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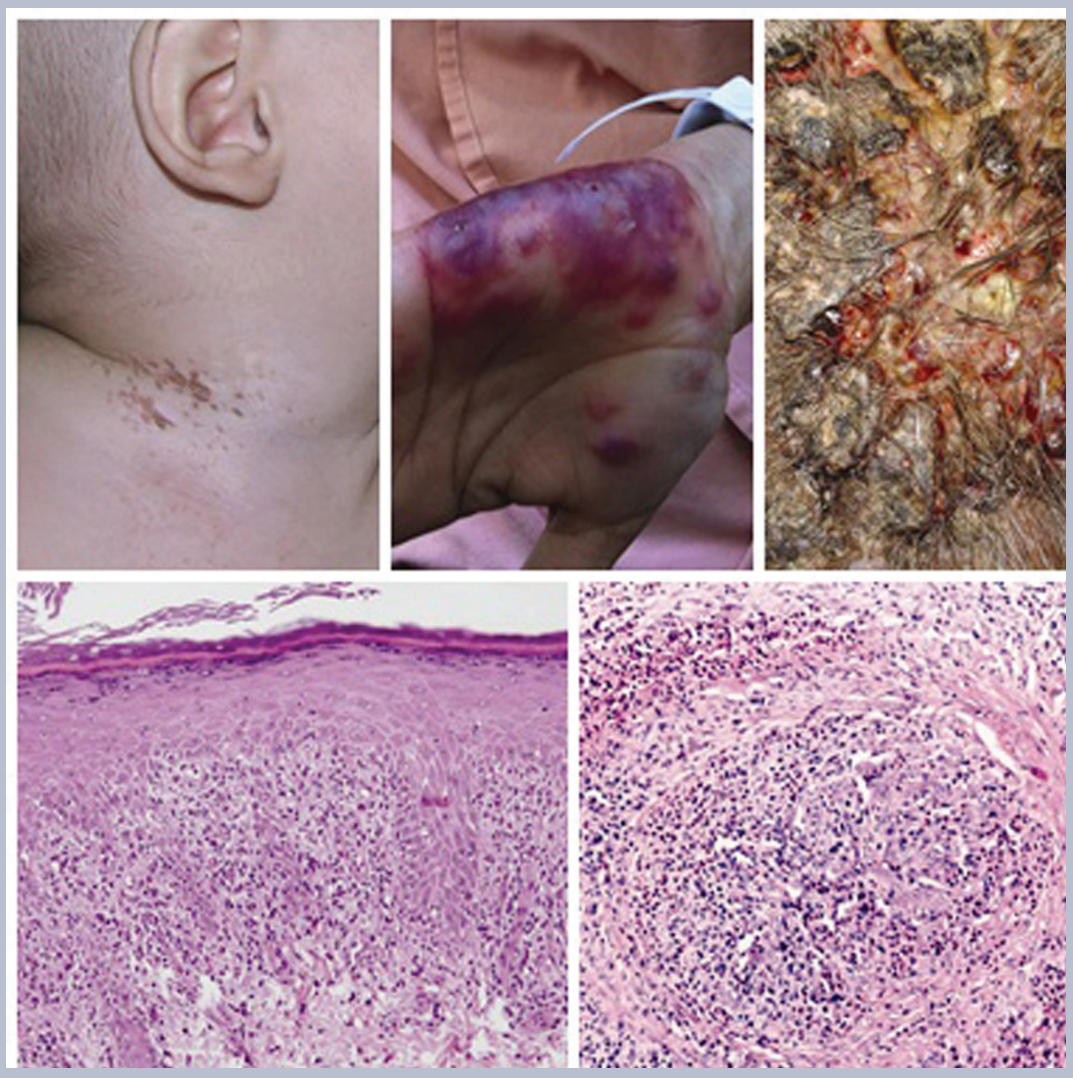

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Editorial Pages

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Editorial Board:

Grupa **Polpharma** dla dermatologii

Flucofast (*Fluconazolum*). **Skład i postać:** 1 kapsułka zawiera 50 mg, 100 mg lub 150 mg flukonazolu. Produkt leczniczy Flucofast 100 mg zawiera laktozę oraz żółcień pomarańczową (E 110). **Wskazania do stosowania:** Flucofast jest wskazany w leczeniu zakażeń grzybiczych. Flucofast jest wskazany do stosowania u pacjentów dorosłych w leczeniu następujących zakażeń: kryptokokowe zapalenie opon mózgowych; kokcydioidomikoza; inwazyjne kandydozy; drożdżakowe zakażenia błon śluzowych, w tym zakażenia gardła, przełyku, występowanie drożdżaków w moczu oraz przewlekłe drożdżakowe zakażenia skóry i błon śluzowych; przewlekłe zanikowe drożdżakowe zapalenie jamy ustnej (związane ze stosowaniem protez zębowych), jeśli higiena jamy ustnej lub leczenie miejscowe są niewystarczające; drożdżyca pochwy, ostra lub nawracająca, gdy leczenie miejscowe jest niewystarczające; drożdżakowe zapalenia żołędzi, gdy leczenie miejscowe jest niewystarczające; grzybice skóry, w tym stóp, tułowia, podudzi, łupież pstry, zakażenia drożdżakowe skóry właściwej, gdy zalecane jest podjęcie leczenia ogólnoustrojowego; grzybica paznokci (onychomikoza), gdy uzna się, że inne leki są nieodpowiednie. Flucofast jest wskazany do stosowania u pacjentów dorosłych w zapobieganiu następującym zakażeniom: nawroty kryptokokowego zapalenia opon mózgowych u pacjentów z podwyższonym ryzykiem nawrotów; nawroty drożdżakowego zapalenia błony śluzowej jamy ustnej, gardła i przełyku u pacjentów zakażonych HIV, u których jest zwiększone ryzyko nawrotów; nawroty drożdżycy pochwy (4 lub więcej zakażeń w ciągu roku); zakażenia grzybicze u pacjentów z przedłużającą się neutropenią (np. u pacjentów z nowotworami krwi, otrzymujących chemioterapię lub u pacjentów po przeszczepieniu krwiotwórczych komórek macierzystych). Flucofast jest wskazany do stosowania w następujących zakażeniach u noworodków, niemowląt, dzieci i młodzieży w wieku od 0 do 17 lat. Flucofast stosuje się w leczeniu drożdżakowego zakażenia błon śluzowych (jamy ustnej, gardła i przełyku), inwazyjnej kandydozy i kryptokokowego zapalenia opon mózgowych oraz w zapobieganiu zakażeniom drożdżakami u pacjentów z osłabioną odpornością. Flucofast można stosować jako leczenie podtrzymujące w celu zapobiegania nawrotom kryptokokowego zapalenia opon mózgowych u dzieci z wysokim ryzykiem nawrotów. Leczenie można rozpocząć przed otrzymaniem wyników posiewu lub innych badań laboratoryjnych. Jednakże po ich otrzymaniu należy odpowiednio dostosować dostępne leczenie. Należy wziąć pod uwagę oficjalne wytyczne dotyczące właściwego zastosowania leków przeciwgrzybiczych. **Dawkowanie i sposób podawania:** Dawkę należy dostosować do rodzaju oraz ciężkości zakażenia grzybiczego. Jeśli w danym zakażeniu konieczne jest stosowanie wielokrotnych dawek, leczenie należy kontynuować do chwili ustąpienia klinicznych lub mikrobiologicznych objawów czynnego zakażenia. Niedostatecznie długi okres leczenia może być przyczyną nawrotu czynnego zakażenia. Kryptokokoza. Leczenie kryptokokowego zapalenia opon mózgowych: Dawka nasycająca: 400 mg pierwszej doby, następna dawka: 200 mg do 400 mg na dobę, zwykle przez 6 do 8 tygodni. W zakażeniach zagrażających życiu dawkę dobową można zwiększyć do 800 mg. Leczenie podtrzymujące w zapobieganiu nawrotom kryptokokowego zapalenia opon mózgowych u pacjentów z podwyższonym ryzykiem nawrotów: 200 mg na dobę. Nieograniczony czas stosowania w dawce dobowej 200 mg. Kokcydioidomikoza: 200 mg do 400 mg przez 11 do 24 miesięcy lub dłużej, w zależności od pacjenta. W niektórych zakażeniach, zwłaszcza w zapaleniu opon mózgowych, można rozważyć zastosowanie dawki 800 mg na dobę. Kandydozy inwazyjne: Dawka nasycająca: 800 mg pierwszej doby. Następna dawka: 400 mg na dobę. Zalecana zwykle długość leczenia zakażenia drożdżakowego krwi wynosi 2 tygodnie po pierwszym negatywnym wyniku posiewu krwi oraz ustąpieniu objawów przedmiotowych i podmiotowych charakterystycznych dla kandydemii. Leczenie kandydozy błon śluzowych. Kandydoza jamy ustnej: Dawka nasycająca: 200 mg do 400 mg pierwszej doby. Następna dawka: 100 mg do 200 mg na dobę przez 7 do 21 dni (do czasu ustąpienia kandydozy jamy ustnej). Można stosować dłużej u pacjentów z ciężkim osłabieniem czynności układu immunologicznego. Kandydoza przełyku: Dawka nasycająca: 200 mg do 400 mg pierwszej doby. Następna dawka: 100 mg do 200 mg na dobę przez 14 do 30 dni (do czasu ustąpienia kandydozy przełyku). Można stosować dłużej u pacjentów z ciężkim osłabieniem czynności układu immunologicznego. Występowanie drożdżaków w moczu: 200 mg do 400 mg na dobę przez 7 do 21 dni. Można stosować dłużej u pacjentów z ciężkim osłabieniem czynności układu immunologicznego. Przewlekła zanikowa kandydoza: 50 mg na dobę przez 14 dni. Przewlekła kandydoza skóry i błon śluzowych: 50 mg do 100 mg na dobę do 28 dni. Można stosować dłużej u pacjentów z ciężkim osłabieniem czynności układu immunologicznego. Zapobieganie nawrotom drożdżakowego zapalenia błony śluzowej u pacjentów zarażonych HIV, u których jest zwiększone ryzyko nawrotów. Kandydoza jamy ustnej: 100 mg do 200 mg na dobę lub 200 mg 3 razy na tydzień. Nieograniczony czas stosowania u pacjentów z przewlekłym osłabieniem czynności układu immunologicznego. Kandydoza przełyku: 100 mg do 200 mg na dobę lub 200 mg 3 razy na tydzień. Nieograniczony czas stosowania u pacjentów z przewlekłym osłabieniem czynności układu immunologicznego. Kandydoza narządów płciowych. Ostra drożdżyca pochwy oraz drożdżakowe zapalenie żołędzi: 150 mg, pojedyncza dawka. Leczenie i zapobieganie nawrotom drożdżycy pochwy (4 lub więcej zakażeń w roku): 150 mg co trzeci dzień, w sumie 3 dawki (doba 1., 4. i 7.), a następnie dawka podtrzymująca 150 mg raz na tydzień. Dawka podtrzymująca przez 6 miesięcy. Grzybice skóry. Grzybica stóp, grzybica tułowia, grzybica podudzi, drożdżyca skóry: 150 mg raz na tydzień lub 50 mg raz na dobę przez 2 do 4 tygodni; w grzybicy stóp może być konieczne stosowanie do 6 tygodni. Łupież pstry: 300 mg do 400 mg raz na tydzień przez 1 do 3 tygodni lub 50 mg raz na dobę przez 2 do 4 tygodni. Grzybica paznokci (onychomikoza): 150 mg raz na tydzień. Leczenie należy kontynuować aż do zastąpienia zakażonego paznokcia przez nowy, niezakażony. Czas potrzebny do odrostu nowego paznokcia dłoni lub stopy wynosi odpowiednio 3 do 6 lub 6 do 12 miesięcy. Szybkość odrostu może jednak różnić się u poszczególnych pacjentów, także w zależności od wieku. Po wyleczeniu przewlekłego zakażenia paznokcie czasami mogą pozostać zniekształcone. Zapobieganie zakażeniom drożdżakowym u pacjentów z przedłużającą się neutropenią: 200 mg do 400 mg. Leczenie należy rozpocząć kilka dni przed spodziewanym początkiem neutropenii i kontynuować przez 7 dni po jej ustąpieniu, kiedy liczba neutrofili zwiększy się powyżej 1000 komórek na mm^3. Szczególne grupy pacjentów: Pacjenci w podeszłym wieku. Dawkowanie należy zmodyfikować w zależności od czynności nerek (patrz „Pacjenci z zaburzeniami czynności nerek"). Pacjenci z zaburzeniami czynności nerek: Jeśli stosuje się pojedynczą dawkę, nie jest konieczna zmiana dawkowania. Pacjentom (w tym dzieciom i młodzieży) z zaburzeniami czynności nerek, otrzymujących wielokrotne dawki flukonazolu, na początku należy podać dawkę od 50 mg do 400 mg, bazując na zalecanej dla danego wskazania dawce dobowej. Po podaniu tej dawki nasycającej dawkę dobową (zgodnie ze wskazaniem) należy ustalić na podstawie poniższych danych: Klirens kreatyniny >50 ml/min – 100% zalecanej dawki. Klirens kreatyniny ≤50 ml/min (bez dializ) – 50% zalecanej dawki. Regularne dializy – 100% zalecanej dawki po każdej dializie. Pacjentom regularnie dializowanym należy po każdej dializie podawać 100% zalecanej dawki; w dniach, w których nie wykonuje się dializy, należy podawać dawkę zmniejszoną odpowiednio do klirensu kreatyniny. Pacjenci z zaburzeniami czynności wątroby: Dane dotyczące stosowania u pacjentów z zaburzeniami czynności wątroby są ograniczone, dlatego flukonazol należy stosować ostrożnie u pacjentów z zaburzeniami czynności wątroby. Dzieci i młodzież. U dzieci i młodzieży nie należy przekraczać maksymalnej dawki dobowej wynoszącej 400 mg. Podobnie jak w zakażeniach u pacjentów dorosłych, długość leczenia zależy od klinicznej oraz mikologicznej odpowiedzi pacjenta. Flucofast podaje się w pojedynczych dobowych dawkach. Dawkowanie u dzieci z zaburzeniami czynności nerek - patrz „Pacjenci z zaburzeniami czynności nerek". Nie przebadano farmakokinetyki flukonazolu u dzieci i młodzieży z niewydolnością nerek (dawkowanie u noworodków (0 do 27 dni), u których często czynność nerek nie jest w pełni rozwinięta – patrz poniżej). Noworodki, niemowlęta i dzieci (w wieku od 28 dni do 11 lat). Kandydoza błon śluzowych. Dawka początkowa: 6 mg/kg m.c. Następna dawka: 3 mg/kg m.c. na dobę. Dawkę początkową można stosować w pierwszym dniu leczenia w celu szybszego osiągnięcia stanu równowagi. Kandydozy inwazyjne oraz kryptokokowe zapalenie opon mózgowych. Dawka: 6 do 12 mg/kg m.c. na dobę, w zależności od ciężkości choroby. Leczenie podtrzymujące w celu zapobiegania nawrotom kryptokokowego zapalenia opon mózgowych u dzieci z dużym ryzykiem nawrotu. Dawka: 6 mg/kg m.c. na dobę, w zależności od ciężkości choroby. Zapobieganie zakażeniom drożdżakami u pacjentów z osłabioną odpornością. Dawka: 3 do 12 mg/kg m.c. na dobę. W zależności od stopnia oraz czasu trwania neutropenii (patrz „Dawkowanie u dorosłych"). Młodzież (w wieku od 12 do 17 lat). W zależności od masy ciała oraz dojrzałości lekarz przepisujący powinien ocenić, które dawkowanie (dla dorosłych czy dla dzieci) jest najbardziej odpowiednie. Dane kliniczne wskazują, że klirens flukonazolu u dzieci jest większy niż u dorosłych. Dawki 100, 200 i 400 mg u dorosłych odpowiadają dawkom 3, 6 i 12 mg/kg m.c. u dzieci, umożliwiającym uzyskanie porównywalnego stopnia narażenia. Nie określono profilu bezpieczeństwa stosowania ani skuteczności flukonazolu w leczeniu kandydozy narządów płciowych u dzieci i młodzieży. Aktualnie dostępne dane dotyczące bezpieczeństwa stosowania u dzieci i młodzieży w innych wskazaniach opisano w punkcie: Działania niepożądane. Jeżeli konieczne jest leczenie kandydozy narządów płciowych u młodzieży (w wieku od 12 do 17 lat), należy zastosować takie samo dawkowanie jak u dorosłych. Noworodki (w wieku od 0 do 27 dni). Noworodki wolniej wydalają flukonazol. Istnieją nieliczne dane farmakokinetyczne potwierdzające sposób stosowania u noworodków. Noworodki (0 do 14 dni): Taką samą dawkę w mg/kg m.c. jak u niemowląt i dzieci należy podawać co 72 godziny. Nie należy przekraczać maksymalnej dawki 12 mg/kg m.c., podawanej co 72 godziny. Noworodki (od 15 do 27 dni): Taką samą dawkę w mg/kg m.c. jak u niemowląt i dzieci należy podawać co 48 godzin. Nie należy przekraczać maksymalnej dawki 12 mg/kg m.c., podawanej co 48 godzin. Flukonazol można podawać w postaci doustnej lub dożylnej (w zależności od preparatu); droga podania zależy od stanu klinicznego pacjenta. W przypadku zmiany drogi podania z dożylnej na doustną i odwrotnie nie jest konieczna zmiana dawkowania. Kapsułki należy połykać w całości, niezależnie od przyjmowanych posiłków. **Przeciwwskazania:** Nadwrażliwość na substancję czynną, pokrewne związki azolowe lub na którąkolwiek substancję pomocniczą produktu. Z badań dotyczących interakcji po podaniu wielokrotnym wynika, że przeciwwskazane jest podawanie terfenadyny pacjentom otrzymującym flukonazol w dawkach wielokrotnych, wynoszących 400 mg na dobę lub więcej. Stosowanie innych leków, które wydłużają odstęp QT i są metabolizowane przez cytochrom P450 (izoenzym CYP3A4), takich jak: cyzapryd, astemizol, pimozyd, chinidyna oraz erytromycyna, jest przeciwwskazane u pacjentów otrzymujących flukonazol. **Ostrzeżenia i zalecane środki ostrożności:** Grzybica skóry owłosionej głowy. Badano stosowanie flukonazolu w leczeniu grzybicy skóry owłosionej głowy u dzieci. Nie wykazano wyższej skuteczności niż gryzeofulwiny, a ogólny odsetek wyzdrowień był mniejszy niż 20%. Dlatego produktu Flucofast nie należy stosować w leczeniu grzybicy skóry owłosionej głowy. Kryptokokoza. Dane dotyczące skuteczności flukonazolu w leczeniu kryptokokozy oraz zakażeń o innych lokalizacjach (np. kryptokokoza płuc lub skóry) są ograniczone, przez co brak dokładnych zaleceń dotyczących dawkowania. Głębokie grzybice endemiczne. Dane dotyczące skuteczności flukonazolu w leczeniu innych postaci grzybicy endemicznej, takich jak parakokcydioidomkoza, sporotrychoza limfatyczno-skórna i histoplazmoza, są ograniczone, przez co brak dokładnych zaleceń dotyczących dawkowania. Nerki. Należy zachować ostrożność podczas podawania flukonazolu u pacjentów z zaburzeniami czynności nerek. Wątroba i drogi żółciowe. Należy zachować ostrożność podczas podawania flukonazolu u pacjentów z zaburzeniami czynności wątroby. Stosowanie produktu Flucofast wiązało się rzadko z ciężkim toksycznym uszkodzeniem wątroby, w tym ze skutkiem śmiertelnym, głównie u pacjentów z ciężkimi chorobami podstawowymi. W przypadkach hepatotoksycznego działania flukonazolu nie obserwowano jednoznacznego związku z całkowitą dawką dobową leku, długością terapii oraz z płcią ani wiekiem pacjentów. Działanie hepatotoksyczne flukonazolu zwykle ustępowało po zaprzestaniu terapii. Jeśli w trakcie leczenia flukonazolem wystąpią zaburzenia wyników badań czynności wątroby, należy dokładnie obserwować, czy u pacjenta nie wystąpi cięższe uszkodzenie tego narządu. Należy poinformować pacjenta, jakie mogą wystąpić objawy świadczące o silnym działaniu na wątrobę (znaczna astenia, jadłowstręt, przedłużające się nudności, wymioty i żółtaczka). Stosowanie flukonazolu należy niezwłocznie przerwać, a pacjent powinien skonsultować się z lekarzem. Układ sercowo-naczyniowy. Stosowanie niektórych azoli, w tym flukonazolu, było związane z wydłużeniem odstępu QT w zapisie elektrokardiograficznym. W badaniach przeprowadzonych po wprowadzeniu produktu do obrotu u pacjentów przyjmujących flukonazol rzadko notowano wydłużenie odstępu QT i zaburzenia rytmu typu torsade de pointes. Dotyczyło to ciężko chorych pacjentów z wieloma czynnikami ryzyka, takimi jak: choroby mięśnia sercowego, zaburzenia elektrolitowe oraz jednoczesne przyjmowanie leków mogących powodować zaburzenia rytmu serca. Należy zachować ostrożność podczas stosowania flukonazolu u pacjentów, u których występują powyższe czynniki ryzyka zaburzeń rytmu serca. Jednoczesne stosowanie innych leków wydłużających odstęp QT oraz metabolizowanych przez cytochrom P450 (CYP3A4) jest przeciwwskazane. Halofantryna. Wykazano, że halofantryna stosowana w zalecanej dawce terapeutycznej wydłuża odstęp QT oraz jest substratem dla izoenzymu CYP3A4. Nie zaleca się jednoczesnego stosowania flukonazolu i halofantryny. Reakcje skórne. Podczas leczenia flukonazolem rzadko obserwowano występowanie skórnych reakcji alergicznych, takich jak zespół Stevensa-Johnsona i martwica toksyczno-rozpływna naskórka. Pacjenci z AIDS są bardziej skłonni do ciężkich reakcji skórnych po zastosowaniu różnych produktów leczniczych. Jeśli u pacjenta z powierzchowną grzybicą, leczonego flukonazolem, wystąpi wysypka, należy przerwać podawanie flukonazolu. Jeżeli wysypka rozwinie się u pacjenta leczonego flukonazolem z powodu inwazyjnego, układowego zakażenia grzybiczego, pacjenta należy uważnie obserwować; w razie wystąpienia zmian pęcherzowych lub rumienia wielopostaciowego należy przerwać podawanie flukonazolu. Nadwrażliwość. Rzadko opisywano przypadki wystąpienia reakcji anafilaktycznej. Cytochrom P450. Flukonazol jest silnym inhibitorem CYP2C9 i umiarkowanym inhibitorem CYP3A4. Ponadto jest również inhibitorem CYP2C19. Należy kontrolować pacjentów przyjmujących jednocześnie flukonazol i leki o wąskim indeksie terapeutycznym metabolizowane z udziałem izoenzymów CYP2C9, CYP2C19 i CYP3A4. Terfenadyna. Należy dokładnie kontrolować pacjentów przyjmujących jednocześnie terfenadynę i flukonazol w dawkach mniejszych niż 400 mg na dobę. Substancje pomocnicze. Kapsułki zawierają laktozę jednowodną, dlatego nie należy ich stosować u pacjentów z rzadko występującą dziedziczną nietolerancją galaktozy, niedoborem laktazy (typu Lapp) lub zespołem złego wchłaniania glukozy-galaktozy. **Działania niepożądane:** Najczęściej zgłaszanymi działaniami niepożądanymi (>1/10) są: ból głowy, ból brzucha, biegunka, nudności, wymioty, zwiększenie we krwi aktywności aminotransferazy alaninowej, aminotransferazy asparaginianowej, fosfatazy alkalicznej oraz wysypka. Podczas stosowania flukonazolu obserwowano i raportowano przedstawione niżej działania niepożądane z następującą częstotliwością: bardzo często (≥1/10), często (≥1/100 do <1/10), niezbyt często (≥1/1000 do <1/100), rzadko (≥1/10 000 do <1/1000), bardzo rzadko (<1/10 000), częstość nieznana (nie może być określona na podstawie dostępnych danych). Zaburzenia krwi i układu chłonnego: Niezbyt często: niedokrwistość. Rzadko: agranulocytoza, leukopenia, trombocytopenia, neutropenia. Zaburzenia układu immunologicznego: Rzadko: anafilaksja. Zaburzenia metabolizmu i odżywiania: Niezbyt często: zmniejszenie łaknienia. Rzadko: hipercholesterolemia, hipertriglicerydemia, hipokaliemia. Zaburzenia psychiczne: Niezbyt często: bezsenność, senność. Zaburzenia układu nerwowego: Często: ból głowy. Niezbyt często: drgawki, parestezje, zawroty głowy, zmiany smaku. Rzadko: drżenie. Zaburzenia ucha i błędnika: Niezbyt często: zawroty głowy pochodzenia obwodowego. Zaburzenia serca: Rzadko: zaburzenia rytmu serca typu torsade de pointes, wydłużenie odstępu QT. Zaburzenia żołądka i jelit: Często: ból brzucha, wymioty, biegunka, nudności. Niezbyt często: zaparcia, niestrawność, wzdęcia, suchość w jamie ustnej. Zaburzenia wątroby i dróg żółciowych: Często: zwiększenie aktywności aminotransferazy alaninowej, aminotransferazy asparaginianowej, fosfatazy alkalicznej we krwi. Niezbyt często: cholestaza, żółtaczka, zwiększenie stężenia bilirubiny. Rzadko: niewydolność wątroby, martwica komórek wątrobowych, zapalenie wątroby, uszkodzenie komórek wątroby. Zaburzenia skóry i tkanki podskórnej: Często: wysypka. Niezbyt często: wysypka polekowa, pokrzywka, świąd, zwiększona potliwość. Rzadko: martwica toksyczno-rozpływna naskórka, zespół Stevensa-Johnsona, ostra uogólniona osutka krostowa, złuszczające zapalenie skóry, obrzęk naczynioruchowy, obrzęk twarzy, łysienie. Zaburzenia mięśniowo-szkieletowe i tkanki łącznej: Niezbyt często: ból mięśni. Zaburzenia ogólne i stany w miejscu podania: Niezbyt często: zmęczenie, złe samopoczucie, astenia, gorączka. Dzieci i młodzież. Profil i częstość występowania działań niepożądanych oraz nieprawidłowych wyników badań laboratoryjnych obserwowanych podczas badań klinicznych z udziałem dzieci i młodzieży, z wyjątkiem stosowania w leczeniu kandydozy narządów płciowych, są porównywalne do obserwowanych u dorosłych. **Podmiot odpowiedzialny:** Medana Pharma S.A., 98-200 Sieradz, ul. Władysława Łokietka 10. Pozwolenie na dopuszczenie do obrotu dla Flucofast 50 mg, Flucofast 100 mg i Flucofast 150 mg odpowiednio nr 4905, nr 14865 i nr 4906, wydane przez MZ. Dodatkowych informacji o leku udziela: Polpharma Biuro Handlowe Sp. z o.o., ul. Bobrowiecka 6, 00-728 Warszawa, tel. +48 22 364 61 00, fax +48 22 364 61 02, www.polpharma.pl. Lek wydawany na podstawie recepty. Cena urzędowa detaliczna dla dawki 50 mg x 7 kaps.; 50 mg x 14 kaps.; 100 mg x 7 kaps.; 100 mg x 28 kaps.; 150 mg x 1 kaps. wynosi odpowiednio w PLN: 14,73; 28,43; 29,00; 109,86; 6,32. Kwota dopłaty pacjenta wynosi odpowiednio w PLN: 8,29; 15,54; 16,11; 58,30; 3,56. ChPL: 2012.09.24.

Trioxal (*Itraconazolum*). **Skład i postać:** Jedna kapsułka twarda zawiera 100 mg itrakonazolu. **Wskazania:** Kandydoza sromu i pochwy; łupież pstry; grzybica skóry wywołana przez dermatofity wrażliwe na itrakonazol (Trichophyton spp., Microsporum spp., Epidermophyton floccosum), np. grzybica stóp, grzybica podudzi, grzybica tułowia, grzybica rąk; grzybica paznokci spowodowana dermatofitami lub drożdżakami; kandydoza jamy ustnej; grzybicze zakażenie rogówki; grzybice układowe: histoplazmoza, aspergiloza, kandydoza, kryptokokoza (w tym kryptokokowe zapalenie opon mózgowych), sporotrychoza, parakokcydioidomikoza, blastomikoza, chromomikoza i inne rzadko występujące grzybicze zakażenia układowe. **Dawkowanie i sposób podawania:** Preparat stosuje się doustnie. W celu uzyskania maksymalnego wchłaniania powinien być przyjmowany niezwłocznie po posiłku. Dorośli: Kandydoza sromu i pochwy: 200 mg dwa razy na dobę przez 1 dzień lub 200 mg raz na dobę przez 3 dni. Łupież pstry: 200 mg raz na dobę przez 7 dni. Grzybica tułowia i grzybica podudzi: 100 mg raz na dobę przez 15 dni lub 200 mg raz na dobę przez 7 dni. Grzybica rąk, grzybica stóp: 100 mg raz na dobę przez 30 dni lub 200 mg raz na dobę przez 7 dni. Kandydoza jamy ustnej: 100 mg raz na dobę przez 15 dni. Grzybicze zapalenie rogówki: 200 mg raz na dobę przez 21 dni. Grzybica paznokci: terapia pulsowa – 200 mg itrakonazolu dwa razy na dobę przez 7 dni. Okresy przyjmowania preparatu (pulsy) są oddzielone 3-tygodniową przerwą w przyjmowaniu leku. W leczeniu grzybicy paznokci rąk stosuje się 2 pulsy, w leczeniu grzybicy paznokci stóp – 3 pulsy. Terapia ciągła: 200 mg raz na dobę przez 3 miesiące. Optymalne efekty kliniczne i przeciwgrzybicze osiągane są po 2 do 4 tygodni po zakończeniu leczenia w przypadku infekcji skóry, sromu i pochwy, jamy ustnej i gardła oraz po 6 do 9 miesięcy po zakończeniu leczenia zakażenia paznokci. Grzybice układowe – Aspergiloza: 200 mg raz na dobę przez okres od 2 do 5 miesięcy. Kandydoza: 100-200 mg raz na dobę przez okres od 3 tygodni do 7 miesięcy. W leczeniu obu powyższych typów grzybic należy zwiększyć dawkę do 200 mg 2 razy na dobę, jeśli przebieg choroby jest ostrzejszy lub zmiany są rozsiane. Kryptokokoza: 200 mg raz na dobę przez okres od 2 do 12 miesięcy. Kryptokokowe zakażenie opon mózgowo-rdzeniowych: 200 mg 2 razy na dobę przez okres od 2 do 12 miesięcy; dawka podtrzymująca (zakażenie opon mózg.-rdz.) 200 mg raz na dobę. Histoplazmoza: 200 mg 1 do 2 razy na dobę przez 8 mies. Sporotrychoza: 100 mg raz na dobę przez 3 miesiące. Parakokcydioidomikoza: 100 mg raz na dobę przez 6 miesięcy. Chromomikoza: 100-200 mg raz na dobę przez 6 miesięcy. Blastomikoza: 100 mg raz na dobę do 200 mg 2 razy na dobę przez 6 miesięcy. Nie stosować u dzieci i osób w podeszłym wieku. **Przeciwwskazania:** Nadwrażliwość na itrakonazol lub inny składnik leku. Leki przeciwwskazane do jednoczesnego podawania z preparatem Trioxal: terfenadyna, astemizol, cisaprid, chinidyna, pimozyd, sertindol, lewacytylometadol, dofetylid, inhibitory CoA-HMG metabolizowane przez CYP3A4, takie jak simwastatyna, lowastatyna, atorwastatyna, triazolam i doustnie podawany midazolam, alkaloidy sporyszu: dihydroergotamina, ergometryna (ergonowina), ergotamina i metyloergometryna (metyloergonowina). Stosowanie preparatu Trioxal jest przeciwwskazane u kobiet w ciąży z wyjątkiem sytuacji zagrożenia życia, gdy potencjalne korzyści przewyższają ewentualny szkodliwy wpływ na płód. Kobiety w wieku rozrodczym powinny stosować odpowiednie środki antykoncepcyjne aż do wystąpienia kolejnej menstruacji po zakończeniu leczenia preparatem. **Ostrzeżenia i zalecane środki ostrożności:** W badaniach na zdrowych ochotnikach z zastosowaniem itrakonazolu podawanego dożylnie obserwowano bezobjawowe zmniejszenie frakcji wyrzutowej lewokomorowej. Itrakonazol wykazywał działanie inotropowe ujemne. Podczas stosowania itrakonazolu występowała zastoinowa niewydolność serca. Nie należy więc stosować preparatu u pacjentów z zastoinową niewydolnością serca występującą aktualnie lub w przeszłości, chyba że potencjalne korzyści przewyższają ryzyko powikłań. Oceniając indywidualnie stosunek korzyści do ryzyka, należy wziąć pod uwagę czynniki, takie jak ciężkość zakażenia, dawkowanie i czas trwania leczenia preparatem Trioxal oraz osobnicze czynniki zagrażające wystąpieniem zastoinowej niewydolności serca. Leczenie tych pacjentów należy prowadzić ostrożnie. Pacjentów zagrożonych rozwojem zastoinowej niewydolności serca należy poinformować o tym, jakie są objawy zastoinowej niewydolności serca, oraz monitorować ich pod względem wystąpienia tych objawów. Jeśli objawy zastoinowej niewydolności serca wystąpią w czasie leczenia itrakonazolem, należy lek odstawić. Należy ostrożnie stosować itrakonazol z antagonistami kanału wapniowego. Itrakonazol może wykazywać klinicznie istotne interakcje z innymi lekami. Wchłanianie itrakonazolu po podaniu doustnym jest zmniejszone w przypadku zmniejszonej kwaśności soku żołądkowego. Leki zobojętniające kwas żołądkowy (np. wodorotlenek glinu) powinny być podawane co najmniej 2 godziny po przyjęciu preparatu Trioxal. U pacjentów z achlorhydrią oraz u pacjentów otrzymujących leki hamujące wydzielanie kwasu żołądkowego (np. antagoniści receptora H2, inhibitory pompy protonowej) zaleca się podawanie preparatu Trioxal z napojem typu „cola". Rzadko występują przypadki hepatotoksyczności, w tym zakończonej zgonem, głównie u pacjentów leczonych itrakonazolem dłużej niż jeden miesiąc. W związku z tym podczas leczenia zaleca się monitorowanie czynności wątroby. Jeśli podczas leczenia u pacjenta wystąpią objawy zapalenia wątroby, takie jak anoreksja, nudności, wymioty, uczucie zmęczenia, bóle brzucha lub ciemny mocz, należy natychmiast zaprzestać stosowania preparatu i ocenić czynność wątroby. U pacjentów ze zwiększoną aktywnością enzymów wątrobowych lub czynną chorobą wątroby, lub u których zaobserwowano działanie hepatotoksyczne innych leków, nie należy rozpoczynać leczenia, chyba że oczekiwane korzyści przewyższają ryzyko uszkodzenia wątroby. W takich przypadkach konieczne jest monitorowanie aktywności enzymów wątrobowych. Itrakonazol jest metabolizowany głównie w wątrobie. U pacjentów z marskością wątroby zaobserwowano niewielkie zmniejszenie biodostępności po podaniu doustnym, które nie było istotne statystycznie. Końcowy okres półtrwania uległ jednak statystycznie istotnemu wydłużeniu. W takich przypadkach konieczne jest dostosowanie dawki. U pacjentów z niewydolnością nerek biodostępność itrakonazolu po podaniu doustnym może być mniejsza. W takim przypadku można rozważyć dostosowanie dawki. W przypadku wystąpienia neuropatii, którą można wiązać z przyjmowaniem itrakonazolu, leczenie należy przerwać. Nie ma dostępnych informacji dotyczących nadwrażliwości krzyżowej pomiędzy itrakonazolem a innymi lekami przeciwgrzybiczymi z grupy azoli. Preparat Trioxal należy przepisywać ostrożnie pacjentom z nadwrażliwością na inne leki z grupy azoli. W kandydozie układowej, jeśli podejrzewa się zakażenie opornymi na flukonazol szczepami Candida, przed rozpoczęciem leczenia należy zbadać wrażliwość tych szczepów na itrakonazol. U niektórych pacjentów z osłabioną odpornością (np. pacjenci z neutropenią, AIDS, po przeszczepach narządowych) biodostępność itrakonazolu może być zmniejszona. Preparat nie jest zalecany w celu rozpoczęcia leczenia bezpośrednio zagrażających życiu grzybic układowych. U pacjentów z AIDS leczonych z powodu grzybic układowych, takich jak sporotrychoza, blastomikoza, histoplazmoza lub kryptokokoza (postać z zajęciem opon mózgowo-rdzeniowych lub bez), u których istnieje ryzyko rozwoju infekcji, należy rozważyć pozostawienie leczenia podtrzymującego. Ze względu na zawartość sacharozy preparatu nie należy stosować u pacjentów z rzadkimi dziedzicznymi zaburzeniami związanymi z nietolerancją fruktozy, zespołem złego wchłaniania glukozy-galaktozy lub niedoborem sacharazy-izomaltazy. **Działania niepożądane:** Podczas leczenia itrakonazolem około 9% pacjentów zgłaszało działania niepożądane. U pacjentów otrzymujących itrakonazol nieprzerwanie przez dłuższy czas (około 1 miesiąca) częstość występowania działań niepożądanych była większa (ok. 15%). Do najczęstszych należały działania pochodzące ze strony układu pokarmowego, wątroby i skóry. Ponadto obserwowano inne, które niemniej występowały bardzo rzadko: hipokaliemia, neuropatia obwodowa, bóle głowy, zawroty głowy; zastoinowa niewydolność krążenia; obrzęk płuc, bóle w nadbrzuszu, wymioty, niestrawność, nudności, biegunka i zaparcie, bardzo ciężkie działania hepatotoksyczne z przypadkami ostrej niewydolności wątroby zakończonej zgonem, zapalenie wątroby, przemijające zwiększenie aktywności enzymów wątrobowych, zespół Stevensa-Johnsona, obrzęk naczyniowy, pokrzywka, wypadanie włosów, wysypka i świąd, zaburzenia cyklu miesiączkowego, reakcje alergiczne, obrzęki. **Podmiot odpowiedzialny:** ZF Polpharma S.A. Pozwolenie nadopuszczenie do obrotu nr 10538, wydane przez MZ. Dodatkowych informacji o leku udziela: Polpharma Biuro Handlowe Sp. z o.o., ul. Bobrowiecka 6, 00-728 Warszawa, tel. +48 22 364 61 00, fax +48 22 364 61 02, www.polpharma.pl. Lek wydawany na podstawie recepty. Cena urzędowa detaliczna dla opakowania 4 kaps.; 28 kaps. odpowiednio wynosi: 19,60; 102,99 PLN. Kwota dopłaty pacjenta dla opakowania 4 kaps.; 28 kaps. odpowiednio wynosi: 12,60; 53,98 PLN. ChPL: 2007.07.18.

Pirolam (*Ciclopiroxi olaminum*). **Skład i postać:** *Ciclopiroxi olaminum*: 1% żel, 1% zawiesina, 1% roztwór. **Wskazania do stosowania:** Leczenie grzybic skóry gładkiej, owłosionej, grzybic stóp, paznokci, podudzia, spowodowanych przez: *Trichophyton rubrum, T. mentagrophytes, Epidermophyton floccosum, Microsporum canis, M. gypseum, Candida albicans, C. tropicalis, C. krusei, C. parapsilosis, Cryptococcus neoformans, Aspergillus fumigatus*. Zakażenia bakteriami Gram-dodatnimi i Gram-ujemnymi oraz mykoplazmami. **Dawkowanie i sposób podawania:** Do stosowania zewnętrznego: dorośli: 2 razy dziennie na zmienioną chorobowo skórę, lekko wcierając lub pozostawiając do wyschnięcia. Leczenie powinno się prowadzić do ustąpienia objawów chorobowych, optymalny czas leczenia wynosi 3 tygodnie. Zaleca się kontynuowanie leczenia przez okres do 10 dni po ustąpieniu zmian (zapobieganie nawrotom). Nie stosować opatrunków i plastrów; wyjątek stanowi grzybica paznokci. W grzybicy paznokci preparat należy nanieść na zmienione chorobowo miejsca i zastosować opatrunek zamknięty. **Przeciwwskazania:** Nadwrażliwość na cyklopiroks i/lub inne składniki podłoża; grzybicze zapalenie oka i okolic oka. **Ostrzeżenia i zalecane środki ostrożności:** U kobiet ciężarnych można stosować tylko w koniecznych przypadkach, nie należy stosować w czasie karmienia piersią; chronić oczy przed kontaktem z lekiem. Preparat nie jest przeznaczony do leczenia grzybic pochwy. Swędzących zakażonych miejsc nie wolno drapać. **Działania niepożądane:** U nielicznych chorych (1–4%) pieczenie, podrażnienie skóry, rumień, świąd, obrzęk. Brak danych na temat stosowania leku u dzieci. **Podmiot odpowiedzialny:** Medana Pharma SA, 98-200 Sieradz, ul. Władysława Łokietka 10. Pozwolenie na dopuszczenie do obrotu: nr 7401 (1% żel), nr 7400 (1% zawiesina), nr 7399 (1% roztwór), wydane przez MZ. Dodatkowych informacji o leku udziela: Polpharma Biuro Handlowe Sp. z o.o., ul. Bobrowiecka 6, 00-728 Warszawa, tel. +48 22 364 61 00, fax +48 22 364 61 02, www.polpharma.pl. Lek wydawany na podstawie recepty. ChPL: 2008.09.29.

Pirolam (*Ciclopiroxum*). **Skład i postać:** 1 g lakieru zawiera 80 mg cyklopiroksu. **Wskazania:** Grzybicze zakażenia paznokci. **Dawkowanie i sposób podawania:** Do stosowania miejscowego. Preparat Pirolam należy nakładać na paznokieć przez pierwszy miesiąc leczenia co drugi dzień, w drugim miesiącu leczenia stosowanie lakieru można ograniczyć do dwóch razy w tygodniu, a od trzeciego miesiąca stosować raz w tygodniu. Cienką warstwę lakieru należy nanieść równomiernie na płytkę paznokciową i pozostawić do wyschnięcia. Raz w tygodniu należy zmyć całą warstwę lakieru kosmetycznym zmywaczem do paznokci. W przypadku uszkodzenia lub starcia warstwy lakieru wystarczy polakierować odsłonięte miejsca. Czas trwania leczenia zależy od ciężkości zakażenia grzybiczego, nie należy jednak stosować go dłużej niż 6 miesięcy. **Przeciwwskazania:** Nadwrażliwość na substancję czynną lub którąkolwiek substancję pomocniczą. Nie stosować u dzieci ze względu na brak wystarczających danych klinicznych. **Ostrzeżenia i zalecane środki ostrożności:** Stosować wyłącznie na paznokcie. Produkt łatwopalny, używać z dala od źródeł ciepła i otwartego ognia. Unikać kontaktu z oczami i błonami śluzowymi. Podczas leczenia nie należy stosować na płytkę paznokciową produktów kosmetycznych. **Działania niepożądane:** U nielicznych chorych obserwowano miejscowe podrażnienie (pieczenie, świąd, rumień, obrzęk, zaczerwienienie i łuszczenie) po kontakcie preparatu ze skórą otaczającą paznokieć. **Podmiot odpowiedzialny:** Medana Pharma SA, 98-200 Sieradz, ul. Władysława Łokietka 10. Pozwolenie na dopuszczenie do obrotu nr 15279, wydane przez MZ. Dodatkowych informacji o leku udziela: Polpharma Biuro Handlowe Sp. z o.o., ul. Bobrowiecka 6, 00-728 Warszawa, tel. +48 22 364 61 00, fax +48 22 364 61 02, www.polpharma.pl. Lek wydawany na podstawie recepty. ChPL: 2009.03.31.

Telfexo 120 mg; Telfexo 180 mg *(Fexofenadini hydrochloridum)*. **Skład i postać:** Jedna tabletka powlekana zawiera 120 mg lub 180 mg feksofenadyny chlorowodorku. **Wskazania:** Dla dawki 120 mg – łagodzenie objawów sezonowego alergicznego zapalenia błony śluzowej nosa; 180 mg – łagodzenie objawów przewlekłej pokrzywki idiopatycznej. **Dawkowanie i sposób podawania:** Dorośli i dzieci w wieku 12 lat i starsze – 1 tabletka raz na dobę; lek nie jest zalecany do stosowania u dzieci poniżej 12 lat w związku z brakiem danych dotyczących bezpieczeństwa i skuteczności; u pacjentów w podeszłym wieku, pacjentów z zaburzeniami czynności wątroby i nerek lek należy stosować ostrożnie. Tabletkę należy połknąć, popijając wystarczającą ilością wody. **Przeciwwskazania:** Nadwrażliwość na substancję czynną lub którąkolwiek substancję pomocniczą. **Ostrzeżenia i zalecane środki ostrożności:** Pacjentów z chorobami układu krążenia w wywiadzie należy ostrzec, że leki przeciwhistaminowe z tej grupy mogą mieć związek z występowaniem działań niepożądanych, takich jak tachykardia i kołatanie serca. Dostępne są jedynie ograniczone dane dotyczące stosowania u pacjentów w podeszłym wieku i u pacjentów z zaburzeniami czynności nerek lub wątroby. W tych grupach pacjentów chlorowodorek feksofenadyny powinien być stosowany ostrożnie. **Działania niepożądane:** W kontrolowanych badaniach klinicznych częstość występowania częstych działań niepożądanych była podobna do obserwowanej w grupie placebo. Zaburzenia układu nerwowego: często – bóle głowy, senność, zawroty głowy. Zaburzenia żołądka i jelit: często – nudności, suchość w jamie ustnej. Zaburzenia ogólne i stany w miejscu podania: niezbyt często – zmęczenie. Następujące działania niepożądane były zgłaszane u osób dorosłych w ramach nadzoru po wprowadzeniu produktu do obrotu. Częstość ich występowania nie jest znana (nie może być określona na podstawie dostępnych danych): Zaburzenia układu immunologicznego: reakcje nadwrażliwości z objawami, takimi jak: obrzęk naczynioruchowy, uczucie ucisku w klatce piersiowej, duszność, nagłe zaczerwienienie skóry i uogólnione objawy anafilaksji. Zaburzenia psychiczne: bezsenność, nerwowość, zaburzenia snu lub koszmary senne/nieprawidłowe sny. Zaburzenia serca: tachykardia, palpitacje. Zaburzenia żołądka i jelit: biegunka. Zaburzenia skóry i tkanki podskórnej: wysypka, pokrzywka, świąd. **Podmiot odpowiedzialny:** ZF Polpharma S.A. Pozwolenie na dopuszczenie do obrotu: Telfexo 120 mg i 180 mg odpowiednio nr 14235 i 14236, wydane przez MZ. Dodatkowych informacji o leku udziela: Polpharma Biuro Handlowe Sp. z o.o., ul. Bobrowiecka 6, 00-728 Warszawa, tel. +48 22 364 61 00, fax +48 22 364 61 02, www.polpharma.pl. Lek wydawany na podstawie recepty. ChPL: 2011.03.30.

Heviran (*Aciclovirum*). **Skład i postać:** Jedna tabletka powlekana zawiera odpowiednio 200 mg, 400 mg lub 800 mg acyklowiru oraz substancje pomocnicze. **Wskazania:** Leczenie zakażeń skóry i błon śluzowych wywołanych przez wirus opryszczki pospolitej (*Herpes simplex virus*), w tym pierwotnego i nawracającego opryszczkowego zakażenia narządów płciowych. Zapobieganie nawrotom opryszczki pospolitej (*Herpes simplex virus*) u pacjentów z prawidłową odpornością. Leczenie zakażeń wywołanych przez wirus ospy wietrznej i półpaśca (*Varicella-Zoster virus*). **Dawkowanie i sposób podawania:** Dawkowanie u dorosłych: Leczenie zakażeń wywołanych przez wirus opryszczki pospolitej (*Herpes simplex virus*): Produkt należy podawać w dawce 200 mg pięć razy na dobę, mniej więcej co 4 godziny, z przerwą nocną. Produkt stosować przez 5 dni, a w przypadku ciężkich zakażeń pierwotnych kurację można przedłużyć. Pacjentom ze znacznie zmniejszoną odpornością (np. po przeszczepieniu szpiku) lub z zaburzeniami wchłaniania z przewodu pokarmowego dawkę można podwoić do 400 mg. Podawanie acyklowiru należy rozpocząć jak najwcześniej po rozpoznaniu zakażenia. W zakażeniach nawracających szczególnie ważne jest rozpoczęcie leczenia w okresie prodromalnym lub tuż po pojawieniu się pierwszych zmian. Zapobieganie nawrotom opryszczki pospolitej (*Herpes simplex virus*): U pacjentów z prawidłową odpornością produkt należy podawać w dawce 200 mg trzy – cztery razy na dobę, mniej więcej co 6-8 godzin. U wielu pacjentów skuteczne oraz wygodniejsze może być podawanie produktu dwa razy na dobę, co 12 godzin, w dawce 400 mg. Zapobiegawczo może również działać dawka zmniejszana stopniowo do 200 mg trzy razy na dobę, mniej więcej co 8 godzin, lub nawet dwa razy na dobę, mniej więcej co 12 godzin. U niektórych pacjentów reakcja na zapobiegawcze podawanie leku występuje po zastosowaniu całkowitej dawki dobowej produktu wynoszącej 800 mg. Stosowanie leku należy przerywać co 6 do 12 miesięcy w celu obserwacji ewentualnych zmian w przebiegu choroby. Leczenie zakażeń wywołanych przez wirus ospy wietrznej i półpaśca (VZV): Produkt należy podawać w dawce 800 mg cztery – pięć razy na dobę (mniej więcej co 4 godziny), z przerwą nocną. Leczenie należy kontynuować przez 5 do 7 dni. Należy rozważyć dożylne podawanie leku pacjentom ze znacznie zmniejszoną odpornością (np. po przeszczepieniu szpiku) lub z zaburzeniami wchłaniania z przewodu pokarmowego. Leczenie trzeba rozpocząć bezzwłocznie po rozpoznaniu zakażenia. Najlepsze wyniki lecznicze zarówno w przypadku ospy wietrznej, jak i półpaśca uzyskuje się, podając lek w ciągu 24 godzin po wystąpieniu pierwszych zmian skórnych – wysypki. Dawkowanie u dzieci: Leczenie zakażeń wywołanych przez wirus opryszczki pospolitej (*Herpes simplex virus*): Dzieci w wieku 2 lat i powyżej – dawka jak dla dorosłych. Leczenie zakażeń wirusem ospy wietrznej: Dzieci w wieku od 6 lat – 800 mg cztery razy na dobę; dzieci w wieku 2 do 5 lat – 400 mg cztery razy na dobę. Dawkę można też określić dokładniej, podając 20 mg/kg masy ciała (do maksymalnej dawki 800 mg) cztery razy na dobę. Leczenie należy kontynuować przez 5 dni. Brak szczegółowych danych na temat zapobiegania nawrotom zakażeń wirusem opryszczki pospolitej oraz leczenia półpaśca u dzieci z prawidłową odpornością. Dawkowanie u pacjentów w podeszłym wieku: U pacjentów w podeszłym wieku należy brać pod uwagę możliwość zaburzenia czynności nerek i odpowiednio dostosować dawkę leku (patrz: Dawkowanie u pacjentów z zaburzeniami czynności nerek). Należy utrzymywać stan właściwego nawodnienia organizmu. Dawkowanie u pacjentów z zaburzeniami czynności nerek: Zaleca się ostrożność podczas stosowania acyklowiru u pacjentów z zaburzeniami czynności nerek. Należy utrzymywać odpowiedni poziom nawodnienia organizmu u tych pacjentów. Podczas leczenia zakażeń wirusem opryszczki pospolitej lub zapobiegania im u pacjentów z umiarkowanym i ciężkim zaburzeniem czynności nerek stosowanie zalecanych dawek doustnych nie doprowadzi do kumulacji acyklowiru w organizmie w stężeniach wyższych niż uznane za bezpieczne podczas podawania leku dożylnie. Jednak pacjentom z ciężką niewydolnością nerek (klirens kreatyniny mniejszy niż 10 ml/min) zaleca się zmniejszenie dawki do 200 mg dwa razy na dobę, mniej więcej co 12 godzin. Podczas leczenia zakażeń wirusem ospy wietrznej i półpaśca u pacjentów z umiarkowaną niewydolnością nerek (klirens kreatyniny 10-25 ml/min) zaleca się zmniejszenie dawki do 800 mg trzy razy na dobę, mniej więcej co 8 godzin, a u pacjentów z ciężką niewydolnością nerek (klirens kreatyniny mniejszy niż 10 ml/min) zaleca się zmniejszenie dawki do 800 mg dwa razy na dobę, mniej więcej co 12 godzin. **Przeciwwskazania:** Nadwrażliwość na acyklowir, walacyklowir lub na jakikolwiek składnik leku. **Ostrzeżenia i zalecane środki ostrożności:** Acyklowir jest wydalany z organizmu przez nerki, toteż dawkę leku u osób z niewydolnością nerek należy zmniejszyć. U pacjentów w podeszłym wieku należy brać pod uwagę zaburzenia czynności nerek, toteż w tej grupie pacjentów należy rozważyć zmniejszenie dawki leku. Osoby w podeszłym wieku oraz pacjenci z niewydolnością nerek należą do grupy zwiększonego ryzyka działań niepożądanych dotyczących układu nerwowego i z tego względu obie te grupy należy uważnie obserwować. Zgłaszane dotąd objawy zwykle ustępowały po przerwaniu podawania leku. Stan nawodnienia: należy zachować szczególną ostrożność podczas stosowania doustnie dużych dawek acyklowiru, aby utrzymać właściwy stan nawodnienia organizmu, np. w przypadku leczenia półpaśca (4 g na dobę), aby uniknąć ryzyka uszkodzenia nerek. Obecnie dostępne dane z badań klinicznych nie są wystarczające, aby wnioskować, że leczenie acyklowirem zmniejsza możliwość wystąpienia powikłań związanych z półpaścem u pacjentów z prawidłową odpornością. Długotrwałe podawanie acyklowiru lub powtarzane cykle leczenia u pacjentów ze znacznie osłabioną odpornością mogą spowodować selekcję szczepów wirusa o zmniejszonej wrażliwości na acyklowir. **Ciąża i laktacja:** Podawanie acyklowiru kobietom w ciąży należy rozważać jedynie wtedy, gdy oczekiwane korzyści ze stosowania leku u matki przewyższają możliwość wystąpienia zagrożeń u płodu. Karmienie piersią: Po doustnym podaniu acyklowiru w dawce 200 mg pięć razy na dobę stężenie jego w mleku kobiecym wynosiło od 60% do 410% stężenia leku mierzonego w osoczu. Takie stężenie acyklowiru w mleku matki mogłoby spowodować przyjmowanie leku przez oseska w dawce dobowej do 0,3 mg/kg masy ciała. Dlatego należy zachować ostrożność, podając lek kobietom karmiącym piersią. **Działania niepożądane:** Następujące zasady zostały przyjęte dla sporządzenia klasyfikacji częstości występowania: bardzo często (≥1/10), często (≥1/100 do <1/10), niezbyt często (≥1/1 000 do <1/100), rzadko (≥1/10 000 do <1/1 000), bardzo rzadko (<1/10 000). Zaburzenia krwi i układu chłonnego: *Bardzo rzadko*: niedokrwistość, zmniejszenie liczby krwinek białych, małopłytkowość. Zaburzenia układu immunologicznego: *Rzadko*: reakcje anafilaktyczne. Zaburzenia psychiczne i zaburzenia układu nerwowego: *Często*: bóle głowy, zawroty głowy; *bardzo rzadko*: pobudzenie, dezorientacja, drżenia, niezborność ruchowa, zaburzenia wymowy, omamy, objawy psychotyczne, drgawki, senność, encefalopatia, śpiączka. Powyższe objawy są zwykle przemijające i występowały głównie u pacjentów z zaburzeniami czynności nerek lub z innymi czynnikami predysponującymi. Zaburzenia oddechowe, klatki piersiowej i śródpiersia: *Rzadko*: duszność. Zaburzenia żołądka i jelit: *Często*: nudności, wymioty, biegunka, bóle brzucha. Zaburzenia wątroby i dróg żółciowych: *Rzadko*: przemijające zwiększanie stężenia bilirubiny oraz aktywności enzymów wątrobowych we krwi; *bardzo rzadko*: zapalenie wątroby, żółtaczka. Zaburzenia skóry i tkanki podskórnej: *Często*: świąd, wysypki (w tym z nadwrażliwością na światło); *niezbyt często*: pokrzywka, przyspieszone, rozsiane wypadanie włosów. Ponieważ przyspieszone, rozsiane wypadanie włosów może być związane z wieloma chorobami oraz ze stosowaniem wielu leków, jego związek z działaniem acyklowiru nie jest pewny; *rzadko*: obrzęk naczynioruchowy. Zaburzenia nerek i dróg moczowych: *Rzadko*: zwiększenie stężenia mocznika i kreatyniny we krwi; *bardzo rzadko*: ostra niewydolność nerek, ból nerek. Ból nerek może być związany z niewydolnością nerki (nerek). Należy utrzymywać właściwy stan nawodnienia chorego. Zaburzenie czynności nerek zwykle szybko ustępuje po uzupełnieniu płynów u pacjenta i (lub) po zmniejszeniu dawki lub odstawieniu leku. W wyjątkowych przypadkach może jednak dojść do ostrej niewydolności nerek. Zaburzenia ogólne i stany w miejscu podania: *Często*: zmęczenie, gorączka. **Podmiot odpowiedzialny:** ZF Polpharma S.A. Dopuszczenie do obrotu dla dawek 200, 400 i 800 mg odpowiednio nr 8400, 8401, 8402, wydane przez MZ. Dodatkowych informacji o leku udziela: Polpharma Biuro Handlowe Sp. z o.o., ul. Bobrowiecka 6, 00-728 Warszawa, tel. +48 22 364 61 00, fax +48 22 364 61 02, www.polpharma.pl. Lek wydawany na podstawie recepty. Cena urzędowa detaliczna dla dawek: 200 mg x 30 tabl.; 400 mg x 30 tabl.; 800 mg x 30 tabl. odpowiednio wynosi w PLN: 16,39; 28,49; 49,83. Kwota dopłaty pacjenta odpowiednio wynosi w PLN: 10,16; 16,03; 24,92. ChPL: 2012.02.22.

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NASZA DERMATOLOGIA Online
OUR DERMATOLOGY Online

A SURVEY OF NAIL INFECTION AND AWARENESS AMONG NON-DIABETIC PATIENTS IN MAURITIUS

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Abstract

Introduction: Nail infection like onychomycosis is mainly caused by dermatophytes and account for almost half of all nail disorders. Prevalence of nail infection has been attributed to several factors such as age, gender, socioeconomic status and predisposition to diabetes amongst others. This study aims at determining the prevalence and level of awareness of non-diabetics towards nail infections in Mauritius.

Material and Methods: A survey was carried out among 471 participants of the non-diabetic population of Mauritius. Data on socio demographic factors, awareness, level of hygiene, family history and quality of life were obtained via questionnaire based studies. Data was analysed using the SPSS software.

Results: Results show almost the same ratio of female to male was affected with nail infection but varies gender wise. Participants within the age group 20-60 with less than US 500 monthly income had a higher incidence of nail infection. No significant relation was obtained between nail infection and education level. A significant relationship was obtained between nail infection and occupation as well as quality of life. More than half of participants did not know about the routes of nail infections or the precautions needed to avoid spreading. However, good level of hygiene was observed among the participants.

Conclusion: Factors like age, gender and socio economic status had a significant relationship on nail infection. Nail infection affects the Quality of Life (QoL) and manual workers or even professionals are prone to nail infections.

Key words: non-diabetic; nail infection; awareness; socio demographic factors; quality of life

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Introduction

There are several types of nail infections among which onychomycosis and Tinea unguium are more common [1]. Both fingernails and toenails are vulnerable to the infection. According to previous reviews, Onychomycosis is the most common nail disease which represents about 50% of all nail changes and for about 30% of all cutaneous fungal infections [2-6]. Nail infections usually exhibits itself as discoloration and thickening of the nail and crumbling edges. The latter manifest itself mostly in toenails [5,6]. Nail infection like onychomycosis is responsible for almost half of all nail disorders and one third of cutaneous fungal infections [5,7]. Research data in the United States have showed a prevalence of 18.5% [8], with the number of persons affected taking an upward trend [9]. Nail infections affect 32% of people between ages 60 and 70 and other studies conducted reported that 48% of the population may be affected by age 70 [10]. Toenail infections are several times more common than fingernail infections and are more difficult to treat because the toenails grow more slowly [6,11].

It has been shown that the increasing incidence of diabetes, HIV infection, changes in lifestyle like an increase in urbanisation, the use of communal bathing facilities and footwear are the main factors leading in an increase in the prevalence of Tinea pedis and onychomycosis [5,12]. In rural Africa, Tinea pedis is uncommon, which is perhaps a reflection of a lack of associated risk factors such as the use of occlusive footwear and associated recreational activities [13]. Comparative study between non-diabetic and diabetic patients with nail changes showed that the latter had a higher proportion of onychomycosis relative to non-fungal onychodystrophy. It was also found that the nature of the fungal pathogens, dermatophytes prevailed mostly over yeast and non-dermatophytic moulds, both in diabetic and non-diabetic patients [14].

It has been shown that there are several important factors that are associated with the occurrence of nail infection such as age and gender [5]. A study of onychomycosis conducted among patients visiting physicians' offices found that the occurrence of onychomycosis considerably increased with age. For example, the prevalence of fungal nail infections was 0.7% in patients younger than 19 years of age, compared with 18.2% in patients 60- to 79-years of age.

As far as gender is concerned and based on several studies, it has been observed that men are more prone to nail infections than women while women are more prone to candida onychomycosis than men [15]. Another important factor is the association of socio economic status (SES) on prevalence of nail infection. The prevalence of Tinea pedis was found to be higher among low SES than compared to high SES and similar results were obtained for prevalence of onychomycosis [16].

Knowledge and level of awareness of nail infection is quite important in either prevention or treatment of nail infection. A survey conducted in Ireland revealed that 84% of participants lack awareness about nail fungal infections and 40% of participants reported to podiatrists when the condition is at a severe to chronic stage [17]. Patients having nail infections had varying degrees of physical impairment and were limited both psychologically and socially thus resulting in a decrease of Quality of Life (QoL). They stated that women generally had a lower QoL compared to men (83% vs. 71%). However patients satisfied with their treatment had an improvement in QoL [18].

To date, there are no documented studies on nail infection and awareness among non-diabetic patients in Mauritius. However a study on onychomycosis in a random sample of Mauritian diabetic patients found that 80% of dermatophyte isolated was Trichophyton species. They also found out that male patients were four times more likely to have nail infection than female patients [19]. Another survey of onychomycosis among 75 agricultural workers found that *Trichophyton tonsurans* was the most frequent fungus isolated in toe nails while no *Candida* infection was observed [20].

In this survey, an attempt has been made to determine the prevalence and level of awareness of non-diabetics towards nail infections. The main objectives are as follows:

1. To assess if there is any relationship between the severity of nail infection and demographic factors such as age and sex.
2. To determine the embarrassment and discomfort associated with nail infection and how quality of life is affected.
3. To identify whether there is a link between patient's occupation and nail infection.
4. To assess the level of awareness of participants towards nail infection.

Material and Methods

The study needed clearance from the UoM Research Ethics Committee and information sheet and consent form were distributed to participants willing to take part in the study.

Two questionnaires were used to obtain information from respondents. One was based mainly on:

a) Demographic information (age, gender, income, level of education, occupational status);

b) Podiatric details (hygiene, difficulties infected participants faced due to their nail infection);

c) Awareness (level of awareness of participants pertaining to nail infection).

The other one was based on standardised and validated question on Quality of life (psychological and physical difficulties faced by nail infected participants base on criteria set by DLQI [21]).

The data collection was performed among members of the general population based on inclusion (general non-diabetic population of both genders of aged between 10 to 70 years old) and exclusion criteria (all diabetic people were excluded from the study while people with genetic nail disease like psoriasis were not considered).

Data analysis:

Statistical analysis of the data collected was done using the Statistical Package for Social Scientist, SPSS version 16.0 and Microsoft Excel.

Results

Demographic details associated with participants

Among the 471 participants, 45.6% of participants were male while 54.4% were female and out of which 15% had nail infections and 85% were not infected. More female (60.2%) were recorded in the group age of 20-30 while higher frequency of male (51.4%) were recorded in the group age of 31-60.

17.2 % of participants who had nail infections were male while 14.1% of participants having nail infections were female. The data was not found to be statistically significant ($p = 0.336$, $r = 0.044$). Participants in the 20-60 age group were found to have a higher rate of nail infection as shown in Figure 1 but this was not found to be statistically significant ($p = 0.782$, $r = -0.013$).

Male having had a tertiary level of education had a higher prevalence of nail infection (44.2%). On the other hand, female having a secondary and tertiary level of education had an equal percentage of nail infection (38.3%). Male having a salary of less than US $ 500 had a higher prevalence of nail infection (38.5%). However, female having no education at all had a higher percentage of nail infection (50.0%). Participants of both gender having a job had higher prevalence of nail infection. 36% of participants having nail infection worked as manual workers while 28% were police officer.

Male living in humid regions was more prone to nail infection (43.6%). However, female in semi- humid region had a higher rate of nail infection (78.9%) but this was not significantly different.

Podiatric details associated with participants

Figure 2 shows that more participants answered that they sometime sweat (62.3%) and rarely came into contact with chemical (51.9%). Same trend were observed for wearing of gloves at work (59.7%) but this was not statistically significant ($p = 0.004$, $r = 0.176$).

More infected participants had their face that sweat the most (37.1%). Male mostly experienced the hardening of the nail (5.1%) while female a higher prevalence of nail discoloration (5.1%). This was statistically significant ($p = 0.000$, $r = -0.853$). In addition, participants of both male and female did not know how they acquired the nail infection they suffered (35.9% and 65.8% respectively). 41% of infected participants did not practice any hobbies while 30% of them regularly do gymnasium's sports. The prevalence of having an affected fingernail was low in both male and female (9.3% and 8.2% respectively) while in male and female, one infected toenail had a higher prevalence that is 7% and 6.6% respectively.

Statistical analysis reveals a positive correlation between participant having nail infection and any other medical problem suffered suggesting that as participants having medical problem relating to nail infection, they were more prone to nail infection. A positive correlation was obtained when sweating and the approximate number of hours participants wear shoes per day were analysed ($r = 0.067$; $p = 0.004$).

Although all participants were non-diabetics, it is found that 45% of infected participants had member of their family suffering from diabetes while 14% had family members having nail infection. Both gender had a higher percentage of response for which they did not felt any discomforting symptoms. Male had a little difficulty to cut their nail compared to female. However more female participants found a little difficulty in wearing shoes that male. All these data were found to be statistically significant.

