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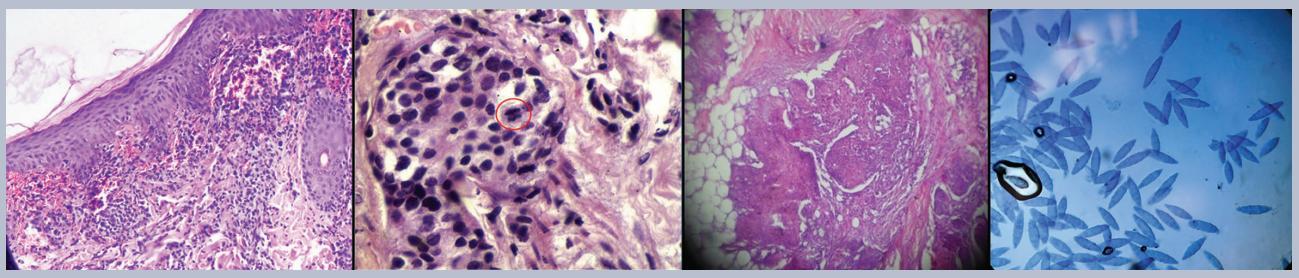

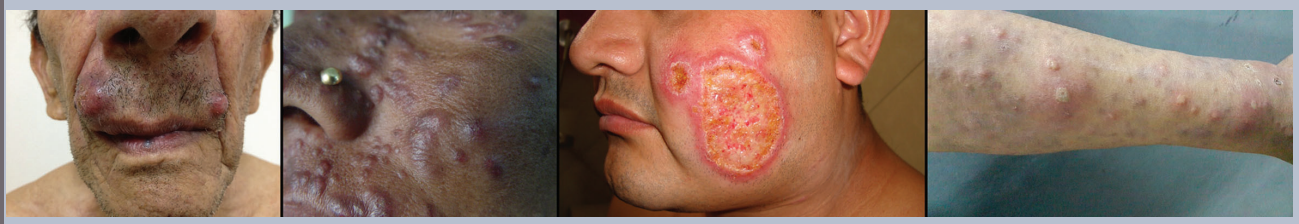

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Original Article

Psoriasis: An eye opener – A cross-sectional study in a Tertiary Care Hospital of South India

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ABSTRACT

Introduction: Psoriasis is a multi-system chronic inflammatory skin disease targeting 2% to 3% of the general population. It is a prototype of immune dysregulation mediated by TH1 proinflammatory cytokines such as TNF-α, IFN-gamma, IL-6, and IL-12 with far reaching systemic effects. There is growing and emerging evidence that psoriasis patients have a higher prevalence of associated comorbid diseases, with severe skin disease portends a serious risk for development of these comorbidities and are found to have a higher association of extracutaneous disease manifestations. **Aim:** To look for eye involvement in psoriasis patients and to evaluate the risk and prognostic factors of disease association. **Material and Methods:** 200 Patients with psoriasis were screened for any eye involvement after few unusual case presentations with eye complications during the period from September 2013 - August 2014. **Results:** First case was a post cataract sudden loss of vision secondary to development of uveitis in a female patient aged 52 years, with past history of psoriasis with minimal skin lesions and no arthritis. Another 5 cases of psoriasis with eye involvement were detected during the screening employed in a series of 200 psoriasis cases. **Conclusion:** The present report highlights the importance of psoriasis and eye involvement, need for collaboration between dermatologists and ophthalmologists for thorough examination and evaluation prior to any surgical intervention and also further long term follow-up studies are warranted for confirmation of this causal relationship.

Key words: Psoriasis; eye complications; opthalmological examination

INTRODUCTION

The relationship between the eye and psoriasis has been recognized for decades, but the precise eye manifestations in patients with psoriasis and psoriatic arthritis are only recently coming to light [1-4]. Psoriatic eye findings may include conjunctivitis, dry eye, episcleritis, and uveitis, all of which may precede articular changes. Uveitis, seen in 7% to 25% of psoriatic arthritis patients, may be recognized by the presence of conjunctival injection, photophobia, pain, lid swelling, or otherwise unexplained visual changes. Early recognition is of paramount because its natural course may lead to vision loss [5]. Immunopathogenesis has shown evidence for T-helper cell (Th) type 1 (Th1) and Th17 involvement in the pathogenesis of uveitis according to the murine experimental autoimmune uveitis model. Corticosteroids are the primary treatment modality; however, increasing emphasis has been placed on immunomodulators and biologics for more intractable cases [6-9]. Referral to an ophthalmologist is essential for definitive diagnosis and treatment. Herein we report our experience to highlight the importance of thorough evaluation of patients with psoriasis and involvement of eye, and coordination between dermatologists and ophthalmologists prior to any interventions.