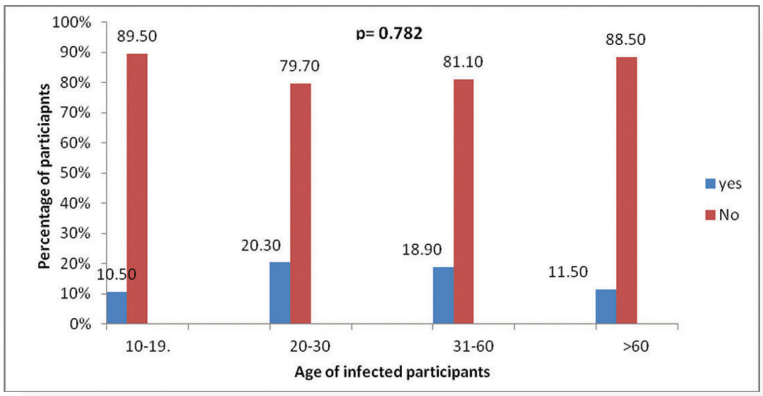

Figure 1. Percentage of infected participants according to age

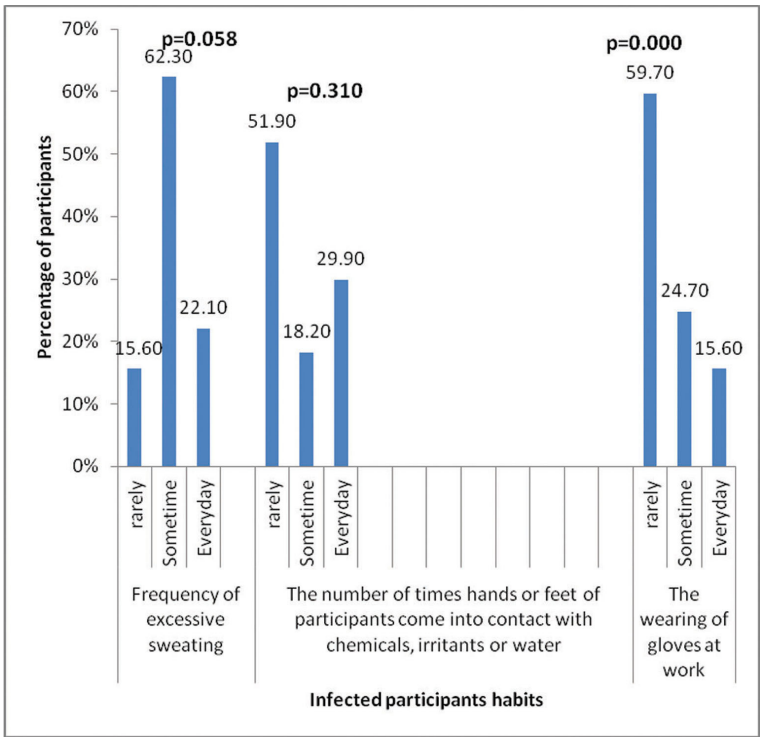

Figure 2. Percentage of infected participants according to their daily habits

Quality of Life (QoL) associated with participants

54.5% of female were unwilling to participate in activities compared to 45.5% of male. 33.3% of male were depressed because of their nail infection compared to 66.7% of female (Fig. 3).

There was a significant correlation observed between nail infection and embarrassment. ($r = 0.951$; $p = 0.000$). Same observation was obtained between nail infection and difficulties in doing sports ($r = 0.945$; $p = 0.000$) as well as problem caused at work or studying ($r = 0.928$; $p = 0.000$).

More male did not feel embarrassed at all about their nail infection (11.2%) while more female (10.2%) did not feel any difficulties in doing sport due to their nail infection. 40% of infected participants did not use any means to hide their infected nails while 34% used socks to hide their infected nail with a significant difference ($p = 0.000$, $r = 0.775$).

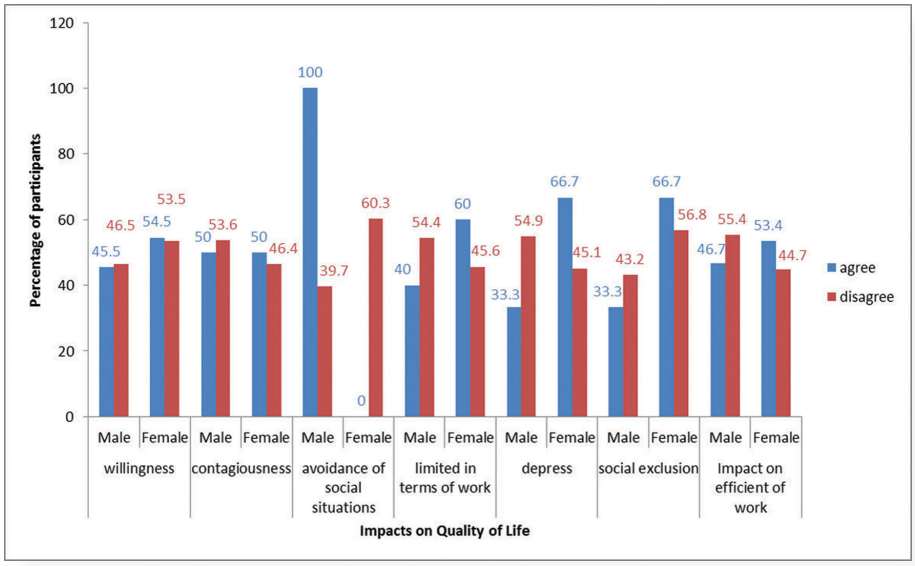

Figure 3. Percentage of infected participants according to Quality of life

Participants' level of awareness

Figure 4 shows that 68 % of participants responded nail infection as disease. More participants said they consulted a doctor for their nail infection (50.7%). 54.8% of them think there is a rapid cure for nail infection. 68.4% of participants were having treatment for their nail infection while 61.9% revealed they did not follow the treatment prescribed. 56.1 % of participants were filling to pay for a cure while 71% of them would accept to follow the treatment even if it is costly. Knowledge on nail infection was higher in male (59.1%) than in female (40.9%). 97.2% of men do not go a manicurist compared to 79.7% among female. higher percentage of male (74%) dried their hand and feet after bath compared to 66% of women. 67.4% of men and 60.9 of female were aware that water could lead to nail infection. Participants washed their hands, feet and clean their nail more than twice a day while they cut their nail once or more per week. The majority of participants changed their socks once a day while the majority rarely cleaned their nail grooming tools.

Only 20.6% of participants having primary level of education were aware of how to prevent the spread of nail infection. 53.2% having done secondary education and 48.2% having done tertiary level of education were unaware of how to prevent the spread of nail infection. The data was found to be statistically significant (p = 0.002).

Discussion

Relationship between the severity of nail infection and demographic factors.

The study shows that more than three quarter of the non-diabetic participants did not suffer from any kind of nail infections (85%) while 15% had at least one kind of nail infection. It has been shown that non- diabetic people had a low prevalence of nail infection [14]. Results herein indicate that more male participants (17.2%) had nail infections compare to female (14.1%) but with similar ratio. However reviews reported that men were three times more prone to nail infection suggesting that this gender difference are not clear but may involve social and/or genetic factors [22].

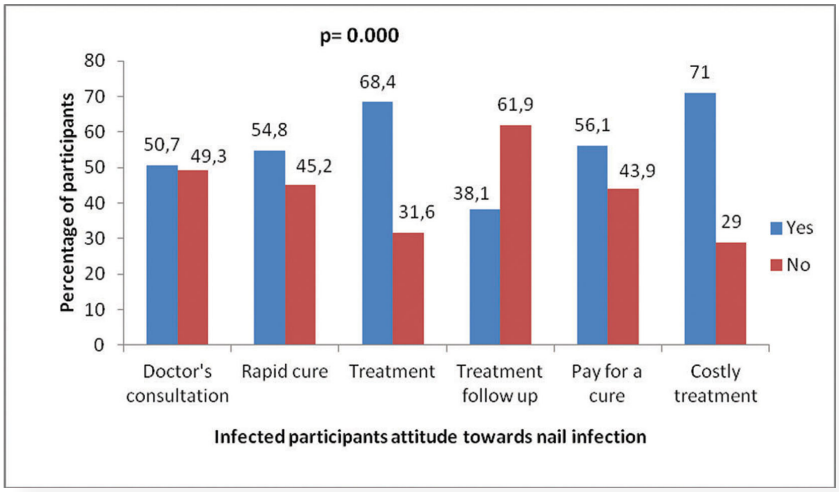

Figure 4. Percentage of participants according to their awareness on nail infection

As far as age is concerned, it was found that participants within the age group 20-60 years had a higher incidence of nail infection contrary to previous finding which reported that elder citizens were more prone to nail infection. Some of their reasons for age related increase in nail infection include repeated nail trauma, poor peripheral circulation or immunosuppression [15]. Diabetic patients above 66 years old were more prone to nail infection [23].

Significant association is reported between socio economic status of participants and the prevalence of nail infection. The percentage of having nail infection were higher in participants having a total monthly salary of less than US 500 (Rs 15,000) and this is in agreement with the study done previously on nail infection [16,23]. Results indicate that those with higher SES had a lower prevalence of nail infection as hygiene level was good. On the other hand, there was no significant correlation between level of education and frequency of nail infection as it was seen that male having had a tertiary level of education had a higher prevalence of nail infection (44.2%). However, it was observed that male living in humid regions was more prone to nail infection (43.6%) compared to 13.2 % of female in humid region. This finding corroborate with previous study which stated that dermatophytes grow well at temperatures of 25–28oC and infection is more prevalent in warm and humid conditions [24].

Out of the 73 infected participants, it was observed that those who were working had a higher percentage of nail infection for both gender which represents 71.8% in male and 60.5% in female. Moreover, it was found that manual workers had more nail infection (36%) when compared to other professions like police officer (28%) and 21% for medical professional. As documented in previous study, manual workers are more prone to nail infection due to the fact they are longer exposed to pathogenic fungi at their place of work [25].

Podiatric links to nail infections

Among the participants, 22% mentioned that they frequently experienced excessive sweating (hyperhidrosis) in various places of their body. A more profound analysis concluded that infected participant primary experienced face hyperhydrosis (37.1%) while 22.3% had hyperhydrosis to their feet. Furthermore, among those subjects who had nail infection, it was found that a significant correlation exists between sweating and the approximate number of hours participants wear shoes per day, implying that prolonged wearing of shoes resulted in nail infection. These findings correspond with previous study which reported that hyperhidrosis provided a conducive environment for proliferation of dermatophytes [25]. It was observed that there was no correlation between contacts with chemical or water and prevalence of nail infection. However, the frequency of wearing gloves at work could be linked with the prevalence of nail infection. The positive correlation implies that as the frequency of wearing gloves increases, the risk of getting nail infection increases too.

It was observed that more male experienced hardening of the nail (5.1%) while 5.1% female had a greater incidence of nail discoloration. Furthermore it was found that more male had multiple signs of nail infection brittleness, discoloration and hardening amongst others which represent 2.8% of the 17.2% male infected. The prevalence of infecting fingernail was low in both male and female representing 9.3% and 8.2% respectively while it was observed that both male and female were more prone of to toenail infection. A possible reason could be fungal nail infections of the toenail have more time to grow and spread, because toenails grow more slowly than fingernails [27].

Data obtained in this study indicates a positive correlation between nail infection and other associated medical problems. When family history was assessed, it was found that 45% of infected participants had member of their family who had diabetes while 26% reported having nail, hair or skin problems in their family. Previous studies report that genetic factors play a fundamental role in nail infection as affected children had at least one parent with Distal Subungual Onychomycosis (DSO) [28].

This study also reports that all studied patients with nail infections experienced at least one of the following sensations that are tingling, burning and numbness. It was also observed that 12.8% male and 31.6% female had difficulties in cutting their infected nails. Furthermore, 7.7% male and 18.4% female had problem while wearing shoes due to their nail infections. This finding support previous research done on podiatric difficulties of infected participants [26].

Association of embarrassment and discomfort of nail infection and participant's Quality of Life (QoL)

Researchers have found that nail infection significantly decreases the Quality of Life (QoL) of patients [18]. A similar scenario is depicted here where participants (45.5% male and 54.5% female) agreed that they were unwilling to participate in activities due to their nail infection. Male suffering from any kind of nail infection avoided social situations more than women. On the other hand, more female (60%) reported that they were limited in terms of work when compared to male (40%). This finding goes in line with what was found in India where it was reported that patients having nail infection faced limitation of physical activities thus making it impossible to perform simple tasks of daily life [29]. Same trend applies to the female gender where depression is concerned. 66.7% of female participants were depressed due to their nail infection compared to only 33.3% of male participants. Higher number of women (66.7%) feel that they were socially excluded due to their nail infection than men (33.3%). 53.4% of female participants felt that their nail infection had a significant impact on their efficiency at work while only 46.7% felt so. It was also observed that nail infection impaired the QoL of women more consequently than those for men. However no statistical significance was noted between age and the QoL of the participants and level of education and the QoL of the participants contrary to what were found in a previous study [18].

A major finding of this study was that nail infection was more likely to cause embarrassment in women (6%) than in men (3.9%). On the other hand, men experienced more difficulties in doing sport activities (3.7%) due to their nail infection compared to women which was just 0.8%. The prevalence of nail infection also had a greater impact on female's work and in studies than the opposite gender. These results are consistent with those obtained in Poland and India by respectively [18,29]. 34% of infected participants admitted that they hide their nail infection using socks while 23% of them used closed shoes and this was statistically significant. The present study also demonstrates a positive correlation among the participants between nail infection and type of shoes participants wears which implies that the types of shoes worn by participants could lead to nail infection. It was reported that only 21.4 % of diabetic having nail infection wore medicated shoes as they did not know about the importance of the medicated shoes or they stated that medicated shoes are too expensive [23].

Level of awareness of participants towards nail infection

The current study found that 68% of participants viewed nail infection as a disease while 12% think it is an aesthetic problem. This contradicts past studies which consider nail infection as a serious medical problem [18]. It was also found that among nail infected participants (n =73), 50.7% visit a doctor for their nail infection and out of this, 68.4% of them were treating the infected nail with prescribed medicine. 45 out of the 73 participants having nail infection revealed neglecting their treatment follow-up suggesting that these participants were unaware of the consequence of the nail infection if left untreated over a long period which may lead to complications ranging from gangrene to amputation [30]. Interestingly, 56.1% of the subject would be willing to pay for a cure while 71% of participants were still willing to pay for a cure even if the treatment would be costly showing that cost was not a factor from preventing them seeking medical help. These finding were found to be statistically significant and goes in line with other studies [9]. Negligence however is not uncommon as 68.4% of diabetic patients having nail infection did not treat their nails while 29.1% never went to the podiatrist at all [23].

As far as knowledge is concerned, it is observed that male was more aware of nail infection (59.1% in men and 40.9% in female) but most infected participants did not know how they acquired nail infection (35.9% in men and 65.8% in women). Male were more delicate in drying their feet or hand after a bath (74%) compared to 26% of women. Hygienic conditions like cutting, cleaning of nails and washing of feet and hands regularly were well known among the participants. However it was observed that a higher incidence of participants rarely or never cleaned their nail cutter before using it (not statistically significant). This finding shows how participants neglect the fact that fungi on nail cutter could contaminate healthy nails. Most participants were aware of the importance of doing a check-up by a podiatrist, to cut nail once a week and to avoid nail injuries amongst others but the results were not found to be statistically significant. However, irrespective of the education level and age, it was found that more than half of participants did not know about the routes of nail infections or the precautions needed to avoid further contamination of healthy nails. This suggests that even mature or well literate participants had little knowledge of the proliferation of nail infections.

Conclusion

In the study nail infection were observed to rarely affect participants below 19 years old but had a greater prevalence in adults of age 20 to 50. Prevalence rate is higher in male. Only 15% of non-diabetic participants had nail infection showing a low prevalence among them. Occupation could be a risk factor for nail infection with manual workers more susceptible. QoL has been found to be impaired in all domains ranging from physical, mental to social functioning. Thus nail infection must be considered as a serious medical problem owing careful consideration from podiatrist. Female were more embarrassed compared to male while more male avoided social situations than female. Toenails were more prone to nail infections than fingernail. Many of the participants were not aware of the existing problem on nail infection even though they show signs and symptoms and majority were unaware of the mode of transmission or means of preventing infection.

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PREVALENCE OF NAIL ABNORMALITIES IN PATIENTS WITH *PSORIASIS*

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Abstract

Introduction: Psoriasis is a chronic inflammatory skin disease that affects about 2% of general population. Clinically, disease can present with cutaneous and nails lesions. Nail abnormalities can be seen in up to two-thirds of patients with psoriasis and both fingernails and toenails may be affected.

Objective: The objectives of our study were to evaluate the frequency and clinical presentations of nail abnormalities in patients with psoriasis. Also, we aimed to find correlation between nail changes and some clinical parameters.

Methods: One hundred and ten patients with psoriasis were included in this study. A detailed history and examination was recorded for all study subjects, including the age and gender of the patients, type of psoriasis, duration, and extent of disease. Finger and toe nails were clinically examined and nail changes were noted. In the case of clinically suspected of fungal infection, further mycological investigations were performed.

Results: Nail abnormalities were present in 67 patients (60.9%) with psoriasis. Nail pitting was the most common lesion observed on fingernails, followed by discoloration of nail plate. Subungual hyperkeratosis of nail plates were significantly more frequent on the toenails. Positive mycological culture was in 14 (20.8%) psoriatic patients with nail involvement. Also, positive correlation between nail abnormalities and duration of psoriasis was found.

Conclusions: Nail involvement is common in patients with psoriasis and accompanies skin lesions on the body surface. Pitting and subungual hyperkeratosis are the most frequent nail abnormality in psoriatic patients.

Key words: nail abnormalities; psoriasis; pitting; subungual hyperkeratosis

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Introduction

Psoriasis is a chronic inflammatory skin disease that affects about 2% of general population [1]. It is classified into several clinical forms. The most common form is chronic plaque psoriasis (CPP) which occurs in 90% of patients [2] and it is usually caracterized by erythematous, scaly plaques on elbows, knees, scalp, but any skin surface may be affected as well. Severe clinical forms are psoriasis pustulosa (PP), psoriasis erythrodermica (PE) and psoriasis arthropatica (PA). The specific pathogenesis of psoriasis is not completly understood, but the underlyng mechanisms involve a complex interplay between epidermal keratinocytes, T limphocytes as well as other leukocytes, and vascular endothelium [3,4].

Even thought the skin lesions are the most typical manifestations of disease, nail involvement can be seen in up to 50% of psoriatic patients with a lifetime incidence of 80% to 90% [5,6]. Nail changes is seen in association with all types of psoriasis of the skin, and is frequently present with psoriatic arthropathy [7]. A wide spectrum of nail abnormalities is seen among patients with psoriasis, and both fingernails and toenails may be affected. Purpose of our study was to determine the frequency and clinical presentations of nail changes in patients with psoriasis.

Material and Methods

One hundred and ten patients with psoriasis were included in this study which was carried out of our Department of Dermatology. A detailed history and examination was recorded for all study subjects, including the age of the patients, age of onset, type of psoriasis, duration of the disease, and extent and severity of disease. Diagnosis of psoriasis was based on clinical findings, and if necessary, a skin biopsy and histopathology examined was performed. Finger and toe nails were clinically observed and nail changes were noted. In patients with nail changes that were suspicious for fungal infection further mycological investigations were performed. Clippings of the affected nails and subungual scrapings from these patients were collected. One part of of nail specimens was subjected to direct microscopic examination with 10% potassium hydroxide aqueos solution and another part of this specimens were cultured on Sabouraud's dextrosa agar medium with cycloheximide (SDA, PB Paureak, Spain).

The other causes of nail changes, like congenital and traumatic dystrophy were excluded from the this study. Statistical comparisons were performed using the chi-square test. The data were considered statistically significant if p values were les than 0,05 ($p<0.05$).

Results

Sixty eight patients (61.8%) were male, and 42 patients (38.2%) were female, and their age ranged from 14 to 61 years (mean age 35.7). The majority of the patients had clinical form of chronic plaque psoriasis 66 (60.0%), followed by psoriasis arthropatica 19 (17.3%), psoriasis erythrodermica 14 (12.7%) and psoriasis pustulosa 11 (10.0%). The age of patients at the onset of the disease had a wide range from 14 to 45 years. The disease duration varied between 2 months to 23.5 years (mean duration: 68.2 month). Nail changes were present in 67 (60.9%) patients with psoriasis, as pitting (47.8%), discoloration of nail plate (17.9%), subungual hyperkeratosis (14.9%), oil spot (8.9%), nail thickening (5.9%) and onycholysis (4.5%). The prominent clinical finding of the observed fingernails was pitting (48.7%). The percentage of nail plate discoloration on the toenails was 9,75%. Subungual hyperkeratosis of the nail plates was significantly more frequent on the thoenails than the fingernails (25% vs 7.6%), ($p<0.05$). Nail changes were more frequent in patients with chronic plaque psoriasis (59.7%) followed by patients with arthropatic psoriasis (19.4%). Male patients were a little more affected than women (54.7% vs 45.3%). There was correlation between the duration of psoriasis and prevalence of nail involvement. Patients with disease duration of more than five years had a higher prevalence of nail changes than those with shorter disease duration. Of total 67 psoriatic patients with nail involvement positive mycological cultures were obtained from 14 (20.8%). The most commonly isolated fugi were *Candida albicans* (64,3%). The prevalence of *Candida albican*s on the fingernails was 49.6 % and on the toenails 14,7 %. *Trichophytone mentagrophytes* was the commonest dermatophite species. It was isolated only on toenails (21,4%) (Tabl. I).

Clinical Type of Psoriasis	Patientsn (%)	Nail Changes n (%)
Psoriasis vulgaris	66 (60.0)	40 (60,6)
Psoriasis arthropatica	19 (17.3)	13 (68,4)
Psoriasis erythrodermica	14 (12.7)	9 (64,3)
Psoriasis pustulosa	11 (10.0)	5 (45,5)

Table I. The association between nail abnormalities and clinical type of psoriasis

Discussion

Nail changes in psoriasis are common and in many cases cause impairment of manual dexterity, pain, and psychologic stress [8]. Most psoriatic nail changes present in patients with clinically manifest lesions of the skin, while isolated nail psoriasis is rare, occurring about 1-5 % of patients [9]. Nail involvement is common in older patients, severe clinical forms and longer duration of diseases, and at the presence of psoriatic arthritis in which the incidence of nails changes is over 80% [10]. Although the pathology of nail abnormality in psoriasis is not completely understood, it implies the association of genetic, environmental and immunological factors (T-cell mediated inflamatory reaction). The clinical presentation of nail changes in psoriasis varies according to the severity and localization of the lesion. The nail matrix is the germinal center of the nail, with the proximal matrix forming the dorsal nail plate and the distal matrix forming the ventral nail plate. Both the proximal and distal matrix can be affected by psoriatic lesions. Disorders of nail matrix manifest as defects of nail plate such as pitting, thinning, onychorrhexis and leuconychia. The nail plate is a specialized epidermal structure formed by a process known as onycholemmal keratinization, whereby matrix cells mature, lose their nuclei and organelles, and become commented in a thick mortar [11]. The involvement of nail bed produces “oil drop” sign, subungual hyperkeratosis, onycholysis and splinter haemorrages [12]. Other less common nail changes include nail fold telangiectasias, red lunulae, punctate red spots in the lunula, transverse leuconychia, leukonychia punctata, half-and-half nail, koilonychia, and onychoschizia [13]. In the most severe forms of psoriasis all the anatomical structures of the nail are damaged. Also, nail alteration in psoriasis can be associated with onychomycosis or paronychia. Nail pitting (psoriasis punctata unguinum, onychia punctata) is the most common changes in psoriasis of nail [12]. Pits in the nails are superficial depressions in the nail plate, single or multiple, that indicate abnormalities in the proximal matrix [14]. Oil drops are translucent, yellow discolorations of nail plate observed beneath the nail plate often extending distally toward the hyponychium, due to psoriasiform hyperplasia, parakeratosis, microvascular changes, and trapping of neutrophils in the nail bed Subungual hyperkeratosis is due to hyperkeratosis of the nail bed and is often accompanied by onycholysis, which usually involves the distal aspect of nail.

In our study 60.9% patients with psoriasis had a nail changes. The commonest change observed was pitting seen in 47.8% patients, followed by discoloration of nail plate 17.9% and subungual hyperkeratosis 14.9%. Pitting and discoloration were significantly more frequent on the fingernails, while subungual hyperkeratosis was observed significantly more often on toenails than on the fingernails, ($p<0.05$).

Our findings are similar to the study of Zaias who also recorded that the most common nail lesion are pitting, nail discoloration, onycholysis and subungual hyperkeratosis [15]. In study of Salomon and al, [16] (78.3%) patients had clinical evidence of nail changes out of total of 106 patients with psoriasis, and subungual hyperkeratosis was the most common nail abnormality observed on both fingernails and toenails [16]. The clinical type of psoriasis associated with nail involvement predominantly was PA (68.4%) followed by PE (64.2%). Although the psoriasis is equally distributed among both genders, some studies showed that the male patients were far more affected [17]. In our study, we observed slight males prepoderance (54.7%). The prevalence of nail abnormality was well connected to the duration of psoriasis.

The longer the psoriasis was present, the more the nail changes prevailed. No association was found of the incidence of nail changes with the age of patients as well as with the extent of skin lesions. Fungal infection of nail is common finding in psoriatic patients. In our study positive mycological cultures from nail specimens were obtained in 14 (20.8%) psoriatic patients. The prevalence of onychomycosis caused by yeasts in psoriatic patients is reported as 19-23 % [18,19]. Similarly to the previous report [16], in our study *Candida albicans* was the commonest isolated fungi in psoriatic patients with nail involvement.

Conclusions

In coclusion, our study confirms that nail involvement is common in patients with psoriasis. Pitting and subungual hyperkeratosis are the most frequent nail abnormality in psoriatic patients. Duration of disease was found to have an impact on the prevalence of nail abnormality.

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TISSUE INHIBITOR OF METALLOPROTEINASE 1, MATRIX METALLOPROTEINASE 9, ALPHA-1 ANTITRYPSIN, METALLOTHIONEIN AND UROKINASE TYPE PLASMINOGEN ACTIVATOR RECEPTOR IN SKIN BIOPSIES FROM PATIENTS AFFECTED BY AUTOIMMUNE BLISTERING DISEASES

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Abstract
Introduction: Proteinases and proteinase inhibitors have been described to play a role in autoimmune skin blistering diseases. We studied skin lesional biopsies from patients affected by several autoimmune skin blistering diseases for proteinases and proteinase inhibitors.
Methods: We utilized immunohistochemistry to evaluate biopsies for α-1-antitrypsin, human matrix metalloproteinase 9 (MMP9), human tissue inhibitor of metalloproteinases 1 (TIMP-1), metallothionein and urokinase type plasminogen activator receptor (uPAR). We tested 30 patients affected by endemic pemphigus, 30 controls from the endemic area, and 15 normal controls. We also tested 30 biopsies from patients with bullous pemphigoid (BP), 20 with pemphigus vulgaris (PV), 8 with pemphigus foliaceus, and 14 with dermatitis herpetiformis (DH).
Results: Contrary to findings in the current literature, most autoimmune skin blistering disease biopsies were negative for uPAR and MMP9. Only some chronic patients with El Bagre-EPF were positive to MMP9 in the dermis, in proximity to telocytes. TIMP-1 and metallothionein were positive in half of the biopsies from BP patients at the basement membrane of the skin, within several skin appendices, in areas of dermal blood vessel inflammation and within dermal mesenchymal-epithelial cell junctions.

Key words: endemic pemphigus foliaceus; autoimmune blistering skin diseases; matrix metalloproteinase 9; tissue inhibitor of metalloproteinases 1; urokinase type plasminogen activator receptor; α-1-antitrypsin

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Abbreviations and acronyms: Bullous pemphigoid (BP), immunohistochemistry (IHC), direct and indirect immunofluorescence (DIF, IIF), hematoxylin and eosin (H&E), basement membrane zone (BMZ), intercellular staining between keratinocytes (ICS), pemphigus vulgaris (PV), cicatricial pemphigoid (CP), autoimmune blistering skin disease (ABD), matrix metalloproteinase 9 (MMP9), tissue inhibitor of metalloproteinases 1 (TIMP-1), extracellular matrix (ECM), urokinase type plasminogen activator receptor (u-Par).

Introduction

Multiple theories have been proposed regarding the pathophysiology of cutaneous autoimmune blistering skin diseases (ABDs). Some involve plasminogen activation, desmoglein compensation, acetylcholine receptor antibodies, and intracellular signal control of autoantibodies [1]. Moreover, human autoantibodies and the presence of complement are primary factors in producing the blisters of human autoimmune skin blistering diseases and are thought to exert their pathogenic effect via proteases [2,3].

Few studies have tested for proteases and protease inhibitors in lesional skin from patients affected by ABDs [4,5]. We decided to investigate enzymes that could be modulated by ions that have been postulated as triggers for ABDs. We also aimed to investigate enzymes that are related to xenobiotics, based on our previous findings of metals and metalloids in skin biopsies of patients with a new variant of endemic pemphigus foliaceus in El Bagre, Colombia (El-Bagre-EPF) that are exposed to significant mercury pollution [5]. Thus, we utilized immunohistochemistry (IHC) to test for anti-human-α-1-antitrypsin, anti-human matrix metalloproteinase 9 (MMP9), anti-human tissue inhibitor of metalloproteinases 1 (TIMP1), urokinase type plasminogen activator receptor (uPAR) and for metallothionein in patients affected by autoimmune skin blistering diseases.

Methods

Subjects of study

We tested 30 biopsies from El Bagre-EPF patients and 30 controls from the endemic area. Of the 30 control biopsies, 15 were taken from healthy first degree relatives and 15 from healthy, non-related persons. We also utilized 15 control skin biopsies from cosmetic surgery patients in the USA, taken from the chest and/or abdomen. The Bagre-EPF patients were previously diagnosed by us, fulfilling specific criteria as previously documented [6-10]. We also tested another group of ABD patients, whose skin biopsies were obtained from the archival files of two private dermatopathology laboratories in the USA. Most of the archival sample patients were not taking immunosuppressive therapeutic medications at the time of biopsy. We evaluated 34 biopsies from bullous pemphigoid (BP) patients, 20 from patients with pemphigus vulgaris (PV), 8 from patients with non-endemic pemphigus foliaceus (PF) and 4 from patients with dermatitis herpetiformis (DH). We also tested biopsies from heart, liver, kidney and lung tissue from 4 autopsies of El Bagre-EPF patients. For all of the El Bagre area patients and controls we obtained written consents, as well as Institutional Review Board (IRB) permission. The archival biopsies were IRB exempt due to the lack of patient identifiers.

Intensity of immunohistochemistry staining

The staining intensity of the immunohistochemistry antibodies was evaluated 1) qualitatively by two independent observers, as well as 2) in a semiquantitative mode by automated computer image analysis (specifically designed to quantify immunohistochemistry staining in hematoxylin-counterstained histologic sections). For the image analysis, slides were scanned with a ScanScope CS scanning system (Aperio Technologies, Vista, California, USA), utilizing bright field imaging at 20× and 40× magnifications. The strength of the staining was evaluated on a scale from 0 to 4, where 0 represented negative staining and 4 the strongest staining.

Immunohistochemistry staining

We performed IHC using antibodies conjugated with horseradish peroxidase (HRP)-labelled secondary antibodies. We utilized multiple monoclonal and polyclonal antibodies, all from Dako (Carpinteria, California, USA). For all our IHC testing, we used a dual endogenous peroxidase blockage, with the addition of an Envision dual link (to assist in chromogen attachment). We applied the chromogen 3,3-diaminobenzidine, and counterstained with hematoxylin. The samples were run in a Dako Autostainer Universal Staining System, as previously described (13-15). Positive and negative controls were consistently performed. For IHC, we utilized Dako antibodies to polyclonal rabbit anti-human α-1-antitrypsin (cat. No. IR505, flex ready to use, antigen retrieval high pH), rabbit anti-human MMP9, (cat. No. A0150, dilution 1:75, antigen retrieval heat), monoclonal mouse anti-human TIMP-1 (cat. No. M0639, dilution 1:50, antigen retrieval heat), monoclonal mouse anti-human metallothionein (cat. No. M0639, dilution 1:50, antigen retrieval high pH), and monoclonal mouse anti-human uPAR (cat. No M7294, dil, 1:25, antigen retrieval high pH). We also utilized control tissue from 4 non-El Bagre EPF patient autopsies (from the El Bagre EPF endemic area), to rule out false positive and false negative results due to spontaneous autolysis. The organs from the autopsies were taken within 12 hours of patient death. The direct immunofluoresecent studies (DIF) were performed as previously described [6-10].

Indirect immunoelectron microscopy (IEM)

Performed as previously described [10]. In brief, postembedding immunogold labeling was performed on samples of El Bagre-EPF sera and controls. Rat skin was utilized as the substrate antigen; the tissue was dissected, fixed in 4% glutaraldehyde with 0.2% paraformaldehyde, and embedded in Lowicryl® resin. The tissue was then sectioned at 70 nm thickness. The samples were blocked with a solution from Aurion™ (Electron Microcopy Sciences/EMS, Hatfield, Pennsylvania, USA). Our tissue grids were then washed with PBS-BSAC (Aurion™, EMS). The primary antibodies were incubated overnight at 4°C.

The next day the grids were again washed; a secondary antibody solution, specifically 10nm gold-conjugated protein A PBS BSAC (Aurion, EMS™) was applied. The samples were then double-stained with uranyl acetate and lead citrate. The samples were reviewed under a Hitachi H7500 transmission electron microscope. Images of immunogold particles displaying any pattern of positivity were recorded, and converted to TIF format.

Statistical methods

Differences in staining intensity and positivity were evaluated using a GraphPad Software statistical analysis system, and employing Student's t-test.

We considered a statistical significance to be present with a *p* value of 0.05 or less, assuming a normal distribution of the samples.

Results

In Table I and Figures 1 through 2 we summarize our primary results. We observed consistent patterns of IHC positivity relative to each autoimmune skin blistering disease. For example, α-1 antitrypsin was positive in all of the lesions of DH within the subepidermal blisters ($p<0.05$). Positivity for this marker was also noted in selected acantholytic areas of hair follicles within DH biopsies. In PV, positivity was seen with TIMP-1, α-1 antitrypsin and metallothionein. Alpha-1 antitrypsin was positive in the majority of active DH active cases in the blisters. El Bagre-EPF patient biopsies and controls stained predominantly positive for TIMP-1, and metallothionein. Contrary to what we expected given the existing literature, most patients with autoimmune skin blistering diseases stained negative for MMP9 ($p<0.05$). A few patients with BP were positive with MMP9 in the area of the upper dermal blood vessels. Only a few patients with a stable, chronic clinical form of El Bagre-EPF and taking low dosage of prednisone daily (e.g 10-20 mgs/per day) showed positivity for this marker, especially in telocyte areas. Specifically, the MMP9 positivity was focally noted in the epidermis, but primarily in mesenchymal-epithelial cell junction transitions (METs) in the dermis ($p<0.05$). Of interest, the same biopsies that stained positive for proteases and/or protease inhibitors demonstrated positive deposits of FITC conjugated IgG in the same areas in the dermis (Fig. 2). In addition, multiple samples from the El Bagre-EPF patients demonstrated positive serum autoantibody deposits (via 10nm Gold particles) on immunoelectron microscopy (IEM)(150 kV) on the METs, highlighted by utilizing using anti-human IgG antibody; these findings correlated with our IHC results, as well as our direct immunofluorescence results for reactivity in the extracellular matrix. Similar positivity was seen in the other autoimmune diseases, demonstrating reactivity to the skin appendices and inflamed dermal blood vessels, and in areas of some type of dermal cell junctions, possibly the METs. IEM only was performed in the El Bagre-EPF patients (Fig. 2).

In 6/10 DH blisters, we found positive staining with α -1 antitrypsin between epidermal keratinocytes, and in the upper dermis under the blister. El Bagre-EPF patient biopsies stained predominantly positive for TIMP-1 and metallothionein. Healthy relatives of El Bagre-EPF patients also displayed higher positivity for these markers, relative to non-related controls (Tabl. I); this finding demonstrates that although the controls are also exposed to the triggering environmental agents, they do not develop the disease.

Based on the fact that El Bagre-EPF patients have autoantibodies to organs such as heart and kidney (mostly directed against plakins and plakophilins), we decided to test for these enzymes in necropsy tissue. In 4/4 biopsy sets from the heart, liver, kidney and lung from El Bagre-EPF patient autopsies, we found positive staining in cardiac tissue for TIMP1 in the cardiac t-tubule area composita, and to individual renal endothelial cells. In the control biopsies, this marker was consistently negative. TIMP1 was also positive in the renal tubules in 4/4 El Bagre-EPF autopsy tissues (Fig. 1). Further, 4/4 kidney, liver, heart and lung El Bagre EPF autopsy biopsy tissue sets were also positive for α-1 antitrypsin. MMP9 staining was positive in the endothelial cells of the liver from 4/4 El Bagre-EPF patients. Moreover, in the controls, MMP9 was positive but present diffusely over the hepatic tissue. Thus, we have evidence of systemic reactivity in El Bagre EPF in that proteases are active in other organs as well as in the skin.

Overall, TIMP-1 was positive in many immunologically active biopsy areas in all the autoimmune skin blistering disease samples studied (Tabl. I). TIMP 1 was positive in most BP biopsies within the blister ($p<0.05$). The presence of α-1-antitrypsin within the blisters favored a diagnosis of DH versus BP. Active cases of PV and PF demonstrated a strong presence of α-1-antitrypsin as well as MMP9 (Tabl. I). Metallothionein was the most common positive marker found in all the autoimmune skin blistering diseases types, as well in controls from genetic relatives of El Bagre-EPF patients (Tabl. I).

Discussion

Contrary to previously published data regarding positivity of MMP9 and uPAR in human ABDs and respective animal models, our studies of in situ biopsies from active clinical lesions demonstrate significant differences [11-15]. Specifically, uPAR was positive only in one part of a lesional blister from one case of BP, where the blister demonstrated blood deposits. Only a few chronic cases of El Bagre-EPF that were under prednisone treatment of less than 40 milligrams per day for more than 10 years stained positive for MMP9. In our necropsy tissue analysis from controls and patients, we found no differences in regard to MMP9 staining. In few cases of active DH, we observed positivity to MMP9 as shown previously [15]. MMP9 and MMP12 have been previously documented to display positive staining in some patients with clinical enteropathy and DH [16]. Some authors have shown variable collagenase expression in autoimmune skin blistering diseases, including induction during re-epithelialization, and decrease by topical glucocorticoid therapy [17]. One of the pitfalls of our study was the fact that with the exception of the skin biopsies from El Bagre-EPF and the controls, we lack definitive data regarding whether specific patients were taking immunosuppressive therapy at the time of biopsy; this limitation of our study is pertinent.

However, our findings are in agreement with some reported previously [18], since many of these autoimmune blistering diseases stained positive for metallothionein and TIMP1. Our results demonstrated stronger staining in areas of active inflammation in most of the ABDs; significant staining was also noted in inflamed appendices, correlating with major deposits of immunoglobulins and complement as determined by IHC (data not shown). Our study results highlight a previously documented increase in expression of metallothionein, coupled with a simultaneous expression of the TIMP1; TIMP1 may thus be expressed to inhibit damaging effects of the metallothionein [19].

Matrix metalloproteinases (MMPs) are a family of extracellular matrix (ECM) degrading enzymes that are collectively capable of degrading almost all ECM components [20,21]. The extracellular activities of MMPs are regulated by tissue inhibitors of metalloproteinases (TIMPs) [20,21]. Both soluble and membrane-anchored metalloproteinases participate in degradation of the ECM. Metallothioneins have the capacity to bind heavy metals, both 1) physiologic, including zinc, copper, and selenium; and 2) xenobiotic, including cadmium, mercury, silver, and arsenic and pesticides (introduced via food supply and/or other routes). Metallothioneins have a high content of cysteine residues that bind various heavy metals; these proteins are transcriptionally regulated by both heavy metals and glucocorticoids.

Markers	BP n=34	PV n=14	PF n=8	DH n=14	Normal skin controls n=15	El Bagre EPF n=30	Control endemic area group n=15
ά -1 anti--trypsin	In 4/34 biopsies, some staining in blister, in dermis and around the eccrine ducts.	Positive in the epidermis in spots, in some blister debris and subcorneal in 8/14.	Positive in the upper vessels and in the inflammatory dermis (3/4).	Upper dermis, blister and under in 8/10. Positive in some fibroblastoid cells.	Mostly negative.	Positive staining in some of the basal keratinocytes hair follicle, neurovascular supplies and subcutaneous fat.	4/15 cases were positive, in neurovascular bundles of the skin and appendices and sweat glands.
MMP-9	Staining in the blister, dermal vessels METS matrix (4/34).	Most cases negative.	Negative.	ICS like, dermis under the blister, neurovascular supplies of appendices (3/10).	Mostly negative.	9/30 of the chronic cases corneal layer, hair follicle some vessels. Positivity in the METS.	Mostly negative.
TIMP1	Weak positive around the blisters, vessels and in the METs and fat (19/34).	Positive in basal keratinocytes, blisters debris, dermal vessels and METs (7/14); linear deposition at the BMZ.	Positive in 2/4 cases around the blisters, upper vessels and METs.	Positive in the blisters in the dermal papillae (3/10).	Mostly negative.	Corneal layer, some epidermis; also, dermal blood vessels and sweat glands.	2/15 Positive sweat and sebaceous glands, vessels and extracellular fibroblastoid cells (8/15).
Metallothionein	Positive in the BMZ of the hair follicles, and some cells of the METs (19/34).	Positive at the BMZ of the hair follicles and sebaceous glands, as well as in some areas in the MTEs matrix (9/14).	Positive in 2/4 cases around the blister and upper vessels and METs.	Positive under the blisters (4/10).	Mostly negative.	Corneal, and cytoplasms of the keratinocytes of the spinous layer. Sebaceous glands in 23/30 patients and some fat tissue.	3/15 positive in the corneal layer. Positive staining to the sweat glands (8/15).
uPAR	Negative	Negative	Negative	Negative	Negative	Negative	Negative

Table I. Summary of staining patterns of proteases and protease inhibitors in multiple autoimmune skin blistering diseases

Several cases of DH were positive for α-1 antitrypsin. We previously described a fatal case of El Bagre-EPF with high levels of α-1 antitrypsin in a patient superinfected by varicella-zoster virus [23]. The El-Bagre-EPF cases also stained positively for MMP9 only in chronic patients under treatment with prednisone for long periods. The MMP9 reactivity was located in areas of newly reported dermal cell junctions, including dermal METs [24] and telocytes [25]. Our finding may explain dermal histologic sclerodermoid changes occasionally noted in El Bagre EPF, with attendant loss of skin appendices.

The fact that the ABDs improve with glucocorticoids may be related to our findings. Other studies of BP have shown altered expression of MMPs and TIMPs within lesional blisters [22].

Conclusions

We conclude that the observed profile expression of proteases, protease inhibitors and other enzymes in autoimmune skin blistering diseases seems to differ from many published animal models, thus highlighting significant immunologic differences between these animal models and the in vivo autoimmune skin blistering diseases of human patients. The TIMP1 and metallothionein seem to be expressed in an inverse correlation, suggestive of one enzyme attempting to repair collateral damage from the other enzyme. It is possible that the capacity to bind heavy metals on these enzymes may indicate some exposure to these xenobiotics in ABDs. The presence of enzymes and their inhibitors (not only in the blister areas, but also in the inflamed dermal vessels, skin appendices and METs) merits further testing of autoimmunity in these areas.

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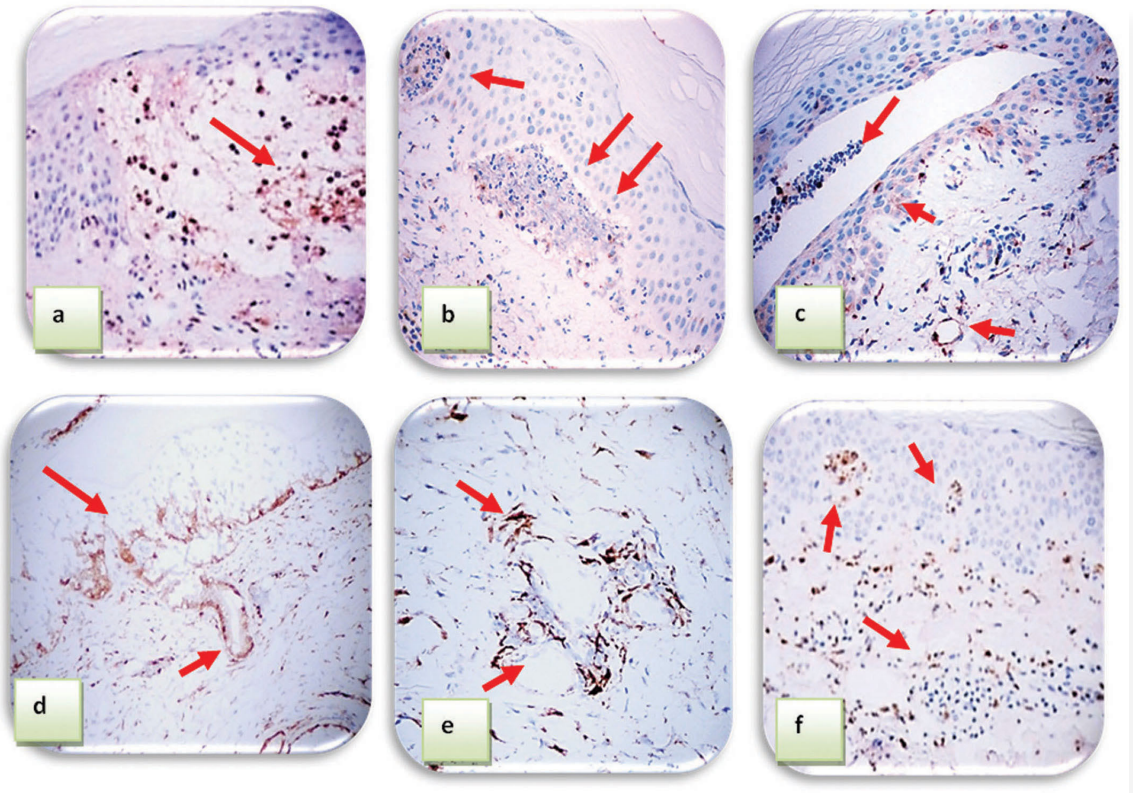

Figure 1. a ά-1 anti-trypsin DIF positive staining in a case of PV inside the blister (red arrow, dark brown staining) and some punctuate staining in upper dermal blood vessels (200x). **b.** Case of DH, demonstrating positive TIMP-1 IHC staining in the blister and punctuate staining in upper dermal blood vessels (red arrows, brown staining) (100x). **c.** Case of PV, with TIMP-1 positive IHC staining in cells within and around the blister, and some in upper dermal blood vessels (red arrows, brown staining). **d.** BP case with positive IHC staining for metallothionein in the base of the blister and around a dermal sweat gland ductus (red arrows, brown staining). A few positive areas of punctate staining are also noted on upper dermal blood vessels. **e.** A BP patient with positive metallothionein IHC staining around dermal blood vessels (red arrows, brown staining). **f.** A DH case, with positive IHC staining in the blister with ά-1 anti-trypsin and on upper dermal blood vessels (red arrows, brown staining).

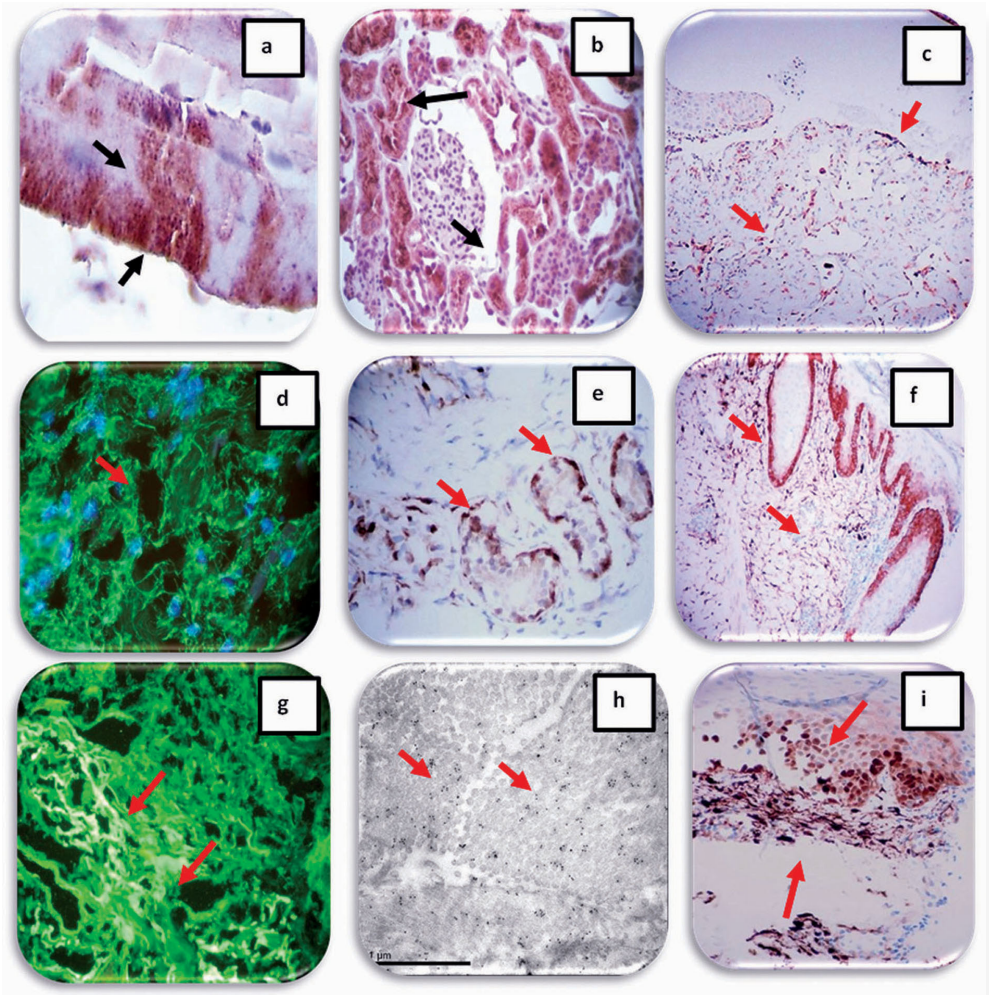

Figure 1. a IHC positive TIMP-1 staining of heart necropsy tissue from an El Bagre-EPF patient; and in **b,** the same patient in renal tubule tissue black arrows, red/brown staining). **c.** A BP case, with positive staining with TIMP1 over the blister BMZ and between dermal extracellular matrix fibers (red arrows, brown staining). **d.** The same case of BP as in c, using DIF with FITCI conjugated fibrinogen and showing that dermal staining is present, possibly related to dermal reactivity(red arrow, light yellow/green staining). **e.** A BP case, demonstrating IHC positive staining in the sweat glands with metallothionein (red arrows, dark staining). **f.** IHC positive to metallothionein in a patient with PV at the base membrane zone as well as in the dermal cell junctions and or the MET. **g.** DIF from an El Bagre-EPF patient using FITCI conjugated anti-human IgG antibody, and showing positive staining between the dermal fibers (red arrows, yellow/white staining). **h.** IEM, showing positive 10 nm Gold labeled anti-human IgG antibodies, positive to several cell junctions in the dermis (red arrows, black dots). **i.** An El Bagre-EPF patient, demonstrating positive IHC metallothionein staining in epidermal acantholytic cells and in the subjacent inflamed dermis (red arrows, brown staining).

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SOCIODEMOGRAPHIC FACTORS AND THEIR ASSOCIATION TO PREVALENCE OF SKIN DISEASES AMONG ADOLESCENTS

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Abstract

Introduction: The pattern of skin diseases in any community is influenced by genetic constitution, climate, socioeconomic status, occupation, education, hygienic standards, customs and quality of medical care. The burden of skin disease also has an impact on the Quality of Life of adolescents. This study aims to investigate the level of awareness and assess the prevalence of different types of skin diseases among adolescents in Mauritius.

Material and Methods: 500 adolescents and young adults of both sexes and aged between 11-23 years were recruited. A questionnaire was used to elicit information and to assess the knowledge status of skin diseases and to determine possible risk factors. In addition, a validated questionnaire based on Quality of Life Index was used to determine the psychosocial effect of adolescents suffering from skin diseases. Data was analysed using IBM Statistics SPSS version 20 and Microsoft Excel 2007.

Results: Incidence of skin diseases was 22.9% in males and 24.7% females respectively. Acne was the most common skin problems in both gender followed by fungal infection (2.9%) in males and eczema (2.4%) in females. Climatic conditions (e.g summer), consumption of oily and spicy foods, sports practice and familial history were correlated positively with prevalence of skin diseases.

Conclusion: Acne, eczema and fungal infection were the most common skin diseases identified. The findings also indicate that more respondents between 15-19 years old were more prone to skin diseases.

Key words: prevalence; awareness; adolescents; skin diseases

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Introduction

Skin diseases are very common in many tropical countries among adolescents [1,2]. The pattern of skin diseases in any community is influenced by genetic constitution, climate, socioeconomic status, occupation, education, hygiene, standards, customs and quality of medical care. The aim of the study was to assess adolescents and young adult's knowledge about skin diseases and its risk factors [1]. Surprisingly not much has been published on interaction with and the role of dermatology in such a setting although skin diseases are quite common in the general population [2].These factors give each community its unique pattern and account for the wide variation reported from different regions of the world and even in the same country [3]. Adolescents' skin problems can be studied at the population level. A study revealed that out of 260 adolescents aged between 18-20 years in Oslo, Norway, 74% had pimples/signs of acne, 40% dry skin, 81% dermatitis/rashes and 83% other skin problems and the prevalence of the adolescents' self-reported complaints were higher than those found during clinical examination by a dermatologist [4].

Skin diseases account for 6-7% of all outpatient visits to primary care clinics and, although dermatologic diagnoses of adolescents overlap with general adult dermatology, data on the former as a distinct entity are rare [5]. In Mauritius, apart from some of the skin cancers, skin diseases are not recorded in any official registry and they vary enormously from mild conditions which may affect only the appearance of the skin to severe diseases which are totally incapacitating. The degree of treatment required, varies accordingly. In Netherlands, adolescents aged 12-18 years attending secondary school participated in a survey and revealed that those with chronic skin diseases are both likely to have emotional and behavioral problems [6].

Nonetheless, every medical practitioner knows that there are plenty people suffering with these conditions [7]. A comprehensive survey of general practitioners' workloads in Australia discovered that skin problems were the primary reason for at least 15% of consultations whereas, a community-based data collections show that physicians are consulted about skin conditions by less than 50% of those who have them. People frequently seek advice from pharmacists, family or friends and naturopaths or they simply prescribe for themselves based on information from elsewhere [5].

A cross-sectional, community-based study in Tehran, Iran by Ghodsi et al. [8] performed to determine the prevalence and severity of acne vulgaris in adolescents reported factors influencing acne severity risk and showed that the secondary outcome measures of family history, relation to nutrition habits, emotional stress, menstruation and smoking were associated with acne. They also stated that personal hygiene is important to inhibit skin diseases such as ringworm, scabies.

According to World Health Organisation 2001 report, the global burden of disease indicated that skin diseases were associated with mortality rates of 20,000 in Sub-Saharan Africa in 2001[9]. An additional point, often overlooked, is that skin problems in the developing world are often transmissible and contagious but are readily treatable [10,11].

Bacterial skin infections or pyoderma are common in most developing countries arised as primary infections of the skin (impetigo) or secondary infections among adolescents [12,13].

Lewis Jones and walker [14] conducted a research among Scottish schoolchildren aged 15-18 years and revealed an 83% high prevalence of acne in teenagers. 11% adolescents perceived their lives to be significantly affected by their acne (8% moderately to severe, 3% severe).

Aim

To assess the prevalence of skin diseases and their awareness among adolescents.

Objectives:

- To investigate which skin disease is more prevalent among adolescents.
- To assess the level of awareness and hygienic practices among teenagers.
- To assess the Quality of Life Index of adolescents suffering from skin diseases.

Material and Methods

Sample Population

A total of 500 random participants including male and female school adolescents and young adults were recruited from different districts of Mauritius. Inclusion criteria for selection were as follows:

1) Age: 11-23 years.

2) Male and Female healthy school adolescents and young adults from secondary schools and universities.

However adolescents and young adults with type 1 and type 2 diabetes were excluded in this study. Following selection the participants were required to fill a designed questionnaire.

Questionnaire design

A questionnaire consisting of both open ended and closed ended questions was designed for the purpose of this study. It included the demographic details (for example age, gender, district etc), the current lifestyle practices with regards to skin disease (for example treatment, face wash), the current awareness of the participants about skin diseases and hygienic practices. Questions on genetic predisposition, possession of tattoos/ piercing, sharing of cosmetics, sports practice, nutrition were also included in an attempt to identify potential risk factors for particular skin diseases.

The last part of the questionnaire dealt with the impact of having skin disease on the social life of the participants and their resulting change in their behaviour. A validated questionnaire based on DLQI (Dermatology Life Quality Index) was used. Prior permission from authors was obtained beforehand.

Data collection

The corrected questionnaires were distributed randomly amongst school adolescents and young university students. Appropriate informed consent was obtained from parents and all participants. Research was approved by UoM Ethic Committee. Information sheet in which all details about the project, the participant's rights and the researcher's statement were enclosed, accompanied the questionnaire. All information collected during the course of this survey was kept confidential and that the data was strictly used for research only.

Data Analysis

Data generated from the questionnaires was analysed both using Excel 2007 (Microsoft corporation) and IBM Statistics SPSS version 20 (IBM corporation). Descriptive frequency tables and Pearson's bivariate correlation in SPSS were used to analyse the information collected during the course of the study.

Analyse carried out also compared the incidence of disease amongst males and females and their current knowledge of skin disease. Potential risk factors for skin disease and the impact of skin disease on the social life of the participants, who had skin disease, were also investigated by performing statistical analysis in SPSS.

Results

The mean age of the sample population was 17.78. The highest levels of education were from tertiary education (27.6%) followed by secondary school (23.8%). Moreover, 63.4% males and 66.1% females were aware about skin diseases and a Pearson correlation revealed a positive correlation between presence of skin diseases and level of knowledge.

Fifteen skin diseases were identified during this survey but acne (13%), fungal infection (2%) and eczema (2%) were the most prevalent and significant among the adolescents and young adults in the general population. 22.9% males and 24.7% females had acne problem. Furthermore participants aged between 15-19 years were more prone to skin diseases such as acne (60%), wart (50%), dart (57.1%), eczema (70%), pimples (55.6%) and those who were between 20-24 years were more affected by fungal infection (50%). Among those who were suffering from skin diseases, the face (62%) was the most affected region in the body followed by the back (11%) (Tabl. I).

Also, it was noted that climatic conditions influenced in the severity of skin diseases and almost everyone (93%) complained to be more prone to get any skin diseases during summer. Moreover, 35.5% respondents grade their skin diseases as 'a little severe' while 5% had 'severe' skin diseases and 39% complained having their skin diseases appeared every month and 12% was every 6 months. An interesting aspect was found that 25.5% of the adolescents came to know about skin diseases via other sources such as parents, friends and teachers and 8.6% from the internet and 19.7% from physician. According to the participants, 27% thought skin diseases were caused by parasites followed by virus (23%). Only 17% thought hormone misbalance and fungi may be the cause.

Moreover, 56% of the adolescents thought nutrition could be a leading cause of skin diseases such as acne (39.6%), eczema (1.8%) and wart (0.6%). A Pearson correlation indicated that presence of skin diseases correlated positively and significantly with spicy and oily foods but 33.3% of the sample population consumed oily and spicy foods (25.5%) and fast foods (22.5%) more than three times a week.

Diseases	Age Group n (%)			Male (%)	Female (%)
	10-14	15-19	20-24		
Acne	8 (12.3)	39 (60.0)	18 (27.7)	35.4	64.6
Wart	-	1 (50.0)	1 (50.0)	50	50
Dart	1 (14.3)	4 (57.1)	2 (28.6)	57.1	42.9
Eczema	-	7 (70.0)	3 (30.0)	30	70
Pimples	1 (11.1)	5 (55.6)	3 (33.3)	44.4	55.6
Fungal Infection	3 (30.0)	2 (20.0)	5 (50.0)	60	40
Scabies	-	2 (33.3)	4 (66.7)	33.3	66.7
Athlete's Foot	-	1 (100.0)	-	100	-
Psoriasis	-	3 (60.0)	2 (40.0)	60	40
Allergies	-	1 (100.0)	-	-	100
Pigmentation	-	-	2 (100.0)	-	100
Furunculosis	-	1 (100.0)	-	-	100
Rashes	-	-	1 (100.0)	100	-
Folliculitis	-	-	1 (100.0)	100	-
Scars	-	1 (100.0)	-	100	-

Table I. Different frequencies and percentage of the different skin diseases in different age group

Discussion

Skin disease is a major health problem [15]. Given the rise in the prevalence of skin infections in many countries and the lack of published data pertaining to the prevalence and awareness of skin disease in Mauritius, this survey was done to assess the level of awareness of skin disease and the prevalence of skin infections among the Mauritian adolescents and young adult's population and found a prevalence of 1:15 among males and females suffering from skin diseases.

Out of 500 participants, it was found that the overall incidence of disease was 24% (n=120). Acne (n=65) was most prevalent among the youngsters followed by eczema and fungal infection in both gender. This finding is in line with the study done by Mancini [16] who revealed that acne vulgaris was the most common skin diseases treated by physicians accounting for more than 14 million visits per year and that generally, acne appeared for the first time in approximately 85% of individuals between the ages of 15 and 17 years. Among the participants who had skin diseases, the majorities (60%) had acne and are within 15-19 years. According to Mancini [16], the first acne lesions among adolescents and young adults were one of the earliest signs of approaching puberty and generally occurred at time of heightened emotional sensitivity.

The incidence of skin diseases in males was 22.9% (n=47) and in females 24.7% (n=73). Further analysis revealed that of the total number of males with or without disease, 11.2% had acne and 14.2% of females also had acne. Eczema and fungal infections were present in 1.5% and 2.9% of males respectively while 2.4% and 1.4% of females who had a skin disease had eczema and fungal infection respectively. An interesting finding is that two males and four females had scabies. Diseases such as wart, dart pimples, scabies, athletes' foot, allergies, psoriasis, pigmentation, furunculosis, rashes, folliculitis and scars though in small amounts, were reported by the participants but in low frequency.

Relationship of age and affected body parts with skin disease

Skin problems were found in all age categories. However, age and presence of disease among youngsters did not correlate (p>0.05). Indeed age was not linked to the presence of disease as acne, dart, fungal infections and other skin diseases were present across all age group implying that a particular disease did not occur at a particular age (Tabl. I). El-Khateeb et al [3] conducted a study in Cairo, Egypt and discovered that only certain skin diseases were related to age. Bacterial infections subgroup was the most common in infants and preschool children, and impetigo was the leading disease [1]. In school and young adult stages, scabies and contact dermatitis were the most common and in old adult and geriatric stages, scabies was the most common. However, this study found that acne, dart, eczema was more prominent between the age of 15-19 years and fungal infections in 20-24 years.

Analysis of impact of skin disease on body parts revealed that face was the most affected. The majority (90.8%) of population who had acne, had their face most affected followed by the back (6.2%). Palmar [17] stated that generally acne began on the face and as it progressed and became more severe, it began to affect other areas of the body as well. Back acne was fairly common among acne sufferers affecting males, females, teens and adult. However, not everyone with acne would experience an outbreak on the body, but those with body acne nearly always have acne on the face too and their causes were the same that is, overactive oil glands, excess dead skin cells, and proliferation of acne-causing bacteria. Moreover body acne was more common and more severe among males [17]. Dart and pimples also affected the face of the participants (57.1% and 66.7% respectively). However, results here showed that as eczema and scabies mostly affected the feet. Of those who specified other places, it was seen that the belly, butt, head, neck and breast were also body parts which were affected by skin disease but there was a minimal percentage.

Analyses also revealed that there are differences in the Frequency and Severity of skin diseases among the participants. Furthermore, this study demonstrated that skin diseases appeared roughly every day to every month. Acne and eczema appeared daily to every month while fungal infections appeared mostly every 4 months and most of participants with dart had the disease every 3 months. The fact of having a skin disease was not considered as a severe problem by a large cohort (35.5%) while a minority (5%) stated that their skin disease was 'very severe'. Acne, dart and fungal infections was considered as a 'very little severe' by the respondents, while those having psoriasis and eczema, the response to the severity of the corresponding disease varied from 'not at all severe' to 'very severe'. This can be explained by the fact that, as a disease progresses, body parts get affected and in the case of psoriasis and eczema, many body parts are affected which the youngsters considered as severe [17].

The attitude of the general study population (n=500) in relation to treatment of skin disease yielded interesting findings. A large percentage (59.4%) of adolescents and young adults seek for advice from dermatologist for treatment following skin disease. Herbal treatment was also an ailment for skin disease while self-medication was in a small percentage (15.2%). A visit to the dermatologist is the best treatment for skin disease depending on the severity of the disease rather than self-medication. A research on retinoids revealed that it has been used widely in the topical and systemic treatments of various dermatoses: psoriasis, disorders of keratinization (DOK), keratotic genodermatosis, and severe acne [18]. The majority of respondents (58.3%) stated that they sought for dermatological consultation at least 1-5 times over the preceding year and they are also of the opinion that a visit to the dermatologist is the best treatment. However, the frequency of dermatologist visits for acne was quite low. The majority of those having scabies (66.7%) did not visit a dermatologist. Nevertheless 2.5% of diseased population specified that they visited pharmacist and 2.5% stated they did nothing to treat their skin disease.

Risk factors and its relationships to prevalence of skin diseases

In the current study one of the objectives was to assess the current awareness of skin diseases of young adults. Various variables pertaining to knowledge of skin diseases were assessed. The majority of males and females were aware of skin diseases. Further analyses between presence of skin diseases and awareness of skin diseases revealed a strong positive association between these two variables (p=0 .00, r= 0.372). This can be explained by the fact that due to the frequent occurrence of skin diseases, the youngsters were more aware. A community-based study of skin diseases especially acne amongst adolescents in Singapore revealed that half of the respondents felt that the following factors in order of priority were important in acne: fried foods, cosmetics, stress, lack of sleep and hormonal changes and in addition two factors, poor skin hygiene (71%) and dirt (75.8%) were identified as most important [19]. In this study, acne was the most predominating skin disorder the sample population was aware of, followed by eczema, pimples, skin cancer, dart and psoriasis. In addition, a case of acne stage II was presented with a long history of firm nodules, large abscesses and sinous tracts, small scars, distributed in the axillary, groin, perianal and infraumbilical areas, associated with lesions on the face [15].

Nutrition is one of the most important parameters that are involved in modulating skin health and condition [20]. The knowledge about main etiological agents of skin diseases was assessed, and the opinions of the participants diverged. Some adolescents were not aware that bacteria, fungi and hormone imbalance could be a possible cause of skin disease. On the other hand, analysis of nutrition and skin disease relationship revealed that, a large cohort (56%) was aware that nutrition is a risk factor for skin disease and most of them, stated that acne was the leading skin disorder caused by nutrition followed by pimple. The role of food in the aetiopathogenesis of skin diseases remains controversial. However, a study done on participants aged between 6-17 years in a paediatric dermatology clinic and found that in a total of 75% (75 of 100) had tried some form of food exclusion. Of these 48% had avoided dairy products, 27% avoided eggs, 20% food additives and colouring, 13% avoided chocolates, sweets (candy), soft or fizzy drinks and nuts. 30% of those restricting foods felt that this had brought about an improvement in their skin diseases such as atopic dermatitis and acne but 51% said they had done so after consultation with a doctor or dietician [21]. Indeed, in the present study presence of skin disease correlated both positively and strongly with spicy and oily foods (r=+ve, p=0.000; r=+ve, p=0.001 respectively). A community based study in Iran showed that sweet and oily foods were recognised as risk factors for moderate to severe acne. However, this relationship does not always stand good as spicy foods were not associated with acne severity [8].

The knowledge about sharing of cosmetics as an agent for skin disease was analysed and it was found that the majority of males and females know that cosmetics could cause skin disease irrespective of age group. Foundation was the cosmetic which was mostly used by males and females and a majority did not share their cosmetics. Many of the participants (91.2%) noticed a positive change in their skin after use of cosmetics while 8.8% had a negative change. Among those who experienced negative changes, acne, pimples, skin rashes, dart and irritations were observed.

In Sweden, Berne et al [22] revealed that the use of cosmetics is rising and adverse reactions to these products are increasing. Among people with self-reported sensitive skin, as many as 57% of women and 31.4% of men reported side effects from using cosmetics or skin care products at some stage in their lives. Their study suggests that 176 patients who visited a dermatologist with specific complaints of reactions to cosmetic products, 45% had dermatoses. Contact dermatitis is the most commonly reported adverse reaction to cosmetics and others such as itching, burning, papules and various others [23]. Moreover, in a recent epidemiological study in UK, 23% of women and 13.8% of men had experienced some sort of negative reaction to a personal care product over the course of 1 year [22]. Findings indicate no correlation between knowledge status and knowledge of cosmetics as a cause of disease and suggest that people are not aware that cosmetics can lead to skin diseases.

In addition all respondents were very aware that tattoo or piercing could be a risk factor for skin disease and this explains why the majority of them were unwilling to have a tattoo or piercing. Tattoos and piercing are increasingly popular in today's society, but it could also give rise to skin diseases.

An investigation was conducted among adolescents of the University of Bari in the region of Apulia, Italy about the knowledge of the risk and practices related to tattoo and piercing.

Of the 1598 students, 78.3% believe it is risky to undergo piercing/tattoo practices, 29% of the sample had at least one piercing or tattoo (excluding earlobe piercing in women). The average age for first piercing was 15.3 years and tattoo 17.5 years. 13.2% of the interviewees who underwent tattoos had skin complication after and 13.1% declared they had had several symptoms [24].

Another major factor contributing positively to a higher incidence of skin diseases is climatic conditions. Hand-foot-mouth disease (HFMD) is an acute viral infection that occurs usually among children in summer [25]. In this study, attempts were made to find possible risk factors for the skin disorders which the youngsters faced. The majority of the study population (92.5%) was more prone to diseases in summer. An association between season and a higher incidence of skin diseases do exist. It has also been found that 8.8% males and 13.6% females were more prone to skin diseases during summer season. For instance, El-Khateeb et al [3] found that there is significant variation in skin diseases mainly in summer (40.7%) and the main skin diseases included dermatitis (58.7%) as most common followed by fungal infection (34.87%), scabies (9.26%), warts (5.51%), and pigmentary disorders (4.24%).

Other factors linked to prevalence of Skin Diseases

Skin hygiene, particularly hands, is considered to be one of the primary mechanisms to reduce risk of infection [26]. Majority of respondents (89%) were fully aware of the impact of humidity can be a prevalence of skin diseases and therefore they did not keep their clothes in a humid environment. A study done in Lebanon among Polish soldiers whose skin diseases pose an epidemiological problem in hot, dry as well as humid climate. High temperature and humidity of air, inappropriate clothing and low level of personal hygiene influence the incidence of skin disease among them. 13.2% of them suffered from dermatoses, 16.2% mycoses, 11.9% from viral diseases and 10% from pyoderma [27].

Most of the youngsters (81.7%) practiced sports. Acne was predominant among those suffering from skin disease and practicing sports, followed by eczema. The correlation between frequency of sports practice and presence of skin disease was not statistically significant. The role of sport in the pathogenesis of acne or skin disease remains to be determined as our data is insufficient enough to relate sports as being a direct risk factor. During the survey only 1 out of 120 participants suffering from skin diseases got furunculosis, which is quite frequent among athletes, was observed. For instance, one study done by [28] revealed that furunculosis in 28% of high school football players and 14% of basketball players.

It is commonly known that the occurrences of some skin diseases are known to be associated with family history. For examples, Tan et al [19] reported a high prevalence of young adolescents in Singapore suffering from acne (88%) when their parents suffered from similar conditions. The hygienic practices of the participants with skin diseases were found to be very good. For instance, the majority did not share their cosmetics (67%), washed their face more than once (49.8%) and most of them bathed twice or more daily. Results also show that many youngsters changed their clothes after heavy perspiration. A study carried out on prevalence of Tinea cruris showed that excessive perspiration is the most common predisposing factor and hence patient education on proper hygiene makes intuitive sense for successful treatment [29].

Dermatology Life Quality Index (DLQI)

Finally, the psychological aspect of skin diseases and its impact on social life of the participants who had skin disease were also investigated. Many of them had a little itching of the skin while very few find their skin itching very much. This finding suggests that depending on the skin disease present, the degree of embarrassment varies. Coincidentally, the impact of having skin disease did not interfere very much with the quality of life of youngsters. This is further supported from evidence that way of dressing, social and leisure activities, family relationships, studies were not affected.

Social, psychological and occupational factors may all contribute to an impaired quality of life. Simmons and Massey [30] found that life choices and employment opportunities are influenced by skin diseases as they may impinge on social life leading to embarrassment, decreased confidence, feelings of rejection and social withdrawal. In addition, domestic life may be affected on many levels.

100 patients with psoriasis had poor quality of life and significant correlation was found between Dermatology Life Quality Index and Beck Depression Inventory [31].

Conclusion

This project has given an account on the prevalence and awareness of skin diseases among school adolescents and young adults in Mauritius. The findings in this study demonstrated that people between the ages of 15-19 years were more prone to skin diseases. Moreover, more females were more affected to skin diseases rather than males.

Acne, eczema and fungal infection were the most common diseases affecting this particular group of people and amongst the different body parts; the face, back and feet were the most affected in particular during summer season. Most respondents view their skin diseases as 'little severe' and the majority preferred to seek dermatologists' advice to avoid worsening skin diseases.

Even if a greater number were aware the fact that cosmetics can be a cause of skin diseases, still most of the respondents made use of them, in particular females. Complaints related to cosmetics include acne, dart, rashes and irritations were the most dominant. The majority were unwilling to have a tattoo/piercing due to the fact that they were aware of its related risk factors.

A large number of adolescents practiced sports. Amongst those who exercised, they suffered from mostly acne. Three quarter of the sample population were aware that perspiration could be a risk factor, hence, after heaving sweating the adolescents did change their clothes and maintain good hygienic practices.

Besides, acne and eczema were found to coincide with family history, that is, some participants said having parents or siblings suffering from acne and eczema and in turns they were affected too.

Also, the psychosocial effect was investigated among adolescents suffering from skin diseases. It was found that some people were a little embarrassed and had an influence in their life, especially problems with their family members, close friends or partners.

Awareness campaigns should organised in schools regarding on preventive measures of skin diseases and advice concerning treatment and regular medical check up in schools as some adolescents might get some skin problems but are unaware. Having a balanced diet and minimum use of cosmetics followed by proper hygiene can also help in preventing skin diseases.

Most importantly providing professional psychological advice and help for adolescents suffering from skin diseases.

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OPTIMIZATION OF *LAMBLIASIS* MICROSCOPIC DIAGNOSTICS BY THE METHOD OF POLARIZED FLUORESCENCE FOR PATIENTS WITH *ROSACEA* AND *URTICARIAL*

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Abstract

Introduction: There is little information about diagnosis of concurrent lambliasis in patients with rosacea and urticaria. We used method of polarized fluorescence to diagnose liambliasis, taking into account belonging of macromolecular structures of unicellular parasites Giardia lamblia to the optically active substances with the properties of liquid crystals.

Material and Methods: Lambliasis was diagnosed on the basis of feces parasitological research and duodenal contents by methods of light and optic microscopy and polarized fluorescence in 105 patients with rosacea and urticaria. Research results were processed by the method of variation statistics in the Statgraf program by using Student's criterion.

Results: Search results of lamblia in patients with rosacea and urticaria depended on the conditions of its holding, patients' preparation and from the previously received basic therapy if it consisted absorbents. Due to the fact that the fluorescence polarization as a physical method does not require the use of any generally toxic, dye- fluorochromes, qualitative cyto fluorescent analysis of lamblia in greeting microdrugs enables to distinguish vegetative forms of cysts.

Conclussions: Polarized fluorescence method allows optimize the microscopic diagnosis of lambliasis, increasing its sensitivity. Previous preparation for the laboratory examination of Giardia lamblia is needed for the best exposure of vermin for patients with rosacea and urticaria.

Key words: rosacea; urticarial; lamblia; polarized fluorescence

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Introduction

Studying the pathogenesis of chronic skin diseases, new methods development of diagnostics and treatment of those dermatoses are still one of the priorities in dermatology [1]. The relevance of this problem is caused by increasing proportion of dermatoses severe clinical forms that are resistant to traditional therapies and involving in the pathogenesis of various infectious agents, including some parasites [2-3].

Our previous studies [4] found aggravating effect of some parasites, such as lamblia, on the course of certain skin diseases – rosacea, urticaria. At the same time, the inclusion of complex anti-parasitic drug therapy of „Ornidazole" increases the treatment effectiveness referred to above dermatosis, resulting in reducing the severity of clinical symptoms, rapid disappearance of rash and itching elements. Complete clinical recovery is possible to achieve in 88.6% of patients versus 18.9% in the application of basic therapy [5].

According to our data, the concomitant lambliasis occurs in 67.7% of patients with urticaria and 52.2% of patients with rosacea. The lack of basic therapy efficiency of mentioned above dermatoses, leads to purposeful data examination of patients with presence of concomitant parasitosis.

Material and Methods

Under the supervision there were 105 patients with rosacea and urticaria on the background of lambliased invasion (lambliasis regarded as concomitant disease), aged from 16 till 69 years, receiving inpatient and outpatient treatment in Ternopil regional Dermatovenerologic Dispensary. The diagnosis of rosacea and urticaria was established clinically.

Lambliasis was diagnosed on the basis of feces parasitological research and duodenal contents by methods of light and optic microscopy and polarized fluorescence with using a fluorescent microscope LYUMAM 8-P 3m with photometric nozzle FMEL-1 for spectral analysis.

Research results were processed by the method of variation statistics in the Statgraf program by using Student's criterion.

Results

Search results of lamblia in patients with rosacea and urticaria depended on the conditions of its holding, patients' preparation and from the previously received basic therapy if it consisted absorbents. Preliminary patients preparation during 5-7 days with the use of spasmolitic „No-spa" and bile-expelling drug „Alohol" helped to increase the exposure of cystic forms of lamblias to 87.5% cases compared with 29.8% in patients receiving absorbents.

As you know, macromolecular structures of unicellular parasites Giardia lamblia belong to the optically active substances with the properties of liquid crystals [6]. Membrane lipids, nucleic acids of nuclei of living cells are inherent the ability to induce elliptic light polarization, which shows up the dependency upon a wave-length phenomenon of circular dichroism [7-9]. Due to the fact that the fluorescence polarization as a physical method does not require the use of any generally toxic, dye- fluorochromes, qualitative cyto fluorescent analysis of lamblia in greeting microdrugs enables to distinguish vegetative forms of cysts (Fig. 1, 2).

The most typical distinction of lamblia fluorescence in polarized light should be considered extremely high level of luminescence intensity of cell nuclei parasite. For example, if the glow intensity of nuclear structures of leukocytes which corresponds to the level of cellular bioenergy DNA and RNA, conventionally taken as 100%, so for similar lamblia intracellular structures this index is founded out as higher [10].

Exactly this fact gets the sign of specificity: even with full blocking primary of primary light stream by polarization filters (polarizer and analyzer) on a background of faint fluorescence by other micro objects, for example, leukocytes, lamblia cells shown especially brightly. The specified diagnostic phenomenon is peculiar to the individuals of exciter at any stage of its life cycle.

In polarized light lamblia are glowing bright golden-yellow and greenish-red light (Fig. 1, 2).

Contrary to the conventional rule about the reliability of parasites detection only in freshly („warm") material, we were able to detect lamblia (both vegetative forms and cysts) in duodenal contents, which is stored in the refrigerator in the syringe, within 72 hours after taking the bile - using both traditional light and optic microscopy and polarized-fluorescence method (Fig. 3).

Another characteristic distinction cyto luminescent parasitological analysis is the dependence of the intensity of Giardia lamblia luminescence in polarized light from the place of parasite staying at the time of diagnostic testing. Thus, the highest intensity of luminescence was in parasites from portions of bile A, taken by us at 100%, while it was lowest in portions of bile C - (71,6 ± 5,9)%.

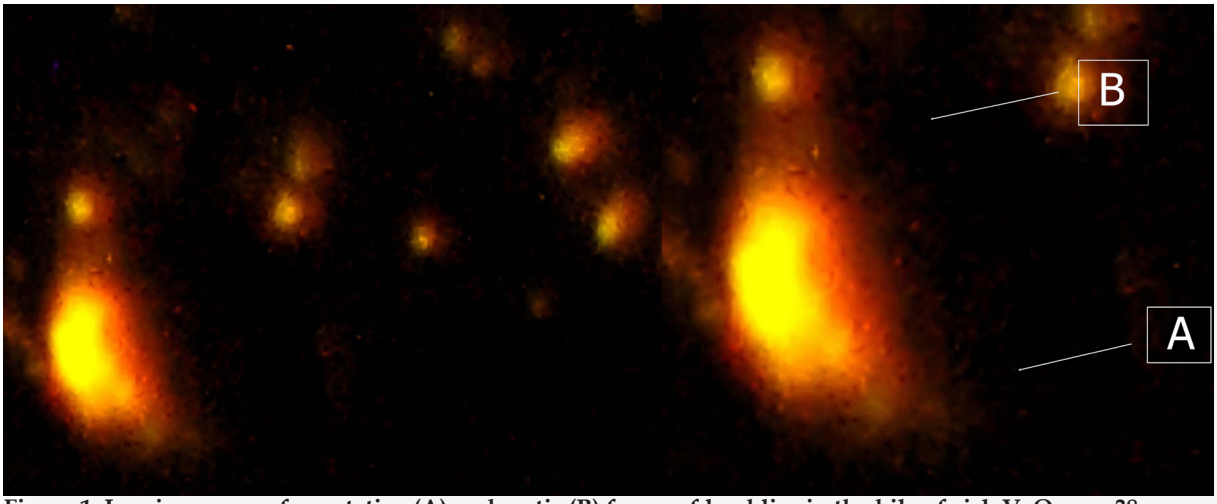

Figure 1. Luminescence of vegetative (A) and cystic (B) forms of lamblias in the bile of sick V. O., age 38. Diagnosis: rosacea, papulo-pustular form, concomitant lambliasis. Microscope LYUMAM P 8. Ok × 10 lens × 9.

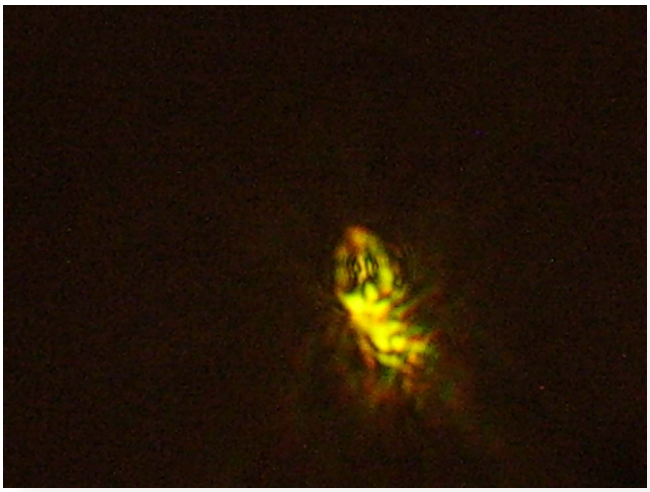

Figure 2. Polarized fluorescence lamblia in bile (portion A) patient V. O., age 38. (Diagnosis: Chronic urticaria associated lambliasis). Microscope LYUMAM P 8. Ok × 10 lens × 9.

Thus, the highest intensity of luminescence was in parasites from portions of bile A, taken by us at 100%, while it was lowest in portions of bile C - (71,6 ± 5,9)%. Intermediate level of fluorescence intensity, namely (82,7 ± 5,1)%, took place at research portion of bile B ($p < 0.05$). The resulted distributing of levels of bioenergetics cell parasites from different portions of bile, in our opinion, is a reflection of reactions from the side of parasites on changing of terms in the microenvironment, namely quantitative composition of bile components (Fig. 3).

In bile research by lamblia polarized fluorescence method it was found out (90,3±3,7) % of patients, whereas the traditional method of light-optical microscopy - only (77,1±5,2) % ($p > 0,05$). In addition, lamblia cysts in separate portions of bile in addition to the results obtained using traditional microscopy were found in 10 patients by polarization-fluorescent method.

Informative were the results of spectral analysis of polarized fluorescence lamblia obtained from different portions of bile in diagnostic duodenal intubations. In all samples of bile were observed two characteristic peaks, namely in the area of 600 nm and 750 nm, that corresponds to emission spectra of DNA and RNA (Fig. 4).

Thus, if the spectral peak areas of RNA differ in terms of intensity, so oscillation wavelengths become character for a similar range of DNA sites, that are evidence of landslides fluctuations bioenergy cells associated with processes of adaptation to altered conditions of parasite survival and parasitism.

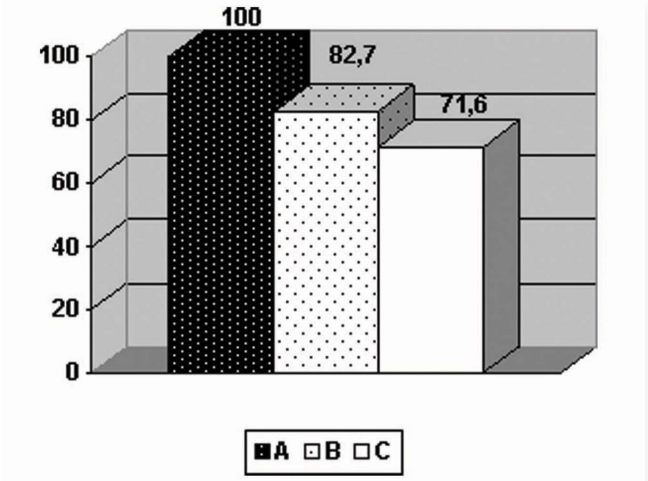

Figure 3. Dependence of Giardia lamblia fluorescence on their localization in portions of bile.

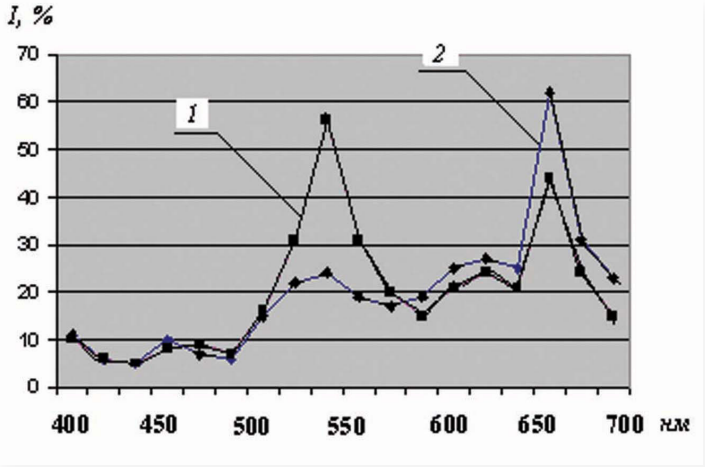

Figure 4. The spectral composition of the polarized fluorescence vegetative forms (1) and lamblia cysts (2) with the bile of patient with urticaria on the background of lambliais. LUMAM-P 8 3m: lens × 9; FMEL-1, 1.5 mm probe.

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This article is dedicated to the blessed memory of talented scientist pathophysiologist, honoured inventor of Ukraine, Professor Vasyl Demyanenko, who conceived the use of polarized fluorescence method for the diagnostics of concurrent lambliasis in patients with rosacea and urticaria.

Conclusions

1. The basis of laboratory diagnostics of concomitant lambliais in patients with urticaria and rosacea remains a classic method of faeces scope of Parasites (95.2%).
2. Polarized fluorescence method allows optimize the microscopic diagnosis of lambliasis, increasing its sensitivity.
3. Spectral analysis of native lamblia radiation in polarized light provides methodical possibilities of differentiation vegetative and cystic forms of parasites by registration and evaluating bioenergy cell parasites in accordance with the terms of their experiencing in patients' body with urticaria and rosacea, and therefore contains diagnostic and prognostic information.
4. Previous preparation for the laboratory examination with the use of antispasmodics and bile-expelling drugs and avoidance of taking absorbents is needed for the best exposure of vermin for patients with rosacea and urticaria.

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A STUDY ON TOPICAL CALCIUM DOBESILATE FOR THE TREATMENT OF LIMITED *PLAQUE PSORIASIS*

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None

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Abstract
Introduction: Topical dobesilate offers the potential for treatment of plaque psoriasis without atrophy or other local side effects associated with the use of topical corticosteroids. Fibroblast growth factor (FGF)-mediated pathways participate in many of the cellular events implicated in the pathogenesis of psoriasis. Thus, targeting FGF signals may be potentially therapeutic.
Aims: To study the efficacy of topical calcium dobesilate for the treatment of 50 patients of limited plaque psoriasis.
Methods: For the present study, fifty clinically diagnosed cases of psoriasis with limited number of plaques (<5) were selected from the outpatient dermatology department. Lesions were treated with potassium dobesilate for a maximal period of 4 weeks. No other modality of treatment was used other than emollients and oral antihistaminics.
Results: The mean duration of disease in our study was 4.74 + 14.64 years in our study. The mean reduction in PASI score with topical calcium dobesilate was statistically significant in our study ($p > 0.05$).

Key words: psoriasis; PASI; treatment; diagnosis; calcium dobesilate; Fibroblast Growth Factor (FGF)

Cite this article:
Neerja Puri, Asha Puri: A study on topical calcium dobesilate for the treatment of limited plaque psoriasis. Our Dermatol Online. 2013; 4(3): 290-293.

Introduction

Psoriasis is a chronic recurrent papulosquamous disorder characterized by epidermal hyperplasia [1]. The management of psoriasis can be challenging. Although, there are many therapeutic modalities available but still there are no clear cut guidelines regarding the usage of different modalities depending on the severity of psoriasis [2]. Fibroblast growth factor (FGF)-mediated pathways participate in many of the cellular events implicated in the pathogenesis of psoriasis [3]. Thus, targeting FGF signals may be potentially therapeutic in the treatment of psoriasis.

There is at present no cure for psoriasis, only suppressive therapy. The most common form for which most types of treatment are tested is plaque-type psoriasis, characterized by welldemarcated, erythematous, scaling plaques. It appears that several cell signaling events regulate the four major signs of this disease: keratinocyte hyperproliferation, low rate of keratinocyte apoptosis, angiogenesis and infiltration of inflammatory cells [4,5]. Targeting such signaling and transcriptional events with pharmaceutical intervention may help to reduce downstream cellular effects in psoriasis. The fibroblast growth factor (FGF) family is an ubiquitously expressed transmembrane signaling family that elicits receptor-mediated and survival [6,7]. The FGF ligands are single regulatory effects on cell growth, function, differentiation polypeptides consisting of 22 genetically distinct homologues and the FGF receptors (FGFRs) are transmembrane tyrosine kinases encoded by four homologous gene products, which form a complex with pericellular matrix heparan sulfates independent of the FGF ligand. Binding of FGF ligands to FGFR-heparan sulfate complexes activates the kinase activity and transmits regulatory signals to downstream signaling mediators or targets [8,9]. FGF stimulates a repertoire of canonical intracellular signaling pathways controlling many of the cellular events implicated in the pathogenesis of psoriasis [10-12]. We have shown previously that elevated plasma levels of FGF in psoriatic patients may be a useful predictor of clinical outcome and affect management [13,14]. Calcium dobesilate has been widely used for the treatment of diabetic retinopathy. Furthermore, it has been reported that this agent inhibits proliferation of vascular smooth muscle cell growth in serum containing, among other things, FGF. Recently, we have shown that dobesilate inhibits cell proliferation and promotes apoptosis in glioma cell cultures acting as an FGF inhibitor [15,16]. Based on the hypotheses about the activities of dobesilate, we assessed the effect of topical dobesilate in chronic plaque psoriasis.

Aims

1. To study the efficacy of topical calcium dobesilate for the treatment of 50 patients of limited plaque psoriasis.
2. To study any side effects of calcium dobesilate.

Material and Methods

For the present study, fifty clinically diagnosed cases of psoriasis with limited number of plaques (<5) were selected from the outpatient dermatology department.

All the patients were subjected to the routine investigations like haemoglobin assessment, complete blood count, Fasting blood sugar, erythrocyte sedimentation rate and urine complete examination, ASO titre and throat swab for culture along with specialized investigation including skin biopsy. A written informed consent was taken from all the patients before starting the study. Prior approval of hospital ethical committee was taken for the study. PASI score was calculated in all patients at the start of study and then every 2 weekly till the remission phase of the disease. The patients were evaluated at 0,2,4,6 and 8 weeks and all patients were photographed. After 8 weeks,no treatment was given and the patients were asked to come for follow up every 4 weeks upto 24 weeks to see for any relapse.

Lesions were treated with potassium dobesilate [hydroquinone monosulfonic acid potassium salt (5 percent in a cream formulation, applied twice daily by the patient himself)] for a maximal period of 4 weeks. No other modality of treatment was used other than emollients and oral antihistaminics. Clinic visits during the treatment phase were at day 0 (baseline), day 7 and day 14. Assessments of efficacy and adverse events were made at each visit. Efficacy was evaluated based on the disease signs and symptoms in lesions. Disease signs include erythema, induration, desquamation and overall severity. Photographs of the lesions were taken at baseline and each visit until study completion. Compliance was judged to be good because of the patient's high motivation.

Results

The results were collected and the data was analyzed statistically.

Duration of Psoriasis (in years)	Number of Cases	Percentage %
Less than 5 years	33	66
Between 5-10 years	13	26
Between 11-15 years	3	6
Between 16-20 years	1	2
Total	50	100

Table I. Total duration of psoriasis

SR no	Triggering Factors in Psoriatics	Number of Cases	Percentage (%)
1	Stress	24	48
2	Trauma	10	20
3	Sore throat	18	36
4	Alcoholism	16	32
5	Drug intake	18	36
6	Photo aggravation	3	6

Table II. Triggering factors in psoriasis

SR no	Mean PASI Score Reduction						Significance
Duration (in weeks)	0 weeks	2 weeks	4 weeks	6 weeks	8 weeks	Mean % age reduction in PASI	
Mean PASI score	20	17.2	15.4	12.2	9.2	PASI 50	t =3.68 p > 0.05 (S)

Table III. Reduction in PASI score with calcium dobesilate

The above table shows that in all the groups the mean reduction of PASI score was statistically significant (p>0.05).

Discussion

In our study, maximum number of cases (22%) were in the age group of 51-60 years. It was followed by 20% in the age group of 31-40 years, 18% in the age group 21-30 years, 16% in the age group 41-50 years, 16% in the age group 11-20 years, 12 % in the age group 0-10 years and 8% of the cases were above 60 years of age. Mean age of psoriasis in our patients was 38.46 + 3.287 out of 50 psoriatics, 31 (62%) were males, while 19 (38%) were females. Male to female ratio was 1.63: 1. The duration of the psoriasis was less than 5 years was seen in 66% of cases, between 5 and 10 years in 26% of cases, between 11 and 15 years in 6% of cases, between 16 and 20 years in 2% of cases. The mean duration of disease in our study was 4.74 + 14.64 in our study. The mean reduction in PASI score (Fig. 1, 1a) after eight weeks of treatment with topical calcium dobesilate was statistically significant in our study (p > 0.05). PASI 50 is defined as a reduction from baseline PASI score of > 50%. These days, PASI 50 (or a reduction in PASI score of 50%) is used to assess severity of psoriasis.

Although psoriasis is rarely life threatening, it can cause significant morbidity, social embarrassment and financial cost and disruption in patients life; while patients with extensive and severe disease may require systemic therapy, less severe psoriasis is typically treated with topical medications [17]. After four weeks of treatment, the patient had almost completed clinical resolution of the lesions with no recurrence after two months of treatment withdrawal. No adverse events were observed. Psoriasis varies widely in its clinical expression, from a single fingernail pit to widespread disfiguring skin lesions and disabling arthritis.

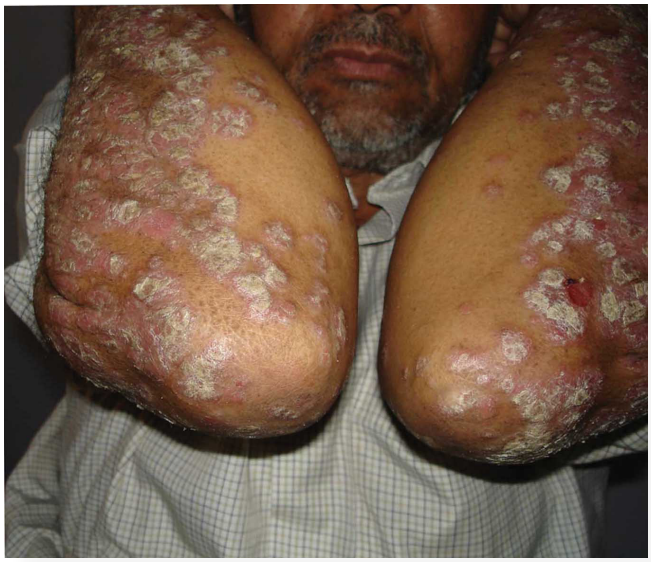

Figure 1. Psoriasis vulgaris before treatment

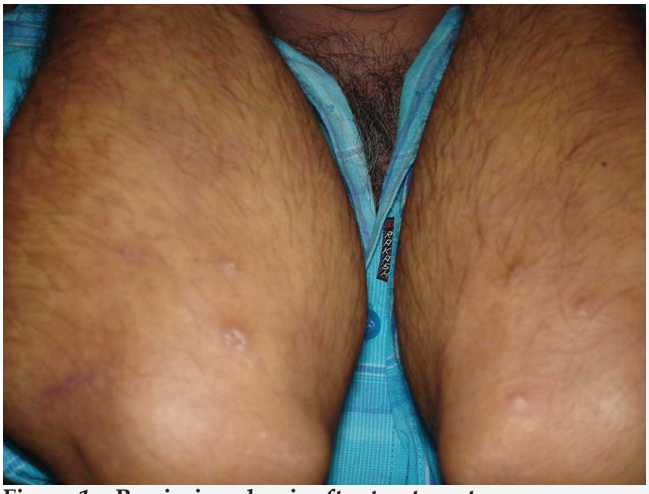

Figure 1a. Psoriasis vulgaris after treatment

Discussion

The primary goal of therapy is to maintain control of the illness so as to avoid disruption of the patient's quality of life, as cure is seldom achieved. Treatment options include systemic agents, topical therapies, and phototherapies. Many of the currently available systemic treatments and phototherapies are associated with unacceptable toxicity or side effects. The most common side effects with topical corticosteroids include skin atrophy, irreversible striae, telangectasia, perioral dermatitis, glaucoma and acne [18,19]. These adverse reactions are more common with use in facial and intertriginous areas. Facial and intertriginous skin is more susceptible to corticosteroid- induced atrophy because of higher percutaneous absorption in these areas. In addition, continued corticosteroid therapy is thought to result in tachyphylaxis, a condition in which stronger formulations of the medication are required to maintain the therapeutic benefit. There may also be a recurrence of the disease if corticosteroid therapy is abruptly withdrawn. A derivate of vitamin D, calcipotriene, another topical therapeutic option for psoriasis, is associated with local skin irritation, particularly in intertriginous areas, often requiring adaptation of the therapeutic regime such as dilution. Thus, from a clinical perspective, a nonatrophogenic, nonirritating topical treatment would address a significant patient need. Potassium dobesilate cream 5% is effective for the treatment of chronic-type plaque psoriasis [20,21]. Calcium dobesilate acts on the the endothelial layer and basement of the blood capillaries. It reduces capillary hyperpermeability by increasing the activity of endothelial nitric oxide synthetase in vascular endothelial cells, leading to an increase in nitric oxide synthesis. This relaxes the vessels, closes the gaps and decreases the capillary hyperpermeability. Substantial and rapid clinical improvement was demonstrated in the assessment of lesions, resulting in improvements in erythema, desquamation, induration and overall severity. Recognition of psoriasis as a T-cell mediated immune disease has led to the development of various therapeutic approaches directed against T cell and T-cell processes such as activation, trafficking and cytokine release. T cells synthesize FGF and have FGF receptors, suggesting that this growth factor may also be involved in T cell activation within psoriasis sites [22]. Thus, in addition to its antiproliferative and proapoptotic functions, dobesilate may also be effective by abolishing T cell activities in psoriasis [23].

Conclusions

Although, calcium dobesilate is a very useful and FDA approved drug for the treatment of plaque psoriasis, still large-scale studies with long-term follow-up are necessary for evaluating the final efficacy of this drug.

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CLINICO - HISTOPATHOLOGICAL CORRELATION IN *LEPROSY*: A TERTIARY CARE HOSPITAL BASED STUDY

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Abstract

Introduction: Leprosy is a chronic infectious disease affecting mainly cutaneous and peripheral nervous system. Histopathology is an important tool to diagnosis leprosy in situation where it mimics other clinical condition. This study was conducted to know the correlation between clinical and histopathological diagnosis of Leprosy.

Material and Methods: This was a retrospective study and patients were enrolled in whom leprosy was clinically diagnosed or suspected and histo-pathological examinations were carried upon.

Results: A total of 71 patients were studied. Of them 48 patients (67.6%) were males and rest 23 (32.39%) patients were females. Mean age of patients at presentation was 37.85 +/- 2.021 years. Clinically in 42 patients (59.1%) type of leprosy could not be specified. Borderline tuberculoid was diagnosed in 7 patients (9.8%), Tuberculoid in 6(8.5%), Relapse in 3(4.2%), lepromatous in 6(8.5%) and Borderline, borderline lepromatous 1(1.4), Indeterminate 1 patient (1.4%). In 7% cases, Hansens disease was considered as differential diagnosis along with other clinical conditions. In 47% cases, data was not available. On histopathological evaluation on skin biopsies, epidermal changes seen were 29.5%. Of the total 71 patient, dermal changes seen were granuloma (42%), dermal infiltrate (11%), adnexal infiltrate (7%), nerve infiltrate (11%), adnexal with nerve infiltrate (6%), perivascular with adnexal infiltrate (20%) and nonspecific (3%). Dermal infiltrates in 46.4% cases constituted of lympho-histiocytes. In 48 patients (69%) leprosy was histopathologically confirmed and in rest 31% cases diagnoses was non-specific in 20 patients (28.1%), vasculitis, Dariers and Fungal infection 1 patient each (1.4%). Borderline Tuberculoid (BT) and TT was the most common diagnosis among leprosy patients around 29.2% each, followed by Indeterminate 25%, LL 8.3%, BL and and Pure neural 4.1% each. When clinical diagnosis and histopathological diagnosis was correlated it was found that the parity was seen in TT as 66.6%, BT 42.9%, LL 16.7%. Where Hansen's disease was kept as differential diagnosis two patients had leprosy.

Conclusion: The study being retrospective the uniformity in clinical diagnosis and histopathological evaluation couldnot be assessed. With the limitations this study still give information about the importance of histopathology to diagnose Leprosy and for proper treatment category and decrease the burden of the disease in the society.

Key words: histopathology; leprosy; granuloma

Cite this article:
Deeptara Pathak Thapa, Anil Kumar Jha: Clinico - histopathological correlation in leprosy: a tertiary care hospital based study. Our Dermatol Online. 2013; 4(3): 294-296

Introduction

Leprosy is a disease affecting mainly skin and peripheral nervous system but can also affect other organs and one of the most common public health problems in this country [1]. In Nepal though Leprosy has been on decline with government declaring elimination of leprosy after achieving a prevalence rate of 0.89 per 10,000 persons, still the disease is prevailing [2]. According to Ridley & Jopling classification it has been classified on the basis of clinical, histopathological and immunological status of the host. Due to its clinical diversity as well as its ability to mimic other diseases sometimes leprosy is difficult to diagnose clinically. In such catch-22 situations, histopathological examination is a helpful diagnostic tool to confirm diagnosis. This study was conducted to know the correlation between clinical and histopathological diagnosis of Leprosy in a tertiary care hospital based scenario.

Material and Methods

We conducted a retrospective study in outpatient department of Dermatology, Nepal Medical College and Teaching hospital. We enrolled patients between 2008 and 2012, in whom leprosy was clinically diagnosed or suspected and histo-pathological examinations were carried upon. The data were retrieved from the records maintained in the department including age, sex, residence, clinical diagnosis, histopathological findings and treatment. To determine clinico- histopathological correlation of skin biopsies in leprosy, statistical evaluation SPSS version 11.5 was used. Chi square test and Fishers exact test was used for statistical significance and p value <0.05 was considered significant.

Results

A total of 71 patients were studied. Of them 48 patients (67.6%) were males and rest 23 (32.39%) patients were females. Youngest patient was 12 years old and oldest was 80 years at presentation; however mean age of patients at presentation was 37.85 +/- 2.021 years. Clinically, in 42 patients (59.1%) type of leprosy could not be specified (Tabl. I). Borderline tuberculoid was diagnosed in 7 patients (9.8%), Tuberculoid in 6(8.5%), Relapse in 3(4.2%), lepromatous in 6(8.5%) and Borderline, borderline lepromatous 1(1.4), Indeterminate 1 patient (1.4%).

In 7% cases, Hansens disease was considered as differential diagnosis along with other clinical conditions. Slit skin smear was positive in 4 cases (5.6%) and negative in 25(35%). PAS stain was positive in 1 patient (1.4%). Fite stain was positive in 2 patients (2.8%) but was negative in 9.8% cases. In 47% cases, data was not available.

On histopathological evaluation on skin biopsies, epidermal changes seen were thinning (11.26%), hyperkeratosis (9.8%), acanthosis (7%) and cleft (1.4%) however it was normal in 70.4% patients Interface dermatitis was seen in 2.8% cases and grenz zone in 7% cases but in 90.1% interface changes were not specified. Of the total 71 patient, dermal changes seen were granuloma (42%), dermal infiltrate (11%), adnexal infiltrate (7%), nerve infiltrate (11%), adnexal with nerve infiltrate (6%), perivascular with adnexal infiltrate (20%) and nonspecific (3%). Dermal infiltrates in 46.4% cases constituted of lympho-histiocytes followed by lymphocyte (39.4%), epitheloid cells (8.4%) and foamy cells (8.4%) but was not mentioned in 3% cases. Of the 4 cases that had infiltrates seen in subcutaneous layer, 2 had giant cells and 1 each had lymphocytes and mixed cellular infiltrates. In 48 patients (69%) leprosy was histopathologically confirmed and in rest 31% cases diagnoses was non-specific in 20 patients (28.1%), vasculitis, Dariers and Fungal infection 1 patient each (1.4%). Borderline Tuberculoid (BT) and TT was the most common diagnosis among leprosy patients around 29.2% each, followed by Indeterminate 25%, LL 8.3%, BL and and Pure neural 4.1% each. When clinical diagnosis and histopathological diagnosis was correlated it was found that the parity is seen in TT as 66.6%, BT 42.9%, LL 16.7%, where it was not classified 69%, relapse 66.7 and Hansens as Differentials 40%. There was no parity seen in BL, Pure Neural and Indeterminate. There were some interesting findings like indeterminate cases were more histopathologically diagnosed. One LL case was found to be TT histopathologically. Clinically where diagnosis was not specified, 69% patients had leprosy. Where Hansen's disease was kept as differential diagnosis two patients had leprosy. Details of the correlation between clinical and histopathological diagnosis is given in Table II.

Clinical Diagnosis	Numbers (%)
TT	6 (8.5)
BT	7 (9.9)
BL	1 (1.4)
LL	6 (8.5)
Pure neural	0 (0)
Intermediate	1 (1.4)
Not Classified	42 (59.2)
Relapse	3 (4.2)
Hansens as Differentials	5 (7.0)

Table I. Clinical diagnosis

Clinical Groups	Histologic Groups							
	TT	BT	BL	LL	Intermediate	Pure neural	Other than Hansens	% Parity
TT	4	1	0	0	0	0	1	66.6
BT	3	3	0	0	0	0	1	42.9
BL	0	0	0	0	1	0	0	0
LL	1	0	0	1	1	0	3	16.7
Pure neural	0	0	0	0	0	0	0	0
Intermediate	0	0	0	0	0	0	1	0
Not Classified	5	9	2	1	10	2	13	69
Relapse	0	1	0	1	0	0	1	66.7
Hansens as Differentials	1	0	0	1	0	0	3	40
Total	14	14	2	4	12	2	23	

Table II. Correlation between clinical and Histopathological diagnosis
P=0.034 according to pearson's rank correlation

Discussion

In developing countries like Nepal, Leprosy is still one of the major public health problems. The Ridley jopling classification is a standard classification to diagnosis leprosy which is based on clinical, histopathological and immunological status of the host. In our study clinicopathological correlation was found in TT as 66.6%, BT 42.9%, LL 16.7% and where it was no classified according to Ridley Joplings criteria found to be 69% which means clinically where hansens was suspected histopathologically it was confirmed and these percentage of patients were treated and rendered noninfectious. On statistical analysis it was found to be statistically significant (P value 0.034). Pandya et al found parity in 68.3%, Moorthy et al in 62.63% [4], Kar et al in 70%, Jerath et al in 68.5% and Mathur et al in 80.4% [2-6,11-13]. In most of these studies like moorthy et al, Kar et al and Jerath et al found parity in TT pole and Mathur et al in LL pole [14]. Our study also found parity in TT and BT. Jha et al also found parity in BT cases [7]. There was lack of uniformity in clinical impression and clinical details in our study. Slit skin smear report was not available in 40% and in 47% fite stain was not mentioned. In histopathology too Ridley jopling classification was not used. Interface changes were not interpreted in 90.1%. In dermal changes none of the reports described about exact location of the granuloma, whether infiltrating appendages or not. In 53%, location of the dermal infiltrate were not mentioned. There were some interesting findings in our study like one case of LL was found to be histopathologically TT. In histopathological evaluation it was found that epitheloid giant cell granuloma was seen. But it was not mentioned it was eroding epidermis or not. Most of the indeterminate cases was diagnosed histopathologically where periadnexal, perineural infiltrate were seen. In two patients even granuloma was also found and histopathologically it doesn't fit in Indeterminate type. Moorthy et al [4] also found indeterminate type more histologically than clinically. Due to non specific histology it becomes difficulty to diagnose IL type. It also depends upon various factors like depth of biopsy, quality of sections, and number of sections examined and staining method including both H&E and acid fast stain [4,8-10]. Clinically where diagnosis was not specified 69% had histopathological diagnosis of leprosy. Where Hansens disease was kept as differential diagnosis two patients had leprosy. Most of the above studies have strictly followed Ridley jopling classification but in our study it was not but still the percentage of parity is similar in their studies compared to our study. It is therefore important to have histopathological evaluation in suspected case of leprosy mostly in the Borderline groups and where slit skin smears are negative. Clinical information like site of lesion, type of lesion, nerve involvement, sensory impairment, treatment history along with immunological status of patients is very important for the pathologist to correlate histopathologically. Histopathological diagnosis also depends on various factors like size of biopsy specimen, age of lesion, depth of biopsy, quality of section and very important interobserver variation has a role in clinico-pathological evaluation [15].

Conclusions

There are certain limitations in our study. The study being retrospective the uniformity in clinical diagnosis and histopathological evaluation could not be assessed. With the limitations this study still give information about the importance of histopathology as in few of the cases where diseases was not specified or Hansens was kept as differential diagnosis, histopathologically different poles of hansens disease as well as others like Dariers or fungal was evaluated and is important for treatment point of view. Sometimes it is difficult on clinical grounds due to its varied presentation and could mimic with other diseases therefore histopathological examination is needed to confirm diagnosis for proper treatment category and decrease the burden of the disease in the society.

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WHAT FACTORS CONTRIBUTE TO A HIGHER FREQUENCY OF SKIN INFECTIONS AMONG ADULTS IN MAURITIUS?

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Abstract

Introduction: Given the rise in the prevalence of skin infections in many countries and the lack of published data pertaining to the prevalence and awareness of skin infection in Mauritius, this survey is the first of its kind to provide data on this issue. The aim of this study is to describe the association of skin infection with various predisposing factors such as socioeconomic status, personal hygiene and level of awareness and to assess the impact of skin infections on quality of life.

Material and Methods: A stratified sample of 500 adults was randomly selected for this study. Subjects were administered a questionnaire to elicit information on sociodemographic factors, awareness, family history and prevalence of skin infections. Quality of life was investigated by a validated questionnaire (DLQI). SPSS Software and Microsoft Excel were used to analyse data.

Results: Among 500 participants, 166 (33%) cases of skin infections were obtained. Acne was found to be more prevalent (n=59). It was found that skin infection varies with gender and higher prevalence was observed during summer as compared to winter (p=0.017). It was noted that family history and income level were associated with an increase incidence of skin infection (p=0.000). With respect to quality of life, psychological distress was mostly affected.

Conclusion: Acne was found to be more prevalent. Respondents with middle income status were mostly affected with skin infection. Those with a family history were more prone to skin infection. The Quality of Life index was found to be an efficient method in assessing the impact of skin infection on the respondents' lives.

Key words: skin infection; prevalence; adults; awareness; personal hygiene; quality of life

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Kotowaroo Goonmatee, Jeewon Rajesh: What factors contribute to a higher frequency of skin infections among adults in Mauritius? Our Dermatol Online. 2013; 4(3): 297-302

Introduction

Several studies have been done worldwide to find the prevalence of skin infections and to assess the level of awareness among adults. In developing countries, the published figures for the prevalence of skin infection range from 20 to 80% [1]. Data from the latest report in Mauritius clearly demonstrate that the rate of skin infection has known an increase from year 2010 to year 2011 [2]. In year 2010, out of 14 048 cases, treated at the dermatology specialist clinics, highest percentage of skin infections were of fungal origin (12.4%) and the lowest percentage of (3.6%) were of bacterial sources as compared to the year 2011, where 12.7% of skin infections were of fungal origin and 3.4% of bacterial origin [2].

Numerous factors can contribute to the development of skin infection such as: poor skin health, low socioeconomic status, low level of hygiene, overcrowding and also lack of awareness [3-6]. In Tigray (Northern Ethiopia), eczema was most common and acne the least common among the outpatient attendance and a positive correlation between these skin infections with factors such as overcrowding, poor hygiene and low socioeconomic status was reported [7]. In Sierra Leone, Bari [8] demonstrated that skin infections was prevalent (42 %) in African population due to the environmental and social factors and most importantly due to the geographical factors such as climate and season. Similarly, Souissi et al [9], reported a high prevalence of fungal infection (16.9%) and eczema (11.9%) in Tunis which was associated to the climatic conditions prevailing there.

Poor socioeconomic status has been identified as the main root of skin infection in developing countries and Tinea versicolor was found to be the most common fungal skin infection in Nigeria [10]. The predisposing factors to this infection were heavy sweating, warm and humid environment, malnutrition and genetics. Moreover it was found that the treatment for these infections is quite expensive and the infected population with a low socioeconomic status cannot afford these costly treatment and this results in a high number of respondents with skin infections [10].

Schofield et al [11] demonstrated that skin diseases have a negative impact on quality of life. Knowledge is an essential prevention factor but however, data pertaining to knowledge of skin infection among adults are inadequate. This research will serve as baseline information that could be related with upcoming follow-up studies.

This study has been designed to assess the level of awareness of skin infections and to determine the prevalence of these skin infections among the Mauritian population and also to describe their association with various predisposing factors such climatic condition, level of education and socioeconomic status. The main objectives of this study are as follows:

1. To investigate the prevalence of skin infection in relation to age, level of hygiene, family history and socioeconomic status.
2. To investigate for any link between the socioeconomic status and awareness with the occurrence of skin infections.
3. To determine which skin problems are most prevalent and if there are gender differences.
4. To assess the impact of skin infection on quality of life.

Material and Methods

Study Population

A stratified sample of 500 adults was randomly selected for this study in 2012. Foreigners and pregnant women were excluded. The participants were well informed about their involvement in the survey with proper informed consent. They were explained about their voluntary participation and all the information gathered would dealt in strict confidentiality and the findings would be used for research purposes only. This research was approved by the Research Ethics Committee.

Assessment

Questionnaire Design

Two questionnaires were used: one questionnaire which consisted mostly of close ended questions was designed to retrieve information such as:

a) *Sociodemographic factors:* Data collected included sociodemographic details such as gender, age group, occupation, level of education, climatic condition, number of general household members and the total family income status [3,5]. Household Income categories were classified as follows [12]: i) Low Income : Less than Rs 15 000 (< 500 USD), ii) Middle Income : Rs 15 000- Rs 30 000 (500-1000 USD) and iii) High Income: Above Rs 30 000 (> 1000 USD)

b) *Awareness:* Questions on type of skin infections were asked together with the risk factors associated with skin infections.

c) *Personal Hygiene:* This section consists of questions such as frequency of shower, sharing of their personal belongings and the associated risk factors [5].

d) *Family History:* Questions were asked on whether there exist any family history of skin infection as some skin condition were due to family history [13,14].

The second questionnaire dealt with e) Quality of Life: Skin infections can have a serious impact on the psychological well being, social and everyday activities on the patient and the patient's family [11]. A validated questionnaire obtained from the Dermatology Life Quality Index (DLQI) has been adapted and used [15].

Statistical Analyses

The Statistical Package for Social Scientist (SPSS statistical package version 20.0) was used for the statistical analyses together with Microsoft Excel 2007. The data were analysed with frequencies, cross tabs, Pearson correlation and chi square test.

Results

Table I shows the sociodemographic details of the respondents. Out of 500 participants, 273 (55%) were male and 227 (45%) were female. The mean age group of the participants were between 26-40 years old (41%).

The majority of respondents [259 participants (52%)] were from a middle socioeconomic status with a middle income of Rs 15 000 - Rs 20 000 (500-1000 USD). The highest level of education for most participants were tertiary level [n= 244 (49%)].

		Frequency	Percentage (%)
Gender	Male	273	55
	Female	227	45
Age Group	18-25	111	22
	26-40	204	41
	41-60	149	30
	Above 60 years	36	7
Household Income Status	Below Rs 15 000 (Below 500 USD)	49	10
	Rs 15 000- Rs 30 000 (500 USD-1000 USD)	259	52
	Above Rs 30 000 (Above 1000 USD)	192	38
Highest Level of Education	Primary	41	8
	Secondary	215	43
		244	49

Table I. The sociodemographic details of the participants

Prevalence of skin infection

Among 500 participants, 166 (33%) cases of skin infections were determined in this study. Acne was found to be more prevalent (n=59) followed by eczema (n=33), versicolor infection (n=30), athlete's foot (n=26) and ringworm infection (n=12). Only 4 cases of wart and 2 cases of psoriasis have been reported (Tabl. I).

With relevance to gender, it can be seen that there is almost the same ratio of female (n=85) to male (n=81) who are affected with skin infection (Tabl. II). However, it can be seen that in some skin infections, females are more affected than male. For instance for acne, 58% are females as compared to males (12 %).

Results also reveal that approximately the same frequency of infections can be seen in the age groups 18-25 and 26-40 years old. Figure 1 shows that acne and athlete foot are more prevalent in the age group of 18-25. The age group 41-60 years old are mostly affected with versicolor infection while the elderly age group (above 60 years old) are more affected with eczema.

A statistical significant relationship was obtained between skin infection and seasonal variation (p value of 0.017). Highest percentage of infections (79%) was observed to be most common in summer season. Summer season correlated with the occurrence of skin infections, hereby showing that seasonal variation has an effect on skin infection. 52% cases of past/ current skin infection have been linked to a positive family history of skin infection (p value = 0.000), and data indicate that skin infections are recurrent in respondents in which there is a past family history of skin infection.

	Skin Infection							Total
	Acne	Eczema	Athlete's Foot	Versicolor Infection	Ringworm Infection	Wart	Psoriasis	
Male	10	19	16	21	10	3	2	81
Female	49	14	10	9	2	1	0	85
Total	59	33	26	30	12	4	2	166

Table II. The distribution of skin infections in both genders

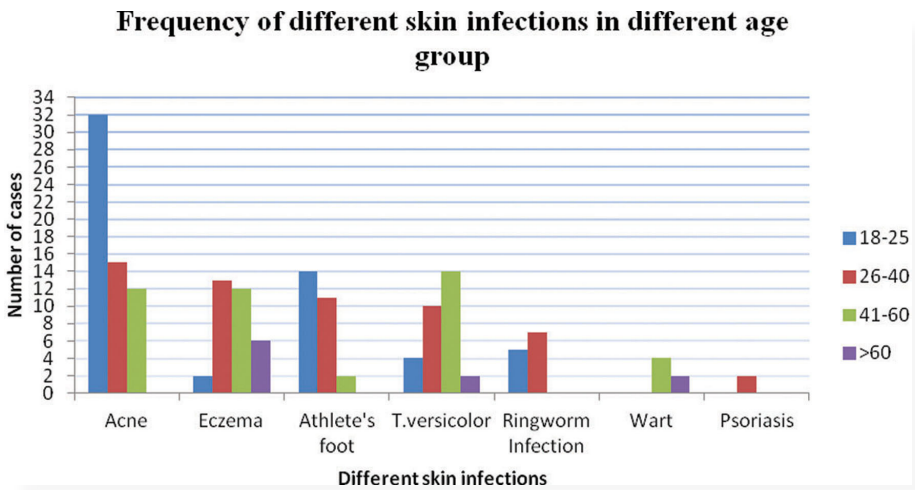

Figure 1. Frequency of skin infection in different age groups

Awareness on skin infection

423 participants (85%) are aware on skin infection. A high frequency of participants are highly aware of skin infection (n=423,85%) and the highest number of participants (n=208,42 %) were from middle socioeconomic status followed by 178 participants (36%) from a high socioeconomic status. Only a minority of the respondents reported no knowledge and awareness on skin infection (n=77,15%). Results obtained also indicate that there is a high number of respondent who reported having good knowledge on skin infection and they were mainly those who had tertiary education (n=234). Participants with a primary education level were those with least knowledge about skin infection (n=25). Data demonstrate that most of the respondents who reported having a good knowledge on skin infection also had good hygiene practices and are highly aware of the risk factors associated with skin infection (Fig. 2). For instance, 73% of respondents knew that use and sharing of cosmetics is a risk factor. In addition, 95% reported that they change their clothes after heavy sweating and 78% of respondents were aware that sharing of personal belonging is a risk factor.

Quality Of Life

The most frequently described aspect was psychological distress due to itchy and painful skin (n=110) and embarrassment (n=100) (Fig. 3). Moreover the burden of the skin infection affected activities such as shopping (n=71) and created problems with partner and closed friends/relatives (n=62).

The problems caused due to people's reaction to the patient's skin appearance lead to an influence on the respondents clothes (n=52). It also affected the social life, work and academic performance of the respondents.

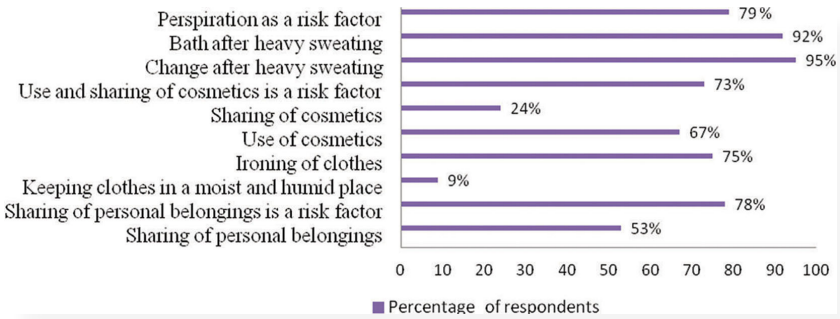

Figure 2. Respondent's awareness on hygiene practices as risk factors for skin infections

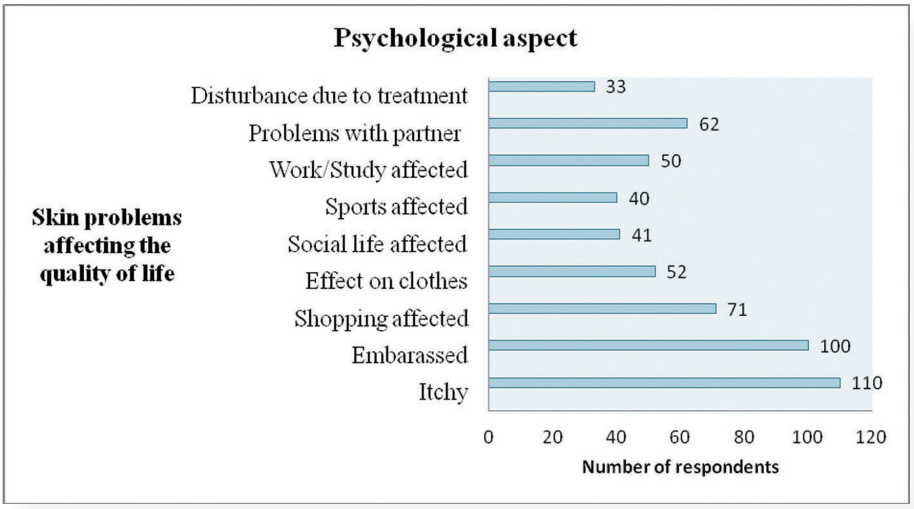

Figure 3. Psychological aspect of skin infection

Discussion

Prevalence of skin infections

Current results demonstrate one third of the respondents (33 %) had skin infection. This result is similar with that of the Mauritian Health Statistics Report 2010, whereby a prevalence of 32.5% of skin infections was observed [16]. This finding is also in line with the results of Hay et al [1] who reports that in developing countries, the published figures for the prevalence of skin infection range from 20 to 80%.

In this study, acne was found to be more prevalent, followed by eczema, athlete's foot, Tinea versicolor and the less common skin infections were ringworm infection, wart and psoriasis.

Gender and skin infection

A major finding of this study was that the ratio of female to male affected with skin infection is almost the same (Tabl. II). However, females (58%) were more affected with acne than males (12%). Similar results were obtained by Khunger and Kumar [17] and Adityan and Thappa [18] in India who reported that females are more affected with acne. Contrasting results were reported by Akyasi et al. [19], who found that in Turkey, men are predominantly affected with acne than women. Although it has been reported that the incidence of Tinea versicolor is almost the same among male and female, findings herein suggest a totally different scenario. Male gender (20%) appears to be an important risk factor in versicolor infection compared to females (12%). These results are consistent with several studies. For instance, Mahmoudabadi et al [20], Rasi et al [21] and He et al [22] found that more males were affected with versicolor infection than women in Iran and China respectively. However, among children, the most common dermatophyte infection is Tinea capitis [6].

Age and skin infection

This study also reveals that age is a predominant factor contributing to a higher prevalence of skin infections. Highest rate of infections were observed in Mauritian adults aged between 18-25 years old and 26-40 years old (Fig. 1). Among the respondents, acne is highly prevalent in the age group 18-25 years old. This result was similar to that found in India by Khunger and Kumar [17] and Adityan and Thappa [18]. Tinea versicolor was more prevalent in the age group 41-60 years (Fig. 1). This result is totally different with the existing published literature. For example, it was reported that highest prevalence of Tinea versicolor infection was among 20-40 year old group and that this age group coincided with the age period when sebum production was highest [21,23]. Mahmoudabadi et al [20] reported the highest frequency were among the 17-28 years age group and suggested an association with hormonal changes and increased sebaceous gland activity. Results herein could not be associated with hormonal changes and sebum production as after the puberty age, sebum production wanes as the level of hormone decreases.

Eczema was more prevalent in the age group 26-40 years old (Fig. 1). This finding corroborate with that of Handa et al [24] who found the most affected age group to be between 21-40 years old and that of Lysdal et al [13] between 22-32 years old. In both gender, eczema was less likely to occur in respondents who were below the age group 26-40 years and above 60 years old. Similar results were reported by Handa et al [24] and this stems from the fact that elderly have several defects in the induction and elicitation of eczema and the younger ones may only have limited exposure to irritants and allergens.

Seasonal variation

Another major factor contributing positively to a higher incidence of skin infection in this current study is seasonal variation [32]. It is generally known that season does have an impact on skin infection. Highest percentage of infections (79%) was observed to be most common in summer season, hereby showing that seasonal variation has an effect on skin infection. For instance, Adityan and Thappa [18] reported that seasonal variation had an effect on acne and Khunger and Kumar [17] reported that a hot climate and summer aggravated acne. All these findings were in line with this current study. In the case of versicolor infection, He et al [22] stated that climate has the greatest impact on appearance, spread and relapse of Tinea versicolor. Athlete's foot was the third most prevalent skin infection. This could be explained by the dry climatic conditions prevailing as Trichophyton species, causing agent of Athlete's foot, thrives in a warm and moist environment [25]. The findings are in line with what have been found by Asadi et al. [26] and Cohen et al [27] that the prevalence of tinea pedis is higher in hot climate and is more prevalent in tropical countries as in Mauritius.

Family history

A positive correlation was established between family history and skin infections (52%). The present study demonstrates that those having a family member with skin infection had a higher risk and some even had the same infection (for example acne and eczema). Luk et al. [28] also reported a significant relationship between family history of atopy and eczema, indicating a correlation between positive family history and eczema [33]. Similarly, He et al [22] observed that in respondents with a positive family history of Tinea versicolor, infection was recurrent and it lasted longer than in those with a negative family history.

Awareness of skin infection and proper hygiene

Data obtained from this study indicated 85% of the respondents have a good knowledge and awareness on skin infection.

Socioeconomic class, level of education and personal hygiene

Results from this present study revealed that majority of respondents who were from the middle household income and tertiary education, had a good knowledge and are aware of skin infection. Lowest level of awareness was indicated among low socioeconomic status who were educated only up to primary education level.

Another key point in this study is that most of the respondents who are knowledgeable on skin infection practiced good hygiene and are aware on risk factors of skin infection (Fig. 3) [34]. Cosmetics can influence the balance of micro flora in the skin [29]. In Sweden, Berne et al [30] revealed that the use of cosmetics is rising and adverse reactions to these products are increasing. In the present study, it was found that 73% of respondents knew that use and sharing of cosmetics is a risk factor (Fig. 3). In addition, more than 90% of respondents reported that they bath and change their clothes after heavy sweating which are good hygiene practices and also 78% of participants were aware that sharing of personal belongings is a risk factor (Fig. 3) [34].

Only 9% of the participants kept their clothes on a humid and moist environment and this shows that the participants were aware that keeping their clothes in such environment would favour fungal growth and in turn this could be a predisposing factor for fungal infection. This was further supported by the fact that 75% of the participants ironed their clothes in order to get rid of any fungal growth on their clothes either humid or dry.

Quality of life

Skin infection can have an impact on respondents' lives and several validated patient-completed questionnaire have been used to assess its impact [31]. In comparison to other studies, Schofield et al [11] observed that skin infections have a serious negative impact on the quality of life. Further analyses do provide further evidence that there are other minor ways in which quality of life due to skin infection are affected [32]. The most commonly reported quality of life was psychological distress due to itchy, painful and stinging skin (n=110) and embarrassment (n=100) (Fig. 4). Moreover the burden of the skin infection affected leisure activities such as shopping (n=71) and created problems with partner and closed friends/relatives (n=62). The lives of some respondents with skin infection are severely affected and in turn the family life of caregivers that are involved with the respondents also are affected. The problems caused due to people's reaction to the respondent's skin appearance, lead to an influence on the respondents clothes (n=52). It also affected the social life, work and academic performance of the respondents.

Conclusion

This study reveals that one third of the studied Mauritian population has been affected with skin infection with acne being the most prevalent skin infection followed by eczema, athlete foot and versicolor infection. A higher prevalence of skin infections correlated with several factors such as age, gender, personal hygiene, level of awareness and climatic conditions.

Age is a key factor in the occurrence of specific skin infections especially for acne and eczema.

Mauritian population have a good knowledge on the awareness of skin infection and had good hygiene practices and were highly aware on the risk factors associated with skin infection.

The Quality of Life index was found to be an efficient method in assessing the impact of skin infection on the respondents' lives. The most commonly reported quality of life was psychological distress and embarrassment. The burden of skin infection remained an issue as it affected the social life of the respondents and created problems with families, friends, partners and relatives.

Acknowledgement

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A STUDY ON *LICHEN PLANUS* IN CHILDREN

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Abstract
Introduction: Lichen planus is considered to be rare in children. However, it does not appear to be uncommon in Indian subcontinent.
Aims: The study was undertaken to analyse the clinical profile of childhood lichen planus.
Material and Methods: We selected 30 children with LP for the study. The children selected were below the age of 14 years of age.
Results and Discussion: In our study, it was seen that that the maximum onset of disease was between 5-9 years of age and mean age of children with LP was 6.8 years. The commonest type of LP in children was classical LP seen in 60% children, followed by actinic LP in 20% children. LP hypertrophicus and linear LP were seen in 10% patients each. Nail changes were seen in 10% patients.

Key words: lichen; autoimmune; childhood; pruritis; childhood; nails

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Introduction

The term ‚lichen' is probably derived from the Greek verb ‚to lick'. However, the use of the term is adapted to a noun in both Greek and Latin for a symbiotic form of plant life. The dermatosis, lichen planus (LP) was first described by Erasmus Wilson in 1869 and is characterized by purple, polygonal, pruritic, papular eruption of unknown etiology affecting skin that can also involve the mucous membranes and the nails. It has been hypothesized that the rarity of associated autoimmune conditions, exposure to drugs and dental restorative materials, infective agents and other environmental triggers that have been known to initiate lichen planus may be responsible for the overall rarity of LP in children [1,2]. The scarcity of reports may further be due to overall rarity of LP in children, 2-3% of total LP occurring in children below 20 years of age. Under-reporting may also influence the apparent rarity of childhood LP [3].

Aims

The study was undertaken to analyse the clinical profile of childhood lichen planus.

Material and Methods

We selected 30 children with LP for the study. The children selected were below the age of 14 years of age. Prior approval of the hospital ethical committee and informed consent from the parents of the children was taken for the study. The patients were diagnosed on the basis of clinical symptoms and signs. Routine investigations wew done in all the patients. Histopathological examination of the patients was done wherever the diagnosis was in doubt and not in every case.

Results

The results were tabulated and the data was analysed.

Sr No	Type of lichen planus	Number	Percentage
1	classical lichen planus	18	60
2	actinic lichen planus	6	20
3	lichen planus hypertrophicus	3	10
4	linear lichen planus	3	10
	TOTAL	30	100

Table I. Various types of lichen planus in children

Sr no	Nail changes	Number	Percentage
1	Pterygium	1	3.3
2	Longitudinal striations and nail discoloration	1	3.3
3	Nail dystrophy and trachyonychia	1	3.3

Table II. Nail involvement in children

Discussion

It was seen in our study that the maximum onset of disease was between 5-9 years of age and mean age of children with LP was 6.8 years. Males outnumbered females Males: Females was 2:1. Koebners phenomenon in our study was seen in 35% patients in our study. In our study, skin involvement alone was seen in 26(86.6%) patients mucosal involvement alone was seen in 1(3.3%) patient. Both skin and mucosal involvement was seen in 3(10%) patients. Scalp involvement was seen in 1(3.3%) patient. The commonest type of LP in children was classical LP seen in 60% children, followed by actinic LP in 20% children. LP hypertrophicus and linear LP were seen in 10% patients each. Nail changes were seen in 10% patients. The common nail changes included pterygium, longitudinal striations with discoloration and nail dystrophy seen in 3.3% patients each. The primary lesion of lichen planus is a violaceous, flat topped, polygonal, pruritic, papule, and represents commonest among all the morphologies of lichen planus in all age groups. Linear LP, LP hypertrophicus, and annular LP are known to be common variants while mucosal involvement is rare in children [4-6]. Actinic LP (Fig. 1) is common in tropical and sub-tropical countries including India. Koebner's phenomenon is considered to be common in children with LP, varying between 24 and 28% [7].

Initially linear LP was thought to be more common in children as compared to adults, but recent studies have shown results on the contrary [8-10]. Linear lichen planus has been observed in 8-30.4 % patients. The high incidence of linear lesions in children may be due to increased tendency of children to traumatize themselves leading to Koebnerization. In general, lesions in linear lichen planus are disposed along solitary strips or segments of skin and are more extensive than those observed with Koebner's phenomenon. Multiple linear lesions resembling a zosteriform distribution may occur. Actinic lichen planus is considered to be the disease of middle aged people (third decade) and has been reported commonly from Middle East. It occurs uncommonly in children. It was observed that patients with actinic LP attended the clinic earlier (3.9 months) due to acute onset of the lesions and cosmetic reasons as compared to other variants of LP [11-13].