METHODS AND RESULTS

Our first case, a 52 year old female was referred from ophthalmology OPD for opinion on her skin lesions present since 30 years. Patient had minimal lesions over the extremities with no itching. There was

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history of winter exacerbation. She gave history of local application of steroids and methotrexate intake for skin lesions 2 years back. There was no history of joint involvement. No long standing debilitating illness like diabetes, tuberculosis and hypertension. She underwent a cataract surgery, phacoemulsification with Intraocular (IOL) implantation for both eyes 1 week apart a month ago. Left eye postoperative was uneventful with visual acquity of 6/6, subsequently she was operated for right eye cataract. Postoperatively when the pad and bandage was removed on the next day she had pain, and no perception of light or projection of rays. The cause of sudden loss of vision could not be explained but on slit lamp examination there was severe anterior uveitis. On examination of right eye there was conjunctival congestion, presence of keratic precipitates with aqueous flare was seen. Upon fundus examination there was no fundal glow, B-scan showed vitreous haze behind the IOL (Fig. 1). Intraocular pressure was 36 mm of Hg. Optical coherence tomography (OCT) was normal in both eyes. Patients was started on antibiotic and steroid eye drops and also a short course of systemic corticosteroids.

On cutaneous examination there were hyperpigmented papules and plaques seen over both lower extremities (Fig. 2). Few post inflammatory hyperpigmentation macules over the back suggestive of old healed lesions. Palms and soles were normal. There were no lesions over the scalp and no nail changes were seen. Hence a clinical diagnosis of psoriasis vulgaris in remission was given. She was advised emollients for regular application.

Retrospectively a literature search was done to look for any association between psoriasis and eye involvement. There was no mention of eye involvement in psoriasis in any of standard textbooks of dermatology. But after extensive research in journals, many published articles of eye involvement in psoriasis with severity of skin lesions and joint involvement were mentioned. This made us to workup the case thoroughly and was referred back to ophthalmologist with relevant information. They investigated for any cause for uveitis and found to be non-infective. Patient was advised few blood investigations along with HLA-B27, but was not done due to logistical reasons. Finally the loss of vision was attributed to development of uveitis, secondary to psoriasis.

This prompted us to screen all our patients with psoriasis with or without joint involvement for any associated eye complications attending our outpatient department or referred cases. In this process over a period from 2013-2014, we screened around 200 psoriasis cases for any involvement of eye and coincidentally we were able to detect 5 cases with eye complications. Two cases had joint involvement, one was HLA-B27 positive. Two cases had extensive psoriasis which was present since more than 20 years (Table 1). All these patients were referred to ophthalmology department with these eye symptoms, they were extensively investigated for any systemic or secondary infective cause and had none. Slit lamp examination confirmed that the eye symptoms were due to anterior uveitis probably secondary to psoriasis. All the cases after initial evaluation were treated and were advised for regular eye follow up to avoid any complications.

Ethical Requirements for Studies Involving live human subjects or animal: Accepted by all authors.

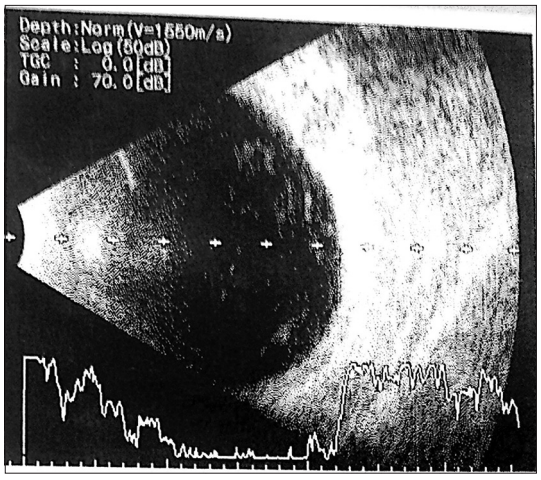

Figure 1: Fundus examination of right eye, there was no fundal glow with B-scan showing vitreous haze behind the IOL indicating anterior uveitis