Histopathology of the lesions revealed band like mononuclear infiltrate (Fig. 2) along the dermoepidermal junction with focal hypergranulosis and saw toothed rete ridges. Nail involvement is rare in children while it occurs in 1-10% of adults. In different studies, nail involvement has been found in 0-8.7% of patients [14]. Longitudinal ridging was the most common finding in 17%, followed by pitting in 15%, thinning of nail plate in 9% patients, trachyonychia, discoloration, nail dystrophy, subungual hyperkeratosis, onycholysis, nail splitting, thickening of nail plate and leukonychia in decreasing order of frequency.

There is no consensus regarding the treatment of childhood LP. Topical corticosteroids and oral antihistamines remain the treatment of choice in most patients with localized classic disease [15]. For mucosal LP, the presence of dental amalgam should be looked for and its removal can be considered, if the lesions do not improve with commonly used medication [16]. Topical treatment options for oral lichen planus include corticosteroids in orabase, topical tretinoin or isotretinoin gel, and topical tacrolimus or pimecrolimus. Oral agents that can be used for mucosal LP are systemic glucocorticoids, griseofulvin, hydroxychloroquine, azathioprine, mycophenolate mofetil and acitretin [17]. Intraleisonal triamcinolone may be used for both oral and cutaneous LP (hypertrophic) if the child can be convinced about the procedure.

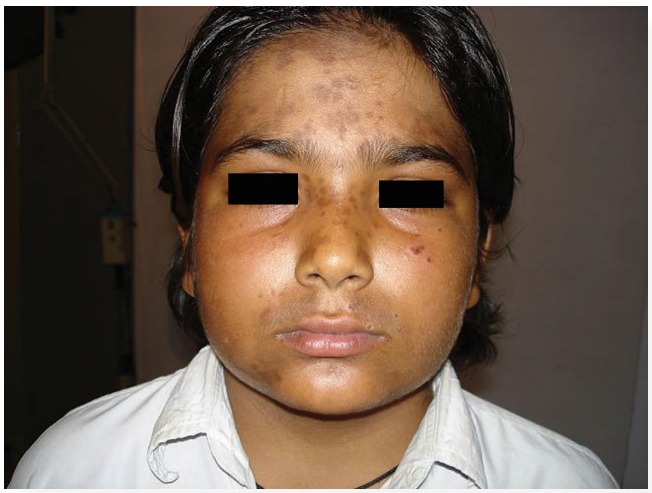

Figure 1. Figure showing actinic lichen planus in an 11 year old child

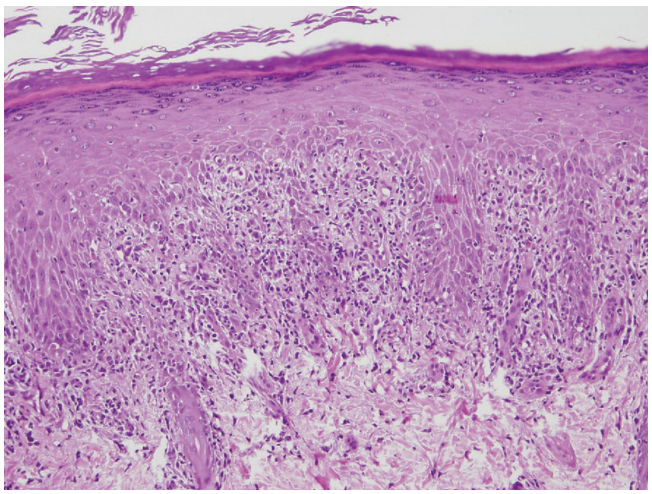

Figure 2. Photomicrograph of lichen planus showing acanthosis, lichenoid mononuclear dermal infiltrate and colloid bodies. (H&E stain 100x)

Conclusions

The natural history of LP in children was essentially similar to that in adults. Unusual features, such as involvement of the palms and soles and upper eyelids, were observed. Actinic LP, mimicking melasma, as reported in adult women, also seems to occur in children.

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STUDY OF THERAPEUTIC COMPARISON OF TACROLIMUS 0.1% AND MINOXIDIL 2% IN *ALOPECIA AREATA*

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Abstract
Introduction: Alopecia areata is a unique, idiopathic disease in which there is patchy hair loss. The variable and uncertain natural history of alopecia areata is accounting for the multiplicity of uncritical claims for a large variety of therapeutic procedures.
Aim: to find the therapeutic comparison between tacrolimus 0.1% ointment and minoxidil 2% solution.
Material and Methods: Patients attending skin out patient department in Navodaya medical college hospital and research centre, Raichur were screened and the consenting consecutive cases of Aopecia Areata (AA) from December 2010 to November 2011 were chosen for study. There were 75 patients in the study. It is a randomized, single blind, intension to treat study. The eligible patients for the study were randomly allocated into two groups-Group A and Group B (38 in Group A and 37 in Group B). Patients in Group A were treated with 2% Minoxidi solution to be applied twice daily over the alopecia patch, where as Patients in Group B were treated with Tacrolimus 0.1% ointment applied twice daily. Patients were followed up at 2, 4, 6, 8, 10 and 12 weeks. Alopecia Grading Score (AGS) was calculated at baseline and 12 weeks. Regrowth Score (RGS) was calculated at 12 weeks.
Results: Total 69 patients completed the study (35 in Group A and 34 in Group B). In our study RGS ≥ 3 was observed in 65.71% of patients treated with Tinoxidil 2% solution and 44.12% of patients treated with Tacrolimus 0.1% ointment.
Conclusion: In our study Minoxidil 2% solution had better stimulatory effect on hair growth compared to Tacrolimus 0.1% ointment in the treatment of mild to moderate patchy alopecia areata. The combination treatment may yield a better clinical response than either of the agents used singly.

Key words: alopecia areata; minoxidil; tacrolimus

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Introduction

Alopecia Areata is one of the most emotionally devastating, dermatological condition.

Alopecia areata is a unique, idiopathic disease in which there is a patchy hair loss that is usually confined on the scalp but may occur on beard region, moustache, eyelashes, eyebrows, axilla, genitalia & general body surface. Alopecia totalis is a condition if all the hair on the scalp is lost and Alopecia universalis is a condition if in addition to scalp, there is complete loss of body hair [1].

It occurs equally in both males and females and onset can be at any age, but most often in children and young adults [2].

The etiology of alopecia areata is not known with certainty. Factors implicated are-autoimmune theory, genetic factors, atopic state, infectious agents and emotional stress.

Alopecia areata progresses as a wave of follicles enter telogen phase prematurely. It is characterized by non-scarring round and/or oval patches of hair loss. The diagnostic hallmark of alopecia areata is an exclamation mark hair at the active hair margin. The lesions are largely asymptomatic, which may manifest either as alopecia areata classic, reticulate alopecia areata, alopecia totalis/universalis, or ophiasis and ophiasis inversa [3].

Associated clinical changes include nail involvement, cataract, vitiligo etc.

Diagnosis is based mainly on the clinical presentation and is corroborated by histology [4].

The variable and uncertain natural history of alopecia areata is accounting for the multiplicity of uncritical claims for a large variety of therapeutic procedures.

Different treatment aspects have been tried in treating alopecia areata [5]. They include,
1. Corticosteroids-topical, intra-lesional and oral.
2. Contact immunotherapy using DNCB (dinitrochlorobenzene), SABDE (squaric acid dibutylester) and diphenceprone.
3. Irritants like Phenol, Salicylic acid, Sulphur, Liquid nitrogen, Anthralin and Croton oil.
4. PUVA (Psoralen with Ultraviolet A) therapy.
5. Minoxidil- topical
6. Tacrolimus- topical

In the present study, a therapeutic comparison between topical tacrolimus 0.1% ointment and minoxidil 2% solution in the treatment of alopecia areata is undertaken.

Minoxidil:
Minoxidil (2,4-diamino-6-piperidinopyrimidine-3-oxide) was initially developed as a drug for antihypertensive therapy. Although minoxidil has been used as a hair regrowing agent for more than 20 years, its mode of action is not fully understood. Minoxidil does not appear to have either a hormonal or an immunosuppressant effect. Minoxidil most likely has a direct mitogenic effect on epidermal cells, both in vitro and in vivo. Anagen-phase hair bulbs plucked from men applying minoxidil showed a significant increase in proliferation index as measured by DNA flow cytometry. Minoxidil also has been shown to prolong the survival time of keratinocytes in vitro. Finally, minoxidil may oppose intracellular calcium entry. Calcium influx normally enhances epidermal growth factors to inhibit hair growth. Minoxidil is converted to minoxidil sulfate, which is a potassium channel agonist and enhances potassium ion permeability, thus opposing the entry of calcium into cells. Local vasodilatation does not appear to play a primary role in hair growth associated with minoxidil. There are some reports indicating that minoxidil also has some immunosuppressive effects [6,7]. Adverse effects- contact dermatitis can occur in 6%, hypertrichosis (facial hair growth) has been a reported side effect in 3% of patients [8].

Tacrolimus:
Initial trials revealed tacrolimus as a potential tool for treatment of AA [9,10]. The peculiarity of tacrolimus was the induction of anagen and hence hair growth promotion was observed with topical but not systemic route of administration. Topical tacrolimus has been tried in several case series in the treatment of AA, but the results have not been encouraging [11-15]. Price et al, showed no positive result with tacrolimus 0.1% applied twice daily even after 24 weeks in patients with AA [11]. Treatment failure with topical tacrolimus 0.1% may be caused by insufficient depth of penetration of the ointment formulation and less than optimal patient selection. Higher concentrations of tacrolimus ointment and large scale randomized controlled trials are needed.

Material and Methods

Source of Data:
Patients attending skin out patient department in Navodaya medical college hospital and research centre, Raichur from Decemberr 2010 to November 2011 were screened and clinically diagnosed cases of Alopecia Areata were taken for study.
75 cases were included in the study.

Inclusion criteria:
1. All patients with circumscribed, bald patch without any signs of inflammation or scarring.
2. Patients with short, easily extractable broken hair at the margin of a bald patch.
3. Skin within the bald patch being normal.
4. Patients above the age of 12 years.

Exclusion criteria:
1. Patients with re-growing hair.
2. Patients with secondary infection.
3. Patients already on some other medication for AA.
4. Patients having scar over the bald patch.
5. Patients below the age of 12 years.

Method of Collection of Data:
It is a randomized, single blind, intension to treat study. An informed consent was obtained. Relevant history taken and clinical examination including general, systemic and local examinations were made.
The total number of patches and their measurements were noted in all quadrants of scalp.
Alopecia Grading Scale (AGS) was calculated as follows - The percentage of hair loss in each quadrant was added and divided by four to get the average. Presence of exclamatory hairs was noted.
Patients eligible for the study, were randomly allocated into two groups-Group A and Group B. Patients in Group A were treated with 2% Minoxidil solution applied twice daily over the alopecia patch where as Patients in Group B were treated with 0.1% Tacrolimus ointment applied twice daily.
Both the groups were explained about the nature and course of the disease and were followed up at 2,4,6,8,10 and 12 weeks. In each visit- history of any side effects, any new patches and patient compliance were noted. Alopecia Grading Score (AGS) was calculated at baseline and 12 weeks. Regrowth Score (RGS) was calculated at 12 weeks as follows – 0 (regrowth < 10%), 1 (regrowth 11– 25%), 2 (regrowth 26–50%), 3 (regrowth 51–75%) and 4 (regrowth>75%).
Serial photographs were taken in each follow up.

Investigations:
Selected investigations were done only in doubtful cases of AA,
· KOH preparation and fungal culture;
· Hair microscopy;
· Skin biopsy;
· Serology for lupus erythematosus;
· Serology for syphilis.

Statistical Analysis:
The primary efficacy measurement was the mean change in the Alopecia Grading Score (AGS) and to compare the hair regrowth rate by using hair regrowth score (RGS). Chi-square test was used to analyze the data.

Results

	Group A	Group B
Total number of patients	38	37
Remained in study	35 (92.10%)	34 (94.59%)
Study left out	3 (07.89%)	3 (08.10%)
Gender		
Male	23	23
Female	15	14
Mean AGS		
Baseline	9.85	10.08
12 weeks	4.17	4.82

Table I. Patient profile

Grading of the Response

Mean AGS for Group A at baseline was 9.85 and at 12 weeks was 4.17.

Mean AGS for Group B at baseline was 10.08 and at 12 weeks was 4.82 (Tabl. II).

Group A		Group B	
Baseline	12 weeks	Baseline	12 weeks
9.85	4.17	10.08	4.82

Table II. Mean Alopecia Grading Score (AGS)

A RGS of 0 and 1 are taken as Poor, 2 is taken as Moderate improvement, 3 is taken as Good and RGS of 4 as Excellent.

From the above graph, it is apparent that the number of patients achieving (Fig. 1).

Excellent regrowth was higher in Gr A (23 patients) compared to Gr B (15 patients).

Total 69 patients completed the study (35 in Gr A and 34 in Gr B). Regrowth Score (RGS) more than or equal to 3 at the end of 12 weeks were considered as improved and RGS less than or equal to 2 were considered not improved.

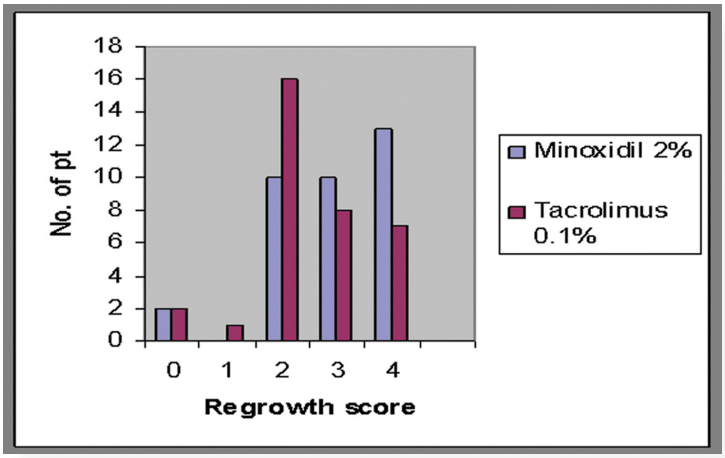

Figure 1. Graph showing regrowth scores for both the groups

Applying Chi-square test to the above Table III.

Chi-Square Test

$\chi 2 = \Sigma (Oi - Ei)\ 2/\ Ei,$

Where Oi is observed frequency and Ei is Expected frequency.

$\chi 2 = (3.73)2/19.27 + (3.72)2\ /15.72 + (3.72)2/18.72 + (3.73)2\ /15.27$

$\chi 2 = 3.25$

	Improved (RGS≥3)	Not improved (RGS≤2)	Total
Gr A	23	12	35
Gr B	15	19	34
Total	38	31	69

Table III. Comparative improvement of both the groups

Side Effects of Treatment
Erythema and scaling were observed in 2 patients and 1 patient respectively each in Minoxidil treated group, whereas tingling and burning sensation was noticed in 2 patients and 1 patient respectively in Tacrolimus treated group (Tabl. IV).

Side effect	Group A	Group B
Erythema	2	-
Scaling	1	-
Tingling sensation	-	2
Burning sensation	-	1

Table IV. Side effects

Discussion

The earlier trials carried out in alopecia areata, compared single agent such as minoxidil and minoxidil with placebo. This is the first study comparing these two topical agents in AA (Fig. 1-4).

Grading of the Response:
The response was graded by assessment of Alopecia Grading Score (AGS) at baseline and after 12 weeks. Only terminal hair growth was taken into account.
Mean AGS for Goupr A at baseline was 9.85 and at 12 weeks was 4.17
Mean AGS for Goupr B at baseline was 10.08 and at 12 weeks was 4.82.
Total 69 patients completed the study (35 in Goupr A and 34 in Goupr B). Regrowth Score (RGS) more than or equal to 3 at the end of 12 weeks were considered as "Improved" and RGS less than or equal to 2 were considered "Not improved".
The data were analyzed using Chi-square test. Group A showed better response then Group B which was found to be of suggestive significance ($0.05<P<0.10$)
Minoxidil 2% showed significantly better response compared to tacrolimus 0.1% in the treatment of patchy AA.

Side Effects:
Erythema and scaling were observed in 2 and 1 patient respectively in minoxidil treated group, whereas tingling and burning sensation was observed in 2 and 1 patient respectively in patients treated with tacrolimus.

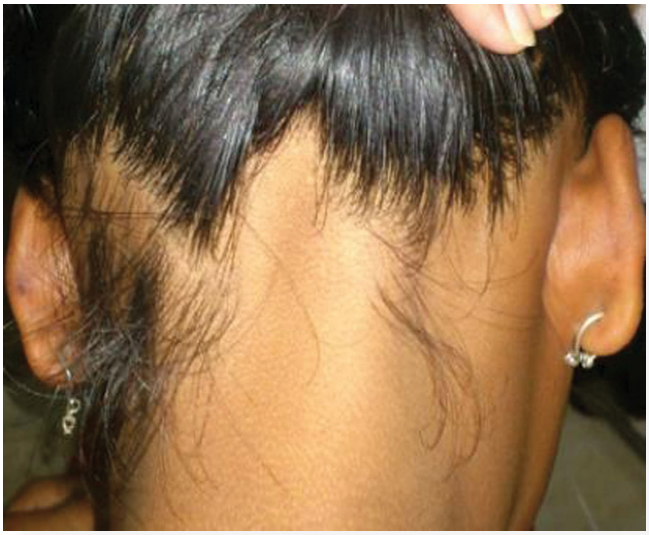

Figure 2. Clinical Photograph showing Alopecia Areata before therapy

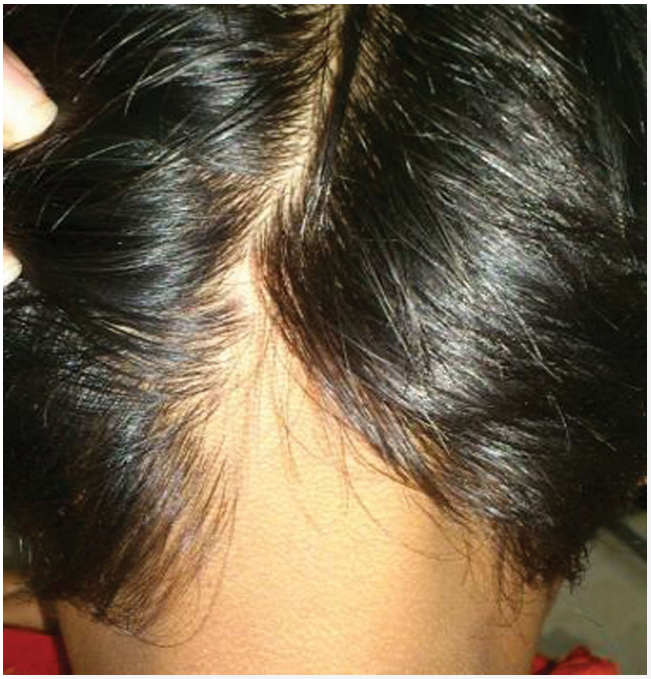

Figure 3. Clinical photograph response to treatment with Minoxidil 2% solution

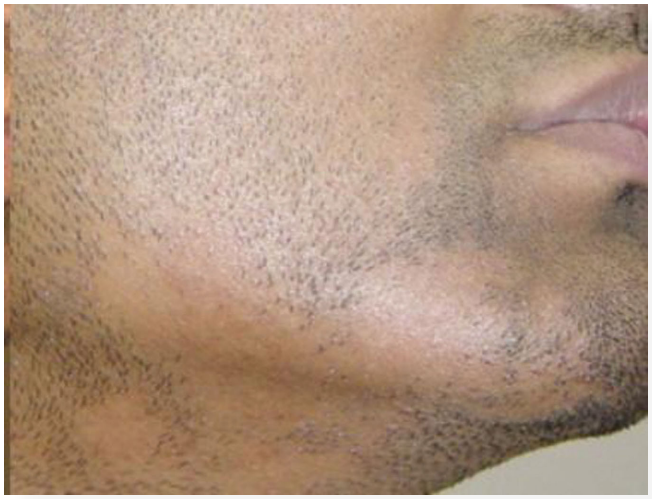

Figure 4. Clinical photograph showing another case of Alopecia Areata (before therapy)

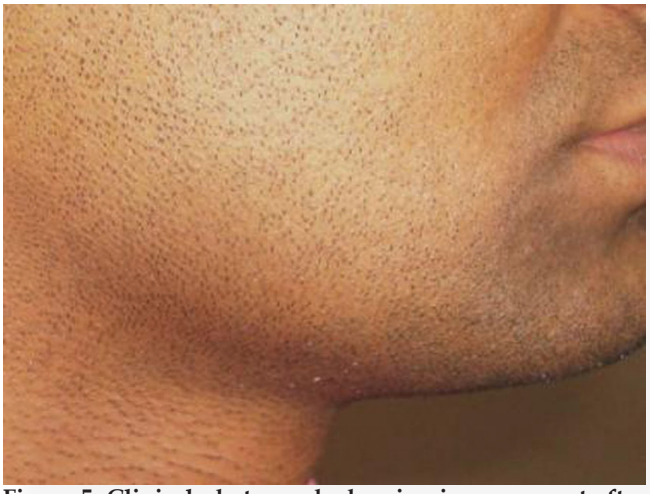

Figure 5. Clinical photograph showing improvement after therapy with Tacrolimus 0.1 %

Conclusion

Total 69 patients completed the study (35 in Gr A and 34 in Gr B).

In our study RGS ≥ 3 was observed in 65.71% of patients treated with minoxidil 2% and 44.12% of patients treated with tacrolimus 0.1%.

Minoxidil 2% showed better response compared to tacrolimus 0.1% in the treatment of patchy AA. Both the treatment modalities showed minimal side effects in the form of mild tingling and burning sensation

Minoxidil 2% has a significant stimulatory effect on hair growth in AA and can be used as in the treatment of AA. Tacrolimus 0.1% is a steroid free topical immunomodulator is safe and well tolerated, but is less efficacious when compared to topical minoxidil. It can be used as an adjuvant therapy. Studies using the combination of topical minoxidil are required to prove if combination is more effective than either alone.

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A CLINICAL AND HISTOPATHOLOGICAL STUDY OF *CICATRICIAL ALOPECIA*

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Abstract
Introduction: Cicatrical alopecia occurs in otherwise healthy men and women of all ages and is seen worldwide
Material and Methods: A study of 40 patients was conducted to study the clinical variants and histopathology of cicatricial alopecia.
Results and Discussion: n our study, it was seen that maximum number of cases of cicatrical alopecia were of LPP (27.5%) followed by 25% of DLE, 20% patients had pseudopelade of Brocq, SLE was seen in 5% cases followed by Scleroderma, dermatomyositis, Keratosis follicularis spinulosa decalvans, aplasia cutis, kerion, follicular mucinosis, pemphigus, dissecting cellulitis of scalp/ pyogenic folliculitis and acne keloidalis nuchae in 2.5% cases each. Regarding the morphology of lesions,epidermal atrophy was seen in 90% patients, erythema was seen in 55% cases, follicular pluging was seen in 40% patients, telangiectasias in 27.5% patients, diffuse scaling in 25% patients and mottled hyperpigmentation was seen in 20% patients. In our study, commonest histopathological feature of alopecia was perifollicular fibrosis seen in 65% patients, basal cell vacuolization was seen in 52.5% patients,perifollicular lymphocytic infiltrate were seen in 50% patients, epidermal atrophy seen in 35% patients and hyperkeratosis was seen in 20% patients.

Key words: cicatrical; alopecia; histopathological; lichen palmopilaris; folliculitis; lupus erythematosis

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Introduction

Cicatricial (scarring) alopecia refers to a group of rare disorders which destroy the hair follicle and replace it with scar tissue, thereby causing permanent hair loss [1]. Causes of cicatricial alopecia are considered either primary or secondary. In primary cicatricial alopecia, the hair follicle is the target of inflammatory destruction, with little effect of the disease process on other components of the dermis [2]. Examples of Primary alopecia include lichen planopilaris, pseudopelade of Brocq, central centrifugal cicatricial alopecia, discoid lupus erythematosus, folliculitis decalvans, and acne keloidalis [3,4]. In secondary cicatricial alopecia, the hair follicle is an „innocent bystander" and is destroyed indirectly. Examples of secondary alopecia include burns and blistering disorders such as pemphigus vulgaris. In primary cicatricial alopecia, there is an inflammatory assault directed primarily at the follicular unit. Although the antigentic trigger for this inflammation is unclear, there is eventually loss of the sebaceous glands and follicular stem cells leading to permanent hair loss. The term „cicatricial alopecia" or scarring alopecia implies the potential of permanent destruction of hair follicle most likely as a result of irreversible damage to epithelial hair follicle stem cells in the region of bulge .

In some cases, hair loss is gradual, without symptoms, and is unnoticed for long periods. In other cases, hair loss is associated with severe itching, burning and pain and is rapidly progressive. The inflammation that destroys the follicle is below the skin surface and there is usually no „scar" seen on the scalp. Affected areas of the scalp may show little signs of inflammation, or have redness, scaling, increased or decreased pigmentation, pustules, or draining sinuses [5].

Aims

1. To study the clinical variants of cicatrical alopecia.
2. To study the histopathology of various types of cicatrical alopecia.

Material and Methods

We selected 40 patients of cicatrical alopecia for the study. Written informed consent of all the patients was taken for the study. Prior approval of hospital ethical committee was taken for the study. All the patients were subjected to detailed clinical examination. Routine investigations of all the patients were performed including complete blood count, fasting blood sugar, Liver function tests, Renal function tests and X ray chest.
Specialized investigations done included antinuclear antibodies, VDRL and scalp biopsy. For performing scalp biopsy (both vertical & horizontal sections), 4mm punch biopsy of all the patients was performed and was sent for histopathological examination.

Results

The data was tabulated and the results were analysed.

Table I shows that maximum number of patients with cicatrical alopecia were between 41-50 years (37.5%), followed by 35% patients between 31-40 years, 20% patients between 21-30 years and 2.5% were between 10 years, between 11-20 years and 51-60 years each.

Table II shows that there were 60% females and 40% males and female: male ratio was 1.5:1.

Table III shows that 30% patients had single patch and 70% patients had multiple patches of alopecia.

Table IV shows that maximum number of cases of cicatrical alopecia were of LPP (27.5%) followed by 25% of DLE, 20% patients had Pseudopelade of Brocq, SLE was seen in 5% cases followed by Scleroderma, dermatomyositis, Keratosis follicularis spinulosa decalvous, aplasia cutis, kerion, follicular mucinosis, pemphigus, dissecting cellulitis of scalp/ pyogenic folliculitis and acne keloidalis nuchae in 2.5% cases each.

Table V shows that epidermal atrophy was seen in 90% patients, erythema was seen in 55% cases, follicular pluging was seen in 40% patients, telangiectasias in 27.5% patients, diffuse scaling in 25% patients and mottled hyperpigmentation was seen in 20% patients.

Table VI shows that the commonest histopathological feature of alopecia was perifollicular fibrosis seen in 65% patients, basal cell vacuolization was seen in 52.5% patients,perifollicular lymphocytic infiltrate were seen in 50% patients, epidermal atrophy seen in 35% patients and hyperkeratosis was seen in 20% patients.

Sr no	Age group (years)	Number of patients	Percentage
1	Below 10 years	1	2.5
2	11-20 years	1	2.5
3	21-30 years	8	20
4	31-40 years	14	35
5	41-50 years	15	37.5
6	51-60 years	1	2.5
	Total	40	100

Table I. Age distribution of patients

Sr no	Sex	Number of patients	Percentage
1	Females	24	60
2	Male	16	40
	Total	40	100

Table II. Sex distribution of patients

Sr no	Number of patches	Number of patients	Percentage
1	Single patch	12	30
2	Multiple patches	28	70
	Total	40	100

Table III. Number of alopecic patches

Sr no	Aetiological cause	Number of cases	Percentage
1	DLE	10	25
2	LPP	11	27.5
3	SLE	2	5
4	Scleroderma	1	2.5
5	Dermatomyositis	1	2.5
6	Keratosis follicularis spinulosa decalvans	1	2.5
7	Aplasia cutis	1	2.5
8	Kerion	1	2.5
9	Follicular mucinosis	1	2.5
10	Pemphigus	1	2.5
11	Dissecting cellulitis of scalp/ pyogenic folliculitis	1	2.5
12	Acne keloidatis nuchae	1	2.5
13	Pseudopelade of Brocq	8	20
	Total	40	100

Table IV. Aetiology of cicatrical alopecia

Sr no	Morphology of alopecia	Number of cases	Percentage
1	Erythema	22	55
2	Diffuse scaling	10	25
3	Follicular plugging	16	40
4	Telangiectasia	9	27.5
5	Mottled hyperpigmentation	8	20
6	Atrophy	36	90

Table V. Morphology of alopecia

Sr no	Histopathological features	Number of cases	Percentage
1	Hyperkeratosis	8	20
2	Follicular plugging	22	5,5
3	Basal cell vacuolization	21	52.5
4	Perifollicular lymphocytic infiltrate	20	50
5	Perifollicular fibrosis	26	65
6	Epidermal atrophy	14	35

Table VI. Histopathological features of alopecia

Discussion

In our study, maximum number of patients with cicatrical alopecia were between 41-50 years (37.5%), followed by 35% patients between 31-40 years, 20% patients between 21-30 years and 2.5% were between 10 years, between 11-20 years and 51-60 years each. There were 60% females and 40% males and female: male ratio was 1.5:1. Out of all the patients, 30% patients had single patch and 70% patients had multiple patches of alopecia. It was seen that maximum number of cases of cicatrical alopecia were of LPP (Fig. 1a) (27.5%) followed by 25% of DLE (Fig. 2), 20% patients had pseudopelade of Brocq, SLE was seen in 5% cases followed by Scleroderma, dermatomyositis, Keratosis follicularis spinulosa decalvans (Fig. 3), aplasia cutis (Fig. 4), kerion (Fig. 5), follicular mucinosis (Fig. 6), pemphigus, dissecting cellulitis of scalp/ pyogenic folliculitis (Fig. 7) and acne keloidalis nuchae in 2.5% cases each.

Regarding the morphology of lesions, epidermal atrophy was seen in 90% patients, erythema was seen in 55% cases, follicular pluging was seen in 40 % patients, telangiectasias in 27.5% patients, diffuse scaling in 25% patients and mottled hyperpigmentation was seen in 20% patients. In our study, commonest histopathological feature of alopecia was perifollicular fibrosis seen in 65% patients,basal cell vacuolization was seen in 52.5% patients,perifollicular lymphocytic infiltrate were seen in 50% patients, epidermal atrophy seen in 35% patients and hyperkeratosis was seen in 20% patients.

The combination of diffuse scaling, erythema, telangiectases, and mottled hyperpigmentation within areas of scarring alopecia was a distinctive feature of DLE [6,7]. In most patients with LP, the histologic changes involved only the follicles and the perifollicular dermis. Less frequently, the inflammatory process extended to the epidermis and the papillary dermis. In all cases, histopathologic features allowed LP (Fig. 1b) to be distinguished from DLE (Fig. 2) regardless of the stage of the disease. The finding of a bandlike fibrotic thickening of the papillary dermis accompanied by fibrotic tracts at sites of destroyed follicles appeared to be a hallmark of „burnt out" lesions of LP. Most early lesions of lichen planopilaris showed a focally dense band like perifollicular lymphocytic infiltrate at the level of infundibulum and the isthmus where the hair 'bulge'is located.

Three types of alopecia have been described in patients with SLE.

1. Discoid lesions with associated scarring alopecia;
2. A diffuse non-scarring alopecia with transient hair loss related to the activity of the disease (a telogen effluvium like picture);
3. Lupus hair which is an unusual non-scarring alopecia characterized by thin weakened hairs at the periphery of the scalp. The hairs fragment and result in a characteristic unruly appearance. In addition alopecia areata has been discovered in patients with SLE rarely scarring DLE and non-scarring AA like lesions may coexist in the same patient.

In a study of 89 patients with scarring alopecia and DLE showed a lymphocytic infiltrate mainly directed to the mid portion of the follicle and a normal anagen: telogen ratio [8]. The authors postulated that the loss of follicle may be due to the destruction of the stem cells which reside in the bulge area where the arrector pili muscle inserts.

Pseudopelade of Brocq (PB) is a permanent progressive scarring alopecia characterized by numerous alopecic patches localized only in the scalp, that tend to coalesce into larger, irregular plaques with policyclic borders. PB can be considered either the final atrophic stage of several scarring disorders such as lichen planus pilaris (LPP) and discoid lupus erythematosus (DLE) (secondary PB) or an autonomous disease (primary PB). PB is a type of scarring alopecia of the scalp associated with a peculiar clinical presentation and evolution, which cannot be considered an autonomous nosologic entity because in 66.6% of patients it is the end stage of other inflammatory chronic diseases such as LPP and DLE [9]. The early evolving lesions of the hair follicles are described in pseudopelade, a type of cicatricial alopecia where clues for the diagnosis of lupus erythematosus or lichen plano-pilaris are lacking.

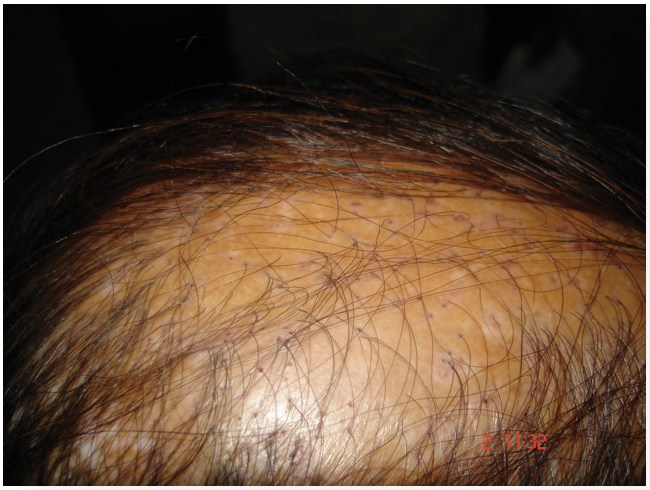

Figure 1a. Atrophic violaceous plaque of lichen plano pilaris

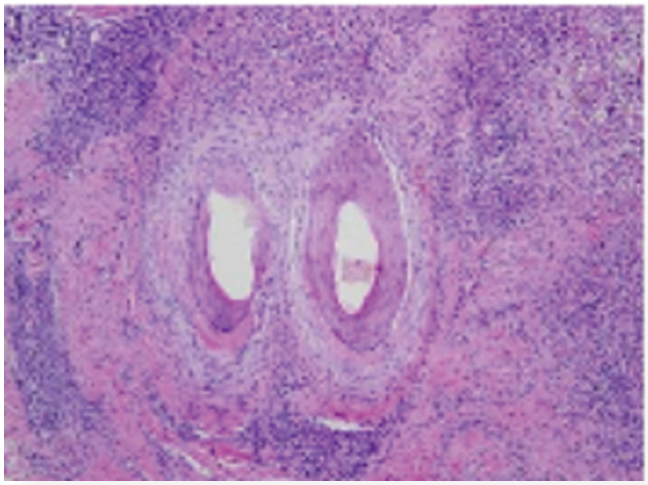

Figure 1b. Photomicrograph showing lymphocytic band like infiltrate involving the infundibulum (H&E stain 100X)

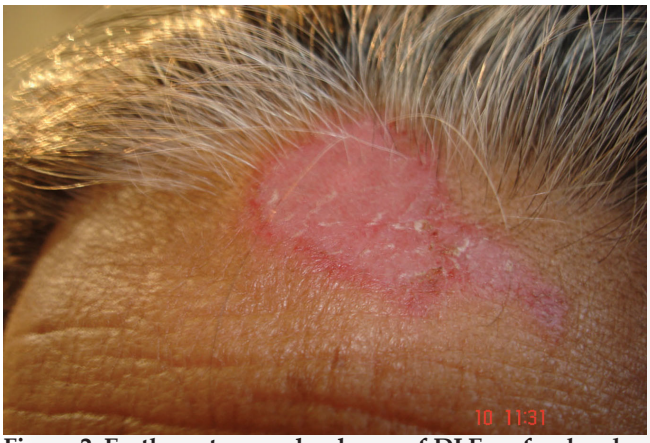

Figure 2. Erythematous scaly plaque of DLE on forehead

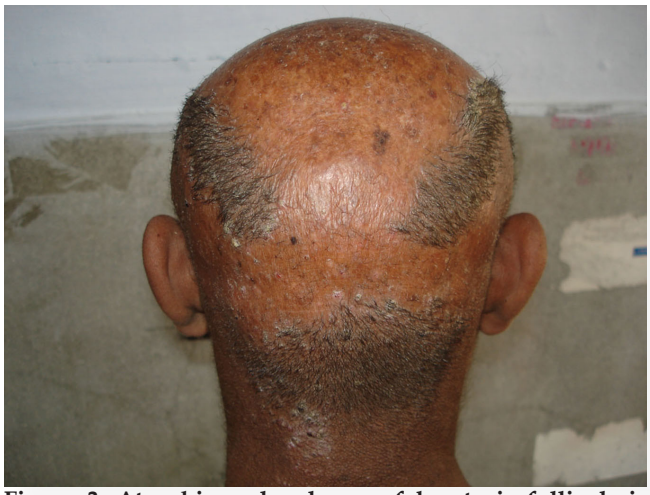

Figure 3. Atrophic scaly plaque of keratosis follicularis atrophicans decalvans

Figure 4. Atrophic patch over the scalp of 8 months old child with aplasia cutis

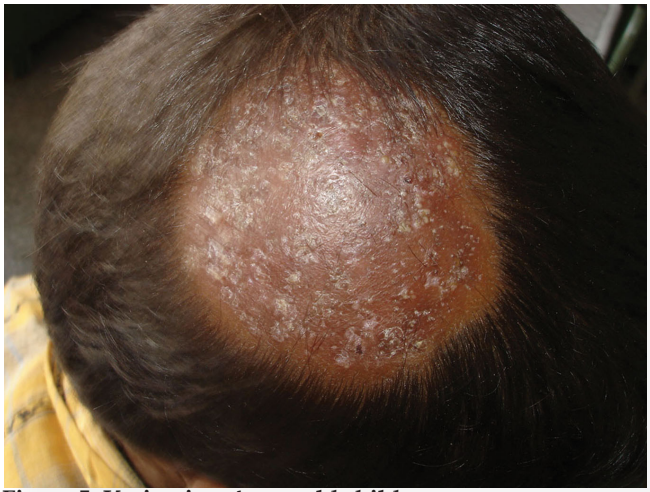

Figure 5. Kerion in a 4 year old child

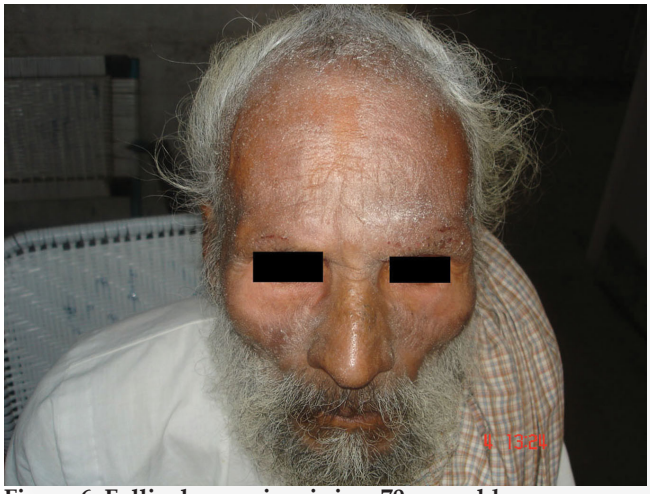

Figure 6. Follicular mucinosis in a 70 year old man

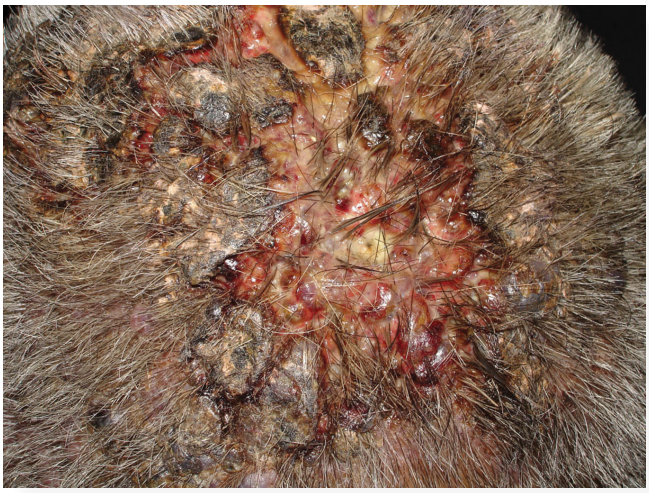

Figure 7. Pustular folliculitis in a 50 year old man

A sudden and synchronized cell death of all the cells of the epithelial sheaths of the hair follicles occurs and is associated with a dense infiltration by lymphocytes. The epidermis remains uninvolved.

The histopathology of pseudopelade of Brocq is of 'burn out' scarring alopecia. The classical description of PPB is one of predominantly follicular scarring chaarcterized by columns of fibrosis replacing hair follicles and sometimes extending into subcutaneous fat. This is accompanied by a loss or decrease of sebaceous glands. Absence of widespread (interfollicular) scarring. Epidermis is normal or rarely atrophic, Sweat glands are normal and marked inflammation is absent. The inflammatory phase is short with lymphocytic inflammation in superficial dermis which is perivascular or perifollicular, centred about the infundibulum or mid point of the follicle. The inflammation remains patchy, mild perivascular and eventually disappears. Follicles are destroyed with marked hair shafts remaining fibrous tracts mark the site of obliterated follicles [10,11].

The histopathology of folliculitis decalvans is characterized by patchy pustular alopecia with areas of scarring with pustules at periphery. Early pustular lesions show an abscess centered about the affected follicle at the level of the lower to the upper infundibulum, which may show comedonal dilataion. Later lesions typically show perifollicular inflammation composed predominantly of lymphocytes with fewer plasma cells, neutrophils, eosinophils and giant cells [12,13]. There may be hyperkeratosis and follicular plugging. Late stage lesions show follicular destruction secondary to diffuse dermal scarring. In such lesions, the inflammation is less pronounced and is composed of lymphocytes, macrophages and some giant cells in response to follicular remnants.

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RECALCITRANT WIDESPREAD *ALOPECIA AREATA* IN A CHILD TREATED SUCCESSFULLY WITH ORAL METHYLPREDNISOLONE PULSE THERAPY

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Abstract
Alopecia areata is a common condition with patchy non scarring hair loss. We report a case of an 11 year old male child with localized patch of hair loss on the frontoparietal region of the scalp since one year. It was a widespread extensive patch of hair loss covering more than 40% of the scalp. On hair shaft microscopy, numerous exclamation mark hairs were present. The patient was put on topical tacrolimus and topical corticosteroids but no response was seen. Since the child was recalcitrant to treatment, methylprednisolone 500 mg/day on three consecutive days in a month was given. After six months 80% regrowth was seen over the affected area of the scalp.

Key words: hair; scalp; alopecia; corticosteroids; treatment; topical

Cite this article:
Neerja Puri: Recalcitrant widespread alopecia areata in a child treated successfully with oral methylprednisolone pulse therapy. Our Dermatol Online. 2013; 4(3): 316-318.

Introduction

Alopecia areata (AA) is a relatively common patchy nonscarring hair loss condition. The annual incidence rate is 20. 2 per 100,000 and the lifetime risk is estimated at 1.7% [1]. Although most small AA lesions resolve spontaneously, 14-25% of AA patients referred to secondary and tertiary centers progress to total loss of scalp hair or to loss of all scalp and body hair, from which full recovery is unusual [2,3].

In the widespread cases in which the remaining hair cannot cover the alopecic sites, there can be tremendous psychological stress. Experimental studies have reported that the pathogenesis of AA is an autoimmune assault on hair follicles [4]. Since the 1950s, oral administration of corticosteroid therapy has been the treatment of choice for recalcitrant AA [5]. However, prolonged use of corticosteroids is limited because of adverse side effects and recurrence after discontinuation. Pulse corticosteroid therapy has also been used to control the active phase of hair loss of AA. According to the recent reports, the dosage of pulse corticosteroids commonly used in treating AA is 500 mg/day or 8 mg/kg/day of intravenous methylprednisolone for 3 consecutive days [6,7]. Lower dosage of oral prednisolone is also used in other studies [8,9]. Severe side effects were not described in those reports. Although acute phases of hair loss are followed by spontaneous hair regrowth in most patients, the disorder may persist for many years or even for life when severe. But even in these cases hair loss is potentially reversible, because the disease usually does not result in destruction of hair follicles or scarring. In consideration of the TH-1 mediated immune attack on the hair follicle in AA, corticosteroids are potentially good candidates for the treatment of this disease.

Topical, intralesional and systemic corticosteroids have been used to treat AA, with different rates of success and side-effects. The failure of topical corticosteroids is most likely due to the insufficient penetration of topically applied drugs from ointments, creams or lotions into the hair bulb. Improving penetration by occlusion has been tried without success.

Case Report

An 11 year old male child reported to the department of dermatology with localized patch of hair loss on the frontoparietal region of the scalp since one year. It was a widespread extensive patch of hair loss covering more than 40% of the scalp. On local examination, the patch of hair loss measured 4cm x 5cm in size (Fig. 1). The scalp was not tender or bruised and there was no evidence of scarring.On hair shaft microscopy,numerous exclamation mark hairs were present. A pottasium hydroxide preparation from the lesional skin did not show any fungal elements. The child had positive family history and history of atopy was also positive. Complete blood cell count, serum chemistry, chest X-ray, electrocardiogram, thyroid function test and antinuclear antigen were checked before starting the pulse corticosteroid therapy.

The patient was put on topical tacrolimus for 8 weeks, but no response was seen. Later, the patient was put on topical corticosteroids for 8-10 weeks without any re growth of hair. Since the child was recalcitrant to treatment, methylprednisolone 500 mg/day on three consecutive days in a month was given.

The steroid pulses were given for three months and the response was seen in six months (Fig. 2). No serious adverse effects were recorded except for transient giddiness,hedadache and epigastric burning. Evaluation of the hair regrowth was made by photo of the patient 6 months after the pulse therapy. Hair growth was assessed on a percentage scale ranging from 0 to 100%. Only growth of terminal hair, not vellus hair from the lesions was regarded as regrowth. After six months 80% regrowth was seen over the affected area of the scalp.

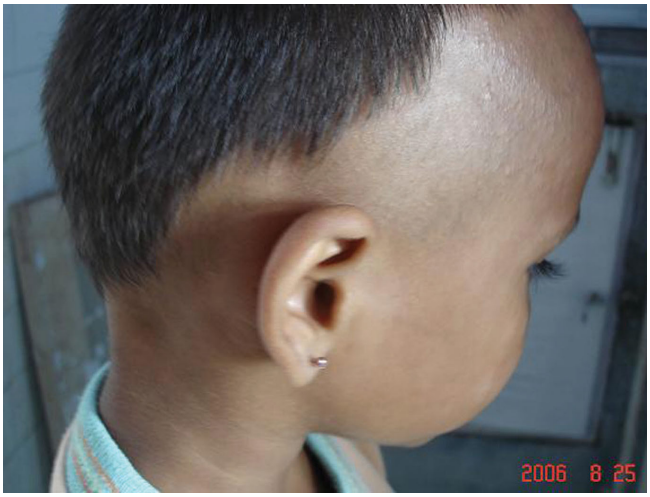

Figure 1. An 11 year old child with patchy alopecia

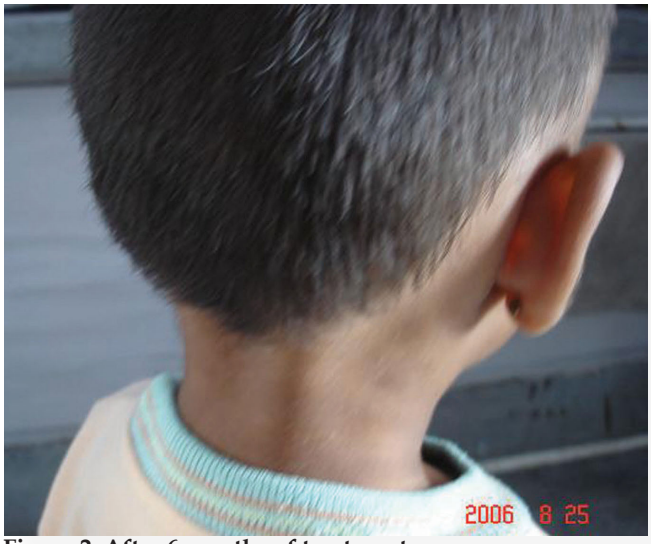

Figure 2. After 6 months of treatment

Discussion

It has been hypothesized that the advantage of pulse therapy compared to regular administration of corticosteroid is due not only to fully ligand-occupied glucocorticoid receptors but also to nongenomic actions, including membrane-bound glucocorticoid - receptor - mediated signaling and direct physicochemical actions on the plasma membrane, which lead to the dysfunction of immune cells [10]. High corticosteroid levels attained during the therapy may help correct the cytokine imbalance systemically or restore the immune privilege locally. Previous studies indicate that good responders to pulse corticosteroid therapy tend to have recent-onset hair loss of plurifocal lesions and that poor responders have alopecia totalis/universalis or ophiasic lesion [11,12]. The dosage of corticosteroid administered in this study was 500 mg/day methylprednisolone on 3 consecutive days. Whereas, initially, oral corticosteroids were used daily or every other day for several months, this continuous use of corticosteroids is obsolete today. Doses that are required to maintain hair regrowth in AA are between 30 and 150 mg daily, giving rise to unacceptable side-effects such as hypertension, diabetes, immunosuppression, osteoporosis and proneness to thrombosis. It is yet to be determined whether pulse corticosteroid therapy during early stages of severe AA will be able to change the long-term prognosis.

Several immunosuppressive agents have also been used for recalcitrant AA patients. Although cyclosporine has been applied for severe AA patients, the efficacy may not be satisfactory because of resistant cases, recurrence after discontinuation and adverse side effects, including hypertension and gingival hyperplasia [13,14]. According to a recent report, methotrexate alone or in combination with low doses of corticosteroids was effective in severe long-term AA [15]. Alefacept, which is a lymphocyte-function-associated antigen 3/IgG fusion protein that blocks T cell activation, has also been used for recalcitrant AA and has achieved some degree of improvement [16].

Conclusion

Since 1975 several authors have performed pulsed administration of corticosteroids in single doses, given once monthly in order to reduce the side-effects of corticosteroids to an acceptable level, but all studies which noted hair regrowth, were uncontrolled and the majority of patients had patchy AA. Moreover, other studies reported treatment failure after corticosteroid pulse therapy. Controlled studies should be conducted to prove the efficacy and long-term value of this treatment. Especially the efficacy in interrupting acute phases of rapid hair loss by pulsed administration of oral corticosteroids should be investigated.

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ERYTHEMA ELEVATUM DIUTINUM AS MOST PROBABLE DIAGNOSIS: A CASE REPORT

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Source of Support:
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Competing Interests:
None

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Abstract
Cutaneous vasculitis can be cause by multiple disorders or can be idiopathic. Many diseases can present with similar findings, therefore histopathologic examination is always require for confirming the right diagnosis. The erythema elevatum diutinum (EED) is a localized vasculitis, classified as a neutrophilic dermatosis. It's a rare cutaneous condition, distribute on the extensor surface of the extremities, more frequently in the dorsum of the hands, knees and elbows. They have a symmetric distribution and can be asymptomatic, painful; or pruritic, sometimes accompanied paresthesias. The most common clinical presentation is round erythematous papules which become erythemato-violaceous or purpuric plaques. There are not pathognomonic histopathological findings, but can present as a leukocytoclastic vasculitis with perivascular neutrophilic infiltration in the middle and superficial dermis. I presented the case of a 61-year-old female, with erythematous purpuric painful plaques, irregular, symmetric and elevated, located in both thenar regions of her hands and paresthesias. The patient's presentation is consistent with multiple characteristics of EED such as the description of the lesions, the anatomical location, the symmetric distribution and the histopathological findings of an initial disease. This patient does not have all the clinical progression and outcome, due to the initial stage of the disease.

Key words: cutaneous; erythema elevatum diutinum; leukocytoclastic vasculitis

Cite this article:
Erick Francisco Sanchez Jimenez: Erythema Elevatum Diutinum as most probable diagnosis: a case report. Our Dermatol Online. 2013; 4(3): 319-321

Introduction

Erythema elevatum diutinum (EED) is a rare disease. It's a vasculitis that affects the small vessels. The most common presentation is red-brown or violaceous papules and nodules over the dorsal hands. The disease is limited to the skin [1]. I am reporting an initial presentation of a case that the most probably diagnosis until now is the EED.

Case Report

A 61-year-old female, Hispanic, complaining of purpuric painful lesions in both of her hands, which develop in one day long. She report paresthesias in both hands and finger tips few days before the onset. She denies any other associated symptom as fever sensation, headache, chest pain, dyspnea, abdominal pain, vomiting, diarrhea, muscle ache or any other. But the last month she was very stress and possibly had some depression symptoms, for which she take clonazepam.

The clinical examination showed (Fig. 1, 2) erythematous purpuric plaques, which were irregular, symmetric, elevated lesions located in both thenar regions of her hands. Also between the main plaques were some blister-like lesions. In the periphery of the main plaque there were some satellite papules of similar color and consistency of the main lesion. There wasn't any other physical finding during the physical examination, including head, eyes, ears, nose, throat, neck, cardiovascular, chest, abdominal, lower extremities and neurologic examination.

The vital signs and laboratory workup was done: including CBC with platelets, coagulation studies, glucose, uric acid, VDRL, HIV ELISA, and urinalysis. There was every test within normal limits.

The preliminary diagnosis was vasculitis vrs pioderma. The patient was treated initially with IV clindamycin and topical aluminum acetate, with mild clinical response to treatment. Then she was treated with oral clindamycin, prednisone and Dapsone, causing improvement of the lesions within 3 days of treatment.

A smear, a gram stain and culture of fluid from the only pustule present was done and was negative for bacteria. The biopsy was done and showed: a dense interstitial neutrophilic infiltrate in the reticular dermis associated with large amount of nuclear dust. There are significant edema of the papillary dermis and some erythrocyte extravasation. Despite the dense infiltrate, there isn't fibrinoid necrosis in the vessel's wall. The epidermis shows hyper and parakeratosis, and the presence of a pustule. The changes describe may correspond to early changes of erythema elevatum diutinum although no frank vasculitis is observed, which would make the definitive diagnosis.

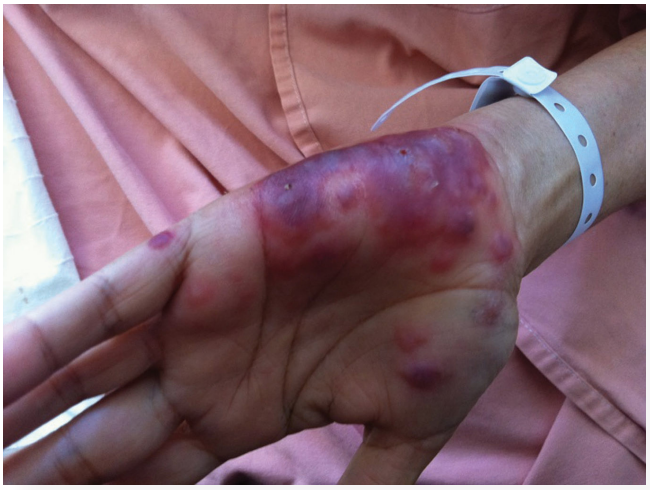

Figure 1. Left hand of the patient, showing the erythematous-purpuric plaque

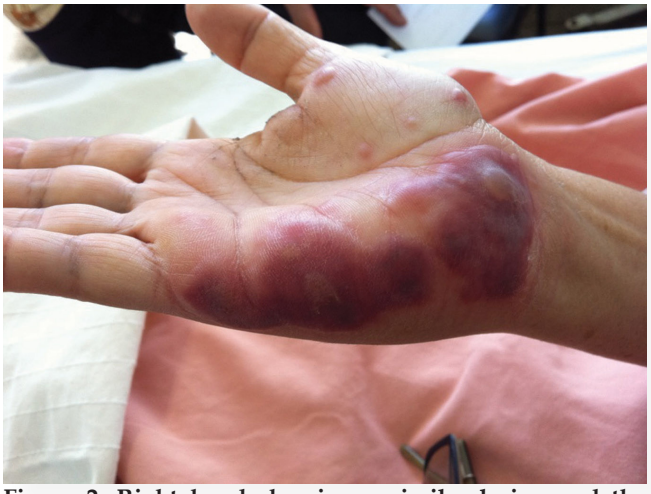

Figure 2. Right hand showing a similar lesion and the presence of the only pustule

Discussion

Cutaneous vasculitis can be cause by multiple disorders or can be idiopathic. Many diseases can present with similar findings, therefore histopathologic examination is always require for confirming the right diagnosis [1]. The nomenclature and classification are based on the histopathological findings. The etiology is still unknow [2]. The EED is a localized vasculitis and is classified into the neutrophilic dermatosis, due to the histopathologic findings [3].

Patients can present with multiple symptoms or physical findings, or can present only with the cutaneous manifestation. Accordingly you should perform multiple laboratory tests or radiologic studies based on the clinical findings of each patient [1].

The erythema elevatum diutinum (EED) is a rare cutaneous condition first describe considered a variant of leukocytoclastic vasculitis. The EED was first described by Hutchinson [4] in 1888 and Bury [5] in 1889. However the introduction of the name was proposed by Radcliffe-Crocker et al [6]. The name describes the lesions, erythema for redness, elevatum for elevated and diutinum for persistent or chronic [7]. The anatomical distribution is usually the extensor surface of the extremities, more frequently in the dorsum of the hands, knees and elbows. They have a symmetric distribution and can be asymptomatic, painful; or pruritic, sometimes accompanied by arthralgias or paresthesias [8].

The most common clinical presentation is round erythematous papules which become erythemato-violaceous or purpuric plaques. They can be accompanied of necrosis, vesicles and blisters. The clinical evolution of the disease is that the lesions can resolve spontaneously, resolve with treatment or can persist as chronic mild lesions with periodic exacerbations. Sometimes they can leave squeals as atrophy or depigmented areas. In addition with time the lesions can become hard nodules [9].

There are not pathognomonic histopathological findings, but can present as a leukocytoclastic vasculitis with perivascular neutrophilic infiltration in the middle and superficial dermis. The vessels can have a fibrinoid degeneration. The epidermis can be intact. With the time the biopsy can show the concentric perivascular fibrosis cause by the deposition of immune complexes. The old lesions have findings consistent with dermis fibrosis with multinucleated giant cells [9-14].

Although some patients have spontaneous resolution of symptoms, most of patients become chronic. The first treatment election is Dapsone which produces a suppressor effect on the lesions, is not curative and some patients have recurrence of symptoms when withdrawal. Some experts recommend 100mg per day as initial dose and then subsequent reduction until find the minimal ideal dose [15-17]. The Dapsone has severe secondary effects as metahemoglobinemia, hemolysis and agranolocytosis, which can be minimized with the combination of vitamin E or cimetidine in the beginning of the treatment. For resistant cases can use colchicine, tetracycline, niacinamida or nicotinamida. For the last option can use intralesional injections of corticoids [18,19].

Conclusion

The patient's presentation is consistent with multiple characteristics describe above as: the description of the lesions, the anatomical location, the symmetric distribution, the isolated cutaneous affection, the histopathological findings of an initial disease and the response to Dapsone. Obviously, the patient does not have the same clinical progression mention above, due to the initial stage of the disease, but I have to wait and see the clinical outcome.

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GRANULAR PARAKERATOSIS: REPORT OF 2 *ECUADORIAN* CASES AND REVIEW OF THE LITERATURE

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Abstract
Granular Parakeratosis is a rare disorder of keratinization usually presented in adults. There are only fews reports in children. We present two cases, one in an adult and the other in a 7-month-old infant.

Key words: parakeratosis; keratosis; infant

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Introduction

Granular parakeratosis (originally termed axillary granular parakeratosis) is a rare, recently recognized, acquired benign disorder of keratinization. It was first described in adults, and there are only a few reports of children with granular parakeratosis (GP), affecting predominantly the diaper area. We describe a case in a 37 years old man, and an additional case of a 7-month-old infant with GP.

Case Report

Case 1

A 32-year-old male patient presented for evaluation of a bilateral papillomatous axillary rash that had persisted for the past 3 months (Fig. 1). He reported that his lesions were slightly pruritic and that he has seen his primary care provider previously for his problem. He has been applying an antifungal cream per his recommendation that resulted in no improvement after 1 month of treatment. He denied the use of new deodorants or antitranspirants but he did mentioned that he sweats profusely and that he needs to reapply deodorant several times a day. Biopsy reported granular parakeratosis. Patient was treated with topical tretinoin.

Case 2

A healthy 7-month-old Ecuadorian boy of Asian descent presented with a 2-month history of an asymptomatic "warty eruption" distributed over his neck and antecubital fossae. The patient's mother denied the use of topical preparations or medications in these areas prior to the appearance of the rash. His past medical history was unremarkable and there was no family history of cutaneous disorders. According to his mother, these lesions had recurred after having partially improved with the application of topical corticosteroids prescribed by his pediatrician.

Clinical examination revealed multiple, discrete, coalescing 2 to 3 mm brownish-eythematous hyperkeratotic papules located in his neck folds (Fig. 2, 3), and similar, but less pronounced lesions along the antecubital fossae (Fig. 4). The eruption was symmetric and no pain could be elicited on palpation. The rest of his skin examination was normal.

A biopsy specimen obtained from his neck showed marked hyperkeratosis and slight waviness of the epidermal surface. Discrete thinning of the stratum malphigii and preservation of the keratohyalin granules within a diffuse parakeratotic straum corneum. A mild superficial perivascular infiltrate of lymphocytes was also present (Fig. 5). These findings are characteristic of those described in granular hyperkeratosis.

After establishing the diagnosis, the patient was treated with 0,025% tretinoin cream with complete clearance of the lesions after 5 days. No known recurrence of the eruption has been documented so far.

Discussion

In 1991, Northcutt et al used the term Axillary granular parakeratosis to describe a peculiar axillary eruption with distinctive histopathological features in 4 middle-aged to elderly patients [1]. The rash consisted of unilateral or bilateral bright red patches with hyperpigmentation associated with pruritus.

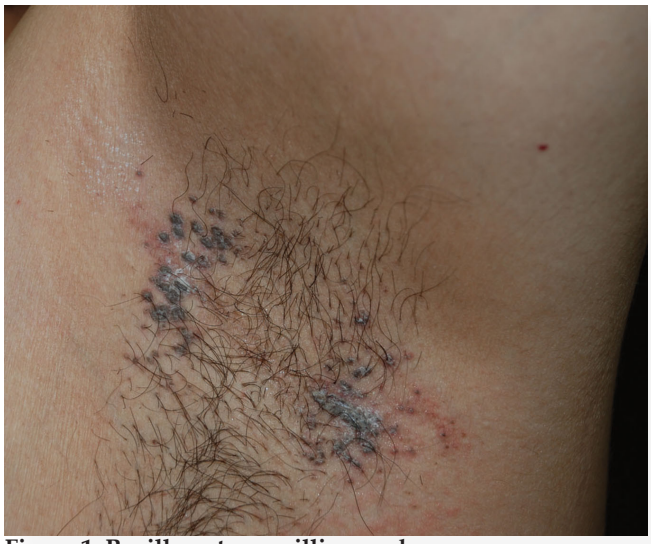

Figure 1. Papillomatous axilliary rash

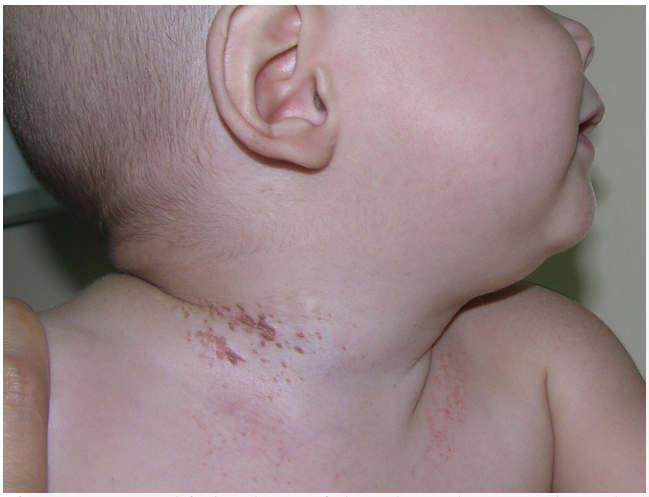

Figure 2. Multiple brownish-red scaly papules that focally coalesce located on the neck fold of the patient

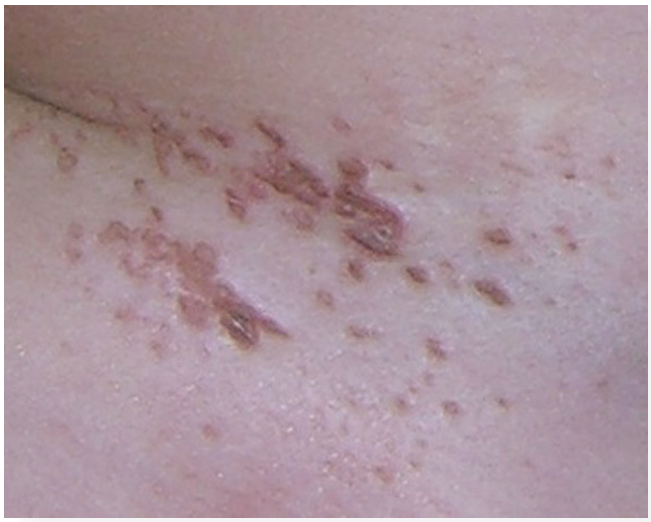

Figure 3. Close up of the neck fold lesions

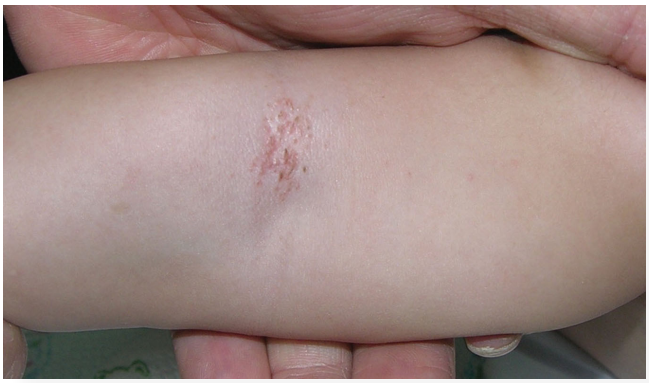

Figure 4. Clinical appearance of granular parakeratosis in the antecubital fossa of the patient

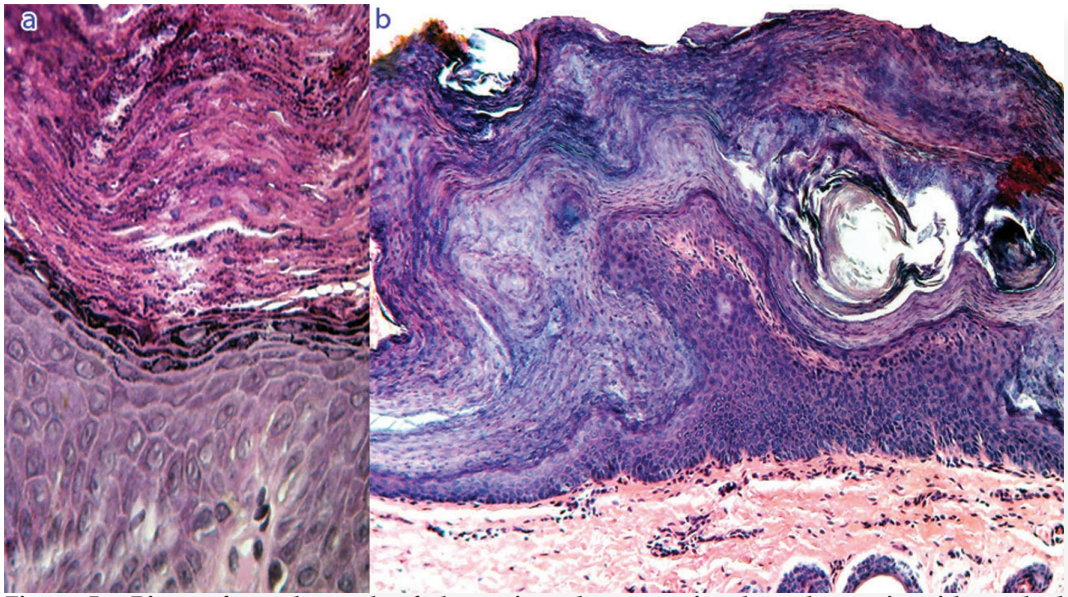

Figure 5a. Biopsy from the neck of the patient demonstrating hyperkeratosis with marked and diffuse parakeratosis.

Figure 5b. High power magnification showing retention of the keratohyaline granules in the stratum corneum

Since then, there have been several additional reports documenting the development of the disease in different intertriginous areas outside the axilae, including the groin, perianal area, inframammary and abdominal folds [2-4]. Therefore, a renaming of this entitiy to "intertriginous granular parakeratosis" or simply "Granular parakeratosis" has been suggested by some authors [2,3].

In a recent study by Scheinfeld et al where the incidence of GP was assessed in 363,343 biopsy specimens, only 18 cases (0.005%) were identified and confirmed as GP and 15 of these cases were adult women and no occurrence in children was found; indicating that this is a rare condition and that adult women are more frequently affected. This study also suggested that there is a lack of awareness of this disease by dermatologist since only in one biopsy requisition form, GP was listed in the differential diagnosis [5].

Before 2002 this disease had only been reported in adults. However, recent publications have demonstrated that this condition can also occur in young children, affecting predominantly the diaper area. Two clinical patterns in the diaper region of infantile GP were described by Chang et al [6]: bilateral linear inguinal plaques and erythematous geometric plaques underlying pressure points from the diaper. Although the lesions in our patient were not located in the groin, they are more consistent with the linear plaques pattern previously described.

The cause of this entity remains unclear. Recent ultrastructural and immunohistochemical studies suggest that the pathophysiologic defect underlying this disorder is a failure in the normal degradation of profilaggrin, resulting in the retention of the keratohyaline granules within the keratinocytes [2]. The histopathologic hallmark of the disease is a markedly parakeratotic stratum corneum that has a granular appearance due to retention of keratohyalin granules.

Early reports had proposed that this disease could represent and allergic contact reaction to deodorants or antiperspirants [1-7]. However, there are several observations that argue against this hypothesis, suggesting that additional factors may be involved. These include case reports of unilateral involvement, non-axillary intertriginous areas affected, failure to improve despite stopping or changing the suspected irritant, and the fact that in some cases no irritant could be identified [8]. Moreover, in the series of cases studied by Scheinfield and Mones, no histopathological evidence supporting an allergic contact or irritant reaction was found [5].

Physical factors such as heat, moisture and friction has also been implicated [3]. In children, occlusion from diaper, the use of baby powder and topical zinc oxide preparations have been speculated as triggering factors, but the mechanisms are unclear [6,9]. In our case, no lesions were observed in the diaper area and no topical products were applied to affected sites prior to the development of the rash.

In adults, the experience in the management of granular parakeratosis is limited. Various treatments have been attempted with variable efficacy. Potent topical corticosteroids have been used with success in a series of three patients [10]; while no response was observed by others [2]. Topical and systemic retinoids have been found to be effective in some patients [8,11,12]. There are reports of clearing with the use of topical vitamin D analogs [4,13,14] and Cryotherapy was used in one patient with good results and no recurrence [1]. Some cases resolved after changing or discontinuing deodorant [2,15] and spontaneous resolution was observed in one patient [3].

Several treatment modalities have also been used in infants with granular parakeratosis, but the optimal therapy is yet to be determined. Tacrolimus, pimecrolimus, topical steroids and emollients have all been used with inconsistent results [6,9]. Keratolytics (3%, 4%, 5% salicylic acid) were used with success in 4 infants reported by Giraldi et al [16]. Similarly to adults, spontaneous clearance of the lesions, as well as, complete resolution of the eruption after discontinuing topical zinc oxide preparations was noted in some patients. Our case responded to treatment with tretinoin 0,025% after 5 days of treatment.

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KIMURA'S DISEASE - A RARE ENTITY

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Abstract
Introduction: Kimura's disease is a benign, but locally injurious disease with a marked predilection for the head and neck. **Case Report:** We present two cases of this rare disease. **Discussion:** Of uncertain aetiology, its tendency to present as a discrete, enlarging mass with associated lymphadenopathy makes it a condition of interest to clinicians who see head and neck pathology. Although rare, there are increasing numbers of reports of the condition and it should become part of the standard differential diagnosis.

Key words: head and neck; eosinophilia; immunoglobulin

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Introduction

Kimura's disease is an unusual condition in several respects. It was first reported by Chinese authors Kimm and Szeto in 1937 [1] and, besides its eponym, has been variously known as epithelioid haemangioma, atypical pyogenic granuloma and cutaneous eosinophilic lymphofolliculosis. The disorder received its current name in 1948, when Kimura et al noted the vascular component and referred to it as an "unusual granulation combined with hyperplastic changes in lymphoid tissue" [2].
Kimura's disease is a chronic inflammatory condition which presents with a characteristic triad of signs and symptoms, namely a painless, slowly enlarging soft tissue mass (or masses), associated lymphadenopathy and peripheral eosinophilia [3]. Eighty-five per cent of cases occur in men. Approximately 67 to 100% of patients develop regional lymphadenopathy and, in longstanding disease, this may become generalized [4]. Patients may complain of local or generalized pruritus and sub acute or chronic dermatitis. There may be proteinuria and laboratory investigations will invariably reveal peripheral eosinophilia and increased serum immunoglobulin (Ig)E [5]. While there has been considerable discussion in the pathology literature concerning this disease, it is still unknown by most surgeons. This report seeks to increase awareness of an interesting condition. Management of this disease is personalized due to lack of consensus and conservative approach is best suited.

Case report

Case 1

This is a second case of 15 years old male who had a swelling in the left cervical area for the past 8 months. The swelling was 5cm x 3cm and was non tender but firm in consistency (Fig. 1). It was non adherent to mandible. The skin overlying the swelling was normal. Patient was treated conservatively with antibiotics and analgesics for two weeks but the swelling persisted. Then the patient was subjected to fine needle aspiration cytological examination. FNAC showed eosinophilia. Biopsy was taken to confirm the diagnosis which revealed the following features: Dilated blood vessels, some with bizarre and irregular shapes in the reticular dermis (Fig. 2). Inflammatory infiltrate contained mainly lymphocytes and eosinophils (HE x 100).

Case 2

A 3 year male presented in surgery OPD with complaints of swellings in the head and neck with involvement of the subcutaneous tissues and cervical lymphadenopathy. The swelling was noticed by his mother 4 months back which was treated by quacks in the near by village which gradually became small in size but again increased in size and now there was swelling 6cm x 3cm on the left side of the neck. The overlying skin was discoloured and the patient was running fever also. He was given antibiotics and was further subjected to fine needle aspiration cytology before doing incision and drainage & wedge biopsy of the swelling.
The histopathological examination revealed lymphoid nodules with discrete germinal centers occupying an area extending from the reticular dermis to the fascia and muscle. A marked eosinophilic infiltrate with eosinophilic abscesses was seen. Capillary proliferation was seen with masses of canalized vessels with flat endothelial cells alongwith fibrosis (Fig. 3).

Figure 1. 15 years male with swelling neck

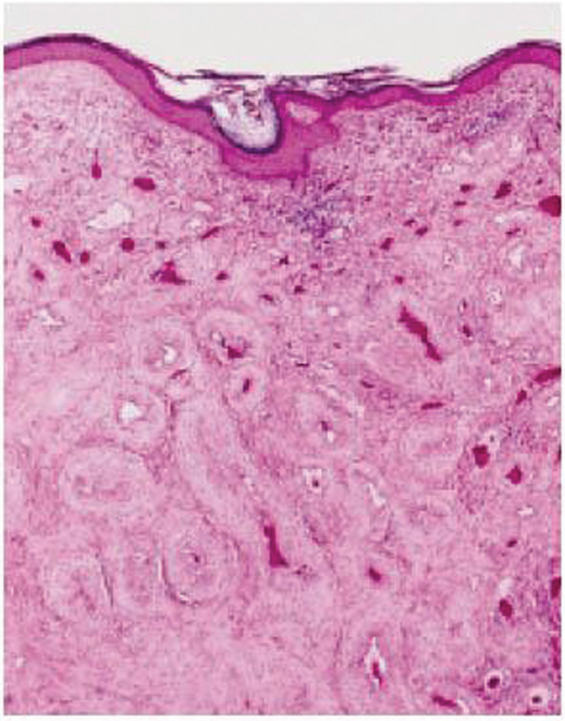

Figure 2. Photomicrograph showing dilated blood vessels alongw

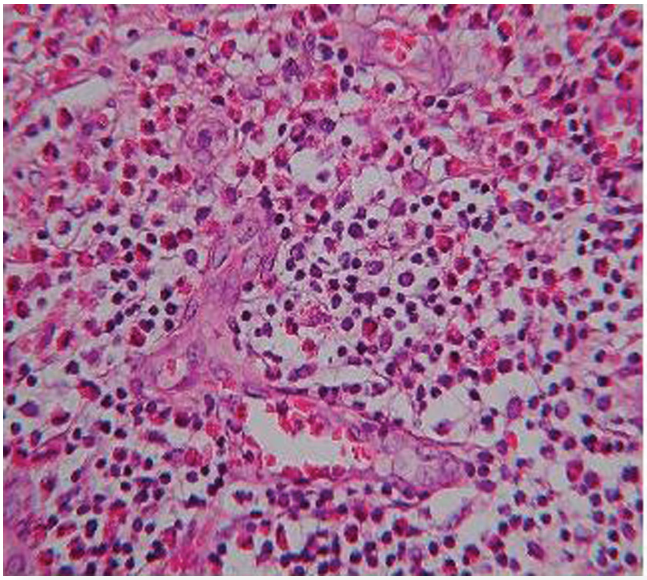

Figure 3. Photomicrograph showing lymphoid nodules with marked

Discussion

The differential diagnosis, while including obvious lesions such as dermatofibrosarcoma protruberans and cylindroma (turban tumours), will ultimately be determined by both the clinical picture and the histopathology. Clinically, malignant lymphoma, parotid tumours, haemangioma, pyogenic granuloma, Mikulicz's disease and Kikuchi's disease are all conditions for which Kimura's disease has been mistaken in the past [6,7]. Other conditions to consider include Kaposi's, sarcoma, angiosarcoma, eosinophilic lymphoma and angioimmunoblastic lymphadenopathy; parasitic diseases responsible for subcutaneous masses with an associated lymphadenopathy, such as tissue-invasive helminth infections, cysticercosis, sparganosis, toxocariasis and several forms of invasive misaim may also need to be ruled out [8].

In Kimura's disease there is classically a dense inflammatory infiltrate characterized by eosinophilic lymphoid tissue with germinal centers and microabscesses. There is often marked fibrosis found within the typical lesions. Pathologically, the picture is perhaps most difficult to distinguish from angiolymphoid hyperplasia with eosinophilia (ALHE), and for a long time these two conditions were thought to represent one and the same pathology, but the current consensus is that they represent two ends of a spectrum of similar diseases [9]. KD is generally limited to the skin, lymph nodes, and salivary glands but patients with KD and nephrotic syndrome have been reported. The basis of this association is unclear. Males are affected by KD more commonly than females, with a 6:1 ratio in one series. KD is usually seen in young adults. A series by Kung et al reported a median age of 28 years [10].

In Kimura's disease there is classically a dense inflammatory infiltrate characterized by proliferating lymphoid tissue with germinal centres, eosinophilic microabscesses and fibrosis. There is often marked fibrosis. The lesion need to be distinguished from angiolymphoid hyperplasia with eosinophilia (ALHE), which is believed to be a true neoplasm of the endothelium [11]. The histology of ALHE is typified by an exuberant proliferation of capillary vessels some of which may not be canalized. These are lined by epithelioid (histiocytoid) endothelial cells which are not seen in Kimura's disease. While there is an inflammatory infiltrate, the associated lymphocytes are not arranged in germinal centres as they are in Kimura's disease.

Clinically, Kimura's disease is believed to be a disease of the Orient, and ALHE one of the western world. ALHE occurs in older (20-40 years), predominantly female populations. Kimura's disease is primarily a disease of younger males.

The pathophysiology of KD remains unknown, although an allergic reaction, trauma, and an autoimmune process have all been implicated as the possible cause. The disease is manifested by an abnormal proliferation of lymphoid follicles and vascular endothelium. Peripheral eosinophilia and the presence of eosinophils in the inflammatory infiltrate suggest that KD may be a hypersensitivity reaction. Some evidence has indicated that TH2 lymphocytes may also play a role, but further investigation is needed [12].

Treatment options range from conservative observation for asymptomatic patients to surgical excision, steroid therapy, and radiotherapy for symptomatic patients. The treatment of choice for localized disease would thus appear to be surgical excision. Conservative management is recommended in anatomically sensitive areas. There had been some case reports in the otorhinolaryngeal, plastic surgery and ophthalmic specialties reflecting problems in management when this lesion affects important anatomical structures. For refractory lesions, Intralesional or oral steroids can shrink the nodules but seldom results in cure. A medium-potency steroid, such as triamcinolone acetonide, used in solution form for intralesional injection usually is well tolerated. Cyclosporine recently was reported to induce remission in a patient with KD of the earlobe. A dose of 5 mg/kg/day was administered for 7 days, then tapered. Radiotherapy has been used to treat recurrent or persistent lesions [13]. In summary, Kimura's disease is an indolent, benign, but locally disfiguring disease, whose true importance lies in its ability to mimic a number of other benign inflammatory and neoplastic conditions of the head and neck. Knowledge of the condition, its clinical appearance, course and histopathology puts the practitioner in a better position to answer questions from concerned patients and primary caregivers, and optimize management strategies.

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FAVRE-RACOUCHOT SYNDROME

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Abstract
This paper describe a typical case of Favre-Racouchot syndrome in a 70-year-old farmer. The exact pathogenesis of Favre-Racouchot syndrome remains obscure but apparently extensive exposure to sun and harsh weather is perhaps largely responsible as had been in the described case.

Key words: chronic actinic skin damage; nodular elastosis; solar elastoses; senile elastosis

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Introduction

Favre-Racouchot syndrome (syn. nodular elastoidosis with cysts and comedones; elastoidosis cutanea nodularis et cystica) is a peculiar complication of solar (senile) degeneration of the skin manifesting with yellowish and atrophic skin, multiple, large, black comedones, follicular cysts, wrinkles and furrows, and yellowish nodules affecting mostly the temporo-periorbital skin of elderly individuals. Its exact pathogenesis is unclear but clinicopathologic and histochemical studies suggest that extensive exposure to sun and harsh weather is largely responsible. The pigmented skin is apparently less predisposed.

Case Report

A 70-year-old male presented with yellowish discoloration, atrophy, wrinkles and furrows, closed and open comedones with dark central plug and patulous opening, small cysts, numerous small yellowish papules and nodules over forehead, periorbital and temporal areas for over 15 years (Fig. 1). The skin over nape of neck was thickened and leathery having accentuated markings and furrows in rhomboid configurations. The patient was a farmer and native of a high altitude area. The patient refused for biopsy. After a clinical diagnosis of Favre-Racouchot syndrome, he was prescribed broad spectrum topical sunscreen creams, avoidance of undue sun exposure, and advised to follow up regularly.

Discussion

Favre-Racouchot syndrome occurs in approximately 6% individuals of >50 years of age and predominantly among whites [1]. Heavy smoking and radiation therapy are other reported predisposing factors [2,3]. Apart from temporo-periorbital skin, lateral neck, postauricular areas, earlobes, and forearms may rarely be involved. Although bilateral and symmetrical, one side may predominate presumably from asymmetrical sun exposure [4]. While cutis rhomboidalis nuchae is usual association, actinic keratosis, basal cell carcinoma, squamous cell carcinoma or keratoacanthoma may appear in sun-damaged skin [1]. Although histopathology is seldom required for diagnosis, it characteristically shows epidermal atrophy with significant solar elasotsis and basophilic (actinic) degeneration of the connective tissue in the upper dermis. The sebaceous glands are small in number and size or absent. The dilated pilosebaceous infundibula form loose keratin-filled comedones and follicular cysts lined with fattened epithelium [5]. Favre-Racouchot syndrome may be misdiagnosed as acne (A. vulgaris, A. comedonica or A. papulopustulosa), syringoma, and trichoepithelioma. These patients are young and readily discerning feature is presence of inflammation in acne vulgaris and absence of comedones in others. Colloid milia or sebaceous hyperplasia seen in later years of age can be differentiated by the absence of associated wrinkling, furrowing and other skin changes of Favre-Racouchot syndrome. Pseudoxanthoma elasticum or plane xanthomas are diagnosed on histology. Chemical peels, dermabrasion, comedo extraction, curettage, multi-staged surgical excision, and CO2 laser peel have produced variable cosmetic results [1,6]. Topical application of tretinoin or retinaldehyde alone or in conjunction with above procedures or oral isotretinoin (0.05-0.1 mg/kg) for 4-6 months is beneficial in some patients [1,7]. Retinaldehyde is less irritating than retinoic acid, significantly increases the surface area of elastic and collagen fibers, and reduces the appearance of the sun-damaged skin [7,8]. Sun protection will benefit in preventing progression.

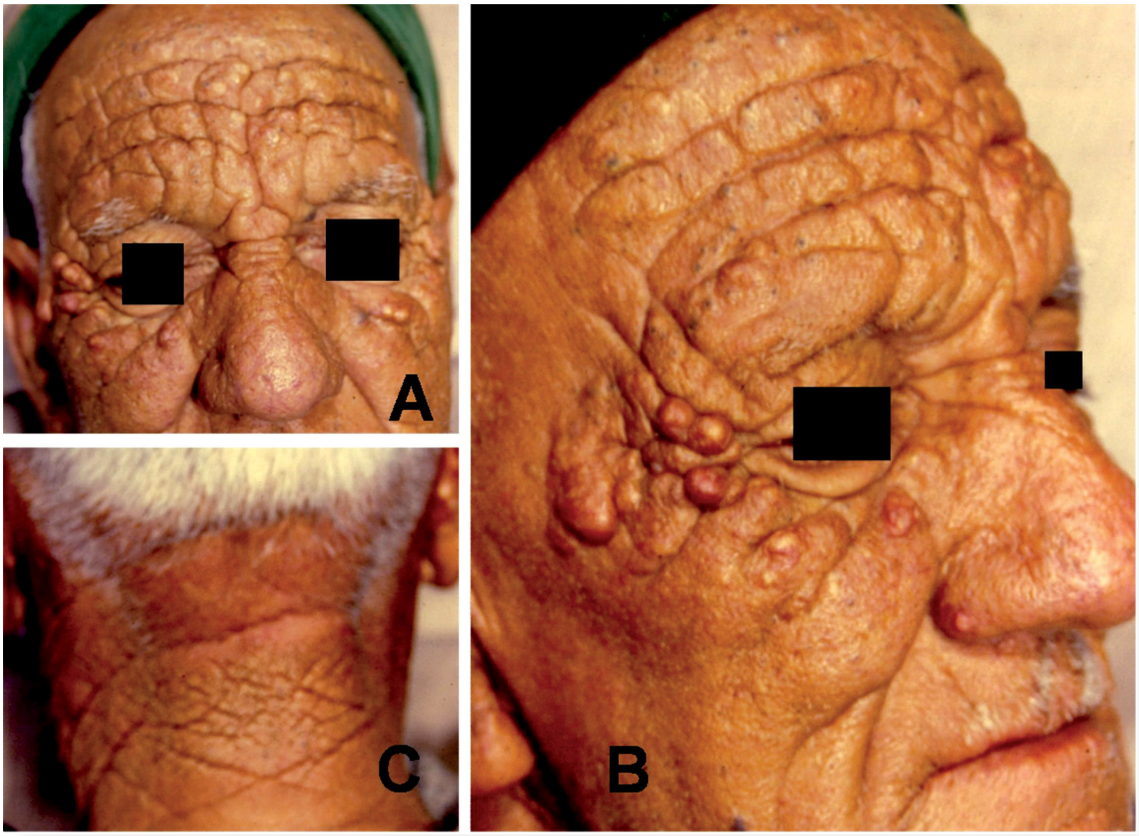

Figure 1A, B. Marked sun-damaged skin with atrophy, yellowish discoloration, yellowish nodules, prominent wrinkles and furrows, multiple, open and closed, non-inflammatory comedones present bilaterally over forehead, periorbital and temporal areas; C. Characteristic thickened, leathery skin of neck with accentuated markings and furrows of Cutis rhomboidalis nuchae.

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LICHEN STRIATUS - CASE REPORTS

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Abstract
Lichen striatus is an acquired linear inflammatory dermatosis, not frequently reported, with a peculiar clinical aspect, most often described in adults, with a poor response to treatment. We described 4 cases of lichen striatus diagnosed over an 8-month period of time.

Key words: lichen; lichen striatus; skin disease

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Introduction

Lichen striatus is a linear inflammatory dermatitis with unclear etiology. It is a self-limiting eruption characterized by pink, tan or hypopigmented small papules distributed in a linear configuration. The diagnosis is based on clinical picture [1-3].
In this report we present 4 cases of Lichen striatus with typical lesions, described in 3 adults and one child, with good evolution and clue for etiology.

Case Report

Case 1.

A 27-year old woman, presented with a 4-week history of pruritus and erythematous papular eruption localized around the left heel. She was on good health status, not on any systemic medications, with no history of atopy.
The clinical differential diagnosis was, at the time of presentation, atypical localization of herpes zoster (serology was negative for varicello-zosterian virus), lichen planus, lupus erythematous and lichen striatus.
A skin biopsy was taken and demonstrated a lichenoid chronic inflammation, perivascular lymphocytic infiltrate, the absence of viral inclusions, so the final diagnosis was lichen striatus.
The patient was treated with potent topical steroids for three weeks and the lesions almost disappeared, with a slight residual erythema and no other complains (Fig. 1, 2).

Case 2.

A 32 year-old female patient was transferred from Rheumatology Department, where she was hospitalized for a suspicion of Rheumatoid Arthritis, with a sudden appearance of pruritus and erythematous papules, in a linear arrangement, distributed on the inner face of left arm. She was not taken any medication, clinically Lichen striatus was suspected. The patient refused the punch biopsy, it was started treatment with topical steroids class II and the patient was transferred back to the Rheumatology Department for further investigations and treatment for Rheumatoid Arthritis (Fig. 3).

Case 3.

A young boy of 13 years old, diagnosed with atopic eczema at the age of 3, came to us for an opinion, regarding a slight hyper pigmentation, with a linear arrangement along the external face of the right arm. He denied any symptoms, he did not remember the day when he had observed the lesions and he could not tell if they were erythematous at the beginning. No other complains, very good clinical health state, no medication, no allergies, all led us to the suspicion of Lichen striatus late phase. We recommended no medication just emollients) for and in 6 weeks after the initial presentation the hyperpigmentation faded away (Fig. 4).

Case 4.

A 45-year old man, in a good condition, presented with erythematous papular eruption and pruritus on the anterior face of left leg, appeared a few months prior to the presentation.

The patient has been seen several times before by different physicians, he had a well established diagnosis of Lichen striatus (confirmed by skin biopsy) and he has tried many different therapeutics schemas, with no improvements: topical steroids for many months, antihistamines orally, antibiotics orally, topical topical application of 0.1% tacrolimus ointment twice daily, topical calcineurin inhibitors; UVB short wave was our therapeutic option, but with no results after 30 seances. We stopped any therapeutically effort and we saw him again in 4 months with the same aspect (Fig. 5).

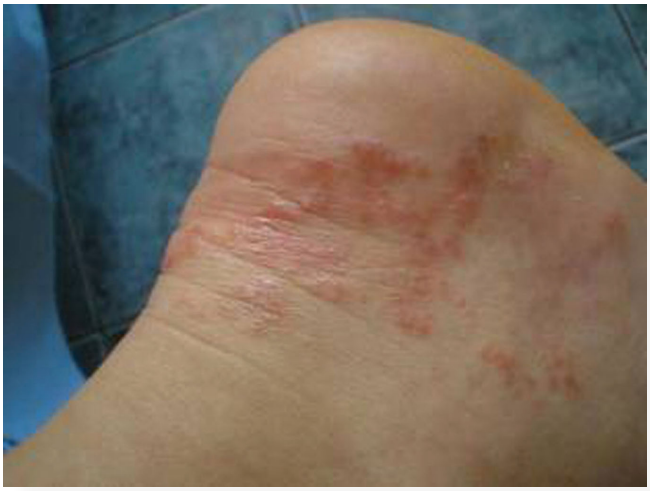

Figure 1. Clinical aspect before treatment

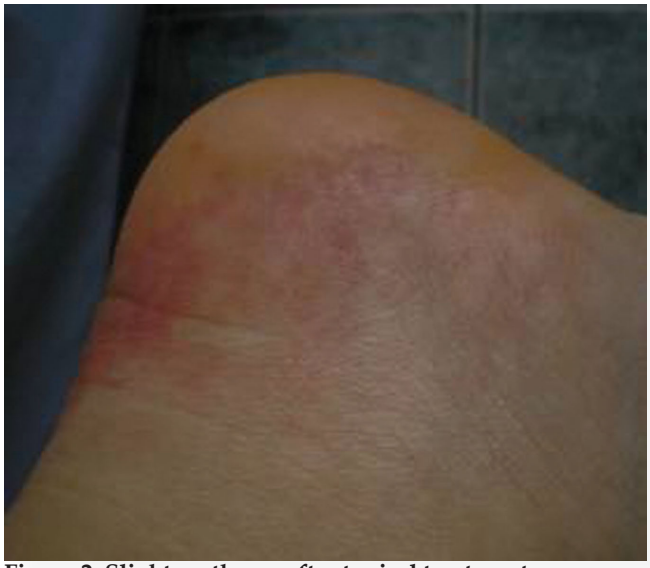

Figure 2. Slight erythema after topical treatment

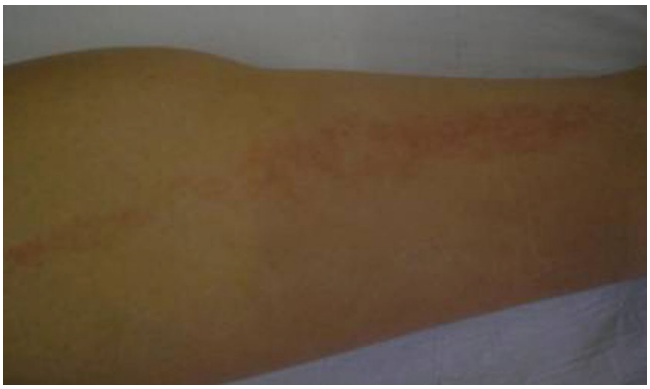

Figure 3. Lichen striatus on the inner face of left arm of a young woman 24 hours after the appearance

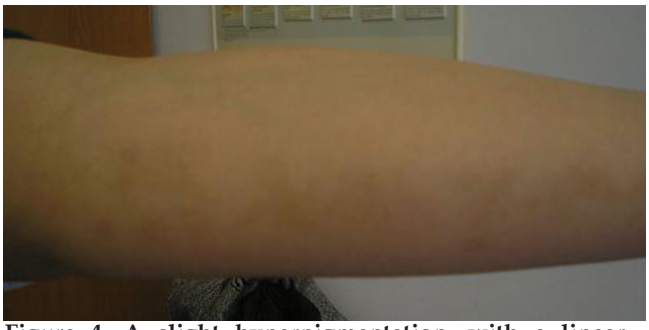

Figure 4. A slight hyperpigmentation, with a linear arrangement along the external face of the right arm: possible Lichen striatus

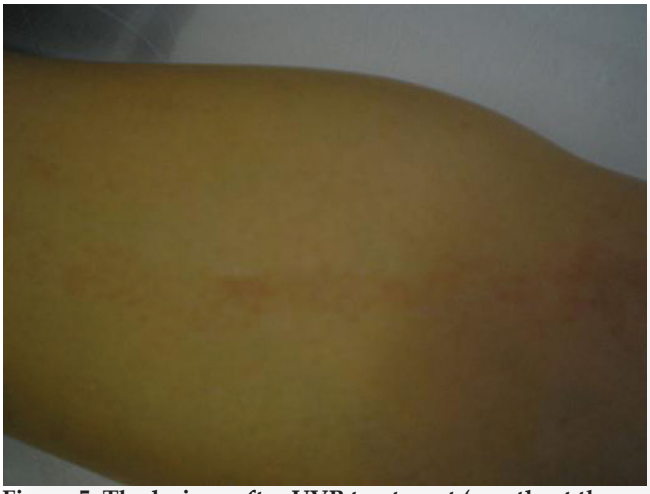

Figure 5. The lesions after UVB treatment (exactly at the beginning of the therapy)

Discussion

Lichen striatus is an inflammatory, linear dermatitis of unknown origin, rarely reported in our country. It is characterized by small (1 to 5 mm), pink, red, tan, or hypo pigmented papules in a linear configuration or Blaschkoid distribution. The etiology remains obscure, although different theories have been proposed: environmental factors, viral infections, cutaneous injury, hypersensitivity acting on a genetic predisposition [4,5].

There is an association between Lichen striatus and atopy which may contribute to its pathogenesis, multiple studies report an increased incidence of lichen striatus in those with atopic family histories (asthma, allergic rhinitis, atopic dermatitis [6].

The appearance of lichen striatus that follows the lines of Blaschko suggests a postzygotic somatic mutation [7-9].

It is more often described in children (especially 5-15 years old), both sexes being equally afflicted, although some studies favor the females [4].

Lichen striatus is a clinical diagnosis; in a doubtful situation skin biopsy is needed o rule out other lichenoid dermatoses (especially lichen planus) [1].
In most cases it is a self limiting disease or with a good response to topical treatments [1,10].

Conclusions

We describe 4 cases, with classical aspects and easy diagnosis, occurred on different anatomic sites, different ages of patients, no causes identified, with good response to treatment or self limiting course and one case with no response and long lasting evolution.

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ERYTHEMA NODOSUM REVEALING *ACUTE MYELOID LEUKEMIA*

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Abstract
Introduction: Erythema nodosum (EN) is the most common type of panniculitis. It may be idiopathic or secondary to various etiologies. However, the occurrence of erythema nodosum in malignant hemopathy had rarely been reported.
Case report: A 42 year-old woman presented with a four week history of recurrent multiple painful erythematous nodules developed on the lower limbs associated with arthralgia of the ankles and fever. The clinical features of skin lesions with contusiform color evolution allowed establishing the diagnosis of EN. No underlying cause was found. The skin lesions were improved with non-steroidal anti-inflammatory drugs and colchicine. Three months later, the patient consulted for recurrence of EN associated with fever, inflammatory polyarthralgia and hepatosplenomegaly. The peripheral blood count revealed pancytopenia. A bone marrow examination confirmed the diagnosis of acute myeloid leukemia type 2. Initiation of chemotherapy was followed by the complete disappearance of skin lesions of EN.
Conclusion: Paraneoplastic erythema nodosum is a rare entity. In the literature, a few cases of association with leukemia have been reported. Exploration for solid neoplasms or hemopathy in case of recurrent EN or resistance to conventional treatment should be systematic.

Key words: erytema nodosum; malignant homeopathy; leukemia

Cite this article:
Chebbi Wafa, Ajili Faida, Boussetta Najeh, Abderrezak Fatma, Othmani Salah, Sfar Mohamed Habib: Erythema nodosum revealing acute myeloid leukemia. Our Dermatol Online. 2013; 4(3): 333-334.

Introduction

Erythema nodosum (EN) is a septal nodular panniculitis, characterized by a sudden onset of painful nodules, most often on the lower limbs. The lesions show spontaneous regression, without ulceration, scarring, or atrophy, and recurrent episodes are uncommon. Cutaneous biopsy is not essential to diagnosis of EN .It may be an idiopathic entity or secondary to multiple causes (Infectious diseases, sarcoidosis, rheumatologic diseases, inflammatory bowel diseases, medication reactions, autoimmune disorders, pregnancy, and malignancies) [1]. Hematologic malignancies, particularly leukemia, are rarely implicated in the occurrence of EN [2,3]. We report a rare case of acute myeloid leukemia revealed by an EN.

Case Report

A 42 years old woman with no past medical history was hospitalized in July 2011 for painful erythematous nodules on the lower limbs, with contusiform color evolution associated with arthralgia of the ankles. The patient reported that at first, the nodules had red color. Within a few days, they become purplish to exhibit a yellow and greenish appearance within 4 weeks. There were no drug intakes, transit disorders or recent infection.

In Physical examination, she had fever of 38° C and symmetrical, tender, erythematous, warm nodules and raised plaques of 20 to 40 mm of diameter, painful on palpation and located in the anterior surfaces of the legs and extensor surfaces of the knees. The existence of painful inflammatory nodules of the lower limbs, with contusiform color evolution allowed establishing the diagnosis of EN.

Laboratory tests showed an erythrocyte sedimentation rate of 90 mm in the first hour, a C-reactive protein of 20 mg/l, a rate of fibrinogen to 3.8 g/l. Blood count, liver and renal functions were normal as well as the chest x-ray. The search for an infectious disease (blood cultures, research of Koch bacillus in blood and urine, intradermal tuberculin test, serology: antistreptolysin O, cytomegalovirus, brucellosis, chlamydia, hepatitis B and C, mycoplasma pneumoniae, rickettsia and HIV) was negative. There was no argument in favor of sarcoidosis, Behçet's disease or inflammatory bowel diseases. The patient was treated with nonsteroidal anti-inflammatory associated to colchicine and EN resolved within 3 weeks. Three months later, the patient was readmitted for a new surge of EN associated to 10kg weight-loss, asthenia and a diffuse inflammatory polyarthralgia.

Physical examination objectified a erythematous nodules, symmetrical and sensitive to palpation located in the lower limbs (Fig. 1) with hepatosplenomegaly. There was no lymphadenopathy. The blood count showed pancytopenia combining leuco-neutropenia (white blood cells at 1200 elts / mm3 and 460 elt/mm3 of neutrophils), anemia to 7.8 g / dl and thrombocytopenia (77000 elts/mm3). The bone marrow objectified infiltration (42%) by blast cells with irregular nucleus and fine nucleated chromatin. The cytoplasm was granular, sometimes with sticks of Aueur bodies . This aspect was in favor of acute myeloid leukemia type 2 according to the International French-American-British classification (FAB). Initiation of chemotherapy was followed by the complete disappearance of skin lesions of EN.

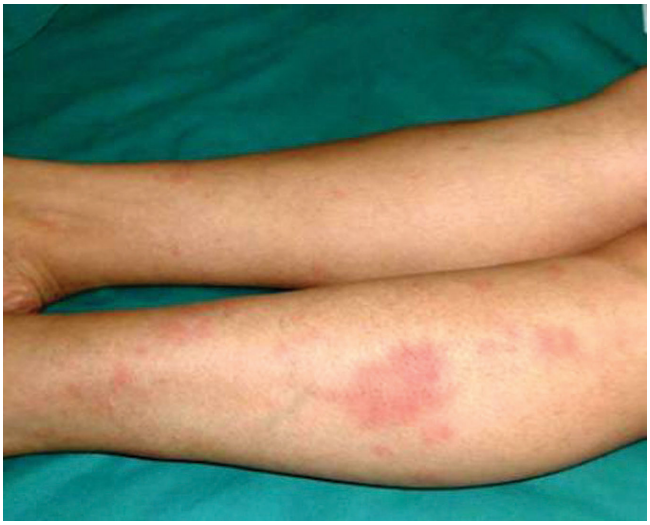

Figure 1. Typical eruption of erythema nodosum along the top surfaces of the lower legs in our patient

Discussion

In leukemia, cutaneous manifestations may be specific by leukemic infiltration or not. The non-specific lesions include mucitis secondary to chemotherapy, hemorrhagic manifestations secondary to homeostasis disturbances and infections due to immunosuppression [4]. Paraneoplastic cutaneous syndromes are rarely observed (erythema multiforme, leukocytoclastic vasculitis, pyoderma gangrenosum, Sweet syndrome and EN) [5].

In our case, we report a satellite cutaneous manifestation rarely described in leukemia. In fact, leukemia does not appear among the common causes of EN reported in large series [6,7] and inversely, EN is not described among the cutaneous manifestations in patients with leukemia [8]. Until today, only a few cases of EN occurring during leukemia have been reported in isolated cases [2,3,9-14]. Usually, the EN precedes leukemia from 1 to 12 months, but it could occur during the evolution of this malignancy [11]. In our patient, the diagnosis of leukemia was established during the second wave of EN and after a time course of 3 months.

The morphology, histologic type and distribution of skin lesions are similar in both paraneoplastic EN and EN of other or idiopathic etiology; however, it is distinguished by its recurrence, like in our patient, and its poor response to conventional therapy. As reported in the literature [2,3,9,11-14], the specific treatment of leukemia had allowed the recovery of EN. Recurrence of EN lesions announces the recurrence of the malignancy [10].

The simultaneous occurrence of EN and leukemia, the absence of other possible causes of EN, the resistance of skin lesions to conventional treatments, their disappearance under chemotherapy and after the remission of leukemia suggests a causal link.

Conclusion

The paraneoplastic EN is a rare entity. In the literature, a few cases of association with leukemia have been reported. Exploration for solid neoplasms or hemopathy in case of recurrent EN or resistance to conventional treatment should be systematic.

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PRIMARY CUTANEOUS NK/T CELL LYMPHOMA-NASAL TYPE WITH *CUTANEOUS ASPERGILLOSIS*. A CASE REPORT AND LITERATURE REVIEW

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Abstract
We report a 66-year-old male who presented with a blackish discolored ulcerated nodule over the right flank of 2 months duration. Biopsy of the lesion revealed ulcerated epidermis with fungal hyphae of Aspergillus overlying dense, angiocentric atypical lymphoid infiltrate involving the dermis, and extending into sub cutis with geographic areas of necrosis. The patient had three episodes of cutaneous recurrence over a three year period. The cutaneous lymphoid infiltrates showed similar immunohistochemical profiles: LCA+, CD3€+, CD20- and CD56-. CD30 was positive in a small percentage of cells. P53 proliferation marker was strongly positive. There was no evidence of systemic involvement by the neoplastic lymphoid and fungal infiltrates. This is one amongst the rare reports of cutaneous aspergillosis with primary cutaneous NK/T cell lymphoma nasal-type.

Key words: NK/T cell lymphoma; skin; aspergillosis

Cite this article:
Geetha Krishnanand, Vidya Monappa, Anuradha C.K. Rao: Primary cutaneous NK/T cell lymphoma-nasal type with cutaneous aspergillosis. A case report and literature review. Our Dermatol Online. 2013; 4(3): 335-338.

Introduction

Nasal-type NK/T cell lymphoma presenting in the skin is a highly aggressive tumor with a mean survival of less than 12 months [1,2]. The WHO-EORTC classification for cutaneous lymphomas describes it as extranodal NK/T cell lymphoma-nasal type [1].

Cutaneous aspergillosis is infrequent and occurs as primary (direct inoculation) or secondary infections (direct extension from adjacent foci or hematogenous dissemination) [3,4]. Reports in literature have described cutaneous aspergillosis in more than 50 cancer patients with leukemia being the commonest underlying malignancy.

In this report, we describe a case of primary cutaneous NK/T cell lymphoma-nasal type with the unusual association of primary cutaneous aspergillosis.

Case report

A 66-year-old-male (farmer), presented with a blackish discolored ulcerated nodule over the right flank with a single enlarged left axillary lymph node. Laboratory investigations revealed peripheral blood eosinophilia (21%), ESR (36mm/1st hr), serum uric acid (5.3), LDH (47.5), alkaline phosphatase (59). Biopsy from skin lesion suggested lymphoma with aspergillosis. Chest x-ray, computerized tomography scan of thorax and abdomen revealed a single 1x1 cm lymph node anterior to arch of aorta with no other abnormality. Excision biopsy of lymph node showed reactive changes. Patient was subjected to wide local excision of right flank lesion followed by local radiotherapy. He received weekly intra-muscular methotrexate 50mg for four weeks; later patient discontinued treatment.

Ten months later the patient developed another swelling on right middle thigh. One month afterwards he had another swelling over right frontal region. Wide excision biopsy of both lesions suggested tumor recurrence. Bone marrow aspiration and biopsy ruled out systemic involvement of the lymphoma.

He returned one year later with progressive swelling in left flank region. On local examination superficial erythematous swelling measuring 5x5 cms on left flank/lumbar region was seen. Another subcutaneous 1x1cm papular lesion was observed over sternal head of left clavicle. Bone marrow aspiration and biopsy revealed no involvement by tumor. Peripheral smear showed eosinophilia (25%). Serum LDH was 844 and ESR was 40mm/hr. The patient received local radiotherapy and has been adviced weekly methotrexate injections. He has been on regular follow-up since then.

Pathological Findings

Gross specimen of Rt. Flank lesion consisted of skin covered oval mass of tissue measuring 5x4.5x1cm, with a surface ulcer covered by necrotic skin. On cut section blackish discoloured area seen infiltrating into the subcutaneous tissue.

Hematoxylin and eosin stained sections of the initial skin biopsy revealed partly elevated ulcerated epidermis with fungal hyphae. Fungal stains revealed narrow based, septate hyphae showing acute angle branching (Fig. 1). Dermis showed nodular, angiocentric and angiodestructive and periadnexal, atypical lymphoid infiltrate of a mixed population of large cells with vesicular nucleus, prominent nucleolus and moderate amounts of cytoplasm along with cells with cerebriform nucleus, mature lymphocytes, histiocytes, eosinophils and epithelioid cells (Fig. 2, 3). Epidermotropism, brisk mitotic activity, extension into subcutaneous fat and geographic areas of necrosis were the other features observed. Immunohistochemical (IHC) analysis revealed a predominant population of LCA+, CD3€+ T cells (Fig. 4) admixed with few CD30+ cells (Fig. 5) and CD20+ B cells in the background. CD56 however was negative in the tumor cells. p53 proliferation marker was strongly positive in the neoplastic lymphoid population (Fig. 6).

Excision biopsy of axillary lymph node showed reactive changes with sinus histiocytosis and vascular transformation of sinuses. Subsequent excision skin biopsies revealed similar histological and IHC features, with no evidence of aspergillosis.

Bone marrow aspiration and biopsy performed on all occasions showed no evidence of involvement.

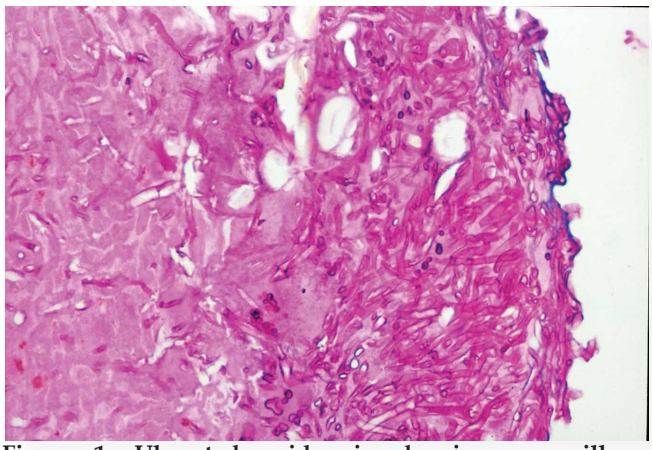

Figure 1. Ulcerated epidermis showing aspergillous hyphae. (PASD, 400x)

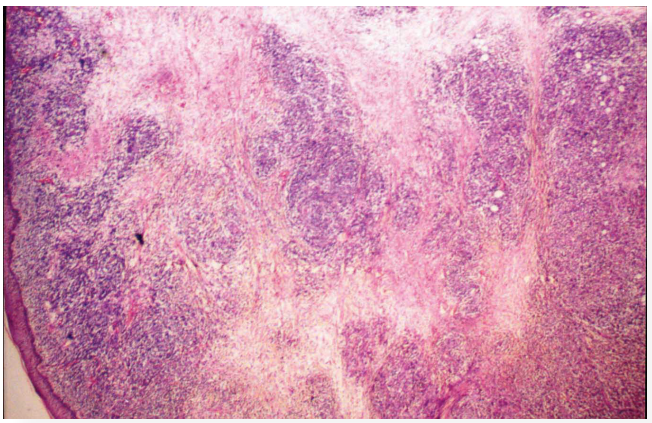

Figure 2. Dermis showing nodular perivascular neoplastic lymphoid aggregates with geographic areas of necrosis. (H&E, 40x)

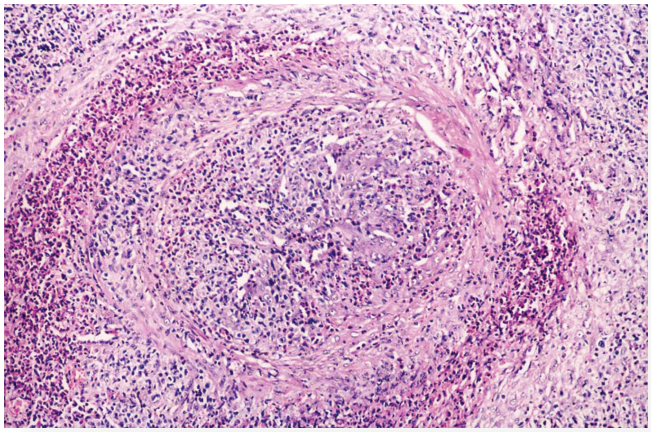

Figure 3. Angiocentric, angioinvasive proliferation of neoplastic lymphoid cells. Eosinophil aggregrates seen. (H&E, 400x)

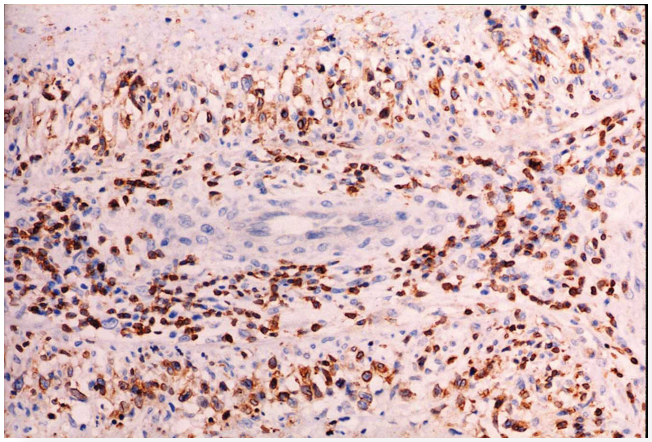

Figure 4. € CD3 cytoplasmic positivity in neoplastic cells. (400x)

Discussion

Extranodal natural killer T (NK/T) -cell lymphoma, nasal-type, is a recently recognized distinct entity within the WHO classification of lymphoid tumors [8]. They show male predominance [6], have a higher frequency of T cell rather than NK cell phenotype and are less associated with EBV [7].

The skin is the most common extranodal site of involvement, and could be either primary or secondary manifestation of the disease. Other sites of involvement as reported in the literature include endometrium [9], breast following renal transplantation [10], skeletal muscle [11], testis [12] gastrointestinal tract, lung [13], soft tissue, spleen [5], kidney, upper respiratory tract and rarely, the eye/orbit [7].

It is an aggressive neoplasm that often pursues a rapidly progressive course, with additional sites of disease appearing within weeks to months. The new sites of involvement are also mostly extranodal and similar to the predilection sites at presentation [5]. Extracutaneous involvement at the time of presentation is associated with a poorer prognosis. The present case had 3 cutaneous recurrances over a span of 3 years.

This lymphoma is more common in Asia, Central and South America. Patients are adults presenting with multiple plaques or tumors on the trunk or extremities. Ulceration and systemic symptoms are common.

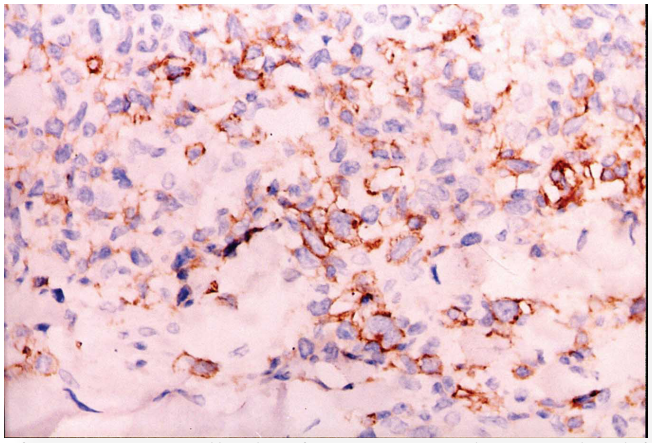

Figure 5. Large cells showing CD30 membrane and golgi zone positivity. (400x)

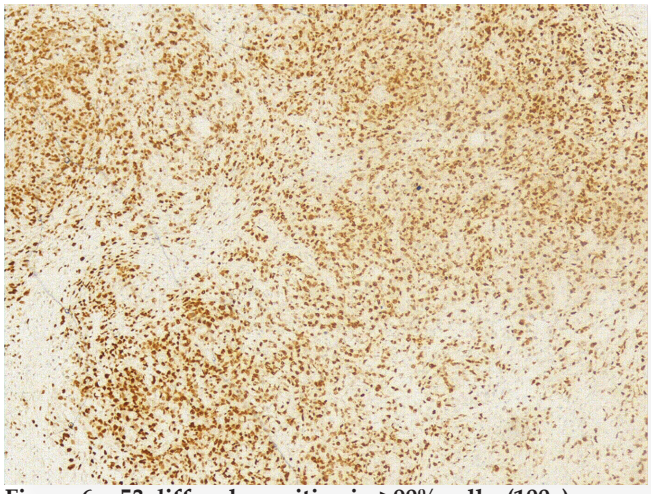

Figure 6. p53 diffusely positive in >90% cells. (100x)

Histologically NK/T cell lymphoma has broad cytologic spectrum with cells ranging from small, medium and large to pleomorphic cells [2] with irregular nuclei, dense chromatin and pale cytoplasm. The cells show prominent angiocentric, angiodestructive growth accompanied by extensive necrosis. Some cases are accompanied by heavy inflammatory infiltrate of small lymphocytes, histiocytes, plasma cells and eosinophils as was seen in this case.

Immunophenotypically the neoplastic cells express CD 3€, CD 56, cytotoxic proteins (TIA-1, granzyme B, perforin). Chan et al [8], y observed that the atypical cells of all 11 cases exhibited T-cell markers [15]. Tseng-Tong Kuo reported 1 case which was CD 3€ -ve. A few reports of CD 56 –ve cases have been reported in literature [2]. Patients with co-expression of CD 30 were observed to have a more favourable outcome [3,16]. Quintanilk-Martinez et al, observed a high prevalence of p53 over-expression in their series of 32 cases [17]; p53 was strongly positive in our case.

Several studies suggest association with EBV associated proteins – EBER-1, LMP-1, EBNA-1 [11,13]. Epstein-Barr virus RNA is present in the majority (80-100 %) of nasal NK/T-cell lymphomas and less often in nasal type NK/T-cell lymphomas (15-40 % or more in some series) [15].

The differential diagnosis includes lymphomatoid granulomatosis, blastic or monomorphic NK cell lymphoma/ leukemia, CD56-positive peripheral T-cell lymphoma, and enteropathy-associated T-cell lymphoma [5]. CD 56+ lymphomas involving the skin are rare and extremely aggressive regardless of their histologic presentation and extent of skin involvement. The risk of death is particularly increased in older patients with CD 30- CD4- lymphomas [14].

NK/T cell lymphoma is associated with an increased risk of developing hemophagocytic syndrome; the systemic histiocytic activation presumably results from cytokines or other products released by the lymphoma cells [5].

Treatment modalities include chemotherapy, radiotherapy, surgery or a combination of the above [15]. Kuo T, observed that local irradiation was more effective than chemotherapy alone. They achieved an overall survival of 63.6% at 5 years as estimated by the Kaplan-Meier analysis, which was better than other series [2]. Mechanisms of drug resistance in T/NK lymphomas have included increased expression of the multidrug resistance proteins and p53 [16]. Multidrug chemotherapy (CHOP regimen) followed by involved field radiotherapy appears to be the most effective treatment approach [19]. Our case was treated with surgery followed by radiotherapy.

A new prognostic model for extranodal NK/T –cell lymphoma, nasal type which included factors like presence of B symptoms, stage, LDH levels and regional lymph node invasion was proposed by Lee et al [20], from their retrospective multicentre study. They divided patients into four different risk groups: group 1, no adverse factor; group 2, one factor; group 3, two factors; group 4, three or four factors. The new model showed superior prognostic discrimination as compared with the International Prognostic Index (IPI).

Cutaneous aspergillosis occurs relatively less frequently and therefore remains poorly characterized. *A. fumigatus* and *A. flavus* are the most frequent causes of cutaneous aspergillosis [3]. Primary cutaneous aspergillosis usually involves sites of skin injury, namely, at or near intravenous access catheter sites, at sites of traumatic inoculation, and at sites associated with occlusive dressings, burns, or surgery. Secondary cutaneous lesions result either from contiguous extension to the skin from infected underlying structures or from widespread blood-borne seeding of the skin [4].

Reports in the literature have described cutaneous aspergillosis in more than 50 cancer patients most of whom had leukemia as the underlying oncologic diagnosis. In greater than 85% of cancer-related cases, primary cutaneous aspergillosis was associated with intravenous catheters, arm boards, or tape securing arm boards [4].

Julin et al [3], reported a case of cutaneous aspergillosis in a patient with cutaneous T-cell lymphoma. As in our case, underlying lymphoma was the major contributing factor which was facilitated by the poor local blood circulation and breach of overlying epithelium .

Review of the literature suggests that this is the very first case of primary cutaneous aspergillosis with extranodal NK/T cell lymphoma-nasal type.

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PRIMARY CUTANEOUS NK/T CELL LYMPHOMA-NASAL TYPE WITH CUTANEOUS ASPERGILLOSIS. A CASE REPORT AND LITERATURE REVIEW

by Geetha Krishnanand, Vidya Monappa, Anuradha C.K. Rao

comment:

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Małgorzata Sokołowska-Wojdyło: comment: Primary cutaneous NK/T cell lymphoma-nasal type with cutaneous aspergillosis. A case report and literature review. Our Dermatol Online. 2013; 4(3): 339-340.

Very interesting case published in Krishnanand G. et al has touched the problem of lymphoproliferation on many levels. It has illustrated the need to remain vigilant in the diagnosis of both proliferative and infectious skin conditions. Extensive necrosis and purulent inflammation may frequently be dismissed as an infectious or benign inflammatory process in case of lymphoma. Extremely rare coincidence of aspergillosis and NK/T cell lymphoma was described just two times before (pubmed database). Relation to HIV infection was noted in one publication and patient died because of oportunistic infection because of invasive aspergillosis after tumor recurrence [1]. What more, in between described by European Organization for Research and Treatment of Cancer/Mycosis Study Group (EORTC/MSG) 2,821 patients with other hematological malignancies (including 597 who had undergone HSCT) the aspergillosis was diagnosed in 23 cases only (pulmonary one, fatal in the course in most of cases) [2]. The case of Krishnanand G. et al is even more interesting because aspergillosis was probably cut out by wide local excision and there were no recurrence in spite of introduction of metotrexate and lack of antifungal treatment. This need a comment of experienced microbiologist.

Affected by NK/T cell lymphoma, nasal type patients typically present with nonspecific rhinitis or refractory chronic sinusitis. But the location not in upper aerodigestive tract can also happened. Ex. between 73 patients published recently by Li S et al [3] 10 had extranasal disease involving skin, small intestine, epiglottis, testis, adrenal glands, kidney, and breast. That is why flank location should not surprise. A correct NK/T cell lymphoma, nasal type diagnosis requires an experienced pathologist, often taking multiple sets of large biopsies. Histologically, angiocentric and angiodestructive growth pattern is frequently present, with fibrinoid changes within blood vessels even in the absense of angioinvasion. Infarction-like coagulative necrosis and admixed apoptotic bodies are very common findings. The angiocentric and angiodestructive features of the tumor cells can mimic a vasculitis, such as Wegener's granulomatosis, what we published before [4]. The typical immunophenotype is CD2+, CD 56+, surface CD3-, with cytoplasmic CD3ε+. Cytotoxic molecules are also positive, such as granzyme B, TIA-1, and perforin. EBER in situ hybridization demonstrates virtually all lymphoma cells as positive. But histopathological pattern can be differ, what was revealed by Krishnanand G. et al case. No CD56 antigen expression, as in noted case, is found in 10% cases, no necrosis can be revealed in 8% cases, no angiocentric/angiodestructive growth pattern in more than 30%. But in situ hybridization for Epstein-Barr virus-encoded small RNA should be positive in every case [3]. The etiology of the lymphoma remains not established, however, a strong association with EBV suggests a pathogenic role of the virus [5]. The disease activity can be monitored by measuring circulating levels of EBV DNA, as a high titer of the DNA may suggest extensive disease, unfavorable response to therapy, and poor survival [6]. The use of Fluorine-18 fluorodeoxyglucose positron emission tomography computerized tomography (18-FDG PET-CT) may offer more accurate diagnosis because it may distinguish lymphoma involvement from inflammatory masses [7].

The prognosis in case of NK/T cell lymphomas, nasal type is still poore. It is well known that P-glycoprotein, a product of the multi-drug resistance (MDR1) gene, is expressed on neoplastic cells of that lymphoma. This is a major cause of the refractoriness of the disease to conventional chemotherapeutic regimens containing anthracycline. Some recent studies, however, have identified that L-asparaginase-containing regimens, such as SMILE (steroid, methotrexate, ifosfamide, L-asparaginase and etoposide), are effective for NK/T cell lymphoma, nasal type. Radiotherapy remains effective for the disease [8,9], but is not effective for occult lesion outside the radiation field. The 5-year overall survival (OS) rate using chemotherapy followed by radiotherapy did not exceed 50% [10-12], which was almost the same as that of radiotherapy alone. Radiotherapy followed by chemotherapy was the standard for the limited stage NK/T-cell lymphoma [13,14].

Recently, a strategy of simultaneous chemoradiotherapy was introduced [15,16]. Both studies showed excellent results with 2-year OS of around 80%, but they have not yet shown the advantage over a radiation-first strategy.

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PERIORBITAL NECROBIOTIC XANTHOGRANULOMA WITHOUT *PARAPROTEINEMIA*

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Abstract
Introduction: Necrobiotic xanthogranuloma (NXG) is a rare histiocytic disease which most frequently involves periorbital areas. NXG is associated with paraproteinemia with a ratio over 80%. However, a few cases of NXG without paraproteinemia (isolated NXG) have also been reported.
Main observation: A 58-year-old Japanese woman complained about asymptomatic dermal nodules on the bilateral lower eyelids. The histopathological examination revealed granulomatous inflammation. Paraproteinemia was not detected either in the serum or in the urine. The size of the nodules has been constant, and she has been under careful follow-up without any systemic therapies.
Conclusions: NXG is frequently associated with paraproteinemia, which may develop later. Patients with NXG need careful follow-up including repeated blood tests.

Key words: necrobiotic xanthogranuloma; no paraproteinemia; periorbital lesions

Cite this article:
Taeko Nakamura-Wakatsuki, Toshiyuki Yamamoto: Periorbital necrobiotic xanthogranuloma without paraproteinemia. Our Dermatol Online. 2013; 4(3): 341-343.

Introduction

Necrobiotic xanthograniloma (NXG) is a rare histiocytic granulomatous disease and it is known about the complication of paraproteinuria. However, we can also see NXG without paraproteinuria and sometimes it may develop later. We herein show the case of NXG without paraproteinuria.

Case report

A 58-year-old Japanese woman visited our department complaining of asymptomatic dermal nodules on the bilateral lower eyelids. The size of the nodules had grown gradually during these two years. She had no relevant personal and family histories. A physical examination showed a circumscribed firm dermal nodule on the right eyelid (Fig. 1a). The overlying epidermis was almost normal with slight telangiectasia. On the left eyelid, a relatively well-circumscribed nodule with yellowish surface was also seen (Fig. 1b). Examination by computed tomography (CT) revealed tumorous iso-density lesions on the bilateral lower eyelids, without invasion into zygomatic bones (Fig. 2). Histopathological examination revealed granulomatous inflammation in the upper to deep dermis. The granulomatous lesions were composed of histiocytes, foam cells, lymphocytes and Touton-type giant cells, surrounding degenerated collagen fibers (Fig. 3a, 3b). Immunohistochemical staining showed that the majority of infiltrating cells were positive for CD68. Based on the clinical and histological features, she was diagnosed as NXG. Laboratory findings did not show any indication of abnormalities, such as liver and renal function, and immunoglobulin levels. Serial investigations by serum electrophoresis resulted in no presence of M-protein. Bence-Jones protein was not detected in the urine. She refused either systemic (intralesional and oral) prednisolone or surgical operation. The size of the nodules has been constant, and she has been under careful follow-up.

Discussion

NXG is a rare, progressive histiocytic disease that often occurs in the fifth or sixth decade. The cutaneous lesions begin as yellowish or red-brown papules and nodules which tend to enlarge slowly. Periorbital areas are most frequently involved, and approximately 50% of the patients had ocular symptoms such as burning, itching or pain. Histopathologically, NXG shows granulomatous inflammation in the dermis, composed of foamy histiocytes, lymphocytes, foreign body-type multinucleated giant cells, and Touton-type giant cells alternating with degenerated collagen bundles [1]. Cholesterin crystals are sometimes seen.

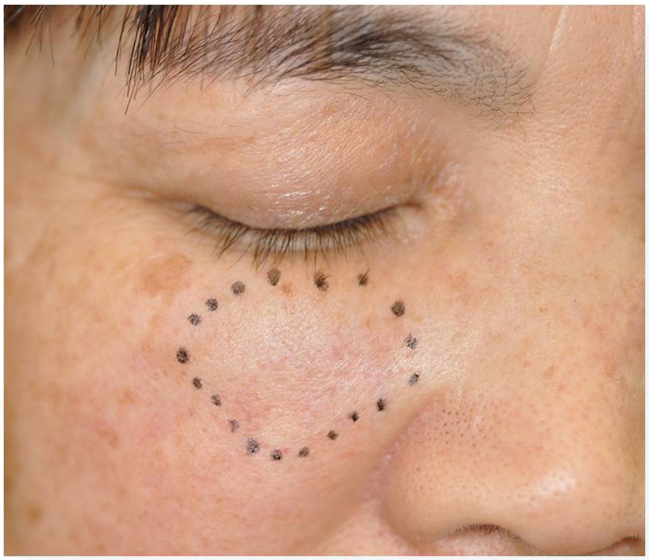

Figure 1a. Border unclear firm nodule with telangiectases on the right eyelid

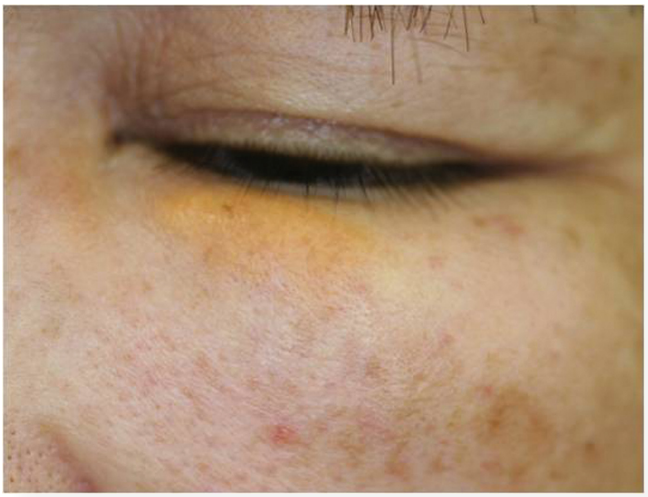

Figure 1a. Yellowish nodule on the left eyelid

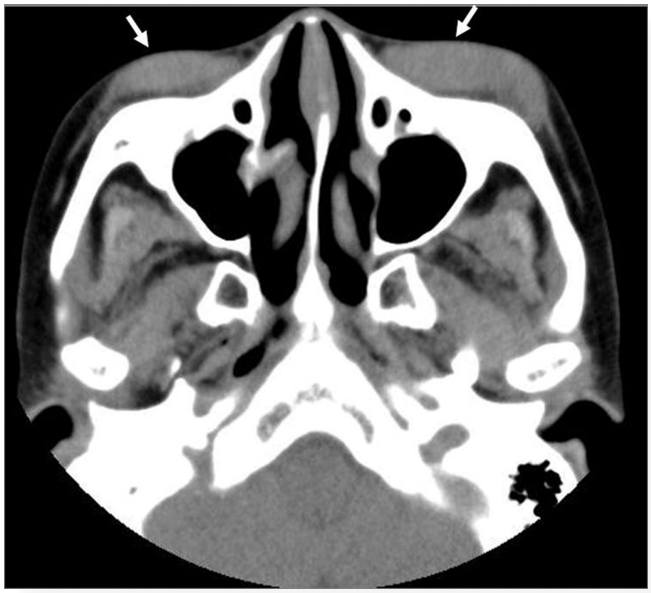

Figure 2. Tumorous lesions on the both lower eyelids (arrow), seen by computed tomography (transverse plane)

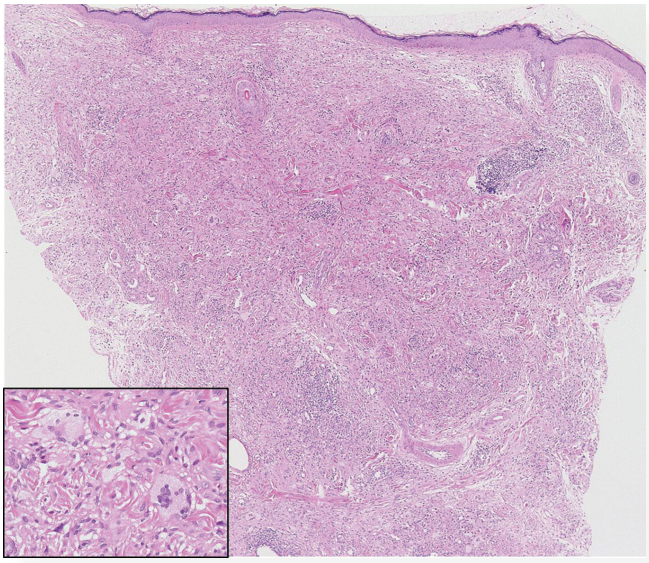

Figure 3a. Granulomatous inflammation is significant in the upper to deeper dermis. Touton-type giant cells are scattered (insert)

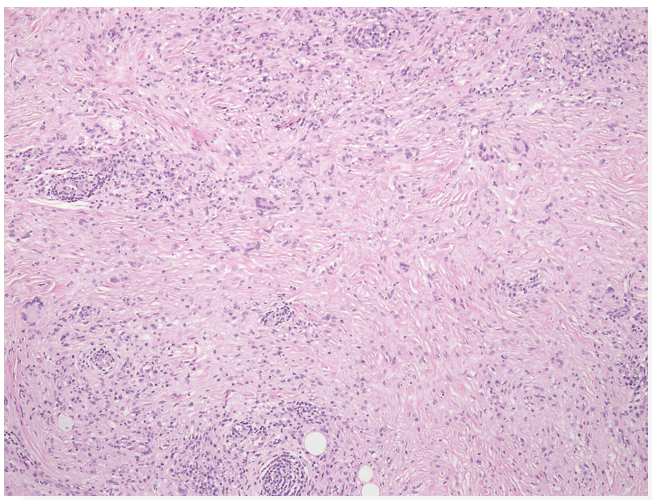

Figure 3a. The granulomas are composed of histiocytes, formy histiocytes, lymphocytes and giant cells surrounding degenerated collagen fibers

Paraproteinemia is closely associated with NXG, and monoclonal gammopathies have been described in approximately 80% of cases. For NXG patients, retrospective analysis indicated that 10-25% of patients with an associated monoclonal gammopathies of undetermined significance may subsequently develop to multiple myeloma and other malignancies such as mycosis fungoides, lymphoma, and leukemia [2]. In addition, we should consider about systemic involvement of NXG including heart, lung and kidney.