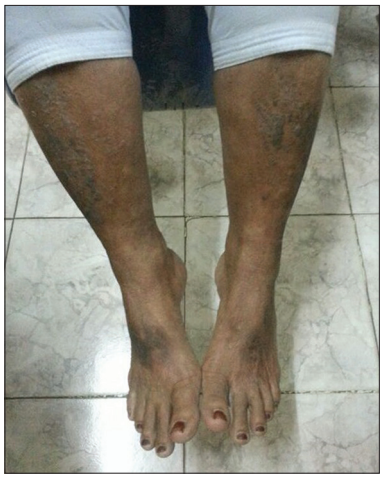

Figure 2: Minimal cutaneous lesions seen as hyperpigmented papules and plaques over both lower extremities suggestive of psoriasis

Table 1: Case details of patients with psoriasis and eye symptoms

S. no	Age/sex	Duration of psoriasis	Eye symptoms	Treatment and outcome
1.	52 yrs/F	30 years	Severe pain in Right eye post cataract. Left eye - normal	Right eye – loss of vision. Left eye – prophylactic antibiotic and steroid eye drops for 2 months. Systemic steroids – 1 week
2.	43 yrs/F	11 years	Redness in both eyes – 6 months	Antibiotic and NSAID drops for 6 weeks
3.	61 yrs/M	17 years with psoriatic arthritis	Pain in both eyes – on and off	Steroid and NSAID drops. Regular follow-up Plan to start – immunomodulatory drugs – Methotrexate
4.	56 yrs/F	22 years, Arthritis, HLA-B27+ve	Pain and photophobia – many years	Eye protection, NSAID Drops. Tapering course of systemic steroids
5.	49 yrs/M	8 years	Reddness in both eyes – 3 months	Antibiotic and NSAID drops for 6 weeks
6.	48 yrs/F	28 years	Watering of eyes, blurred vision – many years	Antibiotic and NSAID eye drops for 6 weeks

The study design was accepted by the Raja Rajeswari Medical College & Hospital.

All subjects gave their informed consent and ethical clearance was obtained from local ethical committee.

DISCUSSION

The relationship between the eye and psoriasis has been recognized for decades, but the precise eye manifestations in patients with psoriasis are only recent findings [1-4]. Psoriatic eye findings may include conjunctivitis, dry eye, episcleritis, and uveitis. Eye findings in conjunction with psoriatic arthritis were reported in 1976 by Lambert and Wright, who noted the presence of ocular inflammation in 31.2% of 112 patients with psoriatic arthritis, with conjunctivitis the most common lesion (19.6%), followed by iritis (7.1%) [5]. Psoriatic arthritis has traditionally been thought to precede psoriatic eye manifestations, but a minority of cases are seen in the reverse order [6].

Uveitis is a loose term that refers to a large group of diverse diseases. The International Uveitis Study Group classifies intraocular inflammation into anterior (iris or ciliary body), posterior (choroid or retina), intermediate (vitreum, peripheral retina, and pars plana of the ciliary body), or panuveitis (generalized inflammation of entire uvea) [7]. Uveitis may manifest solely in the eye, or it may be associated with a systemic disease. Multiple studies quote the prevalence of uveitis in psoriasis and Psoriatic arthritis [4,5,8,9].

Psoriasis and the eye

For patients with psoriasis, uveitis had been commonly thought to occur only in conjunction with psoriatic arthritis; however, there have been many case reports of psoriatic uveitis presenting independent of joint disease [3,16]. Furthermore, the temporal relationship of these two entities has been disputed. Some recent studies suggest that for most spondyloarthropathies (SpAs), inflammatory joint manifestations precede uveitis [11,12,17]. Nevertheless, some cases of uveitis have been reported to occur even before psoriatic skin disease[6], and uveitis has been reported as the first presenting sign of SpAs in 0% to 11.4% of cases [3]. The severity of ocular inflammation does not necessarily correlate with extent of joint findings but may correlate with skin disease [18-20].

Presentation

Acute uveitis attacks typically present with pain, intense photophobia, red eye, blurred vision/miosis (pupil constriction), and varying degrees of lid edema [21]. Conjunctival injection in acute anterior uveitis begins at, and is most intense around, the edge of the cornea. Eyes affected by uveitis may have smaller pupils than on the unaffected side because inflammation may trigger muscle spasm of the iris sphincter, or the pupil could be distorted by posterior synechiae. However, the actual predictive value of symptoms in diagnosing uveitis is unknown. In fact, the only warning sign may be unexplained poor vision [22]. Thus, patients who show no evidence of inflammatory changes should nevertheless be referred to an ophthalmologist if symptoms worsen.