The pathogenesis of NXG is still obscure. It was hypothesized that lipid-laden monocytes and immunoglobulins are deposited in the skin and elicited a giant cell inflammatory reaction [3]. On the contrary, M-protein may be the primary abnormality, and skin lesions arise from secondary proliferation of macrophages bearing receptors for Fc portion of their M-protein [4]. Another study identified spirochaetal organism in NXG lesions, suggesting infectious etiology of NXG [5]. Immunohistochemical analysis of 11 cases of NXG showed a polytypic staining pattern in the inflammatory cells and the number of the IgG4 plasma cells was not increased, suggesting that the skin lesions represent reactive inflammation [6]. Treatment of NXG is usually directed to associated hematologic disorders, with chlorambucil, corticosteroids, melphalan, cyclophosphamide, intravenous immunoglobulin, and radiation therapy.

In our case, either paraproteinemia or other associated hematologic disorders were not detected. So far, only a few cases of NXG without paraproteinemia have been reported, [7,8] suggesting that NXG is not always associated with paraproteinemia or malignancies. By contrast, several papers show paraproteinemia might develop after the onset of skin lesions of NXG as long as 12 years [9] or even 20 years [10]. Further, there was a case which presented NXG after the therapy of lymphoplasmacytic lymphoma [11]. Ugurlu et al summarized long-term outcome of 26 cases with NXG and reported that the time to emergence of hematologic disorder varied from 8 to 11 years after the onset of cutaneous lesion [12]. Thus, paraproteinemia may develop later, and patients with NXG need lifelong careful follow-up by repeated laboratory tests.

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FIXED DRUG ERUPTION OF THE EYELIDS. A DERMOSCOPIC EVALUATION

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Competing Interests: None

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Abstract
Fixed drug eruption (FDE) usually appears as a solitary or a small number of pruritic, well circumscribed, erythematous macules that evolve into edematous plaques; these lesions typically resolve after discontinuation of the offending drug, leaving hyperpigmentation at the site of lesions. Fixed drug eruption has been mentioned previously as a disease model for elucidating the mechanism of how skin inflammation is caused by skin-resident T cells, a multistep process that results in eventual tissue damage. In this article we discuss the utility of dermoscopy as an additional tool which gives significant information aiding us to infer these complex processes seen in FDE and thus to confirm the diagnosis.

Key words: dermoscopy; whale shark pattern; fixed drug eruption; histology

Cite this article:
Manuel Valdebran, Rogelio Isao Salinas, Nelly Ramirez, Alba Rodriguez, Leyla Guzman, Silvia Marte, Max Suazo, Esmirna Rosado: Fixed drug eruption of the eyelids. A dermoscopic evaluation. Our Dermatol Online. 2013; 4(3): 344-346.

Introduction

Fixed drug eruption (FDE) usually appears as a solitary or a small number of pruritic, well circumscribed, erythematous macules that evolve into edematous plaques; these lesions typically resolve after discontinuation of the offending drug, leaving hyperpigmentation at the site of lesions. They recur in exactly the same sites when rechallenged with each administration of the offending drug [1]. Although FDE may occur anywhere on the skin or mucous membrane, the most common locations are the lip, palms, soles, glans penis, and groin areas. Discrete lesions often appear in the same bilaterally symmetrical regions of the skin, particularly in the abdominal and the inner aspect of the arms and legs [2].

There have been many reports describing patients with typical FDE who had no significant history of drug intake preceding the eruptions. Some cases of recurrent exacerbations of FDE lesions without significant history of drug intake might be attributable to nonspecific exogenous factors. Nonmedical factors, such as food and ultraviolet irradiation, have been reported to precipitate exacerbations of FDE lesions [3-5].

FDE has been mentioned previously as a disease model for elucidating the mechanism of how skin inflammation is caused by skin-resident T cells, a complicated multistep process that results in eventual tissue damage [6]. This damage results when intraepidermal CD8+ T cells are activated to directly kill surrounding keratinocytes and release large amounts of cytokines such as IFN [gamma] into the local microenvironment. Cytokine or adhesion molecule-mediated nonspecific recruitment of CD4+, CD8+ T cells and neutrophils to a specific tissue site without recognition of their cognate antigen would serve to enhance tissue damage, thereby contributing to the late stages of development of FDE lesions [6,7].

Case Report

A 4-year-old female patient, Fitzpatrick skin type V, presented in our institution by his father with a 5-month history of a dermatosis affecting periocular area bilaterally, asymptomatic. Clinical examination revealed the presence of oval grayish-violaceous hyperpigmented patches around the eyelids bilateral (Fig. 1). A clinical diagnosis of fixed drug eruption was made. Dermoscopy revealed multiple grouped black, brown and in certain areas steel blue dots (Fig. 2). Histology reveals basal cell hydropic degeneration, Lymphocyte tagging along the dermoepidermic junction and perivascular, necrotic keratinocytes, in the upper and reticular dermis abundant melanophages and pigment incontinence (Fig. 3, 4).

Figure 1. Periorbital greyish-violaceous hyperpigmented patches

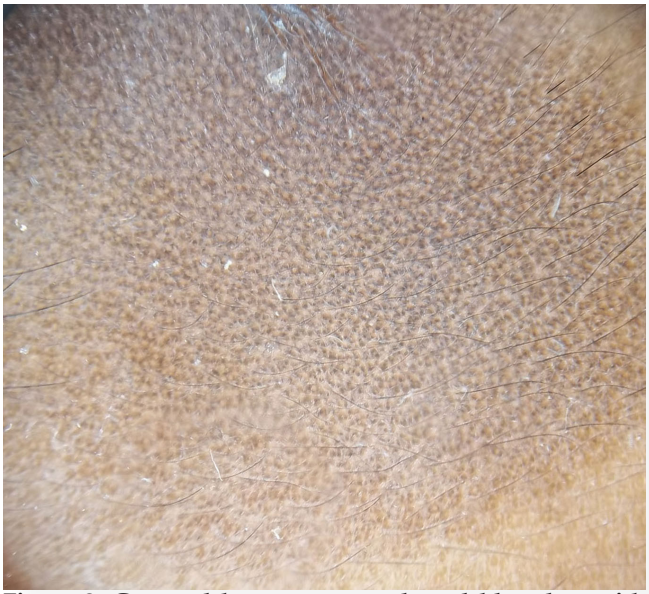

Figure 2. Grouped brown, gray and steel blue dots with perifollicular hypopigmentation in a 4-year-old girl

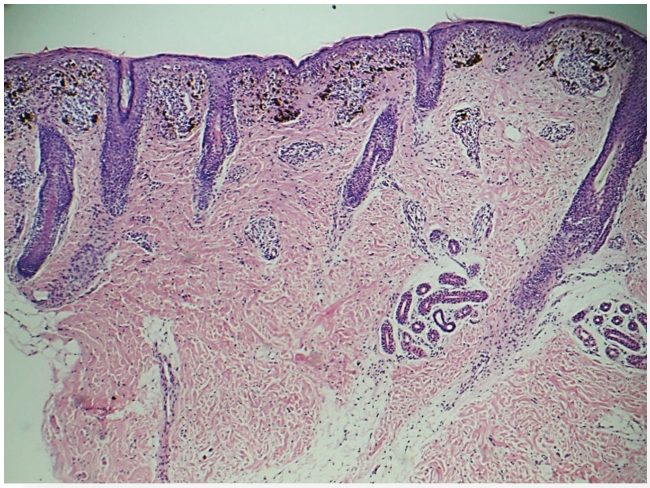

Figure 3. Flat epidermis with vacuolated cells. In superficial and mid-dermis, dense band-like and perivascular inflammatory infiltrate. In follicular and perifollicular areas there is less melanic pigment.

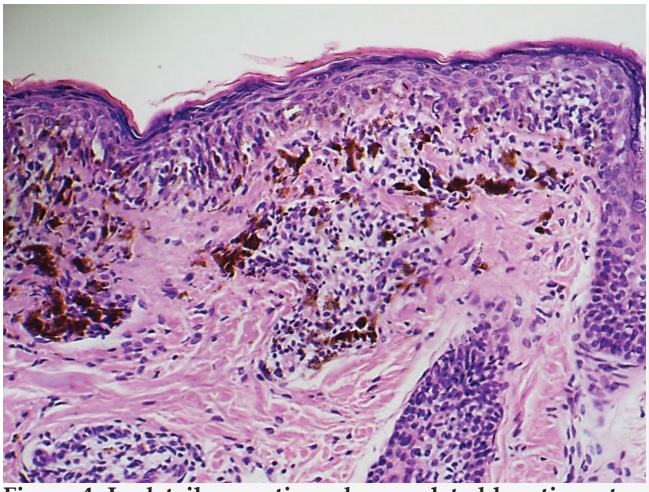

Figure 4. In detail, necrotic and vacuolated keratinocytes. In superficial and mid dermis, dense infiltrate of lymphocytes and abundant melanophages. H&E 20X.

Discussion

Dermoscopy is a noninvasive method that allows the in vivo evaluation of colors and microstructures of the epidermis, the dermoepidermal junction, and the papillary dermis not visible to the naked eye [8,9].

Color variation of melanin depends on its location in the skin. In the stratum corneum and upper epidermis, melanin is jet black; in the basal layer and dermoepidermal junction, it is brown; in the papillary dermis it is blue-gray; and in the reticular dermis it is steel blue. Due to the Tyndall effect, in which short-wavelength visible light (blue) is dispersed and reflected more than long-wavelength light (red), the blue color of otherwise black melanin is explained by the depth of the pigment deep in the dermis (Fig. 5) [10].

These group of structures and colors describe patterns of presentation and are characterized by specifically correlated to histologic features.

In the dermoscopy of the patient (Fig. 2) we observe black dots, light-to-dark brown dots, and steel blue. All this images grouped in a pattern that reminds the image of a whale shark (Fig. 6).

Dermoscopy in this case gives us an approximation of the histology, in which multiple dots colored form black to blue-gray correspond to melanin deposition not only at different levels of the epidermis but also at different levels of the dermis, that information is crucial since we may assume there has been pigment incontinence and damage at the dermoepidermal junction produced by lymphocyte infiltrate.

We can conclude that proper dermoscopy evaluation can give the dermatologist an additional armamentum when aproaching to different dermatoses. Unconventional use of dermoscopy such in fixed drug eruption is valid and can give the dermatologist an information about what is happening underneath the skin.

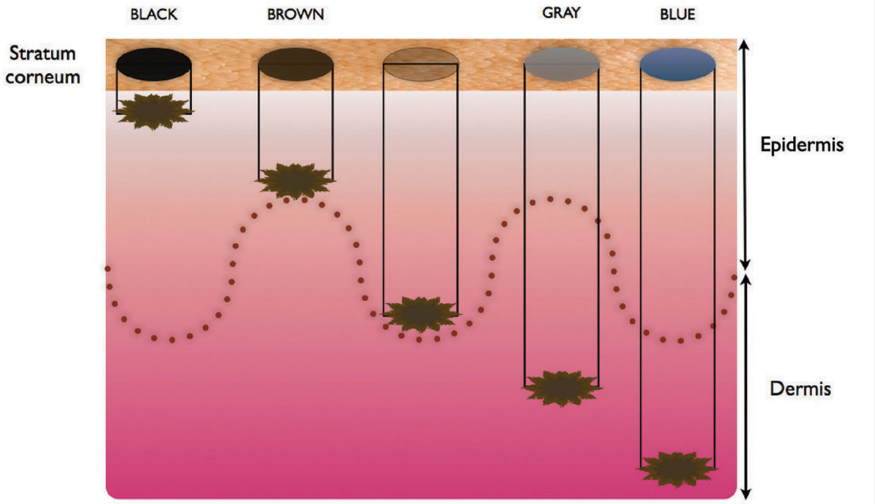

Figure 5. Skin color variations at different melanic pigmentation depths

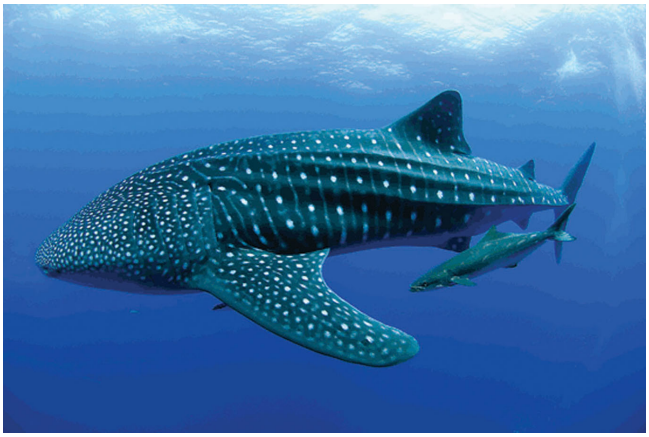

Figure 6. White dots in the surface of a whale shark

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STAPHYLOCOCCAL SCALDED SKIN SYNDROME MIMICKING *TOXIC EPIDERMAL NECROLYSIS* IN A HEALTHY ADULT

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Abstract
Introduction: Staphylococcal scaled skin syndrome (SSSS) presents generalized form bullous impetigo caused by *Staphylococcus aureus* (*S. aureus*) infection, typically seen in infants and children. SSSS may occur also in adults; however, the majority of adult cases are those with immunosuppression. Atypical clinical features of impetigo in adults sometimes make it difficult to diagnose correctly.
Case Report: A 74-year-old healthy woman was hospitalized, complaining of extensive desquamative erythema and a number of erosions. She was administered oral antiviral drugs under suspicion of herpes zoster prior to 10 days. Initial diagnosis on the admission was toxic epidermal necrolysis (TEN) due to antiviral tablets; however, steroid pulse therapy resulted in no effect. Bacterial culture yielded coagulase-positive methicillin-resistent *S. aureus*, producing exfoliative toxin B. A biopsy specimen showed subcorneal splitting of the epidermis. The diffuse erosions gradually improved over 10 days by the treatment with intravenous antibiotics.
Conclusions: The differentiation between streptococcal scaled skin syndrome (SSSS) and TEN is sometimes difficult. It is important to remind SSSS when we suspect TEN, even in healthy adults.

Key words: SSSS; TEN; MRSA; adult

Cite this article:
Tomoko Oishi, Yuka Hanami, Yasunobu Kato, Mikio Otsuka, Toshiyuki Yamamoto: Staphylococcal scalded skin syndrome mimicking toxic epidermal necrolysis in a healthy adult. Our Dermatol Online. 2013; 4(3): 347-348.

Introduction

Streptococcal scaled skin syndrome (SSSS) presents generalized form bullous impetigo caused by *Staphylococcus aureus* (*S. aureus*) infection, typically seen in infants and children. SSSS may occur also in adults; however, the majority of adult cases are those with immunosuppression, overwhelming sepsis, kidney failure, or under immunosuppressive conditions. We herein report a case of SSSS due to methicillin-resistant Staphylococcus aureus (MRSA) in a healthy adult, which mimicked the clinical feature of toxic epidermal necrolysis (TEN).

Case Report

A 74-year-old woman initially visited a practical clinic, complaining of several bullae on the left hip. She was administered oral antiviral drugs under a suspicion of herpes zoster. However, erythema and erosions appeared and spread rapidly all over the body. She visited an emergency room of another hospital 10 days later. Then, she was prescribed oral prednisolone (30mg daily) under a diagnosis of drug eruption, and referred to our hospital on the next day. On physical examination, there were broad erosions around her left hip and lower abdomen with a background of systematic erythema including her face (Fig. 1). Bulbar conjunctival hyperemia was seen. Nikolsky sign was positive on her back skin. She had no special past health histories and there were no significant laboratory findings expect for a slight degree of hypoproteinemia (TP 6.2g/dl, Alb 3.2g/dl) and inflammatory reaction (CRP 2.51mg/dl). Under suspicion of TEN due to antivirus tablets, we started a steroid pulse therapy with gamma globulin, which however resulted in no effects. Histological examination revealed splitting at the level of the granular cell layer (Fig. 2), without inflammation in the dermis. Bacterial cultures from skin erosion yielded coagulase-positive MRSA, producing exfoliative toxin B. Neither toxic shock syndrome toxin-1 (TSST-1) nor enterotoxin was detected. The diagnosis of SSSS was made, and antibiotics (teicoplanin (Targocid^{R}); 200 mg/day for 5 days followed 400mg/day for 4 days) were administered. Because she developed drug eruption, antibiotics were changes to vancomycin (1g/day for 2 days). All eroded surface epithelized in 2 weeks.

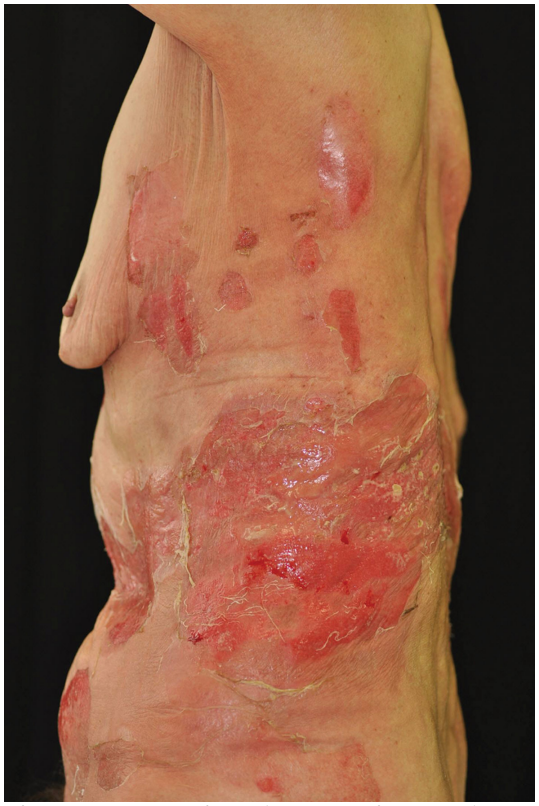

Figure 1. Extensive desquamative erythema, erosions, and scales on the trunk

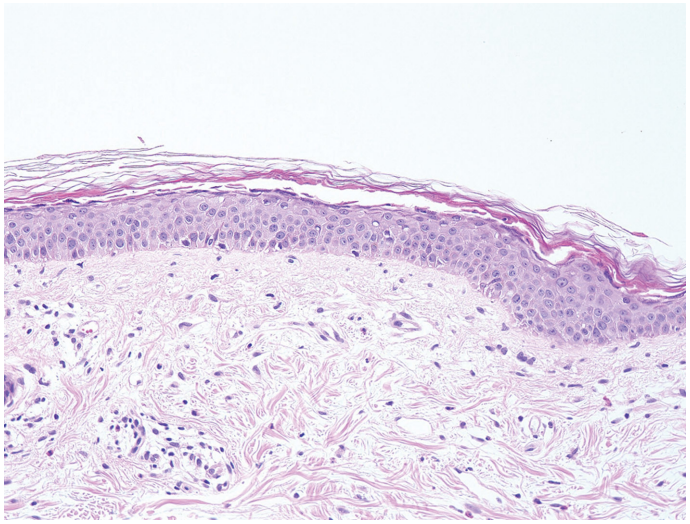

Figure 2. Histopathology showing cleavage in the upper epidermis. (H&E stain, X200)

Discussion

SSSS is an extensive exfoliative dermatitis caused by *S. aureus* infection. The blisters in SSSS is caused by exfoliative toxin (ET) released by *S. aureus*, occasionally by MRSA [1,2]. S. aureus infection results in a loss of keratinocyte cell-cell adhesion through desmoglein-1, leading to blister formation [3]. SSSS usually occurs in children, and is rarely seen in healthy adults [4-6]. SSSS in adults frequently occur in association with kidney failure, malignancy, and immunosuppression [7]. Although our case was an elderly female, she did not either present a prior condition for SSSS such as burn, wounds, or had diabetes, renal failure, or other immunosuppressive conditions. Our case presented diffuse erosive erythema with Nikolsky sign, following intake of antiviral drugs under a misdiagnosis of herpes zoster. Therefore we initially suspected TEN because the patient was healthy adult and had no significant past health history. However, a steroid therapy resulted in no effect and histology examination also denied TEN. Differentiation between TEN and SSSS is sometimes difficult. Nikolsky sign is not specific for TEN. Examination by histological examination by immediate cryosections, Tzank test, and blister roof histology may be useful as rapid tools. In SSSS, blister roof histology shows that the epidermal cleavage is within the stratum granulosum [8].

Conclusion

It is important to remind SSSS in cases suspecting TEN even in healthy adults, because the treatment for both diseases is different and SSSS is still associated with mortality.

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PROGRESSIVE VARICELLA SYNDROME WITH *VARICELLA GANGRENOSA* IN AN IMMUNE-COMPETENT INFANT

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Abstract
Varicella is common and highly contagious and affects nearly all susceptible children before adolescence. Progressive varicella syndrome is a severe complication of primary Varicella Zoster Virus (VZV) infection, with visceral organ involvement, coagulopathy, severe hemorrhage, and continued vesicular lesion development. We report a rare case of progressive varicella syndrome with varicella gangrenosa in a previously well female child of ten months. She presented with history of recurrent vesiculo-bullous skin lesions involving the chest, back and extremities since two months with dry gangrene of 1st, 3rd and right great toe. VZV Polymerase Chain Reaction (PCR) of vesicle fluid was positive. Workup for immunodeficiency state was negative. She responded dramatically to intravenous acyclovir.

Key words: progressive varicella syndrome; varicella gangrenosa; immune-competent

Cite this article:
Sonia Bhatt, Nalini Bhaskaranand, Kashyap Udupa, Meenu Joon: Progressive varicella syndrome with Varicella gangrenosa in an immune-competent infant. Our Dermatol Online. 2013; 4(3): 349-350.

Introduction

Varicella, commonly known as chickenpox, is caused by the varicella-zoster virus and causes primary, latent, and recurrent infections. Varicella is common and highly contagious and affects nearly all susceptible children before adolescence. Infections with varicella-zoster virus (VZV) are usually considered benign infections. However, severe complications including bacterial super infections, coagulopathies, and central nervous system manifestations with a potentially fatal or long term disabling outcome can occur [1,2].

Although most varicella infection confers life-long immunity, clinical reinfections among healthy children have been described [3]. Progressive varicella is a severe complication of primary VZV infection, with visceral organ involvement, coagulopathy, severe hemorrhage, and continued vesicular lesion development [4]. Gangrene of skin and deeper tissues is an unusual complication of varicella. The term varicella gangrenosa has been applied such conditions. However, varicella gangrenosa is a rare complication of this disease, infrequently reported in the literature [5,6].

Very few cases of progressive varicella syndrome have been reported in literature that too in immuno-compromised host. We report a case of progressive varicella syndrome with varicella gangrenosa in an immune-competent female child of ten months.

Case report

A ten month old female baby to us with history of recurrent vesiculo-bullous skin lesions involving the chest, back and extremities since two months with recent progression to palms and perianal area, abdominal distention, tachypnoea, swelling of bilateral lower limbs and discoloration of toes of right foot.

There was no previous history of recurrent infections or recurrent skin lesions; however she had history of vesiculo-bullous lesions in elder sibling four month back. The child was admitted three times elsewhere and treated with multiple antibiotics with inadequate response.

On admission child was lethargic, had multiple confluent hemorrhagic, vesiculo-bullous lesions all over body (Fig. 1), anasarca predominantly in bilateral lower limb with dry gangrene of 1st,3rd and great toe (right) and bilateral crepitations in chest. Investigations revealed normal complete blood count, normal liver functions with low serum albumin (2g/dl) and normal coagulation profile. Blood culture was sterile. VZV Polymerase Chain Reaction (PCR) of vesicle fluid was positive. Chest x-ray was suggestive of bronchopneumonia and Doppler of bilateral lower limbs was normal. Her immunoglobulin levels were normal, Nitro Blue Tetrazolium test (NBT) was normal and P24 antigen assay for HIV was negative.

Patient responded dramatically to intravenous acyclovir. Low molecular weight dextran, Low molecular weight heparin and Pentoxifylline were administered for gangrene. Her general condition improved and her lesions started healing by day five and she was discharged after fifteen days.

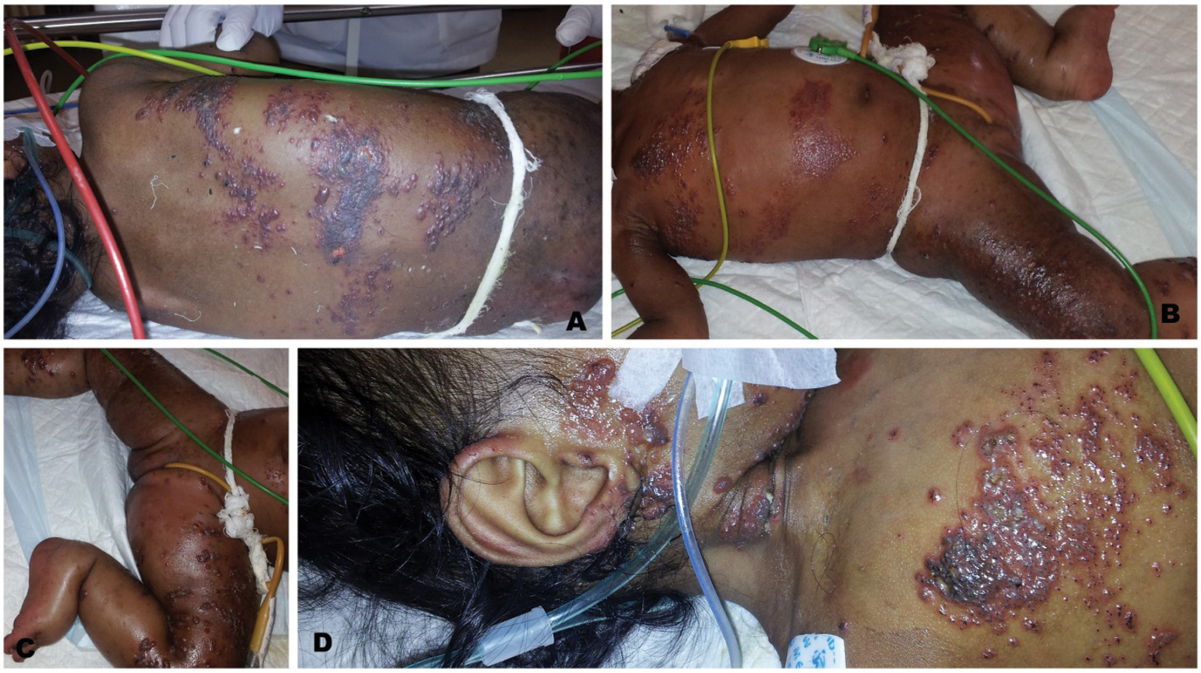

Figure 1. A. Vesiculo-bullous lesions with ulceration over whole back. B. Vesiculo-bullous lesions over thigh, chest and abdomen. C. Edematous lower limbs with lesions. D. Confluenced vesiculo-bullous lesions.

Discussion

Progressive varicella, with visceral organ involvement, coagulopathy, severe hemorrhage, and continued vesicular lesion development, is a severe complication of primary VZV infection [4]. Varicella gangrenosa is a very rare complication [5,6]. Our patient presented with features of progressive varicella along with dry gangrene of toes. Although rare in healthy children, the risk for progressive varicella is highest in children with congenital cellular immune deficiency disorders and those with malignancy [4]. Progressive varicella syndrome has been documented in children with leukemia [7], Wiskott-Aldrich Syndrome [8] and advanced HIV infection, it occurs when the CD4 count is very low [9] and is associated with internal organ involvement such as meningitis, and pneumonitis, which can be fatal. By definition, the skin lesions continue to appear for at least one month. Our patient had skin lesions for two months and was an immune-competent infant. Intravenous foscarnet may be needed for cases that do not respond to acyclovir, however our patient responded well to intravenous acyclovir.

Conclusion

Our encounter with this case highlights that although rare progressive varicella can present in immune-competent child. Prompt diagnosis and treatment with acyclovir leads to complete recovery.

Authors' contributions

SB, NB, KU and MJ were involved in patient management; SB, KU and MJ were involved in manuscript preparation; SB, NB were involved in reviewing the manuscript and final approval.

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CYTOPHAGIC HISTIOCYTIC PANNICULITIS ASSOCIATED WITH *HBE HEMOGLOBINOPATHY* IN A PATIENT WITH *HEMOPHAGOCYTIC SYNDROME*

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Abstract
Introduction: Cytophagic histiocytic panniculitis (CHP) is a rare panniculitis which may occur alone or as a part of systemic manifestation of Hemophagocytic syndrome (HPS). It is described as a chronic histiocytic disorder of the subcutaneous adipose tissue with lymphocytic and histiocytic infiltration showing hemophagocytosis. It may also be noted in bone marrow, spleen, lymph nodes and liver. Treatment includes glucocorticoids, cyclosporine and combined chemotherapeutic medications.
Observation: A 34 years old lady, presented with multiple nodules over the body since 2 years. Hematological investigations revealed that patient had a rare HbE hemoglobinopathy and was treated for that. Skin biopsy showed CHP and subsequently on hematological and biochemical tests, a diagnosis of HPS was given and patient was referred to a hemato-oncologist.
Conclusion: Cytophagic histiocytic panniculitis is a rare and fatal form of panniculitis with multisystem involvement. Awareness of this cutaneous manifestation may help physicians in the early diagnosis of HPS. We report this interesting case of CHP with a brief review of literature. To best of our knowledge this is the first case of Hemophagocytic syndrome associated with HbE hemoglobinopathy.

Key words: cytophagic histiocytic panniculitis; hemophagocytic syndrome; cyclosporine

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Introduction

Winkelmann and Bowie [1] in 1980 described CHP as a rare subtype of panniculitis, histologically characterized by a mixed lobular and segmental panniculitis with a proliferation of benign cytophagic histiocytes exhibiting no nuclear atypia. This may also occur in bone marrow, spleen, lymph nodes and liver [2]. CHP can present as isolated skin lesions or severe systemic involvement as a part of HPS [3]. Hemophagocytic syndrome, initially described by Scott and Robb-Smith [4] is a reactive proliferative disorder which affects the antigen-processing macrophages resulting in uncontrolled hemophagocytosis. We report this unique case where initial diagnosis of CHP helped the physicians to establish the early diagnosis of HPS in this 34 years old lady who presented predominantly with dermatological features. During the course of investigations, on electrophoresis she was found to have HbE hemoglobinopathy. In literature HPS is described to be associated with sickle cell anemias [5]. To best of our knowledge this is the first case of HPS associated with HbE hemoglobinopathy.

Case Report

34 years old lady, came with multiple nodules over the body since 2 years. Nodules were painful, firm, red in color started in the limbs, progressively increased and involved face and abdomen. They were associated with low grade fever and significant weight loss. On examination pallor, generalized lymphadenopathy, non-tender hepatomegaly of 4cms and splenomegaly of 3cms below costal margins were noted. Hematological investigations revealed pancytopenia with Hb of 9.1gm%, normal ESR and hemolytic peripheral smear picture. No hemoparasites were identified. HbE hemoglobinopathy was diagnosed on electrophoresis (Fig. 1).

Bone marrow aspiration and biopsy showed reactive bone marrow with erythroid hyperplasia. Lymph node biopsy revealed sinus histiocytosis with erythrophagocytosis. Mantoux test, ANA profile, chest X-ray, thyroid profile and echocardiography were within normal limits. Bone marrow and blood culture were sterile. She was treated symptomatically with hematinics, improved and was discharged. Patient came 2 months later with similar complaints.

Hematological investigations showed pancytopenia with a Hb of 8.3gm% and deranged coagulation profile. Biochemical tests showed deranged liver function test, reduced fibrinogen and total iron binding capacity. Triglyceride levels, S. ferritin and S. LDH were increased. Serological tests for Hepatitis A, B and C, HIV were negative. PCR for tuberculosis was negative.

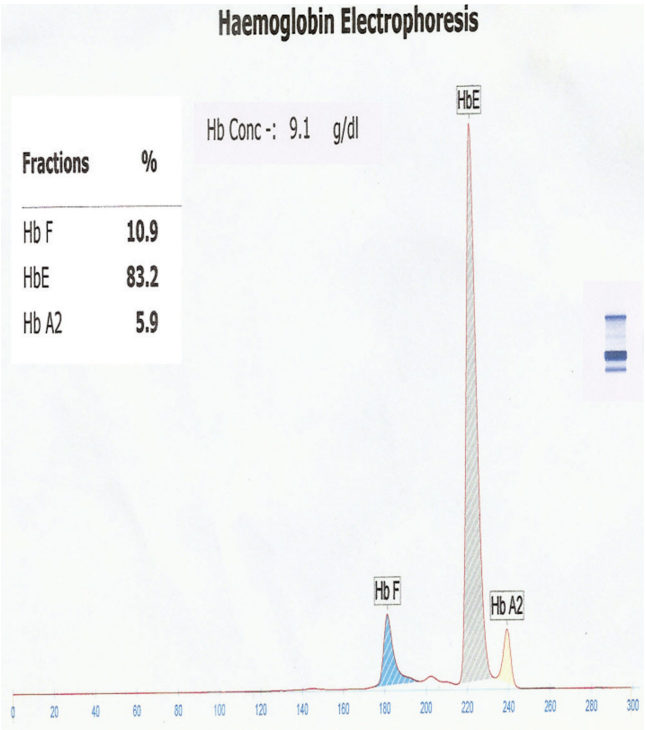

Figure 1. HbE Hemoglobinopathy

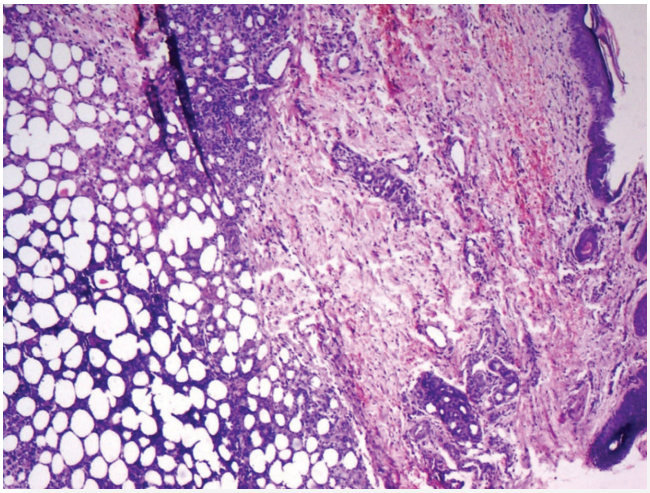

Figure 2. Septal and lobular panniculitis H&E X 40

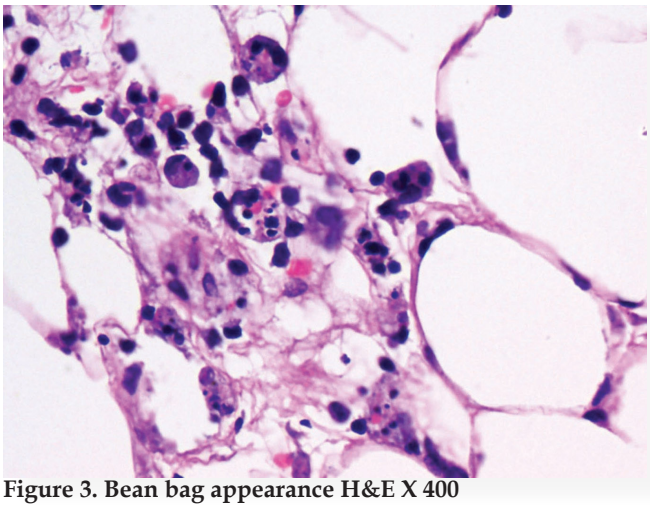

Figure 3. Bean bag appearance H&E X 400

CSF culture was sterile. Biopsy from the skin lesion showed septal and lobular panniculitis composed of macrophages with bland nuclei engulfing erythrocytes, lymphocytes and cell fragments with characterstic "bean bag" appearance along with mixed inflammatory infiltrate (Fig. 2, 3). A diagnosis of CHP was given.

Cytology of the peritoneal ascitic fluid showed reactive mesothelial cells and foamy macrophages with significant hemophagocytosis (Fig. 4). MRI brain and CSF examination were done to rule out CNS involvement by histiocytes. Based on clinical, biochemical, hematological investigations and most importantly skin biopsy diagnosis of HPS in this patient was established. She was referred to hemato-oncologist for further treatment.

Discussion

CHP first described by Winkelmann and Bowie [1] is characterized by a mixed lobular and segmental panniculitis with a proliferation of benign cytophagic histiocytes. It may occur alone or as a part of systemic manifestation of HPS [3]. Scott and Robb-Smith [6] described HPS as distinct clinicopathological entity in 1939 [4] characterized by impaired function of natural killer cells and cytotoxic T-cells [4,7,8]. HPS is a rare, rapidly progressive and potentially fatal disorder of activated histiocytes [9], occuring in all age groups. It is not a single disease and is associated with a variety of underlying conditions leading to the same hyperinflammatory response [7]. The various manifestations are thought to be mediated by inflammatory cytokines [4]. The revised diagnostic criteria of the Histiocyte Society for the diagnosis of HPS requires 5/8 of the following clinical and laboratory features [7].

Fever
Splenomegaly
Cytopenia ≥ 2 cell lines
Hemoglobin < 90 g/L (below 4 weeks < 120 g/L)
Neutrophils < 1 ×109 /L
Hypertriglyceridemia and/or hypofibrinogenemia
Fasting triglycerides ≥ 3 mmol/L
Fibrinogen < 1.5 g/L
Ferritin ≥ 500 µg/L
sCD25 ≥ 2400 U/mL
Decreased or absent NK-cell activity
Hemophagocytosis in bone marrow, CSF or lymph nodes

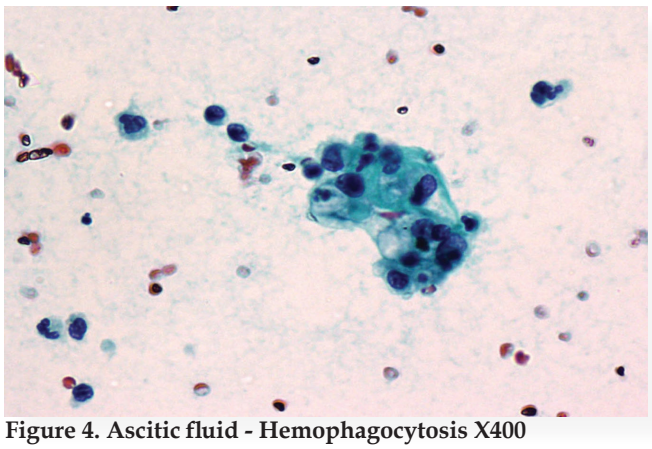

Figure 4. Ascitic fluid - Hemophagocytosis X400

Supportive evidence are cerebral symptoms with moderate pleocytosis and/or elevated protein, elevated transaminases and bilirubin, LDH > 1000 U/L [7].

Two highly sensitive diagnostic marker are an increased plasma concentration of the α chain of soluble IL2 receptor (CD25) and impaired NK cell activity [8]. HPS has variable course, it may be rapidly fatal or can have a long course with intermittent remissions and exacerbations [2].

Our patient fulfilled the criteria for the diagnosis of HPS. The clinical manifestations may be due to increased secretion of cytokines which suppress the hematopoiesis by causing prominent hemophagocytosis in the bone marrow, spleen, liver, and lymph nodes [3,8]. Hemophagocytosis is found at initial presentation only in few cases of HPS, it usually develops as the disease progresses [7]. On bone marrow aspiration, hemophagocytosis may not be present initially and only increased monocytes and monohistiocytic cells may be present [8]. This patient also did not show significant hemophagocytosis in bone marrow aspirate. In about 50% patients there may be elevated cell count, protein or both in the CSF even in the absence of clinical features [8] but CSF cytology and biochemistry in this patient showed normal protein levels. Ascitic fluid cytology showed histiocytes with engulfed erythrocytes and cellular debris in our patient, this was also reported in pleural effusion of a 19 yr old female with sub-cutaneous panniculitis associated with T-cell lymphoma [10]. HPS is associated with various infections and autoimmune diseases [3] however serological tests, blood, CSF and bone marrow culture were negative in our patient.

Cutaneous eruptions are reported to occur in 6% to 65% of cases of HPS. The morphology, configuration and distribution of the skin manifestations are not yet described precisely in literature and are typically reported as nonspecific „transient, maculopapular rashes" [9]. They are to be differentiated from other systemic disorders like myofibromatosis, extramedullary hematopoiesis, langerhans cell histiocytosis and leukemia cutis [9]. Histopathology of CHP is characteristic and shows panniculitis and infiltration by phagocytic benign histiocytes (bean-bag cells) with no nuclear atypia. The benign appearance of the phagocytic histiocytes suggests the reactive response to circulating cytokines, which are secreted by activated macrophages and lymphocytes in the focal cutaneous infiltrates [11]. Hemophagocytosisis by benign histiocytes is also observed in lymph nodes, spleen, liver and bone marrow [3]. CHP is a rare condition and rate of in-hospital deaths in patients of Hemophagocytic syndrome is not significantly associated with cutaneous involvement [12]. But its awareness is important as it may help in early recognition and diagnosis of HPS. CHP is treated with glucocorticoids, cyclosporine, combined chemotherapeutic medications and recently, anakinra, an Interleukin-1 receptor antagonist is suggested. Supportive care, search for underlying malignancies and treatment, and control of associated infections causing HPS are recommended [2,11]. In severe relapse cases, high-dose chemotherapy followed by autologous peripheral blood stem cell transplantation can be considered as an alternative treatment plan [3].

In literature, few cases of HPS associated with sickle cell hemoglobinopathy are described. Kio E et al [5] have hypothesized that hypercytokinemia and impaired NK cell activity induced by zinc deficiency seen in sickle cell anemias might be responsible for it. Hb E is one of the world's most common and important mutations caused by substitution of glutamic acid by lysine at codon 26 of β globin gene. Hb E has a weakened α/β interface, leading to some instability during conditions of increased oxidant stress [13]. To best of our knowledge this is the first documented case of HPS associated with Hb E hemoglobinopathy.

Conclusions

CHP is a rare and often fatal form of panniculitis seen alone or in association with HPS. It is seen as generalized, non pruritic, transient, macula-papular rash in about 6%-65% cases of HPS. CHP is diagnosed by its unique clinical presentation and histological picture of mixed lobular and segmental pannicultis with a proliferation of benign cytophagic histiocytes with no nuclear atypia. Awareness of this cutaneous manifestation in HPS and its early diagnosis may assist physicians in the starting of prompt life saving therapy for HPS. To best of our knowledge this is the first case of HPS associated with Hb E hemoglobinopathy.

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The cutaneous manifestations of hemophagocytic lymphohistiocytosis are varied and non-specific. Many patients with the disease have a non-specific rash that is often vaguely termed maculopapular although it has also been described as ranging from erythroderma to generalized purpuric macules and papules, and morbilliform eruptions [1].

Deep subcutaneous infiltration by histiocytes/lymphocytes giving rise to erythromatous nodules described as cytophagic histiocytic panniculitis by Swati Sharma, et al [2] is yet another skin manifestation of hemophagocytic lymphohistiocytosis [3].

Hemophagocytic lymphohistiocytosis is a rare but potentially fatal disease of normal but overactive histiocytes and lymphocytes that affects all age groups although most reports describe the entity in infants. Fever, hepatosplenomegaly, pancytopenia, lymphadenopathy and rash often comprise the initial presentation. There are two forms of the disease, namely one that is hereditary (or primary) and the other which is acquired (or secondary).

Primary hemophagocytic lymphohistiocytosis is a heterogeneous autosomal recessive disorder found to be more prevalent with parental consanguinity, and is typically seen in infancy and early childhood [4]

Acquired hemophagocytic lymphohistiocytosis occurs after strong immunologic activation, such as that which can occur with systemic infection, immunodeficiency, or underlying malignancy. Both primary and secondary hemophagocytic lymphohistiocytosis are characterized by the overwhelming activation of normal T lymphocytes and macrophages, invariably leading to clinical and hematologic alterations and death in the absence of treatment.

The pathological hallmark of this disease is the aggressive proliferation of activated macrophages and histiocytes, which phagocytosis other cells, namely RBCs, WBCs, and platelets, leading to the clinical symptoms. The uncontrolled growth is non-malignant and does not appear clonal in contrast to the lineage of cells in Langerhans cells diseases [5].

The reticulo-endothelial system namely spleen, lymph nodes, bone marrow, liver, gut, skin, and microglia's cells in the brain and spinal cord are preferential sites of involvement. This disorder may be viewed as a highly stimulated, but ineffective, immune response to antigens, which results in life-threatening cytokine storm. A current accepted theory of hemophagocytic lymphohistiocytosis involves an inappropriate immune reaction caused by proliferating and activated T cells associated with macrophage activation and inadequate apoptosis of immunogenic cells. There are convincing evidence for the role of perforin and natural killer (NK) cells in the hemophagocytic lymphohistiocytosis subtypes. Perforin or pore-forming protein (PFP), gene map location 10q22, is one of the major cytolytic proteins of granules contained in cytotoxic cells [6].

When activated by an antigen, NK cells release granules that contain perforin and granzymes, which form pores in the target cell membrane and cause osmotic lysis and protein degradation, respectively. Patients with perforin deficiency may have impaired defenses against intracellular pathogens and cancers, as has been demonstrated in animal models [7]. Although the mechanism is yet to be determined, decreased NK cell activity results in increased T-cell activation and expansion, resulting in cytokine storm with production of large quantities of cytokines, including interferon gamma (IFNg), tumor necrosis factor-a (TNF–a), and granulocyte-macrophage colony-stimulating factor (GM-CSF). This causes sustained macrophage activation and tissue infiltration as well as production of interleukin-1 (IL–1) and interleukin-6 (IL-6). The resulting inflammatory reaction causes extensive damage and the associated symptoms.

Epstein-Barr virus, is the pathogen that most commonly triggers infection-associated, secondary hemophagocytic lymphohistiocytosis [8] Hemophagocytic lymphohistiocytosis can also be acquired from other infectious and inflammatory conditions [9,10].

The familial form of hemophagocytic lymphohistiocytosis is a rare autosomal recessive disorder that has been classified into 6 different types based on genetic linkage analysis and chromosomal localization; 5 specific genetic defects have been identified, which account for approximately 90% of all patients.

Type 1 is due to a gene defect on chromosome 9, type 2 is due to mutations in the perforin gene, type 3 is due to mutations in the Munc-13-4 (UNC13D) gene, type 4 is due to mutations in the syntaxin 11 (STX11) gene, and type 5 is due to mutations in the gene encoding syntaxin-binding protein 2 (STXBP-2) [11,12].

The diagnostic criteria set forth by the Histiocyte Society for inclusion in the International Registry for Hemophagocytic Lymphohistiocytosis (HLH) is as follows [13].

1. Fever - Seven or more days of a temperature as high as 38.5°C (101.3°F) 2Splenomegaly - A palpable spleen greater than 3 cm below the costal margin

3. Cytopenia - Counts below the specified range in at least 2 of the following cell lineages:

Absolute neutrophils less than 1000/μL

Platelets less than 100,000/μL

Hemoglobin less than 9.0 g/dL

4. Hypofibrinogenemia or hypertriglyceridemia – [1] Fibrinogen less than 1.5 g/L or levels greater than 3 standard deviations below the age adjusted reference range value or [2] fasting triglycerides greater than 2 mmol/L or levels greater than 3 standard deviations above the age-adjusted reference range value

5.Hemophagocytosis - Must have tissue demonstration from lymph node, spleen, or bone marrow without evidence of malignancy.

Three additional criteria are introduced namely, [6] low/absent NK-cell-activity, [7] hyperferritinemia, and [8] high-soluble interleukin-2-receptor levels [14].

Altogether five of these eight criteria must be met before the diagnosis of hemophagocytic lymphohistiocytosis can be made.

Other presenting symptoms include CNS involvement with seizures, ataxia, hemiplegia or mental status changes [15] and clinical abnormalities such as diarrhea, vomiting, jaundice, coagulopathy, due infiltration of other organs or the reticular endothelial system namely gut, bone marrow, liver, spleen and lympnode [16]. Liver involvement and the thrombocytopenia induced by the phagocytic activity of these histiocytes, and splenic activity, leads to life threatening coagulopathy, which is a common cause of mortality in these patients.

T cell lymphomas may present with skin manifestation similar to those seen in hemophagocytic lymphohistiocytosis. A newly described entity namely subcutaneous panniculitis- like T cell lymphoma can be confused with the benign proliferative immune condition hemophagocytic lymphohistiocytosis (HLH), and efforts should be made to differentiate them [17].

Hemophagocytic lymphohistiocytosis (HLH) is a rare life threatening condition and efforts should be made to have prompt diagnosis. Therapy should be instituted at a very early stage.

Familial hemophagocytic lymphohistiocytosis is uniformly fatal if not treated; the median survival time reported in various studies is 2-6 months after diagnosis. Remission is always temporary, as the disease inevitably returns.

The outcomes of secondary hemophagocytic lymphohistiocytosis vary [18,19].

Therapy includes the use of anti-inflammatory agent such as steroids, and anti- neoplastic agents [20]

Intravenous immunoglobulin (IVIG) is also used as an effective form of therapy. Bone marrow transplant is the only hope for cure. Supportive therapy is institutive where ever necessary for example in the treatment of thrombocytopenia and infections. Opportunistic infections especially fungal represent an important cause of death in this population [21].

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LOCALISED INVOLUTIONAL LIPOATROPHY: A CASE REPORT

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Abstract
Localized involutional lipoatrophy (LIL) is a rare distinctive idiopathic form of localized lipoatrophy. The characteristic histopathologic feature of LIL are diminutive fat lobules composed of small adipocyte resembling fetal fat tissue. LIL is not a well-known disorder, there have been only a few reports on LIL in the English literature.We report a case of localised involutional lipoatrophy in a 25 year old lady with bilateral depressed lesions on both arms.

Key words: lipoatrophy; idiopathic; localized

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Introduction

Localized involutional lipoatrophy (LIL) is a rare distinctive idiopathic form of localized lipoatrophy. It is characterized by loss of adipose tissue without antecedent inflammation and was first described by Peters and Winkelmann [1] in 1986. We present a case of LIL in a young lady who presented with features of bilateral LIL on both arms.

Case report

A 25 year old female presented with slowly occurring depressed depigmented lesions over both her arms. She had no other complaints. She was worried about the lesions for cosmetic reasons. On clinical examination there were bilateral, symmetrical, well demarcated depressed plaques measuring 2.5 x 2.0 cms over the lateral aspect of both her arms. Overlying skin showed slight depigmentation (Fig. 1). No similar lesions were seen elsewhere in the body. She denied any history of trauma or injections to the site. She had no associated medical problems or history of drug intake. Her general physical examination and routine laboratory tests were within normal limits.

A skin biopsy from both depressed plaques showed a decrease in the number and size of adipocytes in the subcutaneous fat which was replaced by fibrocollagenous tissue, without any other significant findings in the epidermis or the dermis. There was no evidence of inflammation or increased vasculature (Fig. 2).

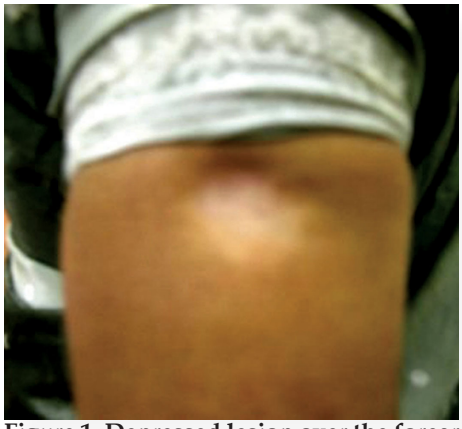

Figure 1. Depressed lesion over the forearm

Discussion

LIL has been defined as a focal loss of subcutaneous tissue on one or several sites, occurring without any significant trigger or autoimmune disease (hence their idiopathic nature). Most reported cases of idiopathic LIL have all been young women, except for a 5 year old boy who was the one exception [1].

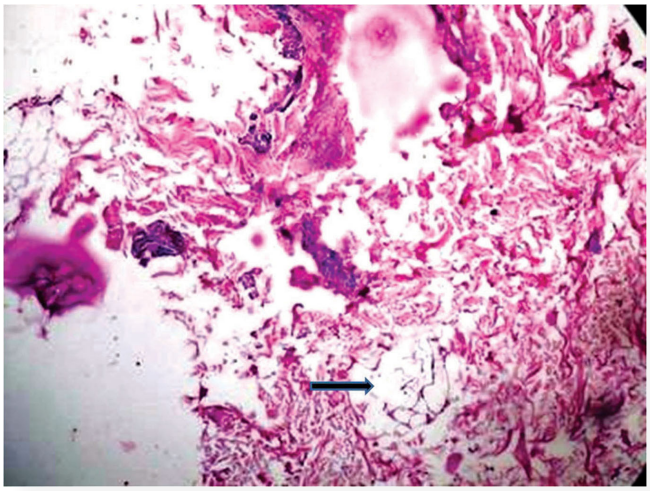

Figure 2. Photomicrograph of dimunitive subcutaneous fat lobules (shown by arrow) surrounded by fibrocollagenous tissue and no inflammation. (H&E 100X)

Clinically, LIL presents as an asymptomatic, non-inflamed, well demarcated, localized, atrophic depression. The differential diagnoses of LIL include lupus erythematosus profundus [2], morphea [3], lichen sclerosus et atrophicus [3], and other types of lipoatrophy associated with triggers like repeated injections with corticosteroids and antibiotics [4-6] or sites of trauma [7]. These disorders can be differentiated from LIL based on the latter's characteristic histopathological feature, which is the presence of diminutive fat lobules composed of small adipocytes that resemble fetal fat tissue without the presence of inflammation. Due to lack of report on idiopathic LIL, the pathogenesis of idiopathic LIL remains unclear, and the female predominance is difficult to explain [8].

It is important to make an appropriate diagnosis of LIL and differentiate idiopathic LIL from lipoatrophy after drug administration or injury [8] and underlying immunological disorders and connective tissue diseases, such as systemic lupus erythematosus, nephritis, Sjögren syndrome, scleroderma, morphea, nephritis, hypocomplementemia, recurrent pyogenic infections, thyroiditis, and ITP.

Therefore, localized lipoatrophy should alert physicians to these diseases. Prompt and appropriate workup is necessary where clinically indicated.

Histopathological examination is the hallmark of diagnosis of LIL which shows dimunitive fat lobules with small lipocytes embedded in hyaline connective tissue absence of inflammatory cells, and myxoid stroma with numerous capillaries.

Treatment of lipoatrophy consists of reassuring the patient that the condition is benign. Anti-inflammatory drugs such as antimalarial or systemic steroids may be helpful in the early stage of the disease .If the lesions persist and are of cosmetic concern, localized fat transplantation may be performed.

Our patient was reassured of the benign nature of the lesion and was treated with Chloroquine, 250mg once a day and topical tacrolimus ointment 0.1% twice daily. She was also advised to discontinue wearing tight fitting clothing, the pressure of which could have resulted in lipoatrophy.

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CALCINOSIS CUTIS METASTÁSICA: *CALCIFILAXIS* (ARTERIOLOPATÍA URÉMICA CALCIFICADA). A PROPÓSITO DE UN CASO

METASTATIC CALCINOSIS CUTIS: *CALCIPHYLAXIS* (CALCIFIED UREMIC ARTERIOLOPATHY). A CASE REPORT

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Resumen
La calcifilaxis es un síndrome clínico caracterizado por una calcificación vascular progresiva que ocasiona la aparición de lesiones violáceas, frecuentemente dolorosas, en la piel de pacientes con insuficiencia renal crónica, diálisis o trasplante renal, asociado usualmente a niveles elevados de hormona paratiroidea.
Se presenta el caso clínico de una mujer de 44 años, diabética con insuficiencia renal crónica, en hemodiálisis desde hace 2 años, que fue diagnosticada de calcifilaxis tras sospecha clínica y biopsia de lesiones cutáneas.

Abstract
Calciphylaxis is a clinical syndrome characterized by progressive vascular calcification that causes the appearance of purplish lesions, often painful, in the skin of patients with chronic renal failure, dialysis or kidney transplantation, usually associated with elevated levels of parathyroid hormone.
We report a case of a 44-year-old diabetic woman with chronic renal failure on hemodialysis for 2 years. She was diagnosed with calciphylaxis after clinical suspicion and biopsy of skin lesions.

Palabras clave: Calcifilaxis, insuficiencia renal; calcinosis cutis
Key words: calciphylaxis; kidney failure; calcinosis cutis

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Introduccion

La calcifilaxis es un proceso cutáneo infrecuente y mal conocido. Afecta casi con exclusividad a pacientes con insuficiencia renal crónica terminal, que son sometidos a diálisis o han sido trasplantados [1].
Se caracteriza por la aparición y rápida progresión de necrosis isquémica y úlceras cutáneas causadas por la calcificación de la íntima de las arterias y las arteriolas de la dermis profunda y la grasa subcutánea. La mayoría de los pacientes afectados tienen aumento de los niveles séricos de calcio y fosfato, además de niveles elevados de hormona paratiroidea. Sin embargo el metabolismo calcio-fósforo es normal en algunos pacientes con calcifilaxis, lo que avala la idea de que también participan otros factores en la patogenia [1,2].
La elevada morbi-mortalidad de este síndrome justifica un diagnóstico precoz y un tratamiento agresivo.
Se presenta el caso clínico de una mujer de 44 años de edad, con insuficiencia renal crónica terminal en hemodiálisis, que fue diagnosticada de calcifilaxis tras sospecha clínica y biopsia de lesiones cutáneas.

Caso Clínico

Mujer de 44 años de edad, procedente de medio rural del Paraguay (Sudamérica), portadora de diabetes mellitus tipo 2, insulinodependiente, insuficiencia renal crónica terminal en hemodiálisis periódicas desde el 2009, secundaria a nefropatía diabética, trombosis de la vena cava superior en julio de 2010, en tratamiento con anticoagulante oral (warfarina), anemia secundaria en tratamiento con hierro parenteral y eritropoyetina. Hiperparatiroidismo secundario (hormona paratiroidea >600), con normocalcemia e hiperfosfatemia.

Consulta por una lesión en abdomen de 6 meses de evolución que se inicia como mancha roja que aumenta de tamaño y se vuelve indurada, violácea y luego negruzca, acompañada de intenso dolor.

En el examen físico se constata escara necrótica de aproximadamente 12 x 8 cm, sobre una base eritematoviolácea mal delimitada en hemiabdomen inferior (Fig. 1) y una placa más pequeña, de características similares con descamación en región de la mama derecha (Fig. 2).

En la analítica general presenta anemia moderada, urea y creatinina elevadas, normocalcemia, hiperfosfatemia, hormona paratiroidea 650 (valor normal hasta 72), producto de calcio x fósforo 60.3 (normal).

Se solicita ecografía abdominal que informa celulitis de pared abdominal y una tomografía axial computarizada de abdomen y ecocardiografía que son normales.

Además se solicitó una ecografía de paratiroides que no pudo realizarse por falta de medios económicos.

Se realiza una biopsia de piel que informa: ulceración epidérmica, necrosis dérmica, paniculitis lobulillar, necrosis grasa, depósitos de calcio en hipodermis y calcificación arterial de vasos hipodérmicos (Fig. 3).

Con los hallazgos clínicos e histopatológicos se llega el diagnóstico final de **Calcinosis cutis metastásica: Calcifilaxis (arteriolopatía urémica calcificada)**.

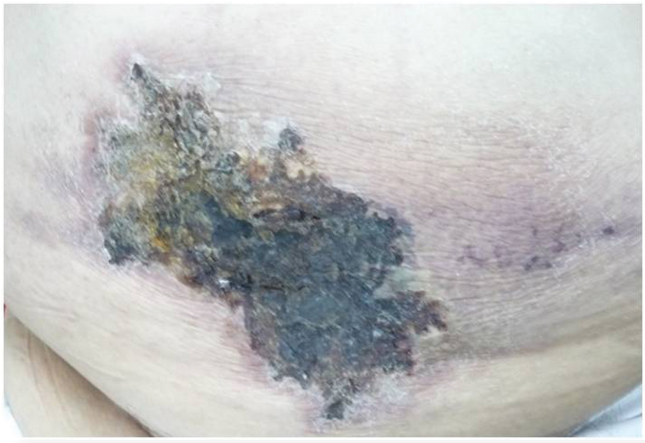

Figura 1. Clínica. Escara necrótica sobre una base eritematoviolácea mal delimitada en hemiabdomen inferior.

Figure 1. Clinic. Necrotic eschar on an eritematoviolaceous base, located in lower abdomen.

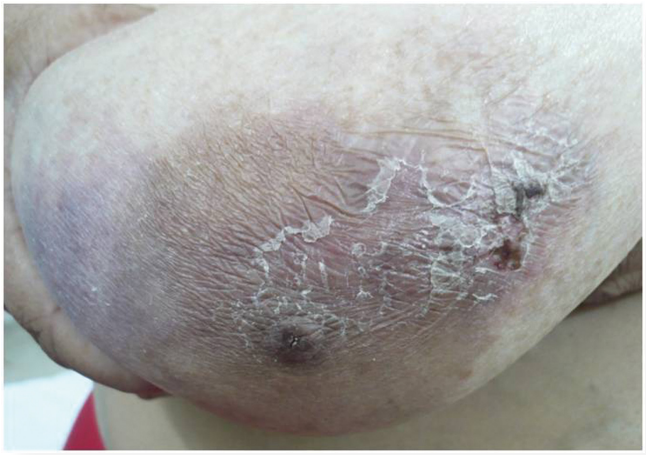

Figura 2. Clínica. Placa eritematosa con pequeña escara necrótica. Se observa descamación.

Figure 1. Erythematous plaque with a small necrotic eschar. Scaling is observed.

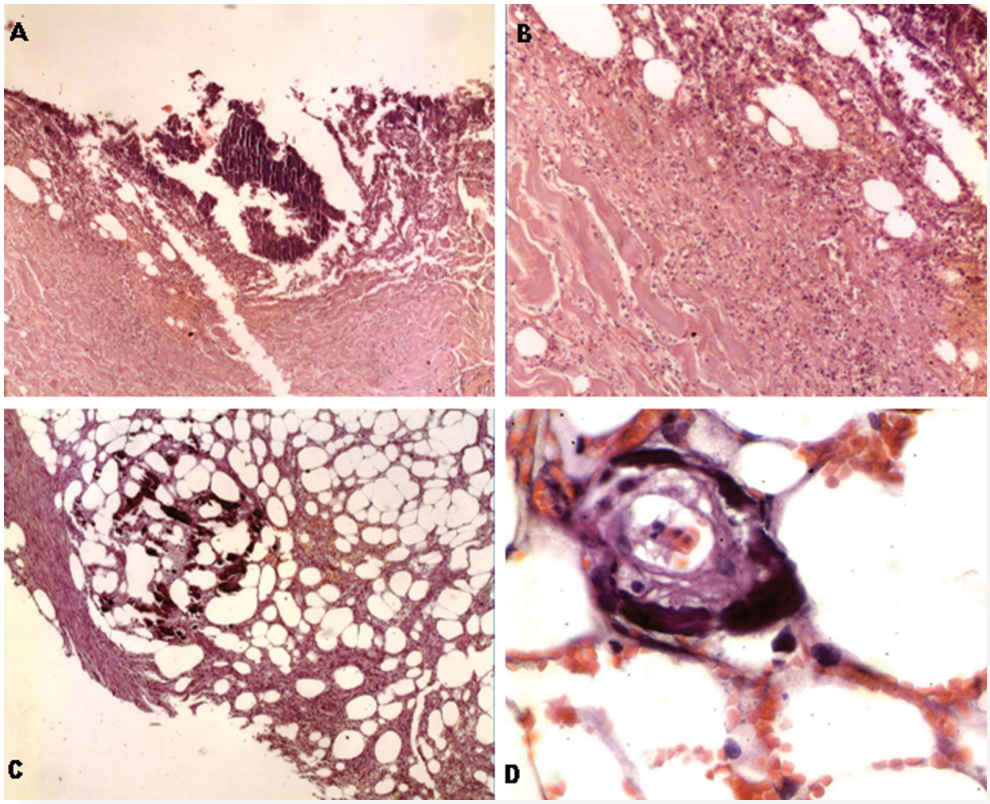

Figura 1. Histopatología. A. Ulceración epidérmica; B. Necrosis dérmica; C. Paniculitis lobulillar, necrosis grasa y calcificación; D. Calcificación arterial.

Figure 1. Histopathology. A. Epidermal ulceration; B. Skin necrosis; C. Lobular panniculitis, fat necrosis and calcification; D. Arterial calcification.

Comentarios

La calcinosis cutis, o cutánea, es el término empleado para describir una serie de trastornos caracterizados por presentar depósitos de sales de calcio a nivel subcutáneo, ocurriendo tanto en hipercalcemia como en normocalcemia [3].

Los trastornos de calcificación de la piel generalmente se dividen en cuatro grandes categorías: distrófica, metastática, idiopática e iatrogénica.

La calcificación distrófica es la calcificación que se produce en el contexto de daño tisular localizado sin anormalidades metabólicas sistémicas en la regulación del calcio. En contraste, la calcificación metastásica se produce en el tejido normal cuando hay una disfunción de los sistemas reguladores de calcio. Cuando no hay factores conocidos locales o sistémicos, la calcificación se clasifica como idiopática y la relacionada con la terapia médica o de prueba es iatrogénica [4].

La calcificación metastásica es más frecuente en la insuficiencia renal crónica y toma la forma de calcificación nodular benigna o calcifilaxis [5].

El aspecto clínico de la calcinosis cutánea varía, debido a que puede asentar sobre una piel normal o bien sobre lesiones preexistentes. Se presenta como neoformaciones subcutáneas, blanquecinas, de color rosa o cafés, pueden ser lesiones únicas o múltiples, simétricas o no, aisladas o confluentes. El tamaño varía, de pocos milímetros a centímetros, pueden ser fluctuantes y en ocasiones tener una disposición lineal. Se describen como de consistencia pétrea y puede haber microulceraciones o eritema en la superficie o eritema perilesional [6].

La calcifilaxis es una enfermedad potencialmente fatal que se caracteriza por una calcificación vascular progresiva, necrosis de los tejidos blandos y necrosis isquémica de la piel [5].

Ocasiona la aparición de lesiones violáceas, frecuentemente dolorosas, asociada con necrosis de tejidos blandos y ulceración [5,7].

Hay dos formas diferentes de presentación clínica, la calcifilaxis acra y la proximal. Los diferentes estudios relacionan la calcifilaxis proximal con los pacientes diabéticos, siendo las alteraciones del metabolismo calcio-fósforo menos severas que en los pacientes con calcifilaxis acra, y suelen tener un pronóstico mucho peor [2].

La calcifilaxis se presenta casi exclusivamente en pacientes con antecedentes de insuficiencia renal crónica e hiperparatiroidismo secundario prolongado. Sin embargo en raros casos se ha observado en ausencia de insuficiencia renal [5].

Su frecuencia se estima en 1% de los pacientes con insuficiencia renal crónica y en 4% en diálisis [7].

Los diferentes casos publicados, identifican una serie de factores de riesgo relacionados con el desarrollo de calcifilaxis: el hiperparatiroidismo, los suplementos de vitamina D, la hiperfosfatemia y los niveles altos o normales de calcio en plasma. De todas formas, estos factores no son suficientes para explicar la presencia de calcifilaxis y no están directamente relacionados con la severidad de la enfermedad [2].

Otro de los factores de riesgo implicados es la obesidad. La razón por la cual se relaciona la obesidad mórbida con la calcifilaxis es probablemente, por la mayor cantidad de tejido adiposo que está en contacto con la circulación sanguínea; es más frecuente en la mujer, siendo las lesiones más abundantes a nivel de caderas, nalgas, infraumbilical y parte superior de muslos, por ser ahí donde se localizan la mayor cantidad de depósitos grasos [2].

El caso clínico que describimos, presentaba como factores de riesgo: obesidad mórbida, niveles elevados de PTH, además de tratamiento anticoagulante desde julio del 2010.

Sin duda la patogenia de la calcifilaxis es multifactorial y hay implicados factores todavía desconocidos.