Psoriatic uveitis is most commonly anterior, although it can be associated with posterior uveitis as well [10,23]. It is also more likely than other forms of spondyloarthropathy-associated uveitis to be insidious in onset, bilateral, with periodic flares [5,10,23-25].

All complaints should be referred to an ophthalmologist for evaluation. Nonophthalmologists can assess a patient's visual acuity and examine the external eye for circumcorneal injection. Physicians may evaluate with a direct ophthalmoscope for evidence of decreased corneal transparency, keratic precipitates (inflammatory cells on the cornea), and posterior synechiae (adhesions of the lens and iris) [22]. However, the diagnosis of

uveitis must be confirmed with a slit-lamp examination performed by an ophthalmologist. HLA-B27, as noted, is not currently considered diagnostically useful [14].

Course of disease

Uveitis is one of the leading causes of visual loss [26]. Long-term ocular complications of psoriatic uveitis have been poorly studied. Acute anterior uveitis is the most common form of uveitis in psoriasis and is the most common uveitis overall. A retrospective study of a cohort of patients with uveitis, irrespective of underlying cause, found that 91% of patients with acute anterior uveitis had normal visual acuity at a final follow-up visit, compared with 64% of those with other forms of uveitis [22]. In B27-associated uveitis, the rates of blindness are up to 11% [27]. Other possible changes secondary to uveitis include secondary glaucoma, retinal vascular occlusions, inflammatory optic neuropathy, retinal detachment, posterior synechiae (adhesions between the iris and the anterior surface of the lens), and hypopyon (a collection of pus inferiorly in the anterior chamber) [22,28].

Other common presentations of eye disease commonly associated with psoriasis include conjunctivitis, keratoconjunctivitis sicca, and episcleritis.

Immunopathogenesis

Although the exact underlying mechanisms contributing to the link between psoriasis and uveitis remain poorly understood, there are common etiologic pathways involved in the pathogenesis of both entities.

Psoriasis

Psoriasis was initially described as a "Th1 disease" because of the presence of interleukin1 (IL-1), tumor necrosis factor-alpha (TNF-α), and interferon-γ, which are classically produced by Th1 cells. Recent research into psoriasis highlights the T-cell population called Th17 cells [29]. The process is thought to be mediated in part by interferon-alpha, a proinflammatory cytokine, which stimulates myeloid dendritic cells to produce IL-12 and IL-23, which are Th17-promoting cytokines [29,30].

Th17 cells are CD4+ T cells that are developmentally and functionally distinct from Th1 and Th2 cells.45 Th17 cells produce IL-17, TNF, and IL-22, which are increased in psoriasis. Both Th1 and Th17 T cells are involved in the pathogenesis of psoriasis. TNF-α is a key inflammatory mediator that is produced by both Th1 and Th17 reactions and is found at elevated levels in psoriatic skin and in joint fluid from patients with psoriatic arthritis [31-33]. TNF-α acts by activating a few possible pathways, such as nuclear factor-kappa B (NF-κB), an inflammatory gene transcription factor, or mitogen-activated protein kinase (MAPK), which activates cellular inflammatory activities. There is notable cross-link in the affected pathways, ensuring that TNF-α activation can incite an inflammatory response. Studies of psoriasis patients treated with TNF-α inhibitors have shown significant clinical response in psoriasis and psoriatic arthritis treatment [34,35].

UVEITIS

Much of the immunology research into uveitis focuses on the experimental autoimmune uveitis (EAU) and endotoxin-induced uveitis (EIU) models. EAU is induced by immunization of species such as mouse, rat, or rabbit with purified retinal antigens such as retinal soluble antigen (i.e., arrestin) and the interphotoreceptor retinoid-binding protein (IRBP). Immunization results in a uveitis that strongly resembles a Th1-induced reaction with strong dependence on TNF-α [36,37], similar to traditional theories of psoriatic uveitis. TNF mRNA expression was increased by 16 times in EAU mice [38]. Notably, intravitreal injection of TNF in rabbits induces uveitis [39], which is characterized by a cellular infiltrate in the aqueous humor consisting primarily of lymphocytes and monocytes. Treatment of EAU-afflicted rats with soluble TNF receptor to inhibit TNF activity inhibited macrophage activity and decreased photoreceptor damage. In a separate open-label study, TNF inhibitor treatment improved visual acuity in refractory posterior segment intraocular inflammation by leading to an increase in IL-10 expression in the peripheral blood CD4+ T cells [34,35].

Treatment of uveitis

Given the immune-mediated nature of both psoriasis and non-infective uveitis, pharmacotherapy has aimed to suppress the inflammatory response implicated in these diseases. Psoriatic uveitis may be anterior or posterior or both and thus may require different treatment strategies. Acute anterior uveitis may often be treated with a dilating eye drops to keep the pupil mobile and prevent formation of synechiae (adhesions between the iris and lens) [40]. Posterior uveitis, although it

may be difficult to appreciate on examination, is more commonly responsible for loss of vision [41], increasing the urgency for inflammation treatment. Recommended pharmacotherapy has evolved as understanding of the pathogenesis has improved and as specific inflammatory mediators have been identified. Although the traditional treatment has involved corticosteroids or immunomodifying drugs, in recent years, the use of drugs that target the TNF pathway has been suggested for use in the more intractable cases.

Our experience in this study and review of literature shows that uveitis in patients with psoriasis may have distinct clinical features. It appears that in this subset of patients, uveitis is more often bilateral, persists for a long duration, and requires oral NSAID therapy more often than the two most common types of anterior uveitis, idiopathic and HLA-B27-associated anterior uveitis. Bilateral attacks have been reported to occur in 7% to 21% of idiopathic and HLA-B27 associated uveitis patients [11]. Observations of a mean attack duration of 11.2 weeks and the high incidence of oral NSAID use compared with the mean attack duration of 6.2 to 5.3 weeks in idiopathic anterior and HLA-B27-associated anterior uveitis and substantially decreased requirement of supplemental therapy seem to underline the fact that uveitis in psoriasis may have a different clinical course and be more recalcitrant than idiopathic or HLA-B27-associated types [50]. The mean age at diagnosis reported for idiopathic and HLA-B27-associated uveitis is 30 to 40 years, in contrast to almost 44 years mean age in our study population of psoriatic uveitis patients [49,50]. This may indicate that uveitis occurs at a later age in this population, perhaps resulting from the fact that the prevalence of psoriasis increases with age, and psoriatic uveitic patients may be older because psoriasis in general occurs in an older population [3].

We believe that psoriasis is indeed a systemic disease with a propensity for skin, joint, and eye involvement. Knox [3], in his review of 10 patients with psoriasis and uveitis, noted that arthritis was present in none. This has been supported by a mounting number of case reports of an anterior uveitis antedating or occurring after the development of psoriatic skin lesions [44-48]. It has been postulated that HLA-B27 positivity may be associated with greater severity of uveitis in patients with psoriasis; demonstrates a significant difference in the maximum grade of cells demonstrated on clinical examination, and the HLA-B27 patients required systemic nonsteroidal anti-inflammatory drugs more often for the control of intraocular inflammation than did HLA-B27 negative patients. These findings are almost certainly indicative of more resistant, difficult to control, recurrent uveitis in psoriatic patients who are HLA-B27 positive. Indeed, HLA-B27 positivity may contribute to disease expression in patients with psoriatic arthritis as well and has been associated with an earlier age of onset of psoriasis, arthritis, and bilateral sacroileitis [50].

Posterior involvement (retinal vasculitis, cystoid macular edema, and papillitis) was a frequent occurrence. This contrasts with Knox's [3] observation of boggy retinal congestion and edema and pigmentation of both maculae seen in his series of patients with psoriasis. Our study suggests that psoriatic uveitis is usually anterior, recurrent, often bilateral, and may be associated with a high incidence of posterior involvement. Anterior uveitis in such patients typically requires oral nonsteroidal anti-inflammatory drug therapy to achieve and maintain remission of ocular inflammation. Further epidemiologic studies are required to determine the strength of association between psoriasis and uveitis; definition of such an association may allow more frequent ophthalmic monitoring in patients with psoriasis, allow the institution of appropriate treatment with NSAIDs or systemic immunomodulators early on in their treatment, and prevent vision loss in patients with psoriatic uveitis.

CONCLUSION

Psoriatic eye manifestations, uveitis in particular, can lead to serious consequences, including vision loss. These manifestations have been reported more frequently in psoriasis patients with arthritis, but they have also been reported in psoriatic patients without arthritis. Psoriatic eye manifestations may precede articular changes. Uveitis may be recognized by the dermatologist by the presence of conjunctival injection, photophobia, pain, lid swelling, or otherwise unexplained visual changes. Referral to an ophthalmologist is essential for definitive diagnosis and treatment. Corticosteroids are the primary treatment modality. However, increasing emphasis has been given to immunomodulators and TNF blockers for the more intractable cases. TNF blockers may be promising for the prevention of induction and recurrence of uveitis in psoriasis patients.