En la histopatología, por lo general hay ulceración epidérmica, necrosis dérmica focal y calcificación vascular. La calcificación implica a pequeñas y medianas arterias sobre todo en el tejido subcutáneo. Trombos de fibrina pueden estar presentes en capilares. Una paniculitis calcificante aguda y crónica es un hallazgo común. Necrosis grasa está presente a menudo [8].

La elevada morbi-mortalidad de este síndrome, alrededor de un 80%, justifican la mayoría de las veces, la agresividad del tratamiento, siendo vital, en los pacientes tributarios de padecer dicho síndrome, un diagnóstico precoz [2].

El tratamiento actual de la calcifilaxis consiste en normalizar los productos de calcio-fosfato y el cuidado de las lesiones. Se utiliza diálisis con bajo calcio, ligadores de fosfato que combinan acetato de calcio y carbonato de magnesio, tiosulfato de sodio, y paratiroidectomía. La paratiroidectomía permite mejorar la supervivencia. Para disminuir la incidencia de sepsis y muerte en estos pacientes, debe hacerse un tratamiento agresivo de la infección y limpieza de las lesiones [5,9,10].

En el caso presentado se procedió a la realización de debridamientos quirúrgicos en dos oportunidades. Se planteó la alcoholización de la glándula paratiroidea y el tratamiento con tiosulfato endovenoso que no llegaron a realizarse. Luego de 13 meses del inicio del cuadro, observamos una mejoría de la lesión con desaparición del dolor a dicho nivel.

Conclusión

Se presenta el caso por tratarse de una patología poco frecuente, que implica un reto terapéutico y condiciona un pronóstico reservado para el paciente. Dada la elevada morbimortalidad, la prevención de las calcificaciones, el diagnóstico precoz, la normalización de los niveles de calcio y fósforo, el control del hiperparatiroidismo y la profilaxis de la infección secundaria, serían las mejores armas terapéuticas.

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HISTOPLASMOSE AFRICAINE DISSEMINEE CHEZ UN ENFANT IMMUNOCOMPETENT AU BURKINA FASO: UN CAS

DISSEMINATED AFRICAN HISTOPLASMOSIS IN AN IMMUNOCOMPETENT CHILD IN BURKINA FASO: ONE CASE

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Résumé
Introduction: L'histoplasmose à *Histoplasma capsulatum var. duboisii* est une affection rare en Afrique. Les lésions cutanées localisées sont les plus fréquentes. Nous rapportons une forme disséminée chez un enfant immunocompétent.
Observation: Une élève de 8 ans est hospitalisée pour des nodules cutanés, généralisés, associés à des douleurs ostéo-articulaires très intenses de la quasi-totalité des articulations. L'examen a noté une malnutrition aiguë modérée, des nodules sous cutanés, multiples, des papules rosées, à surface plane, des papules ombiliquées, des tuméfactions nodulaires très douloureuses de plusieurs articulations, de multiples adénopathies fermes, mobiles, une atteinte osseuse multiple à la radiographie, une hépatosplénomégalie et des ulcérations secondaires douloureuses. L'histologie d'un nodule cutané et d'une papule ombiliquée a mis en évidence *H.capsulatum var. duboisii*. Après l'échec d'un traitement au fluconazole, l'évolution a été favorable sous l'amphotéricine B. La patiente a bénéficié de la collaboration Nord-Sud et de l'aide des structures sociales.
Conclusion: Cette observation nous a permis de décrire les particularités cliniques et socio-économiques, les difficultés diagnostiques et thérapeutiques d'un cas d'histoplasmose africaine disséminée et de démontrer encore l'efficacité de l'amphotéricine B.

Abstract
Introduction: Histoplasmosis due to *Histoplasma capsulatum var. duboisii* is a rare affection in Africa. Localized cutaneous lesions are the most common form. We report a disseminated form in an immunocompetent child.
Case report: An 8-year-old student has been hospitalized for generalized, cutaneous nodules associated with very severe osteo-articular pains of almost all the joints. The examination has noted a moderate acute malnutrition, multiple and sub-cutaneous nodules, pinkish and plan papules, umbilicate papules, very painful nodular tumefactions of several joints, multiple, firm and mobiles adenopathies, hepatosplenomegaly and secondary painful ulcerations. Multiple bones have been affected at the radiography. Histology of a cutaneous nodule and an umbilicate papule has identified *H.capsulatum var. duboisii*. After the failure of treatment with fluconazole, the evolution has been favourable with amphotericin B. The patient has benefited from collaboration North-South, the help of social structures.
Conclusion: This observation allowed us to describe clinical and socio-economic characteristics, diagnostic and therapeutic difficulties of a case of disseminated African histoplasmosis and has demonstrated the effectiveness of amphotericin B.

Mots-clé: Histoplasmose; africaine; disséminée; immunocompétent; enfant
Key words: Histoplasmosis; african; disseminated; immunocompetent; child

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Introduction

L'histoplasmose est une mycose profonde due à un champignon, *Histoplasma capsulatum* qui possède deux variétés à savoir *Histoplasma capsulatum var. capsulatum*, agent de l'histoplasmose dite américaine (à tort, car de répartition mondiale) et *Histoplasma capsulatum var. duboisii*, agent de l'histoplasmose africaine. Ce sont des affections rarement décrites en Afrique. En effet, la fréquence réelle de la forme africaine n'est pas connue, la plupart des études ayant porté sur des cas cliniques [1-9]. Les lésions cutanées, qui sont les plus fréquentes, prédominent au thorax et à la face [5,10]. Les formes disséminées sont rares, et se rencontrent de plus en plus chez les patients immunodéprimés par le virus de l'immunodéficience humaine (VIH) [11,12]. Nous rapportons un cas d'histoplasmose africaine disséminée chez un enfant immunocompétent au Burkina Faso pour décrire les particularités cliniques et les difficultés socio-économiques, diagnostiques et thérapeutiques.

Observation

Une élève de 8 ans, de père cultivateur, est référée le 12 janvier 2010 pour des nodules cutanés, généralisés. Le début remonterait à 3 mois auparavant (octobre 2009) par un amaigrissement progressif, une anorexie et des douleurs ostéo-articulaires fixes, permanentes des grosses articulations (l'épaule, le coude et le poignet gauches, les genoux, la cheville gauche), à type de brûlure, exacerbées par la mobilisation, sans fièvre ni notion de traumatisme. Un mois plus tard, sont apparues des tuméfactions osseuses et articulaires du coude, de l'avant bras et du genou gauches et des deux jambes associées à des nodules cutanés, non prurigineux, indolores du dos puis disséminés à tout le corps. Les antécédents médicaux étaient sans particularités. L'interrogatoire notait dans son environnement habituel un important élevage traditionnel de poulets à domicile, et la fréquentation d'un abri de chauves-souris sur le trajet de l'école.

L'examen à l'entrée a noté : un mauvais état général avec amaigrissement, une température à 37,2°C, un périmètre brachial à 15cm, un poids de 18kg, une taille de 124 cm (rapport poids/taille entre 75 et 80 %), ce qui traduisait une malnutrition aiguë modérée. L'examen dermatologique montrait trois types de lésions, disséminées à tout le tégument: des nodules sous cutanés, multiples, de 0,5 à 2 cm de diamètre, de consistance tantôt ferme tantôt fluctuante (abcès froids), indolores, mobiles par rapport au plan profond et cutané mais parfois adhérents à la peau ; ces nodules étaient associés à des papules rosées, arrondies ou ovalaires, de 3 à 5 mm, indolores, à surface plane, et à des papules ombiliquées (Fig. 1a, 1b). L'examen de l'appareil locomoteur avait noté des tuméfactions nodulaires (Fig. 2a, 2b), de 2 à 3 cm de diamètre, dures, très douloureuses du coude et l'avant-bras gauches, du poignet et du genou gauches et des jambes avec une attitude antalgique du membre supérieur gauche et une légère boiterie gauche à la marche. Il n'y avait pas de déformation visible au niveau du rachis.

L'examen du système spléno-ganglionnaire a montré de multiples adénopathies fermes, mobiles, non inflammatoires, de 1,5 cm à 3 cm de diamètre, siégeant dans les régions sous angulo-maxillaires, axillaires et inguinales sans splénomégalie. Il n'y avait pas d'hépatomégalie. Nous avons évoqué une histoplasmose disséminée, une cryptococcose disséminée et une tuberculose multifocale.

Les examens complémentaires montraient une vitesse de sédimentation accélérée (1ère heure = 84 mm), le fibrinogène élevé à 9,65 g/l, la CRP élevée à 198,9 mg/l), une anémie à 10,2 g/dl, normochrome, microcytaire, des ostéolyses multifocales péri articulaires notamment de l'acromion gauche, de la quasi-totalité de l'olécrâne gauche (Fig. 3a) et des régions métaphyso-épiphysaires des fémurs et des tibias (Fig. 3b, 3c) avec tuméfaction des parties molles en regard à la radiographie des articulations en janvier 2010; la radiographie pulmonaire et l'échographie abdominopelvienne étaient normales. L'intradermo-réaction à la tuberculine, la recherche de bacilles acido-alcoolo-résistants dans les crachats, la sérologie syphilitique (TPHA-VDRL) et celle pour le VIH étaient négatives. La glycémie, le bilan rénal et hépatique étaient normaux; l'électrophorèse de l'hémoglobine était AA.

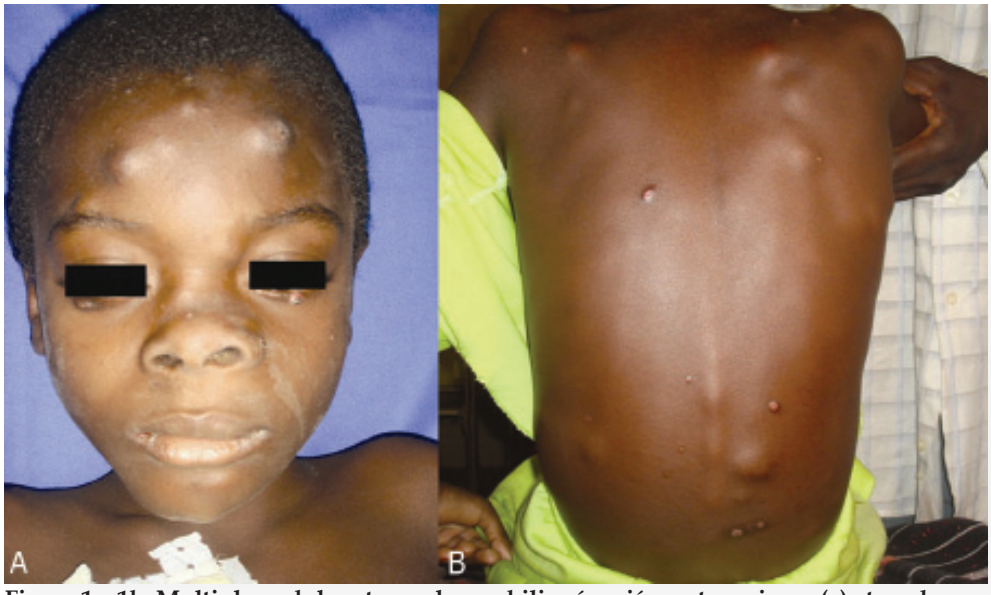


Figure 1a, 1b. Multiple nodules et papules ombiliquées siégeant au visage (a) et au dos (b) à l'admission (janvier 2010).

Figure 1a, 1b. Multiple nodules and umbilicate papules on the face (a) and the back (b) at entry (January 2010).

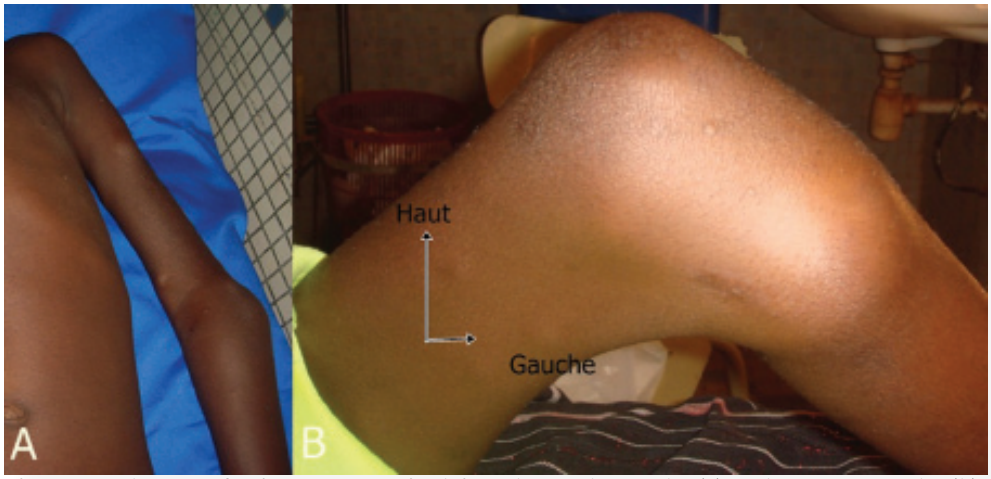


Figure 2a, 2b. Tuméfactions ostéo-articulaires du coude gauche (a) et du genou gauche (b) à l'admission (janvier 2010).

Figure 2a, 2b. Osteo-articular tumefactions of the left elbow (a) and the left knee (b) at entry (January 2010).

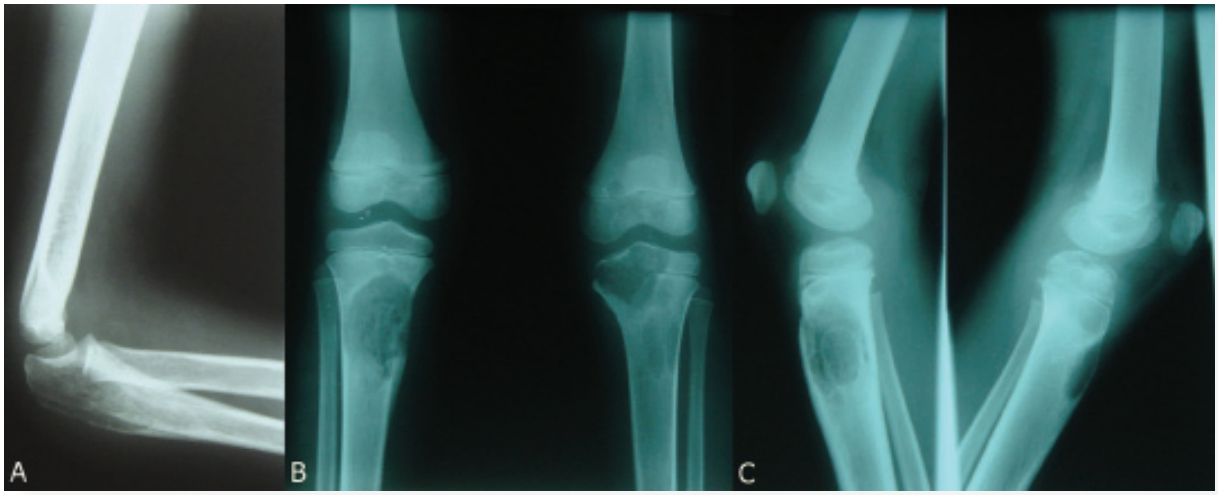


Figure 3a. Radiographie du coude gauche (de profil) : ostéolyse prenant la quasi-totalité de l'olécrâne gauche avec réaction uni lamellaire postérieure à l'admission en janvier 2010.
Figures 3b, 3c. Radiographie des genoux de face (3b) et de profil (3c). Ostéolyse métaphyso-épiphysaire intéressant les fémurs et les tibias à l'admission en janvier 2010.

Figure 3a. Radiography of the left elbow (in profile): osteolysis of the quasi-totality of left olecranon with posterior uni-lamellar reaction at entry in january 2010.
Figures 3b, 3c. Radiography of the knees from the front (3b) and in profile (3c). Metaphyso-epiphysial osteolysis concerning the femurs and the tibias at entry in january 2010.

L'examen direct et la culture du pus d'un nodule, réalisés chez nous à l'hôpital, étaient négatifs. Les parents de notre patiente n'ayant pas les moyens financiers pour prendre en charge les frais de l'examen anatomopathologique, nous avons envoyé les échantillons de biopsie d'un nodule cutané et d'une papule ombiliquée à nos collaborateurs en France (l'examen fait gratuitement par l'anatomopathologiste Gilles Lemasson de Brest), ce qui a retardé la confirmation diagnostique et le traitement. Un traitement symptomatique a été institué (repos au lit, Paracétamol, Ibuprofène), avec la mise à plat de certains abcès, des pansements quotidiens avec des solutions antiseptiques.

L'évolution au cours du premier mois d'hospitalisation (avant la confirmation du diagnostic) a été marquée par une intensification des douleurs ostéo-articulaires devenues insomniantes, ayant nécessité l'utilisation d'antalgiques de 2ème (tramadol par voie orale) puis de 3ème palier (morphine par voie injectable et orale) et la confection d'attelle plâtrée à visée antalgique des membres supérieur et inférieur gauches.

L'histologie mettait en évidence un infiltrat cellulaire fait d'éléments histiocytaires qui comportaient de très nombreuses cellules géantes multinucléées, caractérisées par la présence dans leur cytoplasme de grandes levures typiques d'histoplasmose à *H. capsulatum var. duboisii* nettement colorable par l'HE (Fig. 4a), le PAS (Fig. 4b) et le Gomori-Grocott. Il n'y avait pas de parasites, ni d'éléments bactériens (coloration de Ziehl négatif).

Le traitement étiologique au fluconazole injectable à raison de 200 mg/j (soit 11mg/kg/j) a effectivement débuté le 20 février 2010 après un bilan pré-thérapeutique normal. Cette molécule a été choisie du fait de sa disponibilité et de sa gratuité dans notre dépôt pharmaceutique à l'hôpital (l'amphotéricine B, l'itraconazole et le kétoconazole cités en première intention dans la littérature n'étaient pas disponibles et sont coûteux), de son coût (les parents de l'enfant n'avaient pas de moyens financiers), de ses moindres effets secondaires (notamment troubles gastro-intestinaux et hépatiques).

Ce traitement a permis pendant 45 jours une stabilisation des lésions cutanées puis une aggravation est survenue, marquée par une exacerbation des douleurs ostéo-articulaires, une poussée de nouvelles lésions cutanées (Fig. 5) puis un ramollissement et une fistulisation simultanés de la quasi-totalité des nodules et des tuméfactions articulaires préexistantes aboutissant à des ulcérations douloureuses, bourgeonnantes (Fig. 6a, 6b). Par ailleurs, nous avons observé une hépatomégalie (FH à 12cm) indolore, ferme, à surface lisse et à bord mousse avec un bilan biologique normal et une splénomégalie de type I de Hackett. La prise en charge chirurgicale de certaines lésions sous anesthésie générale s'est avérée nécessaire en mi-avril 2010. En fin mai 2010, soit 3 mois après le début du fluconazole, nous avons constaté une aggravation des lésions radiologiques avec ostéolyse intéressant l'ulna et l'humérus gauches (Fig. 7a), le tibia, la fibula et le calcanéum gauches (Fig. 7b, 7c) avec un début de genu varum à gauche associée à des douleurs très intenses.

Cliniquement, en fin juin, une deuxième poussée de lésions cutanées et ganglionnaires est survenue avec augmentation de la taille de l'hépato-splénomégalie. Nous avons décidé un changement d'antifungique. En effet, le 15 juillet 2010, malgré la crainte de sa toxicité, nous avons commencé le traitement à base d'amphotéricine B par voie injectable (commandé et obtenu gratuitement avec l'aide de la pharmacie de l'hôpital et des structures sociales), à dose progressive pour atteindre au bout de 3 jours, 15mg/j soit environ 0,8 mg/kg/j, 3 fois par semaine. L'évolution a été spectaculaire : en un mois de traitement, les ulcérations étaient presque toutes cicatrisées (Fig. 8a, 8b) avec la disparition quasi complète des nodules et des adénopathies, une régression de l'hépato-splénomégalie. Au 4ème mois de traitement, nous avons observé une nette régression des lésions osseuses radiologiques, et un gain pondéral de 2,500 kg. Une kinésithérapie douce a été alors associée au traitement.

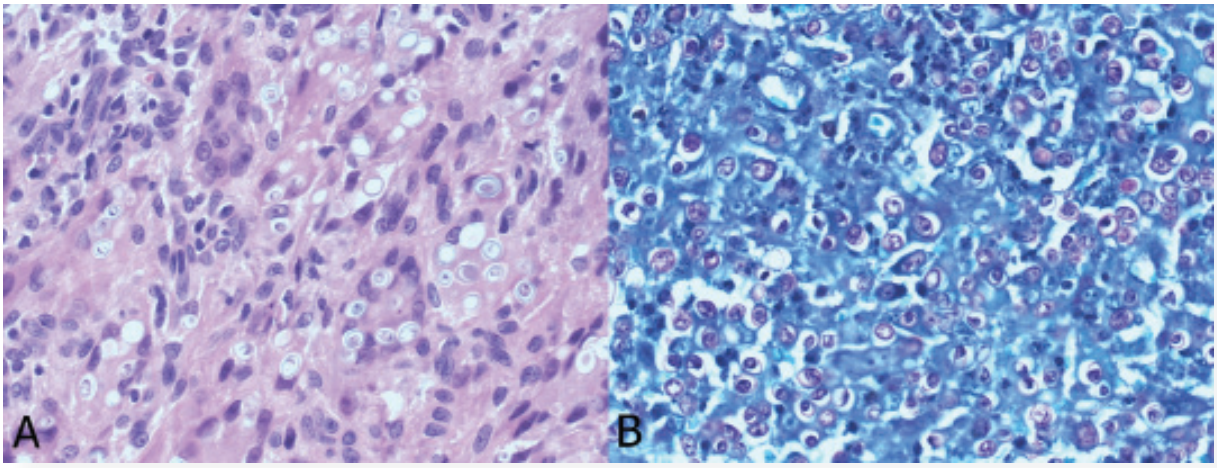


Figure 4a. HE x 400. Présence de grandes levures d'Histoplasma duboisii dans le cytoplasme de cellules géantes multinuclées.
Figure 4b. PAS x 400. Présence de très nombreuses levures d'Histoplasma duboisii, bien limitées par une capsule transparente.

Figure 4a. HE x 400. Presence high yeasts of Histoplasma duboisii in the cytoplasm of giant multinuclear cells.
Figure 4b. PAS x 400. Presence of very numerous yeasts of Histoplasma duboisii, well limited by transparent capsule.

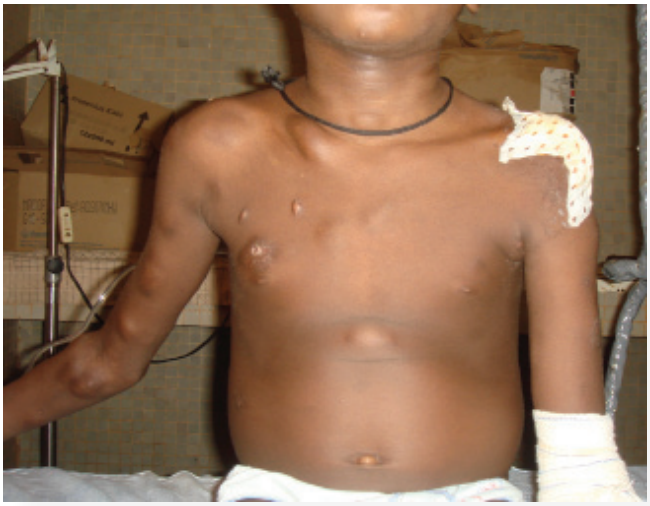


Figure 5. Poussée de nodules au tronc et au membre supérieur droit sous fluconazole (juin 2010).

Figure 5. Extension of nodules at the trunk and right thoracic limb during the treatment with fluconazole (June 2010).

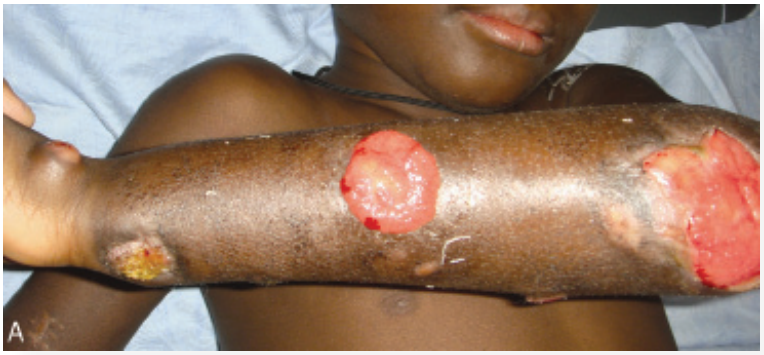


Figure 6a. Multiples ulcérations à l'avant bras gauche sous fluconazole (juin 2010).
Figure 6a. Multiples ulcerations on the left forearm during the treatment with fluconazole (June 2010).

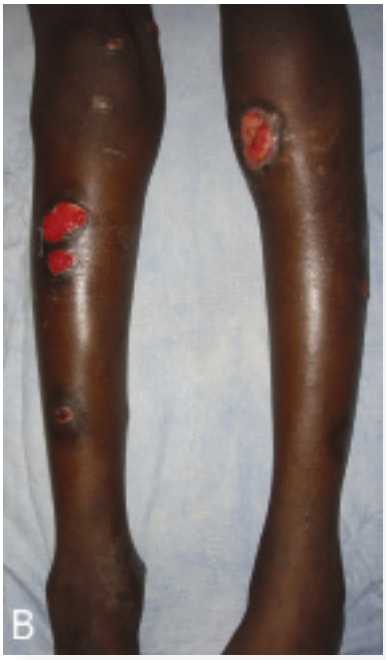


Figure 6b. Multiples ulcérations aux jambes sous fluconazole (juin 2010).
Figure 6b. Multiples ulcerations on the legs during the treatment with fluconazole (June 2010).

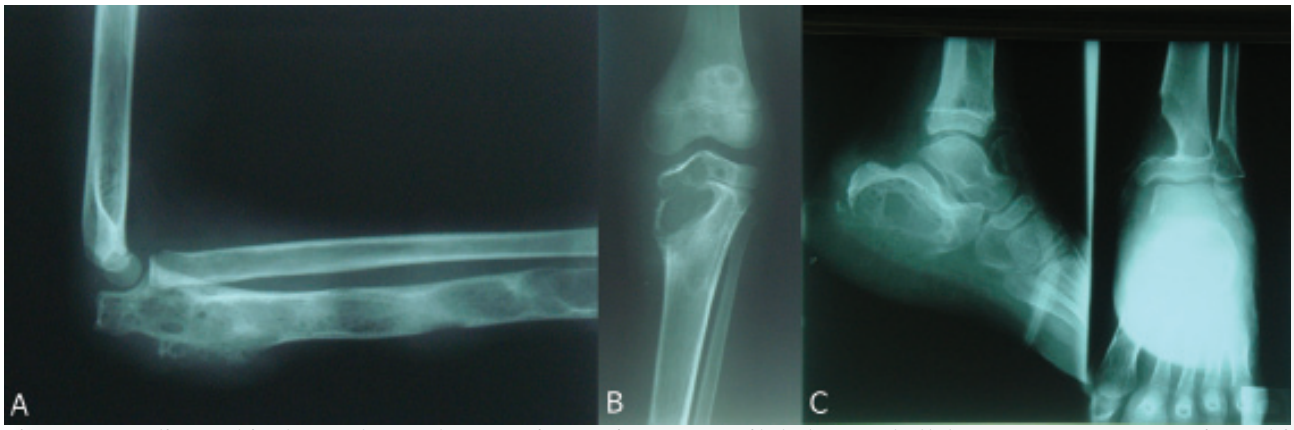
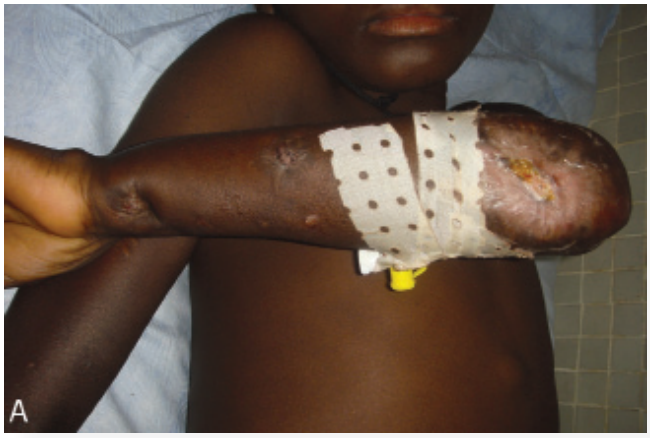
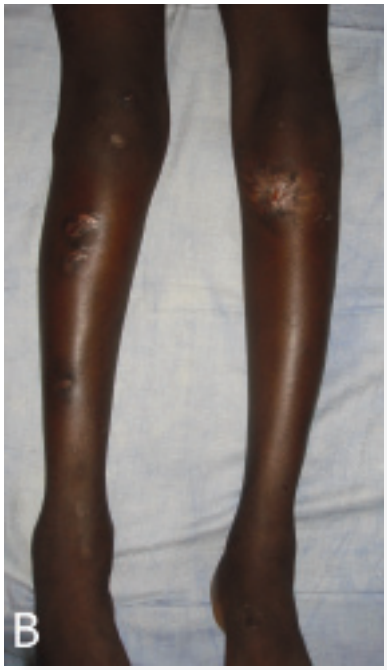


Figure 7a. Radiographie du coude gauche: Réaction périostée en poil de brosse de l'olécrâne et aspect remanié multi lacunaire de toute la diaphyse ulnaire en mai 2010 (sous fluconazole).
Figures 7b, 7c. Radiographie du genou gauche (a) et de la cheville gauche (b) en mai 2010: Majoration de l'ostéolyse métaphyso-épiphysaire supérieure et inférieure du tibia et de la fibula gauches, avec extension de l'ostéolyse à la patella et importante ostéolyse de type II du calcaneus sous fluconazole.
Figure 7a. Radiography of left elbow: periosteal reaction of olecranon with multilacunar remodeled aspect of the whole ulnar diaphysis in may 2010 (treatment with fluconazole).
Figures 7b, 7c. Radiography of left knee (a) and the left ankle (b) in may 2010: augmentation of the higher and lower metaphyso-epiphyseal osteolysis of the left tibia and the left fibula with extension of the osteolysis of the patella and important osteolysis of the calcaneum during the treatment with fluconazole.

La tolérance clinique et biologique à l'amphotéricine B a été bonne (quelques effets secondaires à type de douleurs abdominales intenses, de fièvre et de frissons à la première semaine du traitement). Nous avons effectué une surveillance rigoureuse avec un bilan biologique bihebdomadaire (NFS, transaminases, ionogramme sanguin, urée, créatininémie) et parfois un électrocardiogramme. La mère et l'enfant ont bénéficié d'une psychothérapie. Nous avons réalisé le 7 mars 2011 un scanner du corps entier (les parents n'ayant pas les moyens financiers, il a été réalisé avec l'aide de structures sociales) pour rechercher d'autres atteintes et apprécier l'évolution des lésions osseuses radiologiques; il notait seulement la présence de multiples lésions lytiques résiduelles au niveau du squelette périphérique (Fig. 9a, 9b, 9c). Le 15 mars 2011, soit à 8 mois de traitement avec de l'amphotéricine B, cliniquement, toutes les lésions cutanées étaient cicatrisées (Fig. 10a, 10b), les adénopathies et l'hépato-splénomégalie avaient disparu. Devant la déviation des membres inférieurs en coup de vent (séquelles des lésions osseuses) composé d'un genou varum gauche et d'un genou valgum droit (Fig. 11a et 11b), le port diurne, mais surtout nocturne d'orthèses de correction a été prescrit, en attendant une éventuelle ostéotomie à froid. La dose cumulée de 2g d'amphotéricine B a été atteinte en fin mars 2011 et le relais pris en avril par le kétoconazole par voie orale (offert gratuitement) à raison de 100mg/jr (soit environ 5mg/kg/j) pour prévenir les récidives. Le patient a continué ce traitement pendant un mois puis l'a arrêté sans avis médical. Un bilan biologique effectué était normal. La surveillance clinique a été maintenue à cause du risque de récidives. En juillet 2012, soit un recul de 15 mois après l'arrêt du traitement, il n'y avait aucune récidive cliniquement mais l'enfant a été ensuite perdu de vue.





Figures 8a, 8b. Lésions cicatricielles à l'avant bras gauche (a) et aux jambes (b) après un mois de traitement à l'amphotéricine B (aout 2010).

Figures 8a et 8b : Cicatricial lesions at the left forearm (a) and at the legs (b) after one month with amphotericin B treatment (August 2010) .

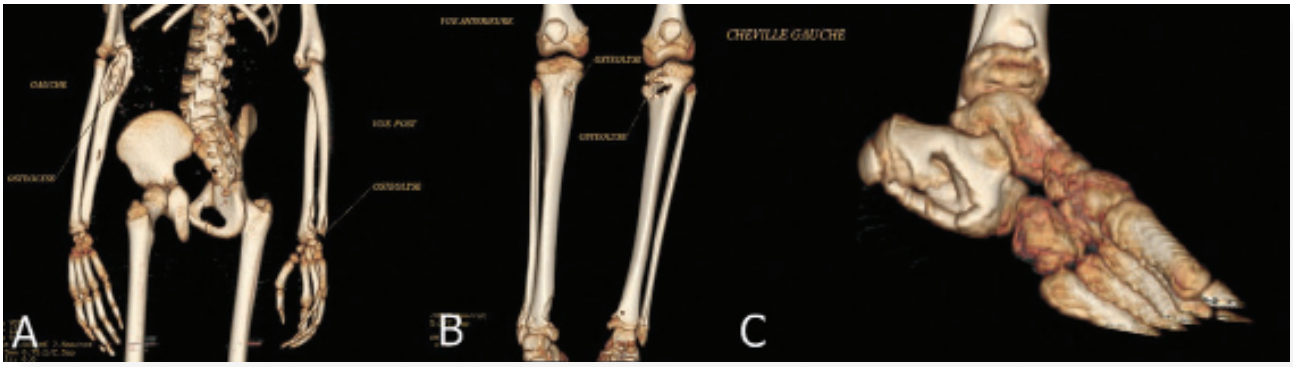


Figure 9a. Reconstruction osseuse en 3D à partir d'un bodyscan révélant les lésions résiduelles d'ostéolyse des os des avant- bras après 8 mois de traitement à l'amphotéricine B (mars 2011).

Figure 9b, 9c. Reconstruction osseuse en 3D montrant des lésions résiduelles d'ostéolyse des os de la jambe (b) et du calcaneus (c) après 8 mois de traitement à l'amphotéricine B (mars 2011).

Figure 9a : Bony reconstruction in 3D with bodyscan showing residual osteolysis of the bone of the forearms after 8 months of amphotericin treatment (March 2010).

Figure 9b, 9c. Bony reconstruction in 3D with bodyscan showing residual osteolysis of the bone of the legs after 8 months of amphotericin treatment (March 2010).

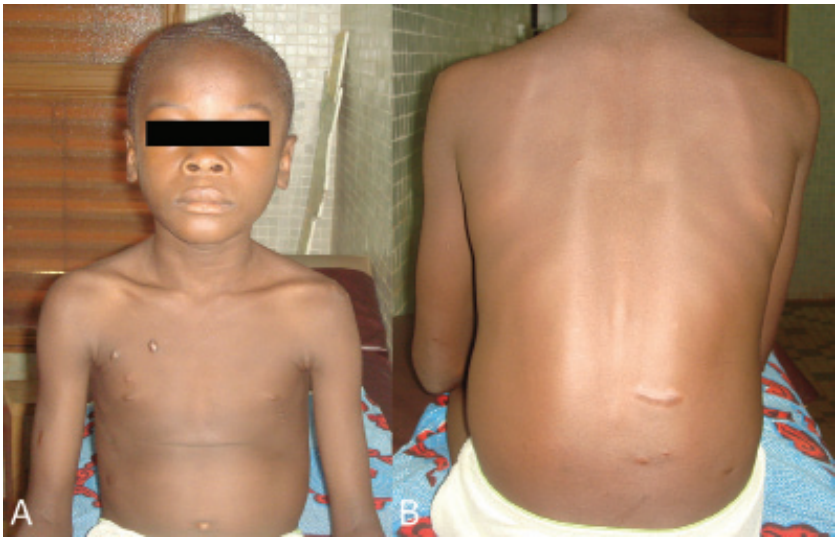


Figure 10a, 10b. Disparition complète des lésions cutanées (du visage et du tronc) de face (a) et de dos (b), après 8 mois de traitement à l'amphotéricine B en mars 2011. Noter les cicatrices hypertrophiques à la poitrine et au dos

Figure 10a et 10b : complete disparition of cutaneous lesions (face and trunk) in front (a) and the back (b) after 8 months of amphotericin treatment (March 2010).

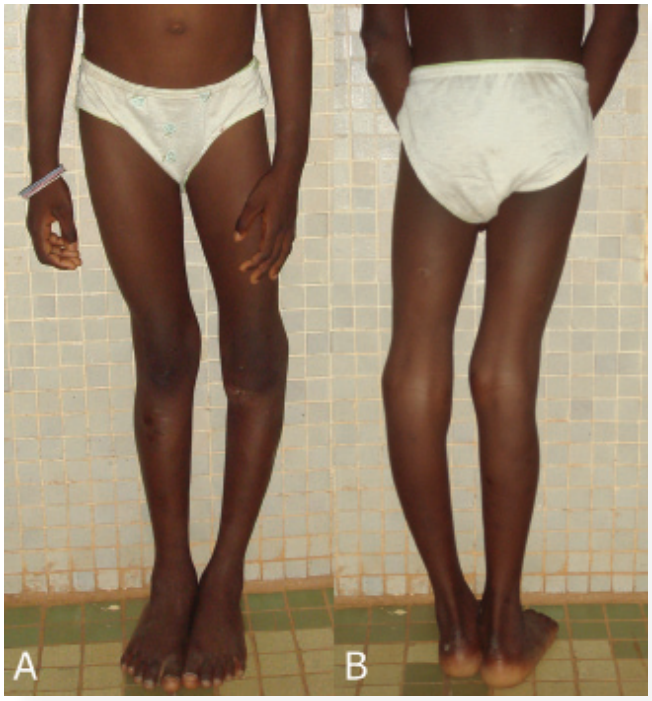


Figure 11a, 11b. Déviation des membres inférieurs : genu varum à gauche, et genu valgum à droite de face (a) et de dos (b) en mars 2011.

Figure 11a, 11b. Deviation of the lower limbs : genu varum at the left and genu valgum at the right in front (a) and on the back (b) in March 2011.

Discussion

L'histoplasmose africaine demeure encore une affection rare en dehors de quelques foyers dans certains pays d'Afrique [13]. Au Burkina Faso, à notre connaissance selon la littérature, nous rapportons le 9ème cas publié mais nous n'avons pas trouvé d'observation sur les six premiers cas. Les 2 derniers cas étaient des enfants comme le nôtre [1,2] alors que l'histoplasmose africaine prédominerait chez les adultes jeunes. En Afrique, d'autres cas ont été décrits chez des enfants immunocompétents [1-9]. La prédominance masculine est notée dans la littérature [10] avec un sex-ratio variant entre 2 et 3 mais notre cas est une fille.

Contrairement à l'histoplasmose américaine, la porte d'entrée de l'histoplasmose africaine fait toujours l'objet de débat. Dans notre cas, la voie aérienne pourrait être incriminée compte-tenu de l'environnement de l'enfant où le père avait un important élevage de poulets à domicile, et de la fréquentation d'un arbre qui était un abri de chauve-souris (sur le trajet de l'école) mais il n'y avait pas d'atteinte pulmonaire; l'affection ayant commencé par des douleurs ostéo-articulaires puis les nodules articulaires et cutanés, la voie transcutanée pourrait être privilégiée; l'analyse du sol de son environnement par un laboratoire d'analyse mycologique qualifié aurait été d'un grand apport. Calzolari et al [1], Vieira et al [14] et Arlet et al [15] ont incriminé respectivement la voie aérienne, la voie transcutanée et la voie digestive chez leurs patients.

Bien que les lésions soient souvent localisées, des formes disséminées ont été décrites chez des enfants par d'autres auteurs [1,3,9,10,16] mais notre patiente avait une forme multifocale disséminée d'histoplasmose africaine associant une localisation cutanée généralisée, ostéo-articulaire multiple, pluri-ganglionnaire, hépatique et splénique. Le polymorphisme des lésions cutanées a été décrit par d'autres auteurs [2,6,8,10]. En effet, notre patiente avait des nodules, des lésions de pseudo-molluscum contagiosum, des papules planes, des abcès froids, des ulcérations bourgeonnantes mais notre cas était particulier par la diffusion et la multiplicité des lésions sur tout le corps, y compris le cuir chevelu et les paupières. Les lésions osseuses étaient particulières par les douleurs très intenses et par l'atteinte multifocale (plusieurs os et articulations atteints) entrainant une déformation des membres. Les ulcérations cutanées et les lésions ostéo-articulaires étaient si douloureuses que nous avons été obligés de prescrire de la morphine. Bien qu'ayant noté des lésions cutanées au visage et au niveau du cuir chevelu, nous n'avons pas observé de lésions osseuses du crâne, ni de la face chez notre patiente. Toutefois, selon Simon [17], les os de la face sont des sièges électifs (14,4%) d'histoplasmose africaine chez les enfants et les jeunes patients. L'hépato- splénomégalie pourrait être aussi due à un envahissement du foie et de la rate par la mycose chez notre fillette car elle n'était pas présente à l'admission et a régressé au cours du traitement par l'amphotéricine B; cette atteinte hépatique pourrait expliquer l'anorexie et l'amaigrissement progressif. Nous n'avons pas pu effectuer la ponction-biopsie du foie pour y rechercher *H.capsulatum var. duboisii* du fait du manque de moyens financiers du patient et du risque encouru, notre plateau technique étant limité. Les localisations viscérales dans l'histoplasmose africaine sont rares [14,15] et d'une extrême gravité, avec une évolution souvent fatale surtout dans sa localisation hépatosplénique [18]. Nous n'avons pas observé d'atteinte pulmonaire; en effet, elle est rare dans l'histoplasmose africaine [1].

Le diagnostic chez notre patiente a été posé à partir de l'examen anatomopathologique de deux prélèvements cutanés. L'examen direct et la culture du pus, réalisés chez nous à l'hôpital, étaient négatifs ; cela retarde le diagnostic et le traitement, et témoigne des difficiles conditions de travail dans notre pays.

Concernant le traitement, Onwuasoigwe [19] suggérait l'utilisation du fluconazole dans le traitement de l'histoplasmose du fait de sa meilleure tolérance et de sa facilité d'administration par voie orale. Cependant, dans notre cas, nous avons eu un échec avec le fluconazole; la patiente a eu au cours du traitement (qui a duré 4 mois et trois semaines) deux épisodes de poussées de lésions cutanées et ganglionnaires, une aggravation des lésions osseuses et l'apparition d'une hépatosplénomégalie. Par contre, grâce à une bonne tolérance clinique et biologique, l'amphotéricine B a prouvé une efficacité remarquable chez notre patiente dès la deuxième semaine de traitement, avec une rémission clinique quasi complète au bout de 8 mois. L'efficacité de l'amphotéricine B a été prouvée par de nombreux auteurs, notamment par Vieira et al [14], Arlet et al [15] et Garcia-Guiñon et al [6]. Cependant, quelques cas de rechutes et de toxicité, voire de décès [7] liées à cette molécule ont été décrits. L'évolution a été favorable dans notre cas mais le traitement a duré 8 mois alors qu'il est normalement de 4 mois [10]. Le coût de ces molécules reste hors de portée de la plupart de nos populations dans notre pays comme en témoignent d'autres auteurs africains [9]. Ce manque de moyens financiers expliquait le retard à la consultation, fréquent dans nos régions, du diagnostic et celui du traitement à l'amphotéricine B qui n'était pas disponible au dépôt pharmaceutique de notre hôpital ; en effet, notre patiente a bénéficié pour sa prise en charge, de l'aide de structures sociales et de notre dépôt pharmaceutique, de la gratuité du fluconazole dans notre pays.

Nous avons eu recours aux chirurgiens pour le parage des lésions cutanées fistulisées et pour la correction des déformations osseuses. La prise en charge de notre patiente a été donc multidisciplinaire (médicale, chirurgicale, orthopédique et psycho-sociale). La déformation des membres constituait un préjudice fonctionnel et moral (la patiente affirmait être la cible de moqueries de ses camarades d'école) qui pourrait jouer sur les résultats scolaires de l'enfant. Le pronostic vital est toujours réservé compte-tenu du risque de récidives tardives voire de décès dans les formes viscérales d'histoplasmose africaine ; une surveillance à long terme de cette patiente s'imposait, ce qui s'avérait difficile du fait qu'elle résidait dans une autre localité éloignée de notre hôpital.

Chez notre patiente, la sérologie pour le VIH était négative. S'il est établi que l'histoplasmose disséminée à *Histoplasma capsulatum var. capsulatum* est considéré comme « un bon marqueur » de l'immunodépression due au VIH, le cas de l'histoplasmose à *Histoplasma capsulatum var. duboisii* n'est pas encore élucidé [20]. La malnutrition aiguë modérée chez notre patiente pourrait diminuer ses défenses immunitaires, expliquant cette contagion par cette mycose. La prévalence réelle de l'histoplasmose africaine est sous-estimée du fait de sa rareté en dehors des zones d'endémie, du retard au diagnostic (polymorphisme clinique occasionnant la confusion avec la tuberculose), du décès souvent rapide des patients (manque de moyens financiers, inaccessibilité géographique aux hôpitaux), du plateau technique limité dans notre pays, et l'inaccessibilité au test du VIH dans les zones rurales.

Conclusion

L'histoplasmose africaine est rare chez le patient immunocompétent au Burkina Faso. Cette observation nous a permis d'identifier chez le même patient, les différentes manifestations de cette affection. Ainsi, nous avons noté l'atteinte de plusieurs appareils (la peau, les ganglions, les os, le foie et la rate), le polymorphisme des lésions cutanées, la diffusion des lésions et le caractère très douloureux des lésions osseuses, le retard à la consultation et les problèmes financiers qui ne permettent pas de confirmer nos diagnostics précocement. Ce cas nous a prouvé que le fluconazole n'est pas toujours efficace et que l'amphotéricine B reste le traitement de choix dans nos pays à moyens limités.

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SUNSCREENS AND ANTIOXIDANTS AS PHOTO-PROTECTIVE MEASURES: AN UPDATE

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Abstract
There are many photo-protective measures adopted for protection from the solar radiation especially the UV radiation spectrum, sunscreens being the main agents. Besides the traditional approach of topical use of sunscreens, both chemical and physical, a new approach has emerged to use systemic agents in the form of vitamins and minerals. In this review, we are describing the major aspects related to sunscreens and anti-oxidants as photo-protective measures.

Key words: photo-protective measures; sunscreens; antioxidants

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Introduction

Ultraviolet (UV) radiation spectrum is the major component of solar radiation, with multitude of effects on the skin. In order to provide protection from the deleterious effects of solar radiations, especially the UV component, various measures have been adopted since time immemorial. Besides the physical protective measures like protective clothing, shields and others, various medicinal preparations which provide a barrier between the sun and skin have been in use in the form of sunscreens. Of late, a new trend has emerged of using antioxidant preparations which increase the antioxidant defence system to cope up with the oxidative damage induced by solar radiations. We hereby present a comprehensive and precise review of sunscreens and anti-oxidants as photo-protective measures, keeping in mind the newer trends that have emerged over the years.

UV radiation spectrum

The most important biologically active functional components of UV radiation spectrum are UV A (~320-400 nm) and UV B (~290-320 nm) components.

UVB is responsible for more severe damage to skin, with acute erythematogenic effect and long term carcinogenic potential, inducing photo-aging and mutagenic damage to nucleic acids.

UVA,less absorbed by biological targets in the skin, penetrates deeper than UVB and is less erythematogenic. It promotes reactive oxygen species (ROS) accumulation and induces direct cell damage, carcinogenesis and contributes to photo-aging and many photo-dermatoses, including polymorphous light eruption [1].

Sunscreens

Most common types of sunscreens presently in use are the topical preparations, designated as physical and chemical sunscreens. Various systemic agents in the form of antioxidants, vitamins and minerals, designated as systemic sunscreens, have emerged as new photo-protective measure. The main goals of sunscreens are to protect against UVB radiation and long-wavelength UVA radiation, scavenge ROS, activate cellular repair systems, including DNA repair [2,3].

Topical sunscreens

Topical sunscreens are available as ointments, lotions, creams or sprays. In order to ensure optimal patient compliance, an ideal sunscreen would be: combination of physical and chemical agents, broad spectrum, cosmetically elegant, substantive, non-irritant, hypoallergenic, non-comedogenic and economical.

The activity of a sunscreen is judged based on sun protection factor (SPF), which measures their capacity to block UV radiation. SPF is defined as a ratio of minimal erythema dose (MED) with sunscreen application to the MED without sunscreen application and is measured using solar simulated radiation and a defined sunscreen application density (2 mg/cm-2). Higher SPF denotes higher efficacy.

High SPF sunscreens almost always contain a physical filter and at least two organic filters,one with optimal screening for UVB wavelengths and the other for UVA photons.

Due to their ease of use, topical sunscreens are the most common photo-protective measure in use [4-6].

Topical sunscreens include the following categories of preparations:

i) Those which reflect or scatter UV photons (physical sunscreens),
ii) Those which absorb them, preventing their effect on the cells of the skin (chemical sunscreens),
iii) Preparations with antioxidant properties

Inorganic (physical) sunscreens

Inorganic sunscreens are formulations containing opaque particulate particles (0.1-1mm diameter), which act by scattering, reflecting or absorbing solar radiation in the UV andvisible radiation spectrum. The factors which affect the effectiveness of inorganic sunscreen are their reflective index, particle size, dispersion in base and film thickness. Their opaque nature and `whitening effect` is an inherent disadvantage, which may be minimized by the use of micronized or ultrafine particles. Various types of inorganic sunscreen agents available include:

a) Zinc oxide (ZnO)
b) Titanium dioxide (TiO).
These are by far the two most commonphysical blockers. Micro-fine ZnO is a betterblocker than TiO7.
c) Others - iron oxide, red veterinary petrolatum, kaolin, calamine, ichthammol, talc,

Organic Sunscreens

Organic Sunscreens are active ingredients which absorb specific wavelengths of UV radiation, not allowing them to reach the viable cells of epidermis. There are more than 21 US FDA approved chemicals used as organic sunscreens. Most common ones are shown in table I.

UVB Absorbers	UVA Absorbers	Newer generation broad spectrum (UVA + UVB) filters
1. PABA derivatives a) Padimate O b) PABA 2. Cinnamates a) Octinoxate b) Cinoxate 3. Salicylates a) Octisalate b) Homosalate c) Trolamine d) Salicylate 4. Others a) Octocrylene b) Ensulizole	1. Benzophenones a) Oxybenzone b) Sulisobenzone c) Dioxybenzone 2. Dibenzoyl methanes a) Avobenzone or Parsol 1789 3. Anthranilates a) Meradimate	1. Ecamsule (Mexoryl SX) 2. Silatriazole (Mexoryl XL) 3. Bemotrizinol (Tinosorb S) 4. Bisoctrizole (Tinosorb M)

Table I. Most common organic sunscreen ingredients

Antioxidants

Antioxidants are commonly added in commercial sunscreen preparationsin order to reduce the photo-oxidative damage that results from UV-induced ROS production, providing a sort of non-sunscreen photo-protection and supplement the photo-protective effects of sunscreens [8]. These include several well characterized vitamins including vitamins C, E and β-carotene [9]. These substances in general help by their antioxidant, anti-inflammatory, anti-carcinogenic effects. Common compounds and effects specific to each are mentioned below.
* Hydroxicinnamic acids such ascaffeic or ferulic acids prevent UVB-induced erythema in vivo and in vitro, and decrease UV-induced oxidative damage in skin cells and lymphocytes [10-13].
* Polyphenolics such as flavonoids and phenolic acids, green tea polyphenols, resveratrol, astaxanthin have been found useful [14].
* Anthocyanins and tannins, present in several fruits such as grapes, pears act by inhibiting UVB-dependent activation of NF-kB, MAP kinase and COX-2 pathways downstream of the signalling kinases MKK4, MEK1, and Raf-1 [15,16].
* Pycnogenol, an extract of French maritime pine (Pinuspinaster Ait), prevents UV induced erythema as well as long-term effects, such as immune-suppression and tumour formation [17,18]. It also possesses regenerative skin properties, and prevents UVB-induced photo-aging [19,20].
* Fernblock, an extract obtained from the fern *Polypodium leucotomos*, inhibits UVB and PUVA therapy-induced erythema in vivo [21]. It is a potent antioxidant and has shown immune-modulating capability and inhibition of pro-inflammatory cytokines, such as TNF-α or IL-6 [22]. PL also inhibits the depletion of langerhan cells induced by irradiation with UV light and PUVA therapy [22-24] and reduces chronic elastosis and matrix metalloprotease expression [25,26].
* Dihydroxy-acetone: Photo-protective agent that provides SPF 3-4 and protects against UVA photons [27].
* Caffeine and caffeine sodium benzoate: inhibit UVB-induced apoptosis [28].
* *Polygonum multiflorum* thumb (PM): an extract that possesses antibacterial properties.
* N-(4-pyridoxylmethylene)-L-serine (PYSer): Suppresses ironcatalyzed ROS generation [29].
* Creatine: Topical use of creatine has been shown to decrease UV-induced damage in vitro and in vivo, and postulates its use to fight photo-aging [30].
* Idebenone: Clinical studies have suggested its efficacy in preventing photo-aging [31].
* COX-2 inhibitors: Topicalcelecoxib, a COX-2 inhibitor, has been shown to decrease UVBmediated erythema, inflammation and prostaglandin E2 production [32,33].
* DNA repair enzymes: Constitute an emerging approach to enhance DNA repair after UV exposure such as photolyase [34,35].

* T4 endonuclease: Assayed in patients with xerodermapigmentosum [36,37].
* DNA oligonucleotides: Enhance the cellular response to subsequent UV irradiation,regardless of the existence of previous DNA damage [38].

Systemic sunscreens

Photo-protection by oral/parentral medication is a novel approach in skin care. They complement the topical sunscreen use by preventing photo-aging and photo-carcinogenesis. They increase the basal threshold of systemic and cutaneous antioxidant systems [39]. Various biologically active compounds evaluated include:

Vitamin derivatives: Carotenoids, such as lycopene, which has been suggested to be a very efficient singlet oxygen quencher present in tomatoes, and xanthophylliccarotenoids such as lutein and zeaxanthin, exhibit beneficial photo-protective effect, singly or in combination, along with topical preparations [40,41]. Tocopheroland ascorbatealso exhibit photo-protective effect, especially when used in combination with other compounds such aslycopene, beta-carotene, selenium yeast, proanthocyanidins [42,43]. Oral use of these delays the onset of UVB induced erythema and inhibits the expression of matrixmetalloproteinases, delaying an effect on photo-aging [44].

Dietary animal and plant extracts: Their composition is rather heterogeneous, but most contain dietary flavonoids and phenolics. Some examples include:

* Genistein, which can be used as a dietary complement as well as in topical formulations, decreases UVB induced skin photo-aging and tumour genesis in rodent models, postulating its use for cancer prevention [45].
* High doses of omega-3 polyunsaturated fatty acids from fish oil have been shown to decrease UVB induced erythema and inflammation [46].
* *Polypodium leucotomos* extract (PL) can also be administered orally with very low toxicity, in addition to its topical use as already described.Oral PL scavenges free radicals and reactive oxygen species such as superoxide anion, singlet oxygen, hydroxyl radical and hydrogen peroxide, and prevents lipid per-oxidation [47,48]. Besides the effects already mentioned, PL also prevents oxidative DNA damage (8-hydroxyguanine) and accelerates repair of thymine dimers [24,49]. In addition, it also inhibitstrans-urocanic acid photo-induced isomerization and inactivation, as well as UVA-induced cyclobutane pyrimidine dimer deletions and mitochondrial DNA damage [50,51].
* Green tea poly-phenols (GTPP), e.g. epigallocatechin-3-gallateprevents UV-induced skin tumourgenesis in mice. Several mechanisms underlie this effect, e.g. induction of interleukin 12, which prevents immune-suppression and boosts DNA repair through excision repair mechanisms, inhibition of angiogenic factors, stimulation of T cell-dependent cytotoxicity and tumour cell clearance [52]. Oral GTPPs can also decrease UV-induced expression of skin matrix metalloproteinases, postulating an effect in photo-aging [53].

Indications of sunscreen use

There are innumerable prophylactic and therapeutic indications for sun protection and potential benefits of sunscreens and antioxidants. The major ones are listed in table II [54].

Guidance for usage

Sunscreens protect the skin by absorbing and/or reflecting UVA and UVB rays. The FDA requires that all sunscreens contain a sun protection factor (SPF) label. In order to obtain maximum performance from sunscreen it is important that it is applied correctly and sufficiently with the right thickness. Application thickness has a significant effect on the amount of protection provided by a sunscreen. When not enough sunscreen is applied, the effective SPF of the product will be reduced significantly. This reduction in SPF may potentially lead to sunburn, particularly if the sunscreen used has a low or medium SPF to begin with [55].

An average size adult should apply at least one teaspoon of sunscreen to each arm, leg, frontand back of body, and at least half a teaspoon to the face (including theears and neck). Sunscreen should be applied at least 10-15 minutes before sun exposure to allow the sunscreen time to form a protective film on the skin. Sunscreen should be re-applied every two hours at minimum, even on cloudy days, and after swimming, heavy sweating, and towelling. Re-applying sunscreen doesn't extend the length of time a person is protected from sunburn. It just guarantees that the actual SPF of the product is realized [55]. While using sunscreen sprays, the product should be both sprayed on and rubbed in to ensure uniform coverage [56].

1. Sunburn
2. Freckling, discolouration
3. Photo-aging
4. Skin cancer
5. Phototoxic/ photo-allergic reactions
6. Photosensitivity diseases
   - Polymorphous light eruption (290-365 nm)
   - Solar urticaria (290-515 nm)
   - Chronic actinic dermatitis (290 nm-visible)
   - Persistent light reaction (290-400 nm)
   - Lupus erythematosus (290-330 nm)
   - Xeroderma pigmentosum (290-340 nm)
   - Albinism
7. Photo-aggravated dermatoses
8. Post-inflammatory hyper-pigmentation (post-procedure)

Table II. Main indications of sunscreen use and sun protection

Some issues of concern

The use of sunscreen as photo-protective measure is non controversial. But some concerns exist in a few special situations, as mentioned below.

* *Sunscreen use in infants:* Although not known to be hazardous, the use of sunscreens is not recommended for infants younger than 6 months. Sun protection in children plays a significant role in preventing skin cancer later in life. Research indicates that regular use of sunscreen for the first 18 years of a child's life can reduce the lifetime incidence of skin cancers by more than 70% [55].

* *Contact dermatitis:* The most common cause of contact dermatitis (photoallergy) due to sunscreens is oxybenzone [57].

* *Nano-sized particles:* Nano-sized particles range in size from 1-100 nm. Micro-fine forms of zinc oxide and titanium dioxide have a particle size of 20-50 nm. Nanotechnology makes inorganic sunscreens more cosmetically acceptable (less whitening of skin after application). Studies show that these particles remain on the surface of the skin or in the stratum corneum, and are hence safe for human use [58].

* *Vitamin D production:* UVB radiation is responsible for more than 90% of vitamin D production in the skin. A few minutes exposure of the face, arms, and hands to mid-day summer sunlight two or three times a week is sufficient for vitamin D synthesis [59]. There have been concerns that widespread use of sunscreens, particularly those with high SPF, may lead to a significant decrease in vitamin D production. However, there is evidence that normal usage does not generally result in vitamin D insufficiency though sunscreens can significantly reduce the production of vitamin D under very strictly controlled conditions [60]. In fact, vitamin D and calcium levels have been found to be relatively normal in xeroderma pigmentosum patients, in spite of strict photo-protection [61].

* *Hormonal effects*: Some sunscreens (oxybenzone, avobenzone, octinoxate, padimate O) have been tested for their estrogenic/ anti-androgenic properties in animal studies. However, the endocrine effects of these agents remain controversial, warranting further human studies.

Sunscreen related indices

Various indices have been formulated by in vitro and in vivo methods to assess the efficacy of sunscreens with respect to specific components of the UV spectrum [1,57,58,62-64]. These are as follows:

i) Sunburn protection factor (SPF)

SPF= MED of photo-protected skin with sunscreen/ MED of unprotected skin without sunscreen.

Grading of sunscreens according to SPF:
Low: SPF 2 – 15; Medium: SPF 15 – 30; High: SPF 30 – 50; Highest: SPF >50

It is noteworthy that a sunscreen with an SPF 15 blocks about 93% of UVB radiation, while one with SPF 30 blocks about 97% of UVB radiation. This small difference of 4% in protection may make a big difference between an aesthetically pleasing sunscreen and an undesirable one, as products with higher SPF generally tend to be uncomfortable and cosmetically unpleasant due to the higher concentration of the active ingredients [65].

ii) Japanese standard (persistent pigment darkening; in vivo method)

UVA dose that induces persistent pigment darkening 2-24 hours after exposure in sunscreen protected skin/ UVA dose that induces persistent pigment darkening 2-24 hours after exposure in sunscreen unprotected skin.

iii) Australian / New Zealand standard (in vitro method)

8-µm layer of the product should not transmit more than 10% of radiation of 320 to 360 nm
OR
20-µm layer of the product should not transmit more than 1% of radiation of 320 to 360 nm

iv) European union guidelines

UVA protection factor (persistent pigment darkening method) = 1/3 of SPF
AND
Critical wavelength = 370nm

v) Boots star rating system (used in the United Kingdom)

In vitro measurement of the ratio of a product's UVA (320-400 nm) absorbance over its UVB (290-320 nm) absorbance is used to calculate its Boots star rating, shown in Table III. Products with better UVA absorbance have a higher Boots star rating.

New Sunscreen Technologies

Sun spheres

Sun-spheres are styrene/acrylate copolymers that do not absorb UV irradiation but enhance the effectiveness of the active sunscreen ingredients. The Sun-sphere polymer beads are filled with water, which migrates out of the particle, leaving behind tiny air-filled spheres, which have a lower refractive index (1.0) than the dried sunscreen film (1.4-1.5). As a result, scattering of UV radiation occurs, increasing the probability of contact with the active UV filters in the sunscreen. Sun-spheres are also available in a powder form, and can boost SPF by 50 -70% making it possible to reduce the concentration of active ingredients [66].

Microencapsulation

Active sunscreen ingredients are entrapped within a silica shell, as a result of which, allergic or irritant reactions to the active ingredient can be minimized, and incompatible sunscreen ingredients can be safely combined, without loss of efficacy [66].

Ratio of UVA:UVB absorbance		Boots star rating
Before irradiation	After irradiation	
< 0.6	< 0.56	No star
> 0.6	> 0.57	3
> 0.8	> 0.76	4
> 0.9	> 0.86	5

Table III. Boots star rating for sunscreens

Conclusion

Sunscreens are an important prophylactic and therapeutic armamentarium for dermatologists and also used as over the counter products as photo-protective measures. Sunscreens are constantly evolving and a dermatologist should be well versed with various aspects of these.

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POLYMORPHOUS LIGHT ERUPTION - A REVIEW

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Abstract
Polymprhouos light eruption is the most common idiopathic photodermatosis. It is a sun induced cutaneous reaction characterized by onset itchy erathematous papules, plaques, vesicles or erythema multiforme type of lesions after brief exposure to sunlight. Sun-exposed areas of the body or rarely the partially covered areas are commonly involved.
PLE is more common in temperate climates than in tropics. It begins usually at the onset of summer and moderates as the summer progresses. In most patients it usually runs a benign course. Diagnosis is mainly on clinical grounds. Therapy involves avoidance of sun-exposure and use of sunscreens. Cases not responding to simple measures require PUVA (Psoralen and Ultraviolet A) or UVB (ultraviolet B) therapy. Other alternative suggested therapies with variable success include oral hydroxychloroquine, beta-carotene, thalidomide and nicotinamide.

Key words: Polymorphous Light Eruption; UV-A radiation; UV-B radiation; Sunscreens; sun-induced reaction

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Introduction

Polymorphous Light Eruption (PMLE), also termed Polymorphic Light Eruption, is the most common photodermatosis encountered in clinical practice. It is an idiopathic acquired disorder in which a delayed cutaneous response to ultraviolet radiation occurs in the form of skin eruptions consisting of papules, vesicles or plaques over the sun-exposed and rarely on partially covered areas. The reaction usually follows the brief spring or summer sun exposure and occurs after a latent period of hours to days. It moderates as the summer progresses and usually subsides on absence of further sun exposure [1].
Polymorphous light eruption causes lot of psychological stress amongst those suffering from the disease especially in women with longstanding illness [2].

History

The first description of PMLE was probably that of Robert Wilson as reported by Bateman [3]. These authors used the term eczema solare to describe recurrent eczematous skin lesions that appeared on light-exposed body areas during the summer months. Jonathan Hutchinson introduced the term summer prurigo to describe a disorder that he observed in 13 Patients that probably represented a form of PMLE [4]. He described this disorder as a papular eruption that began at puberty and affected primarily the face and upper extremities. Hutchinson noted that it occurred in the summer and was related to sun exposure.
Sellei and Liebner attempted to differentiate the eczema solare and the summer prurigo types of PMLE; they believed that the lesions of eczema solare are confined to exclusively sun-exposed parts of the body whereas the papules of summer prurigo appear on certain predisposed areas, such as forehead, the outer aspects of arms and ankles. In addition, they showed that, in one patient, sun exposure of a single body area not only produced local erythema in situ but also evoked the development of papular lesions in previously involved areas [5].
Lamb et al reviewed their experience with PMLE and called the condition solar dermatitis [6]. They noted that, in their patients from south western United States, plaques were the most common lesions, appearing in 75 percent of patients, and that vast majority of affected individuals were males.
McGrae and Perry reviewed the Mayo clinic experience with PMLE and observed that persistent erythema should be included with eczema solare, summer prurigo and solar dermatitis as part of PMLE [7]. Magnus asserted that summer prurigo identified by Hutchinson is a disorder separate from PMLE [8]. Harber and Bickers opined that the terms summer prurigo, solar eczema, prurigo, plaques and persistent erythema (sun induced) to be included under a single term PMLE [9].
However, the current literature includes clinical lesions consisting of intermittent, delayed and transient cutaneous reaction to sun exposure as PMLE. The reaction is usually non-scarring, is pruritic and the lesions consist of either papules, vesicles, plaques, eczema, erythema multiforme-like lesions or insect bite reaction-like lesions as a spectrum of lesion in PMLE.

Some authors do not include eczema, erythema-multiforme-like lesions or insect-bite like reactions as a part of spectrum since they are a source of confusion, and they may occur in conjunction with papules, plaques or vesicles at other sites in the body but not alone [10].

Epidemiological Aspects

Several population-based prevalence surveys have been conducted, and the results of these studies suggested that the prevalence of PMLE is 10-20 % in North America populations [11]. Berg interviewed 809 randomly selected office workers from four Swedish cities, and observed that 100 (12.4%) had a history consistent with PMLE [12]. In this study, there was a predominance of women with a history of PMLE. Pao et al interviewed 182 subjects in England and 368 subjects in Australia and found that the prevalence of PMLE to be 14.8% in London and 4.3% in Australia [13]. They suggested that the prevalence of PMLE may be higher in regions further away from the equator because of variations in the proportions of UVA and UVB radiation at different latitudes.

Morison and Stern interviewed 271 random individuals entering a medical library in Massachusetts. Ten percent of this sample reported a history consistent with PMLE, and the reported prevalence was higher among females than males (14% VS 7%) [14]. Only 15% of individuals with a history consistent with PMLE had sought previous medical attention for their symptoms. Morrison and stern compared the PMLE patients identified from their survey of 38 patients with PMLE who presented to the photosensitivity clinic at General Hospital, Massachusetts. Only one significant difference between the two groups was observed; clinic patients required a mean exposure of 30 minutes to induce symptoms compared to a mean exposure of 3 hours among survey cases [15].

Ros and Wennernstern interviewed 397 workers in a Swedish pharmaceutical company and found 21% had a history consistent with PMLE. Their sample study primarily included women (86%) and so after adjusting, a prevalence estimate of 7.4% was reported. Only 3% of these patients had sought medical attention for their symptoms [16].

The results of these prevalence studies suggest that PMLE is a relatively common condition in North America and European populations.

PMLE is more common in temperate climates than nearer equator. The explanation for this is unknown, but lesion development may be inhibited by UVB-induced immunological reactivity in sunnier climates. In addition, variations in the proportions of UVA and UVB in terrestrial sunlight at different latitudes may play a role, as UVA appears to be important in lesion induction. Thus, the greater proportion of UVA to UVB in temperate climates may cause more PMLE than in tropical regions. Furthermore, greater UVA exposure may also occur because of a slower rate of sun burning [13].

Jansen observed 138 PMLE cases in Finland during the early 1970s. 62% of these were women, 51% reported seasonal hardening effect, and 60% reported symptom development with 30 min of sun exposure [16]. 57% were able to identify the exact onset of their first symptoms. The mean age of onset was 36.6 years, and a mean duration of symptoms prior to clinical presentation was 10.5 years. Petzelbaner et al studied 198 patients and reported that the mean age at onset of symptoms was 35 years and the mean duration of PMLE prior to diagnosis was 12 years [17]. Lesional morphologies reported in these series include urticaria-like plaques (25.1%), blistering (36%), papular lesions (25%) and lesions with scales or crusts (6%) [17].

In a study of 110 patients by Boonstra et al, average age onset of disease in men was 46 yrs as compared to 28 yrs in females [18]. The mean duration of complaints before they came to the clinic was 9.2 years. The course of disease activity during the period (from 1985 to 1991) was progressive in 86 patients, stationary in 19, and unknown in 5. The morphology of lesions, according to patient history and clinical inspection, was papular (61 Patients), papulovesicular (27 patients), eczematous (18 patients), or erythematous with infiltration of the skin (4 patients). The Minimum Erythema Doses (MEDs) for UVB and UVA were lowered in 43% and 37% respectively in men. In women only 4% and 11% MEDs were reduced for UVB and UVA respectively [18].

The photoprovocation tests showed a pathologic reaction to both UVB and UVA in 88% of the men and in 52% of the women. In the remaining patients they found pathologic reactions to UVB alone (3% men, 24% women). Abnormal reactions to visible light were mostly observed in those patients who reacted pathologically to UVB and UVA [19].

Etiology and Pathogenesis

Pathogenic mechanisms in PMLE have not been fully elucidated. An abnormal immunological response of Gell and Coombs type IV to a sunlight–induced cutaneous neoantigen, first proposed in 1942, because of the delayed reaction time and histological appearance, remains a favored hypothesis, although possible abnormalities of arachidonic acid metabolism have also been suggested as being responsible [20,21]. Far et al studied the effects of indomethacin on UVB and UVA induced erythema in patients with PMLE [22]. They found that topical application of indomethacin inhibited UVB but not UVA erythema in 13 of 23 patients. In the remaining 10 patients there was an augmented response to both UVA and UVB. This finding indicates that PMLE embraces two or more disease states- the more severe group, perhaps associated with the abnormal metabolism of arachidonic acid in response to UV irradiation, and a milder form [22].

In some PMLE lesions induced by UV-A, keratinocytes were found to express intercellular adhesion molecule 1 (ICAM-1) [23,24]. Induction of ICAM-1 occurs either directly by effects of UV on ICAM-1 gene or indirectly by effect of interferon gamma produced by activated lymphocytes in the lesions. Intravascular deposits of fibrin, C3 and Immunofglobulin-M were noted in certain patients suggesting the possible role of vascular injury and ensuing activation of clotting cascade in the pathogenesis. Immunohistochemical analysis by Schornagel et al in 2004 showed a significant decreased neutrophil infiltration in PMLE skin after UV-B irradiation compared with healthy case control subjects ($P < .05$) [25]. The authors concluded that PMLE is marked by an altered immune response resulting in decreased skin infiltration of neutrophils after UV-B irradiation.

Induction of PMLE: Difficulty in reliable laboratory induction of clinical lesions has frustrated investigators into the pathogenesis of PMLE. No particular wavelength induces lesions consistently. In most series, however, UVA has been more reliable effective in inducing lesions than UVB [26].

Although chromopheres for PMLE have not been identified, the induction of lesions by a UVA sun-bed in the non-tanning sacral pressure area suggests that UV absorption, at least some patients, may be oxygen independent [27,28].

The reported percentage of patients with family history of photosensitivity ranges from 15% to 56%. Several authors have speculated that PMLE is inherited as an autosomal dominant gene with reduced penetrance. Some published studies have investigated the genetics of PMLE in greater detail, and the results of these studies suggest that a polygenic model can also explain PMLE inheritance. Millard et al examined 420 adult female twins enrolled in a twin registry in England. The prevalence of PMLE was 23% in monozygotic twins and 18% in dizygotic twins [29]. Both a polygenic model of inheritance and a dominant single gene model explained these data. Although results of the genetic studies suggest that environmental factors, other than UV radiation, may be involved in the pathogenesis of PMLE. Oral contraceptive use was evaluated in one small case series. 3 out of 87 women in this study noted some improvement in their PMLE symptoms after discontinuation of oral contraceptives, but this alleviation of symptoms was only temporary [29].

Most authors agree that PMLE results from delayed cell-mediated hypersensitivity to some unknown sunlight-induced antigen. Three commonly reported findings support this hypothesis: delay in onset of symptoms from 30 minutes to several days; dense perivascular infiltrate in the dermis resembling that observed in allergic contact dermatitis; and the pattern of adhesion molecule expression is similar to that seen in a delayed hypersensitivity response [30].

Histopathology

The histological features of PMLE are characteristic but not pathognomonic and vary with the different clinical presentations. There is a moderate to intense, tight perivascular infiltrate in the upper dermis and mid-dermis in all clinical types, the infiltrate consisting predominantly of T cells; although neutrophils are also present. Eosinophisls are infrequent [31].

Epidermal changes may be absent or variable in severity [31].

Epidermal spongiosis occurs along with perivascular infilitration and dermal edema. In older lesions dermal edema and perivascular infiltrate may extend into deep dermis. Acanthosis and parakeratosis can occur along with epidermal spongiosis [12]. Occasional dyskeratosis, exocytosis may be seen [1].

Sunburn cells are notably absent. The liquefactive degeneration at the dermo-epidermal interface, commonly observed in cutaneous lupus erythematosus, may also be seen in PMLE [32]. Dermal edema may be accompanied by perivascular edema and endothelial swelling [31].

Influence of time

The manifestations of a normal sunburn response must be considered in the description of abnormal findings in the epidermis of a skin biopsy from a patient with PMLE. For example necrosis of epidermal cells which is not a specific feature of PMLE, but is response seen in normal skin 24 hours after irradiation with UVB, may be seen in lesions of PMLE [9].

Influence of site

Biopsy specimens obtained from light-exposed areas, such as the face and the arms, may show chronic degenerative changes due to repetitive actinic damage; among them are hyperkeratosis, epidermal atrophy and solar elastosis [9].

The dermal infiltrate is composed primarily of lymphocytes. CD4+T cells dominate in the first 5 hours after irradiation, while CD8+T cells dominate 72 hours after exposure. Delayed Langerhan's cell depletion has been observed in PMLE. In normal skin CD11b+ cells decrease in the dermis following UV exposure. In PMLE patients, CD11b+ cells increase in both epidermis and dermis after UV exposure [33].

Most histopathological studies have focused papular type lesions; other lesion type may have slightly varied appearances. For example, spongiotic vesicles and subepidermal blisters are often formed in vesiculobullous lesions and, in plaque lesions, the dermal infiltrate tends to be lichenoid and spongiosis is widespread [34].

The picture may resemble that seen in early lesions of subacute cutaneous lupus erythematosus (SCLE), except that the infiltrate is periadnexal in case of SCLE and perivascular in case of PMLE [31].

Clinical Features

The eruption typically begins in each spring often moderating as summer progresses. It rarely occurs in winter except after exposure to UVR reflected from snow. Individual susceptibility varies considerably; the period of sunexposure needed to trigger the eruption usually begin from 30 min to several hours, occasionally more or less. Following exposure, new lesions appear after a latent period of hours to days, but not less than 30 minutes, although pruritus may develop sooner. In the absence of further exposure, these lesions subside completely, usually without scarring, over 1 to 7 days or occasionally longer. In any one patient, PMLE always tends to occur on the same areas, although the distribution may gradually spread or recede overall. Lesions generally occur symmetrically and usually affect only some exposed sites, often those covered in winter such as the upper chest and arms. Associated systemic symptoms are rare, but chills, headache, fever and nausea are possible [15]. Over 7 years, 64 of 114 patients (57%) reported diminution in their sun sensitivity, including 12 (11%) that totally cleared [14].

PMLE has been subdivided into several morphologic variants, namely papular, papulovesicular, plaque, vesiculobullous, eczematous, insect bite-like, and erythema multiforme-like forms, with one type of lesions usually predominating in a given individual [1].

In some patients only pruritus occurs without any lesions. "Polymorphic light eruption sine eruption" is used to describe such an entity in patients. They probably represent milder form of PMLE or subclinical of PMLE [35].

The papular form is the most common followed by papulovesicular and plaque variants, while the rare vesiculobullous, eczematous, insect bite like, and erythema multiforme-like forms are controversial and are a source of confusion. They are excluded altogether by many authors. It is unlikely that such variants represent true subgroups, because lesion of different as morphology may occur at different skin areas in the same patient. Diffuse facial erythema and swelling, for example, may accompany typical papular lesions at other sites. A variation in susceptibility of exposed skin areas to PMLE is an important distinguishing characteristic feature of the disorder from other photodermatoses, and juvenile spring eruption [36]. Juvenile spring eruption commonly affects boys aged 5 to 12 years, apparently represents this phenomenon. This condition is a self limiting eruption of pruritic grouped papules and vesicles confined to the light exposed helices of the ears and histopathology is similar to that seen in PMLE.

Sometimes a patient having PMLE lesions elsewhere can have lesions involving the helices of ears, similar to those seen in juvenile spring eruption.

The most commonly affected sites include 'V'area of the neck and forearms. The face and hands of PMLE cases may be spared, because these sites often receive daily sun exposure and thus undergo hardening [11]. The onset of PMLE usually occurs in second to third decades, but symptoms may begin in early childhood or late adulthood. PMLE is reported to occur in all skin types; however, fair-skinned individuals are most commonly affected.

Women are more often affected than men, usually in 2:1 or 3:1 ratio. The observed gender differences in PMLE occurrence probably reflects differences in underlying genetic and hormonal pathways, and possibly differences in the daily and seasonal patterns of sun exposure between men and women. Women may also be more cognizant of their skin symptoms and are more likely to seek medical attention than men, which could result in an over representation of women in clinical studies [11].

Differential Diagnosis

PMLE can be differentiated from actinic prurigo because the onset of actinic prurigo typically occurs in early childhood. Actinic prurigo lesions often persist for months even after cessation of UVR experience, and chelitis and scarring are common features [37]. Solar urticaria develops almost immediately after sunexposure and resolves within hours, lesions being wheals; lesion development and resolution in PMLE are less rapid [38]. Chronic actinic dermatitis primarily affects elderly men and is characterized by scaly or eczematous lesions [37,39], while PMLE lesions predominately affect women in early to mid adulthood. Other differential diagnosis that should be considered includes drug-induced photosensitivity, photocontact dermatititis, airborne contact dermatitis, hydroa vaccinforme, lupus erythematosus and porphyrias. Careful history, including questions about age at symptom onset, exposure to known photosenitizers, the time interval between the sunexposure and the onset of symptoms, family history of photosensitivity, sunscreen use and possible involvement of other organ system may aid in diagnosis. Sometimes subacute cutaneous lupus erythematosus may present with lesions similar to PMLE. In case of doubt, measurement of serum antinuclear factor, serum anti-Ro and anti-La would exclude SCLE. More persistent plaque-type PMLE must be differentiated from Jessner's lympholytic infiltrate of the skin by histopathological examination of skin biopsy [40].

Prognosis

Studies of the natural history of PMLE have demonstrated that the course of this condition is highly variable, ranging from complete remission to development of debilitating symptoms and possibly other autoimmune disorders. After 38 years of follow-up, Ferguson and Ibbotson observed a 24% spontaneous remission rate in their cohort [41]. Jansen and Karvonen followed 114 patients for 7 years after diagnosis, and found that 57% improvement in their patients during the follow–up period [42]. After 4 years of follow up of 110 Dutch PMLE patients, symptoms worsened in 86, stayed the same in 19, and were unknown in 5. Hasan et al observed 24% of their patients went into complete resolution of lesions, 51% showed improvement of the conditions, and in 24% condition remained unchanged or worsened [43].

Treatment

The mild disease of many patients is satisfactorily controlled by the moderation of sunexposure at times of high UV intensity and regular application of broad-spectrum sunscreens with a high protection factor particularly against UVA. Thus, the use of sunscreen protecting against mostly UVB may lead exacerbation of UVA-sensitive PMLE by permitting patients longer sunexposure without burning and should be avoided [44]. More severely affected subjects, however require courses of prophylactic low-dose photochemotherapy or phototherapy [45].

In a study of 42 patients of PMLE, Murphy et al found that 6 weeks of thrice weekly low-dose PUVA and UVB irradiation therapy in early spring were found to be excellent prophylactic treatments [45] PUVA was more effective than UVB from patients' subjective reports and from clear clinical trend in that direction. In another study by Addo et al, 36 Patients with PMLE were treated with either UVB photo therapy or PUVA therapy during the spring and the early summer [46]. Both the forms of therapy were found to be effective in 90% of cases. Similar efficacies were found in other studies as well [47].

The UV exposure of prophylactic UVA or UVB may sometimes trigger the eruption, particularly in severely affected individuals, necessitating concurrent administration of systemic glucocorticosteroids on occasion. However, some patients are unsuitable for this or their disease remains uncontrolled, and therefore is inappropriate for further courses. Such PUVA – intolerant patients or those unable to commute for treatment may instead be tried on suggested alternative therapies such as hydroxychloroquine, thalidomide, beta-carotene and nicotinamide [47,48]. A study by Corbett et al reported that beta-carotene was effective in reducing erythema and irritation [47]. Chloroquine also reduced irritation and erythema. They concluded that they are only moderately effective in controlling the disease. Similarly Murphy et al reported only moderate improvement with hydroxychloroquine. Hence except for thalidomide, in cases of persistent case of PMLE, these are of only occasional or limited therapeutic value, and phototherapy-resistant cases thus pose a management problem [48]. Sometimes, short-term (less than a week) oral glucocorticoid therapy rapidly suppresses the eruption once developed although no controlled studies are undertaken. Thus glucocorticoids can be given for young, fit patients or in those who need only intermittent therapy for vacations or other occasional sun exposure [49]. Topical corticosteroids and oral antihistamines are effective in alleviating symptomatic relief but are of not much benefit [47]. There remain, however, a small proportion of patients, who are unsuitable for, or unable to tolerate, or not helped by any of these measures, and UV avoidance remains only safe and effective option. A further few of them are so sensitive that they are continuously affected in spite of all reasonable UV avoidance measures, and in these, short-term immuno- suppressive therapy with low-dose azathioprine may be appropriate, and has lead to marked clinical improvement in two such patients [50].

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MOLLUSCUM CONTAGIOSUM OF SCALP IN A CHILD

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We report a male patient of 7 months old with redish papule on his scalp (Fig. 1a, b) the rest of the clinical examination was normal. Personal and family history non contributory.
The lesion of the scalp began 4 months ago asymptomatic but began to grow and bleeding for that reason his pediatrician sent to us to evaluate him.
The diagnosis of nevoxantoendothelioma was done and a biopsy was performed.
The histogical slides showed a lesion become enlarged as a consequence of the accumulation of masses of viral material purplish red bodies of mollusccum contagiosum was seen (Fig. 2).
Molluscum contagiosum is caused by a virus that is a member of the poxvirus family. The infection can get in a number of different ways.
This is a common infection in children although it is rare under the age of one year and occurs when a child comes into direct contact with a lesion. It is frequently seen on the face, neck, armpit, arms, and hands but may occur anywhere on the body including mucous membranes except the palms and soles.
A second peak occurs in young adult due to sexual transmission with involvement of genital and perineal skin [1].
The virus can spread through contact with infected persons, fomites and sexual transmission.
In conditions that involve altered immunity such as atopic dermatitis, corticosteroid and immunosuppressive therapy, sarcoidosis, leukemias, Wiskott Aldrich syndrome and acquired immune deficiency syndrome, atypical lesions of molluscum contagiosum may occur, often reaching a large size on an unusual site [2].
Typically, the lesion of molluscum begins as a small, painless umbilicated papule that may become raised up to a pearly, flesh-colored nodule. The papule often has in the center central core or plug of white, cheesy or waxy material.
The papules are about 2-5 millimeters wide. There is usually no inflammation and subsequently no redness unless you have been digging or scratching at the lesions.
In adults, the lesions are commonly seen on the genitals, abdomen, and inner thigh.
The localization of molluscum contagiosum exclusively on scalp is rare White [3] and Hill, Messina [4] each reported a case of molluscum contagiosum located exclusively on the.
Sometimes the molluscum contagiosum can be only on the scalp or can also be in other sites [5] at the same time, but the single lesion localized on scalp is uncommon
Molluscum contagiosum on the scalp can affect patients in all ages since newborn to adult in old age and in immunocompetent or no immunocompetent persons [6].
This is a little report of molluscum contagiosum of the scalp for its uncommon localization.

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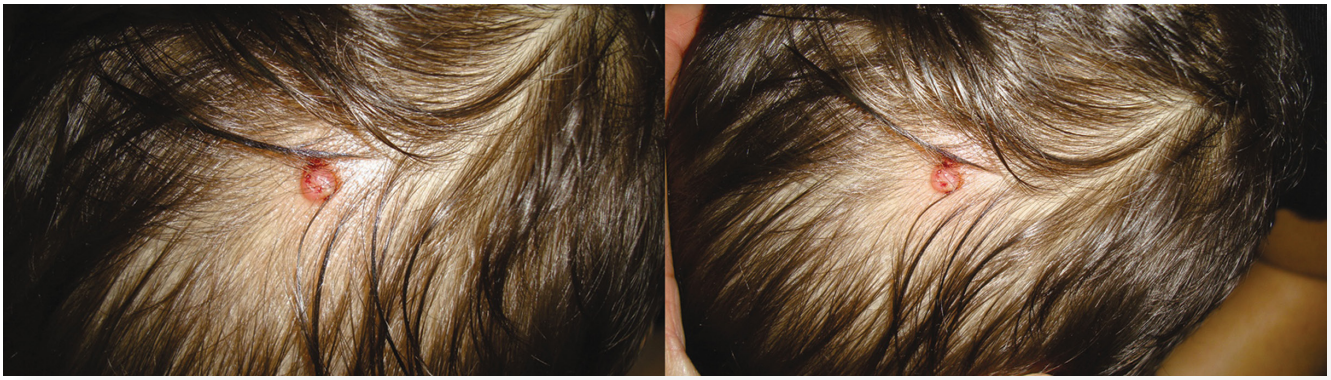

Figure 1a, b. Male patient of 7 months old with redish papule on his scalp

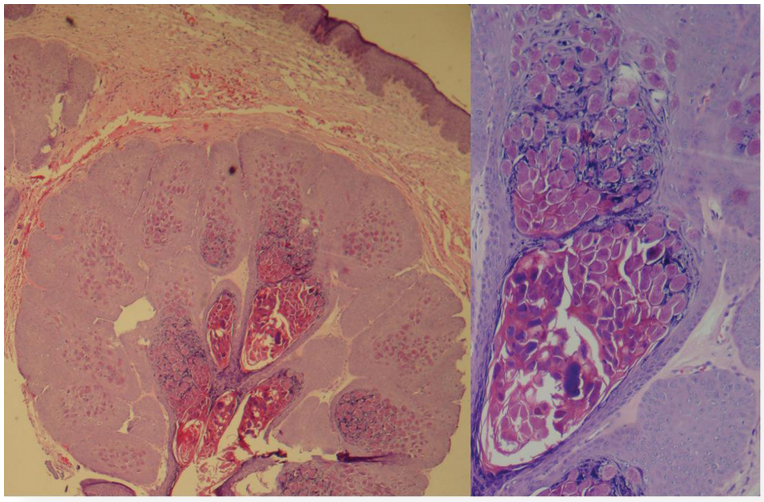

Figure 2. Close up of the scalp lesion

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MEES' LINE FOLLOWING CHEMOTHERAPY

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Sir

Cytotoxic chemotherapeutic agents has many systemic affect specially involving rapidly proliferating organs, such as skin, hair, and the gastrointestinal tract manifesting as exfoliative dermatitis, alopecia, and diarrhea, respectively. We are presenting here effect of chemotherapy on nail which is a "skin" appendage. A 19-year-old tribal boy from rural Maharashtra was diagnosed as Acute Myeloid Leukaemia (M4) and was on combination chemotherapy as cytarabine and daunorubicine (cycles of 3-week intervals). This time he came for 3rd cycle. On physical examination his nails had transverse line parallel to the lunula across the entire nail bed with no palpable ridges which were white and nonblanching (Fig. 1). These lines are known as Mees' lines (true leukonychia). Distance between them is usually related to the cycles intervals after each chemotherapy cycle [1]. As most of the time patients are not aware of appearance of the lines, the timing of the disease process may be estimated by measuring the distance from the line to the nail bed assuming that nails grow about 1mm every 6 to 10 days [2]. Mees' lines are signs of toxicity to the distal nail matrix, resulting in parakeratosis of the nail plate, which becomes white and opaque. Drug-induced true leukonychia (Mees' lines) appears as one or several parallel transverse white bands affecting all nails at the same level and moving distally with nail growth [3]. Another line which may be confused with Mees' lines are Muehrcke's lines (apparent leukonychia). These are paired white lines caused by vascular congestion in the nail bed and they do not fade after digital compression and migration with the growth of the nail [4]. Other causes of Mees' lines are arsenic and thallium intoxication, carbon monoxide poisoning, Hodgkin's disease, myocardial infarction, congestive heart failure, acute and chronic renal failure, systemic lupus erythematosus, immune haemolytic anaemia, leprosy, malaria, chemotherapy, and other systemic insults [2].

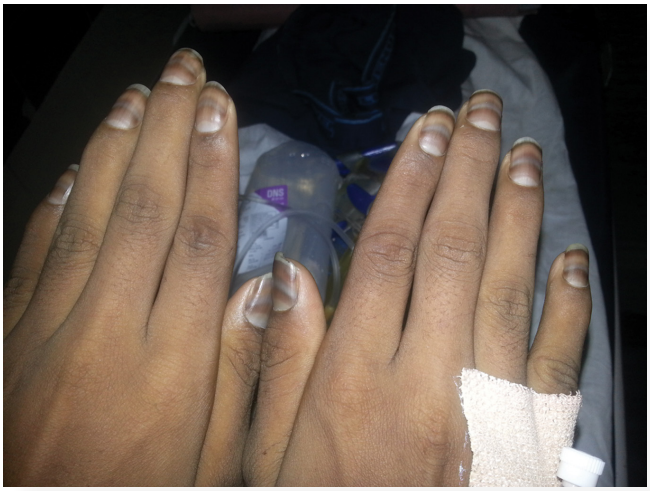

Figure 1. Mees'line on nails

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EPONYMS IN THE DERMATOLOGY LITERATURE LINKED TO THE *HISTIOCYTIC DISORDERS*

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A histiocyte is a type of cells and it is a part of the mononuclear phagocyte system.It is derived from bone marrow and develops into macrophage (CD68), or dendritic, Langerhans cell (CD1a).
Histiocytes have common histological and immunophenotypical characteristics. Their cytoplasm is eosinophilic and contains variable amounts of lysosomes. They bear membrane receptors for opsonins, such as IgG and the fragment C3b of complement. They express CD45, CD14, CD33 and CD4 .

There are many histiocytic disorders, and our aim is to highlight on selected eponyms linked to them, which we listed in Table I [1-7].
Last but not least we want to stress on one thing, that, It is important to remember, not only the names of the scientists behind the eponyms but also to realize the great contributions made by those scientists. Hand, Christian, Schüller, Letterer, and Siwe represent far more than names to attach to eponyms [1].

Eponyms in the dermatology literature linked to the histiocytic disorders	Remarks
Erdheim–Chester disease [2-4]	Erdheim-Chester disease (ECD) is a rare, systemic, non-familial histiocytic disorder, named for, Jakob Erdheim (1874-1937), an Austrian pathologist, and William Chester, an American pathologist. The first case of ECD was reported by William Chester in 1930. Most patients have multiple sites of involvement at presentation. The most common site of involvement is the long bones of the axial skeleton. Cutaneous involvement is rarely a presenting symptom of ECD, with handful reported cases in the English literature.
Eponyms of Histiocytosis X [1]	There are few eponyms for Langerhans cell histiocytosis (LCH), from a time where LCH was thought to be several different diseases. These are, Letterer-Siwe disease, Hand-Schuller-Christian disease, Eosinophilic granuloma and Hashimoto-Pritzker disease. Later they were all put together under the name Histiocytosis X. Letterer-Siwe disease stands for Erich Letterer and Sture Siwe. Hand-Schuller-Christian disease is named for Alfred Hand, Artur Schüller, and Henry Asbury Christian.
Langerhans cells [5]	Langerhans cells are dendritic cells (antigen-presenting immune cells) of the skin and mucosa, and contain large granules called, Birbeck granules. It is named for Paul Langerhans (1847-1888), (Fig. 1), who was a German pathologist, physiologist and biologist. Birbeck granules were discovered by Michael Stanley Clive Birbeck (1925–2005), a British scientist and electron microscopist.

Table I. Selected Eponyms in the dermatology literature linked to the histiocytic disorders

Figure 1. Paul Langerhans (1847-1888)

Figure 2. Juan Rosai

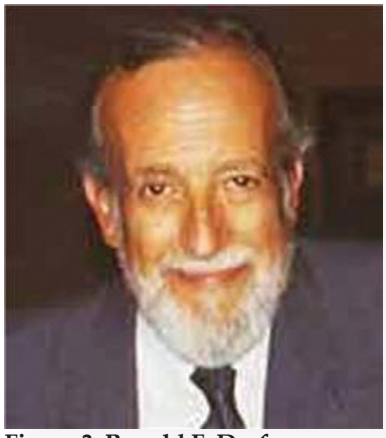

Figure 3. Ronald F. Dorfman (1923-2012)

Eponyms in the dermatology literature linked to the histiocytic disorders	Remarks
Rosai–Dorfman disease [6,7]	Rosai–Dorfman disease, also known as sinus histiocytosis with massive lymphadenopathy, is a rare disorder of unknown etiology that is characterized by abundant histiocytes in the lymph nodes throughout the body. Cutaneous involvement may occur. This condition has been named afterJuan Rosai and Ronald F. Dorfman.Juan Rosai, (Fig. 2), is an Italian-born American physician who has contributed to clinical research in the subspecialty of surgical pathology.He was born in 1940. Ronald F. Dorfman (1923-2012), (Fig. 3), was a Professor of Pathology at Stanford Hospital. An alternative eponym of this condition is known as Destombes-Rosai-Dorfman syndrome, part of which is named afterbPierre-Paul Louis Lucien Destombes, a French pathologist, Born 1912.

Table I. Selected Eponyms in the dermatology literature linked to the histiocytic disorders (continued)

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EPONYMS IN THE LITERATURE OF *CUTANEOUS LYMPHOMAS*

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Lymphoma is a cancer that starts in cells called lymphocytes, which are part of the body's immune system.
In most lymphomas and leukemias, cutaneous involvement occurs through hematogenous dissemination.
One can see several eponyms in cutaneous lymphomas. However, some of them are no longer used in the current nomenclature.
For example, In the World Health Organization (WHO) and European Organization for Research and Treatment of Cancer (EORTC) classification of cutaneous lymphomas, Woringer-Kolopp disease (WKD) is classified as a relatively indolent variant of mycosis fungoides (MF), whereas Ketron-Goodman disease (KGD), which is not classified yet, is generally considered an aggressive lymphoma with bad prognosis similar to the aggressive CD8-positive cutaneous T-cell lymphoma, the cutaneous γ/δ-positive T-cell lymphoma and the tumor stage of MF [1].
In Table I [1-24], we listed selected eponyms in dermatology literature linked to cutaneous lymphomas.

Eponyms in the literature of cutaneous lymphomas	Remarks
Burkitt's lymphoma [1,2]	Burkitt lymphoma is an aggressive non-Hodgkin lymphoma which can be classified into endemic, sporadic, and immunodeficiency variants. Although each variant frequently involves extranodal sites, cutaneous involvement with Burkitt lymphoma is very rare. This lymphoma is named after, Denis Parsons Burkitt (Fig. 1), British surgeon (1911-1993), who first described the disease in 1956 while working in equatorial Africa.

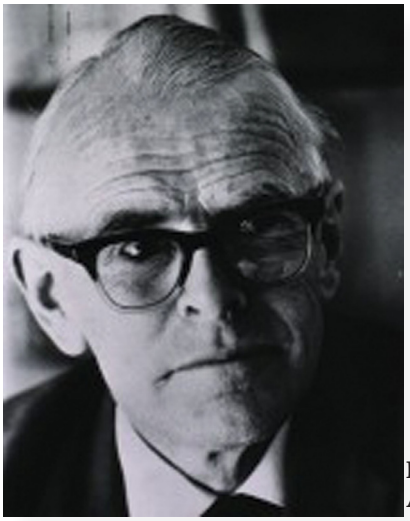

Figure 1. Denis Parsons Burkitt (1911-1993). A courtesy of National library of Medicine.

Table I. Selected Eponyms in the literature of cutaneous lymphomas

Figure 2. William Russell (1852-1940). Reproduced from reference 8.

Figure 3. Thomas Hodgkin (1798-1866). A courtesy of National library of Medicine.

Figure 4. Dorothy Reed Mendenhall (1874-1964)

Eponyms in the literature of cutaneous lymphomas	Remarks
Crosti lymphoma [3,4]	In 1951, Crosti reported on seven patients with ‚reticulo-histiocytoma of the back' who presented with figurate erythematous plaques and nodules on the back or lateral trunk. Reticulo-histiocytoma of the back was later classified as a primary cutaneous follicle center lymphoma (PCFCL). It is named after, Agostino Crosti, (1896-1988), an Italian dermatologist, and Professor of Dermatology in Milan. Crosti's syndrome and Gianotti-Crosti syndrome are named after him.
Dutcher bodies [5-9]	Dutcher bodies are PAS-positive, diastase-resistant nuclear pseudoinclusions of eosinophilic cytoplasm found in plasma cells described by Dutcher and Fahey in Waldenstrom macroglobulinemia. Dutcher bodies are a feature of clinically indolent, mucosa-associated lymphoid tissue (MALT) lymphomas. There are no essential differences between Dutcher bodies, single or multiple Russell bodies, and the inclusions of Mott cells. They are all aspects of the same phenomenon, representing spherical cytoplasmic inclusions that are either clearly within the cytoplasm or are overlying the nucleus or invaginated into it. Russell bodies, is named after William Russell (1852-1940) (Fig. 2), Scottish pathologist and physician. Mott cell is named after Mott, who described it in 1905. Dutcher bodies may rarely occur in a benign reactive condition, such as synovitis. While Dutcher bodies may be a clue to the presence of low-grade lymphoma, they are not a definitive feature, particularly in unusual contexts.
Hodgkin lymphoma [10-15]	Cutaneous Hodgkin's disease is a rare condition that usually occurs late in the course of Hodgkin's lymphoma. Hodgkin lymphoma was named after Thomas Hodgkin, who first described abnormalities in the lymph system in 1832. Thomas Hodgkin (1798-1866) (Fig. 3), was an English physcian and pathologist. The multinucleated Reed–Sternberg cells (RS cells) are the characteristic histopathologic finding of this disease.This type of cells are named after Dorothy Reed (1874-1964) (Fig. 4), an American pathologist, and Carl Sternberg (1872-1935), an Austrian pathologist.
Kettron-Goodman disease [16-18]	Pagetoid reticulosis (PR) is a rare form of cutaneous T-cell lymphoma. Two variants of the disease are described: the localized type Woringer-Kolopp disease (WKD) and the disseminated type Ketron-Goodman disease (KGD). KGD is named after Lloyd W. Ketron and M.H. Goodman.The term PR has been introduced by Braun-Falco et al. in 1973 to identify this clinical entity [5], first described by Woringer and Kolopp in 1939, for the resemblance of infiltrating cells characterizing this condition with Paget's cells present in the epidermotropic infiltrate of mammary Paget's disease. Pierre Kolopp was French physician and Frederic Woringer (1903-1964) (Fig. 5), was one of Pautrier's students, who had been in charge of the Laboratoire d'Histopathologie Cutanée in Strasbourg from 1930 until his death.

Table I. Selected Eponyms in the literature of cutaneous lymphomas (continued)

Figure 5. Frederic Woringer (1903-1964)

Figure 6. Karl Lennert (1921-2012). Reproduced from reference 19.

Figure 7. Lucien-Marie Pautrier (1876-1959)

Eponyms in the literature of cutaneous lymphomas	Remarks
Lennert lymphoma [19,20]	Lennert lymphoma (LL), or the lymphoepithelioid variant of peripheral T-cell lymphoma, is an uncommon entity with rarely seen or reported presentations in the skin. It was first characterized in 1952 by Karl Lennert (1921-2012) (Fig. 6), who was an eminent German physician and pathologist
Pautrier microabscesses [21]	An intraepidermal collections of malignant lymphocytes, seen in cutaneous cell lymphoma. It is named after Lucien-Marie Pautrier, although he did not first describe them. Lucien-Marie Pautrier (1876-1959) (Fig. 7), was a French dermatologist, who headed a leading department at the medical school of Strasbourg.
Richter syndrome [22]	Richter syndrome (RS) is large-cell transformation of chronic lymphocytic leukemia (CLL). It commonly involves lymph nodes and bone marrow, but may rarely manifest in skin. Certain triggering factors, such as Epstein-Barr virus infection and p53 overexpression, have been implicated in the pathogenesis of RS.It is named for the American pathologist Maurice Nathaniel Richter (Fig. 8), born in 1897.  **Figure 8. Maurice Nathaniel Richter. A courtesy of National library of Medicine.**
Sézary syndrome or Sézary disease [23]	In a series of papers from 1938 to 1949, Albert Sézary (1880-1956) (Fig. 9), a French dermatologist and syphilologist, described erythroderma with cellules monstrueuses (monster cells) in the skin and blood, which is now known as Sézary syndrome or Sézary disease.

Table I. Selected Eponyms in the literature of cutaneous lymphomas (continued)

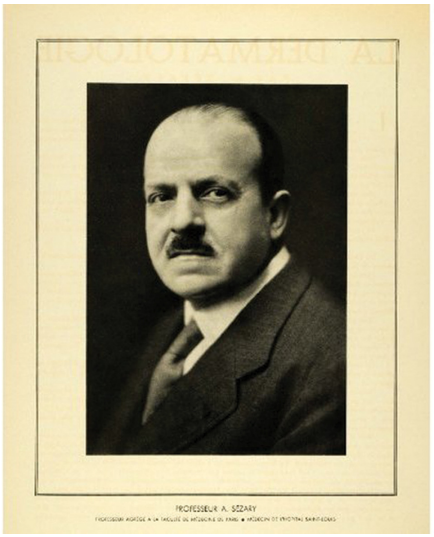

Figure 9. Albert Sézary (1880-1956)

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NASZA DERMATOLOGIA Online
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EPONYMS IN THE DERMATOLOGY LITERATURE LINKED TO THE *SKIN* AND *SOFT TISSUE TUMORS*

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The term "eponym" originates from the Greek word "eponymous", which means "named after". An eponym was a simple way to describe tumors and tumor like lesions that initially were not well understood [1].
Most of the tumors in the skin and soft tissues are named according to its histopathological features under the microscope. Nevertheless, few of them are named eponymously.
With the exception of Evans tumor which is currently best known as Low-Grade Fibromyxoid Sarcoma, the eponyms linked to the tumors in the skin and soft tissue maintain their position in the medical literature over the years.
In this communication which is based, essentially [1], we aimed to highlight on selected eponyms in dermatology literature linked to the skin and soft tissue tumors, which we listed it in in Table I [1-10].

Eponyms in the dermatology literature linked to the skin and soft tissue tumors	Remarks
Bednar tumor	It is a name given to the pigmented type of Dermatofibrosarcoma protuberans (DFSP). DFSP is a locally aggressive soft tissue neoplasm with intermediate- to low-grade malignancy. Bednar tumor is named after a well-known Czech pathologist, Blahoslav Bednar (1916-1998) (Fig. 1).

Figure 1. Blahoslav Bednar (1916-1998). Reproduced from reference number 2.

Table I. Selected Eponyms in the dermatology literature linked to the skin and soft tissue tumors [1-10]

Figure 2. Harry L. Evans

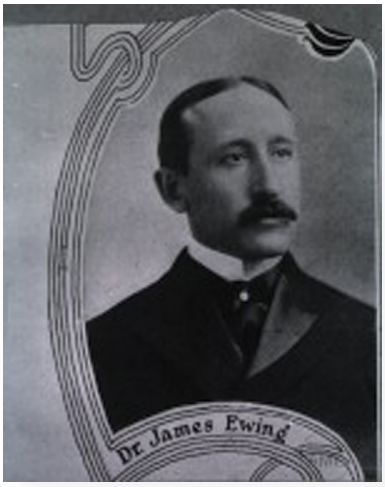

Figure 3. James Ewing (1866–1943). A courtesy of National library of Medicine.

Figure 4. Moritz Kaposi (1837–1902). A courtesy of National library of Medicine.

Eponyms in the dermatology literature linked to the skin and soft tissue tumors	Remarks
Evans tumor	Evans tumor is another name for the tumor which is currently best known as Low-Grade Fibromyxoid Sarcoma. The tumor typically presents as an intramuscular soft-tissue mass in the lower extremity or trunk and is most commonly seen in young to middle--aged adults. It was first described, in 1987, by, Harry L. Evans (Fig. 2), who is a contemporary Professor of Patholog, in the University of Texas MD Anderson Cancer Center. Evans made other important scientific contributions. As an example, he defined the diagnostic criteria for monophasic synovial sarcoma.
Ewing sarcoma	Ewing sarcoma is a malignant osseous neoplasm that affects mostly children and young adult males. It was initially described as "endothelioma of bone" by James Ewing (1866–1943) (Fig. 3), in 1921. Ewing became the first professor of pathology at Cornell University, Weill Cornell Medical College. He was recognized as a central figure in emerging tumor pathology at that time and was dubbed "Cancer Man". Clinically, the neoplasm presents with oedema, swelling, and pain of the involved area. Histopathologically, Ewing's sarcoma consists of solid sheets of small round cells, with vesicular nuclei and scant cytoplasm, arranged in irregular masses separated by strands of fibrous tissue, with areas of necrosis en masse intermingled with intratumoural haemorrhage. Cutaneous metastases from Ewing's sarcoma are very uncommon. While, primary cutaneous Ewing sarcoma very rarely occurs and the prognosis has been reported to be better in some small series.
Kaposi sarcoma	It is a mesenchymal tumor that involves blood and lymphatic vessels and that affects multiple organs, most commonly the skin.It was first described as "idiopathic multiple pigmented sarcoma" by Moritz Kaposi Kohn (1837–1902) (Fig. 4), in 1872. Kaposi was born in Hungary, and graduated in medicine from the University of Vienna. He was one of the first to establish dermatology based on anatomic pathology. His book, Pathology and Therapy of the Skin Diseases in Lectures for Practical Physicians and Students, became one of the most significant books in the history of dermatology and was translated into several languages.

Table I. Selected Eponyms in the dermatology literature linked to the skin and soft tissue tumors (continued) [1-10]

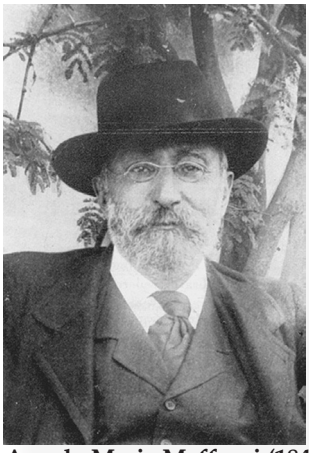

Figure 5. Angelo Maria Maffucci (1845-1903)

Figure 6. Louis Xavier Édouard Léopold Ollier (1830–1900). A courtesy of National library of Medicine.

Eponyms in the dermatology literature linked to the skin and soft tissue tumors	Remarks
Maffucci syndrome	It is characterized by multiple enchondromas and soft-tissue hemangiomas, less commonly lymphangiomas, affecting the skin and musculoskeletal system. It is named after, an Italian pathologist, Angelo Maria Maffucci (1845-1903) (Fig. 5), who described it for the first time in 1881. He made also important scientific contribution in the field of tuberculosis. When multiple enchondromas, is not associated with hemangiomas, it is called Ollier disease, after a French doctor, Louis Xavier Édouard Léopold Ollier (1830–1900) (Fig. 6), who reported it, in 1898. Ollier is recognized for his contributions in orthopedic and reconstructive surgery.
Morton neuroma	It consists of perineural fibrosis and nerve degeneration of the interdigital nerve at the level of the metatarsal heads. It is not a true neuroma and is caused by compression and irritation of the nerve beneath the intermetatarsal ligament. It was first described in 1876, by Thomas George Morton (1835–1903). Morton was born in Philadelphia. He was the son of Samuel George Morton, a famous scientist and doctor. Morton became a surgeon after obtaining his medical degree at the University of Pennsylvania in 1856.

Table I. Selected Eponyms in the dermatology literature linked to the skin and soft tissue tumors (continued) [1-10]

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NASZA DERMATOLOGIA Online
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EPONYMS IN THE DERMATOLOGY LITERATURE LINKED TO THE *VASCULAR TUMORS*

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The term "eponym" originates from the Greek word "eponymous", which means "named after". Dermatology literature is rich in eponyms [1].

In this communication, we aimed to highlight on selected eponyms in dermatology literature linked to the vascular tumors, which we listed it in in Table I [1-7].

However, we want to stress that this table is by no mean conclusive as some eponyms linked to vascular lesions in the skin are not included.For examples; Campbell De Morgan spots (also known as senile angiomas or cherry angiomas), which is named after the nineteenth-century British surgeon Campbell De Morgan (1811-1876). Also Kasabach-Merritt syndrome, in which a vascular tumor leads to decreased platelet counts and sometimes other bleeding problems, It is named after Haig Haigouni Kasabach (1898-1943) and Katharine Krom Merritt (1886-1986), the two American pediatricians who first described the condition in 1940.

Eponyms in the dermatology literature linked to the vascular lesions	Remarks
Angiokeratoma of Fordyce [1]	Named after an American dermatologist, John Addison Fordyce (1858 -1925) (Fig. 1).  **Figure 1. John Addison Fordyce (1858 -1925)**
Dąbska tumor (DT) [2,3]	It is a rare, low-grade angiosarcoma that often affects the skin of children. It is named after, Maria Dąbska, a Polish pathologist, born 1920 (Fig. 2). She originally described DT in 1969 and named it malignant endovascular papillary angioendothelioma of the skin in childhood. She described 6 patients during a 14-year period (1953-1967) at the Maria Sklodowska-Curie Institute of Oncology in Warsaw, Poland, where she was a member of the Pathology faculty.

Table I. Selected Eponyms in the dermatology literature linked to the vascular tumors

Figure 2. Maria Dąbska. Reproduced from reference number 3.

Figure 3. Moritz Kaposi (1837–1902). Reproduced from reference number 4.

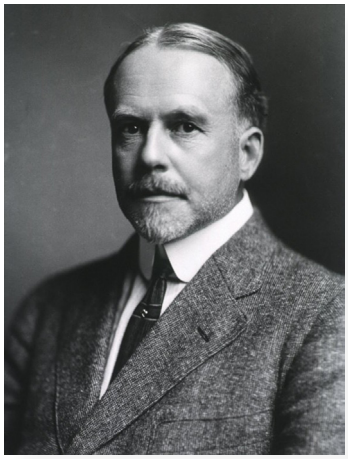

Figure 4. Aldred Scott Warthin (1866-1931). A courtesy of National library of Medicine.

Eponyms in the dermatology literature linked to the vascular lesions	Remarks
Kaposi sarcoma [4]	It is a mesenchymal tumor that involves blood and lymphatic vessels and that affects multiple organs, most commonly the skin. It was first described as "idiopathic multiple pigmented sarcoma" by Moritz Kaposi Kohn (1837–1902) (Fig. 3), in 1872. Kaposi was born in Hungary, and graduated in medicine from the University of Vienna. He was one of the first to establish dermatology based on anatomic pathology. His book, Pathology and Therapy of the Skin Diseases in Lectures for Practical Physicians and Students, became one of the most significant books in the history of dermatology and was translated into several languages.
Kimura disease [5]	Kimura disease is a chronic inflammatory disorder of unknown etiology that most commonly presents as painless lymphadenopathy or subcutaneous masses in the head or neck region. The first report of Kimura disease was from China in 1937, in which Kimm and Szeto described 7 cases of a condition they termed „eosinophilic hyperplastic lymphogranuloma". The disorder received its current name in 1948, when Kimura et al, noted the vascular component and referred to it as an „unusual granulation combined with hyperplastic changes in lymphoid tissue". In the histopathology of this disease, one may see, Warthin-Finkeldey giant cells. This cell which can be seen also in measles is named after, Wilhelm Finkeldey, a German pathologist and Aldred Scott Warthin (1866-1931) (Fig. 4), an American pathologist .
Masson tumour [6]	This is another name for, Intravascular papillary endothelial hyperplasia. It was first described by Claude L. Pierre Masson (1880-1959) (Fig. 5), French-born Canadian pathologist.

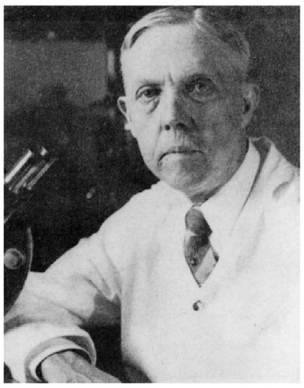

Figure 5. Claude L. Pierre Masson (1880-1959). Reproduced from reference number 6.

Table I. Selected Eponyms in the dermatology literature linked to the vascular tumors (continued)

Eponyms in the dermatology literature linked to the vascular lesions	Remarks
Sucquet-Hoyer canal [7]	This is part of glomus body from which glomus tumor arise. Masson studied a tumor and found that its cells are similar to those found in the coccygeal gland or glomus coccygeum and named the tumor glomus (latin for ball) tumor. He also gave the name "Sucquet-Hoyer", based on the earlier report s of Sucquet in 1862 and Hoyer in 1877.

Table I. Selected Eponyms in the dermatology literature linked to the vascular tumors (continued)

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NASZA DERMATOLOGIA Online
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EPONYMS IN THE DERMATOLOPATHOLOGY LITERATURE LINKED TO THE *NEURAL TISSUES*

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We want to refresh the memory of our readers with some of the eponyms present in dermatopathology literature linked to the neural tissue, which we listed it concisely, in Table I [1-13]. The notes presented in the table are only inclusive and by no means conclusive, and are only intended to define only each eponyms.We utilized the information available for each eponyms from Wikipedia. However, the readers are free to refer to the references below for further reading about each eponyms.

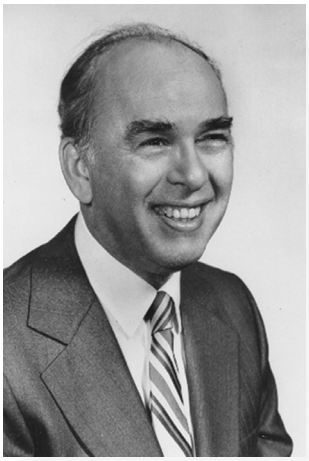
Eponyms in the dermatopathology literature linked to the neural tissues	Remarks
Antoni A and B [1]	These are histopathological pattern seen in schwannomas, consisting of hypercellular area (Antoni A) and hypercellular area (Antoni B). Described in 1920, by Nils Ragnar Eugene Antoni (1887-1968), a Swedish physician who became doctor of medicine and associate professor of neurology at the Karolinska Institute, Stockholm, Sweden.
Bodian stain [2]	Special stain for nerve fibers and nerve endings. Named after David Bodian (1910-1992), (Fig. 1). Bodian received his Ph.D. in anatomy in 1934 and his M.D. in 1937 from the University of Chicago. He made major contributions to the knowledge of the basic structure of nerve cells.  **Figure 1. David Bodian (1910 - 1992)**
Bourneville disease [3]	This is not a common name for what is best known today as Tuberous Sclerosis Complex (TSC). It is named after, Désiré-Magloire Bourneville (1840-1909), (Fig. 2), a French neurologist born in Garencières.

Table I. Selected Eponyms in the dermatopathology literature linked to the neural tissues

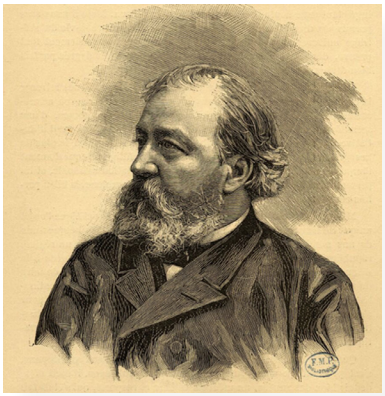


Figure 2. Désiré-Magloire Bourneville (1840-1909)

Figure 3. J. Aidan Carney

Figure 4. Simon Flexner (1863–1946)

Eponyms in the dermatopathology literature linked to the neural tissues	Remarks
Carney complex [4]	Schwannomas may occur in association with Carney complex. The latter is an autosomal dominant condition comprising myxomas of the heart and skin, hyperpigmentation of the skin (lentiginosis), and endocrine overactivity. It is different from Carney triad, which describes the coexistence of several neoplasms, including: gastric epithelioid leiomyosarcoma, pulmonary chondroma, and extra-adrenal paraganglioma. Both are named after, J. Aidan Carney, (Fig. 3), a contemporary Professor of Pathology at Mayo Medical School.
Flexner-Wintersteiner rosette [5]	It is a peculiar microscopic pattern seen in retinoblastoma and certain other ophthalmic tumors. They are true rosettes, which contain an empty lumen. They were first described by Simon Flexner (1863–1946), (Fig. 4), a physician, scientist, administrator, and professor of experimental pathology at the University of Pennsylvania. The observation of Flexner was later confirmed by, Hugo Wintersteiner (1865–1946) an Austrian ophthalmologist.
Homer-Wright rosettes	Homer-Wright rosettes are a type of rosette in which differentiated tumor cells surround the neuropil. Examples of tumors containing these are neuroblastoma, medulloblastoma, andpinealoblastoma. They are considered „pseudo" in the sense they are not the true rosettes.
Lisch nodule [6]	It is a pigmented hamartomatous nodular aggregate of dendritic melanocytes affecting the iris, named after Austrian ophthalmologist Karl Lisch (1907-1999), (Fig. 5), who first recognized them in 1937.
Masson neuronevus [7,8]	It is more commonly, known as neural nevus, or neurotized melanocytic nevus. Named after, Claude L. Pierre Masson (1880-1959), (Fig. 6), French-born Canadian pathologist.
Meissner's corpuscles [9-11]	There are four major types of mechanoreceptors. These Meissner's corpuscles, Pacinian corpuscles, Ruffini endings and Merkel's discs. Meissner's corpuscles are named after, Georg Meissner (1829-1905), (Fig. 7), a German anatomist and physiologist. Pacinian corpuscles, are named after, Filippo Pacini (1812-1883), (Fig. 8), who was an Italian anatomist, posthumously famous for isolating the cholera bacillus Vibrio cholerae in 1854. Ruffini endings are named after, Angelo Ruffini (1864-1929), (Fig. 9). He was an Italian histologist and embryologist. Merkel's discs are named after, Friedrich Sigmund Merkel (1845-1919), (Fig. 10). He was a leading German anatomist and histopathologist in the late 19th century.

Table I. Selected Eponyms in the dermatopathology literature linked to the neural tissues (continued)

Figure 5. Karl Lisch (1907-1999)

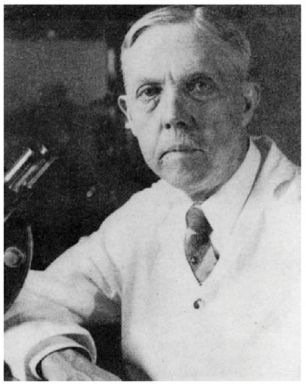


Figure 6. Claude L. Pierre Masson (1880-1959). Reproduced from reference number 6.

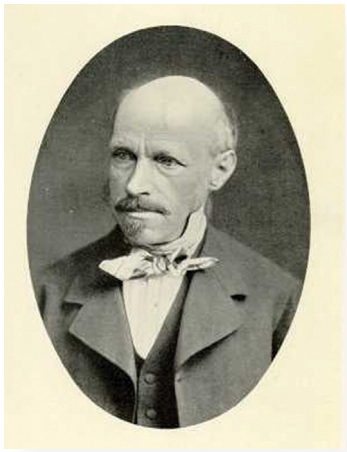


Figure 7. Georg Meissner (1829-1905)

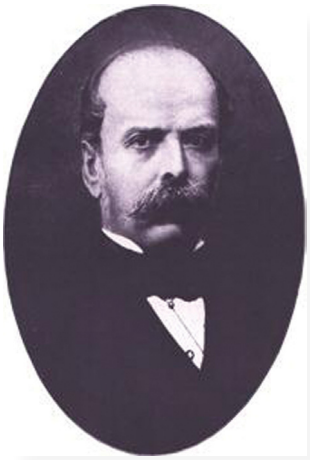


Figure 8. Filippo Pacini (1812 -1883)

Figure 9. Angelo Ruffini (1864-1929)

Figure 10. Friedrich Sigmund Merkel (1845-1919)

Eponyms in the dermatopathology literature linked to the neural tissues	Remarks
Schwann cells [12]	Schwann cells are the principal glia of the peripheral nervous system. Named after Theodor Schwann (1810-1882), (Fig. 11), who was a German physiologist.
Verocay bodies [1]	A peculiar microscopic pattern seen in schwannomas, consisting of palisading cell around a cellular area. It is named after, Jose Juan Verocay (1876-1927), (Fig. 12). He was a Uruguayan physician who trained and worked for most of his adult life in Europe in the late nineteenth and early twentieth century.
von Recklinghausen syndrome [13]	This is a synonym to neurofibromatosis. It is named after Friedrich Daniel von Recklinghausen (1833-1910), (Fig. 13), who was a German pathologist.

Table I. Selected Eponyms in the dermatopathology literature linked to the neural tissues (continued)

Figure 11. Theodor Schwann (1810-1882)

Figure 12. Jose Juan Verocay (1876-1927)

Figure 13. Friedrich Daniel von Recklinghausen (1833-1910)

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DERMATOLOGY EPONYMS – SIGN – LEXICON – (J)

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Abstract
Eponyms are used almost daily in the clinical practice of dermatology. And yet, information about the person behind the eponyms is difficult to find. Indeed, who is? What is this person's nationality? Is this person alive or dead? How can one find the paper in which this person first described the disease? Eponyms are used to describe not only disease, but also clinical signs, surgical procedures, staining techniques, pharmacological formulations, and even pieces of equipment. In this article we present the symptoms starting with (J) and other. The symptoms and their synonyms, and those who have described this symptom or phenomenon.

Key words: eponyms; skin diseases; sign; phenomenon

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JACQUET'S SIGN

Baldness and dental anomalies [1]. Papulo-lenticular erythema of the napkin area. A minor form of congenital ectodermal defect is associated with other tegumentary changes, including congenital absence of nails and dental anomalies. Alopecia may be present at birth, or develop in first month of life. The syndrome is rare and may be partial or complete. Autosomal dominant inheritance reported; autoimmune mechanism suggested. Also Jacquet's reflex alopecia and Jacquet's syndrome.

LÉONARD MARIE LUCIEN JACQUET

French dermatologist, 1860–1914 (Fig. 1). He obtained his doctorate in 1888, became médecin des hôpitaux 1896 and from 1903 worked in the Hôpital Saint-Antoine. He chose dermatology and syphilology as his speciality and concerned himself with pruritus, the pathogenesis of pruriginous eruptions and the alopecia areata. With his "bio-kinetic" treatment he gave new ways in the treatment of certain dermatoses [2]. Jacquet's syndrome, Vidal-Jacquet syndrome, diaper dermatitis.

Figure 1. Léonard Marie Lucien Jacquet

JADASSOHN'S SIGN

=Maculopapular erythrodermia, pityriasis lichenoides chronica [3].

The term applied to a group of relatively uncommon inflammatory, maculopapular, scaly eruptions of unknown etiology and resistant to conventional treatment. Eruptions are both psoriatic and lichenoid in appearance, but the diseases are distinct from psoriasis, lichen planus, or other recognized dermatoses. Proposed nomenclature divides parapsoriasis into two distinct subgroups, pityriasis lichenoides and parapsoriasis en plaques (small- and large-plaque parapsoriasis).

JOSEPH JADASSOHN

German dermatologist, 1863-1936 (Fig. 2). Jadassohn, who was born at Liegnitz (current Poland), studied at Breslau (current Poland). He was an assistant of Albert Neisser at Allerheiligen Hospital in Breslau until 1892, the director of the university skin clinic in Bern (1896–1917), and a professor of dermatology at Breslau University (1917–1932). Jadassohn was a pioneer in the field of allergology and was among the first to take an immunological approach in the research of dermatological disorders, contributing to the understanding of the immunopathology of tuberculosis and trichophytosis. Jadassohn is credited for introducing patch testing to diagnose contact dermatitis, and in 1901, he described a rare childhood dermatological disorder, known as granulosis rubra nasi (a papular red lesion of the nose associated with increased sweating).

He was particularly interested in drug reactions, leprosy, eczema, tuberculosis, syphilis, and mycotic infections. His awareness of the social aspects of venereal diseases led to his appointment to the Committee on Hygiene of the League of Nations. He was a corresponding member of the British Association of Dermatology, and in the year prior to his death, he was made an honorary fellow of the Royal Society of Medicine. Jadassohn devoted much of his time to research. Maculopapular erythematosa, a scaling skin affection, is known as „Jadassohn's disease" because he first identified it and his name is also associated with the Jadassohn-Bloch skin test for allergic conditions. He described the patch test and nevus sebaceus (1895). His publications include Krankheiten der Haut und die venerischen Krankheiten written in collaboration with Albert Neisser (1900–01) and Allgemeine Aetologie, Pathologie, Diagnose und Therapie der Gonorrhoe (1910). He edited Handbuch der Haut-und Geschlechtskrankheiten (1927–32) and coedited the Archiv fuer Dermatologie und Syphilis [4].

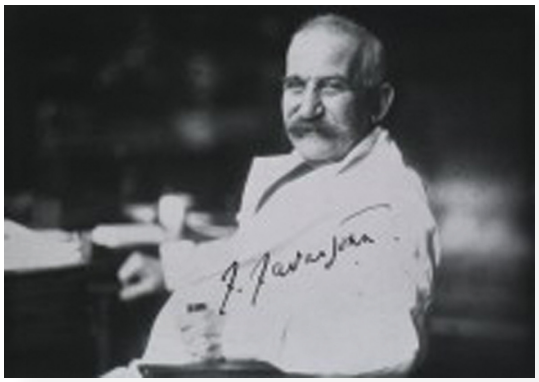

Figure 2. Joseph Jadassohn. History of Medicine (NLM)

JAIL-FEVER SIGN

=typhus fever (endemic typhus) (Fig. 3). Also called „camp fever", „hospital fever", „ship fever", „famine fever", „putrid fever", „petechial fever", „Epidemic louse-borne typhus", and „louse-borne typhus". It is usually seen in areas where hygiene is poor and the temperature is cold [5,6].

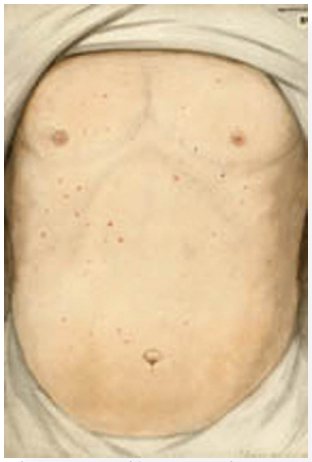

Figure 3. Jail-Fever sign

JAKE LEG SIGN (c. 1930)

A form of leg paralysis, caused by Jamaican ginger extract adulterated with tri-orthoceresyl phosphate (Fig. 4).

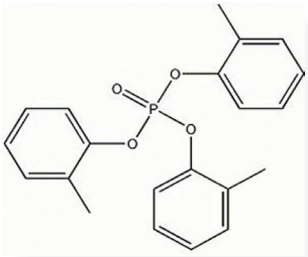

Figure 4. Tri-ortho cresyl phosphate (TOCP)

Jamaican Ginger Extract, known colloquially as „jake," was a patent medicine that happened to be up to 80% ethyl alcohol, yet was legal to import to the United States. But to keep it from being drunk as an alcoholic beverage, the government insisted that the manufacturers add so much ginger that it was impossibly bitter (Fig. 5).

To test for this ginger content, inspectors would often boil it down and weigh the solids.

Figure 5. Motimer's box and bottle for Jamaica Ginger, Boston (alcohol 90)

Eventually a pair of unscrupulous chemists found another chemical that would pass the inspectors' test, while still leaving the jake drinkable: a neurotoxin called Tricresyl phosphate (TOCP).
TOCP caused paralysis at the spinal cord which left sufferers with a characteristic limp-footed walk. Either one or both feet would be paralyzed such that they dangled loose from the leg, and had to be picked up and flopped down in a tap-shuffle rhythm that became part of the „jake walk" lore [7,8].

JANEWAY'S SIGN
Erythematosus lesions on the palm or sole essn in subacute bacterial endocarditis [9].

THEODORE CALDWELL JANEWAY
American physician, 1872-1917 (Fig. 6). He was educated at the Sheffield Scientific school, Yale university, and the College of Physicians and Surgeons, Columbia university. From 1898 to 1906 he taught medical diagnosis in New York university. In 1907 he became associate in medicine in Columbia university, and two years later professor of medicine. In 1914 he was called to Johns Hopkins university as professor of medi cine, and became physician-in-chief to Johns Hopkins hospital.
His investigations in the phenomena of blood pressure opened up a hitherto unexplored field of medical research. During the World War, he became major in the Medical Officers' Reserve Corps and was engaged in research in Washington (D.C.). He died at Balti more (Md.) Dec. 27, 1917. He was a member of the board of scientific directors of the Rockefeller Institute for Medical Re search. He was the author of The Clinical Study of Blood Pres sure [10].

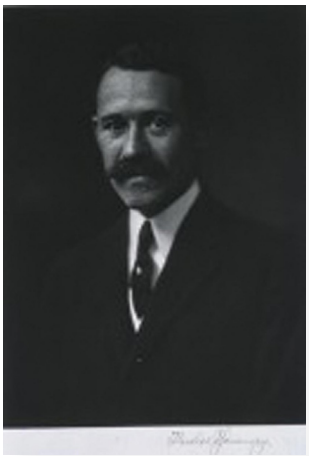

Figure 6. Theodore Caldwell Janeway. History of Medicine (NLM)

JELLINEK'S SIGN
The pigmentation, usually brownish, occurring on the lid margins in many cases of hyperparathyroidism [11]. In Graves disease, a brownish pigmentation of the eyelids, especially the upper ones. Also jnown as Rasin's sing.

STEFAN JELLINEK
Austrian physician, 1871-1968 (Fig. 7). He studied medicine at the University of Vienna from 1892 to 1898. From December 1898 to April 1899 Senator's assistant at the clinic in Berlin. In the years 1900-1903 the aspirant in the third clinic in Vienna, from 1903 sekundariusz in the Department of Dermatology. In December 1908 his habilitation in internal medicine. Since 1910 assistant at the Institute Elektropatologicznym. May 14, 1929 elektropatologii was an associate professor at the University of Vienna. In 1938, because of his Jewish origin had lost his job, then emigrated to the UK. He practiced at Queen's College [12].

Figure 7. Stefan Jellinek

JUNIN SIGN (South America)
Fever and bleeding caused by the zoonotic Argentinean hemorrhagic fever Arenaviridae virus (Junin virus) [13]. A member of the genus Arenavirus, Junin virus characteristically causes Argentine hemorrhagic fever (AHF). AHF leads to major alterations within the vascular, neurological and immune systems and has a mortality rate of between 20 and 30%. Symptoms of the disease are conjunctivitis, purpura, petechia and occasional sepsis. The symptoms of the disease are relatively indistinct and may therefore be mistaken for a different condition.
Since the discovery of the Junin virus in 1958, the geographical distribution of the pathogen, although still confined to Argentina, has risen. At the time of discovery, Junin virus was confined to an area of around 15,000 km². At the beginning of 2000, the distribution had risen to around 150,000 km². The natural hosts of Junin virus are rodents, particularly Mus musculus, Calomys spp. and Akodon azarae. Direct rodent to human transmission only transpires when contact is made with excrement of an infected rodent. This commonly occurs via ingestion of contaminated food or water, inhalation of particles within urine or via direct contact of broken skin with rodent excrement.

JUZAM SIGN
=Elephantiasis graecorum.

„.....No mention is made in the Hippocratic writings of elephantiasis graecorum, which was really a type of leprosy, and is now considered synonymous with it. According to Rayer, some writers insist that the affection then existed under the name of the Phoenician disease. Before the time of Celsus, the poet Lucretius first speaks of elephantiasis graecorum, and assigns Egypt as the country where it occurs.

Celsus gives the principal characteristics, and adds that the disease is scarcely known in Italy, but is very common in certain other countries. Galen supplies us with several particular but imperfect cases--histories of elephantiasis graecorum, with a view to demonstrate the value of the flesh of the viper, and in another review he adds that the disease is common in Alexandria. Aretaeus has left a very accurate picture of the symptoms of elephantiasis graecorum; and Pliny recapitulates the principal features and tells us that the disease is indigenous in Egypt. The opinion of the contagiousness of elephantiasis graecorum which we find announced in Herodotus and Galen is more strongly insisted upon by Caelius Aurelianus who recommends isolation of those affected. Paulus aegenita discusses the disease. The Arabian writers have described elephantiasis graecorum under the name of juzam, which their translators have rendered by the word lepra. Later, Hensler, Fernel Pare, Vesalius, Horstius, Forestus, and others have discussed it. affected in the East....." [14,15].

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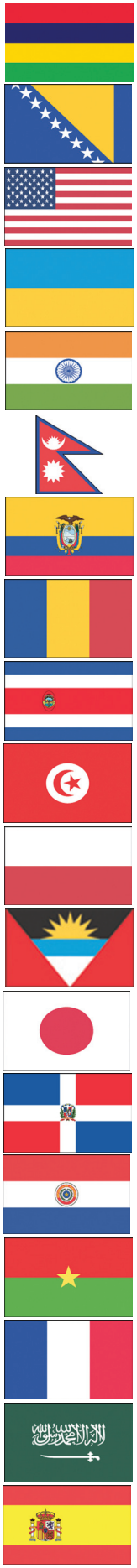
We are pleased to extend a warm welcome to the 23RD World Congress of Dermatology (23RD WCD), to be held in Vancouver, Canada from June 8-13, 2015. Held under the auspices of the International League of Dermatological Societies, the 23RD WCD will be the largest international gathering of dermatologists and people dedicated to skin health from all sectors. Our vision for the world's premier dermatology conference includes celebration, innovation, and inclusiveness. Our award-winning world class Vancouver Convention Centre will serve as one of the most beautiful venues to ever host the WCD. Strategically situated on the waterfront in the heart of downtown Vancouver, participants will enjoy spectacular views of the harbour and mountains as they move between their sessions. This unique convention centre is within walking distance of a spectacular variety of accommodation, dining, shopping, tourist attractions, and transportation.

We look forward to celebrating with you in Vancouver, where the world of dermatology will gather in 2015.

Dr. Jerry Shapiro and Dr. Harvey Lui
President and Secretary-General

http://www.derm2015.org



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