More research on the relationship between uveitis and psoriasis is needed. In particular, a greater understanding

of the frequency of psoriasis-specific uveitis may shed light on the importance of surveillance. Current experimental eye models for the study of uveitis do not specifically address the pathophysiology of psoriatic uveitis. Long-term follow-up of psoriasis patients with eye manifestations would provide more insight into treatment methods.

Given the serious nature of untreated disease, the dermatologist should have a high index of suspicion for eye findings in psoriasis patients. We recommend regular surveillance of psoriasis patients for visual changes and eye symptoms. Collaboration between ophthalmologists and dermatologists is essential to optimize disease management.

CONSENT

The examination of patients is conducted according to the Declaration of Helsinki principles. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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Original Article

Comparative study of efficacy of excimer light therapy vs intralesional triamcinolone vs topical 5% minoxidil: an observational study

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ABSTRACT

Introduction: Alopecia Areota is a chronic inflammatory disease that involves hair follicles, and sometimes nails, caused by T-cell mediated autoimmune mechanism. Current treatment modalities includes corticosteroids (oral, topical or intralesional), Minoxidil, Contact sensitizers like DNCB, DPCP and SADBE, Immunosuppressants like Methotrexate or Azathioprine, DMARDs like Sulfasalazine, and Phototherapy. **Materials and methods:** After taking consent, 40 patients treated with excimer light, 46 patients treated with triamcinolone injection intralesionally and 14 patients treated with topical minoxidil 5% were compared by their photographs taken prior to treatments, at 2 months and 6 months follow up. **Results:** Among the excimer group, 21/32 (61.76%) with single patch and 1/6 (16.67%) with multiple patches achieved >50% hair regrowth. Among Triamcinolone group, 23/30 (76.67%) with single patch and 10/16 (62.5%) with multiple patches achieved >50% hair regrowth. Among the Minoxidil group, 4/12 (33.33%) with single patch and none .i.e 0/2 with multiple patches achieved >50% regrowth. **Conclusion:** After comparing the efficacy of Excimer light therapy, intralesional triamcinolone and 5% Minoxidil, it was concluded that intralesional triamcinolone seems to be the most efficacious. Multiple patches were more resistant than single patch. Scalp response much better than beard.

Key words: Alopecia areata; Minoxidil; Triamcinolone; Excimer light therapy

INTRODUCTION

Alopecia Areata is a chronic inflammatory disease that involves hair follicles, and sometimes nails, caused by T-cell mediated autoimmune mechanism. It is the most common hair loss after Androgenic Alopecia. It affects all ages, predominantly 2nd to 4th decade and both sexes equally [1]. It is a non-scarring telogenic Alopecia, predisposed by HLA's such as DQ3, DQ7, DR4 and DR11, CD4+ T helper cells and is associated in some patients with Thyroid dysfuctions, Psychological problems, Atopy, Pernicious anemia and infections [2]. Strong association between autoimmune polyglandular syndrome type 1 (APS1), caused by mutations in the 7 AIRE gene on chromosome 21 and AA has also been reported [3].

It can present as well demarcated patch of hair loss, multiple patches or extensive hair loss as in Alopecia totalis / universalis [3]. It causes significant cosmetic and psychological distress in most of the people it affects.

Current treatment modalities includes corticosteroids (oral, topical or intralesional), Minoxidil, contact sensitizers like DNCB, DPCP and SADBE, Immunosuppressants like Methotrexate or Azathioprine, DMARDs like Sulfasalazine and Phototherapy [4-6].

MATERIALS AND METHODS

The aim of the study is to compare the efficacy of Excimer light therapy, intralesional Triamcinolone and topical Minoxidil 5%. This was an observational study which was done at Department of Dermatology, RNT Medical college, Udaipur, Rajasthan. The study was conducted between June 2013 to September 2014. For the purpose

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of easy comparison and segregations of data, the following inclusion and exclusion criteria were followed.

Inclusion criteria

- Patients who give consent for the study
- Patients presenting with Alopecia Areata, 1 to 6 patch/patches, sizes 2 cm to 10 cm
- Subjects having patch for at least 3 months, with no evidence of hair regrowth
- Who never taken treatment before or who has not taken any treatment for at least 8 weeks
- No history of Photosensitivity
- Patients who were willing and capable of cooperating to the extent and degree required by the protocol.

Exclusion criteria

- Patients who do not give consent
- Patients who received treatment for alopecia areata within the past 8 weeks.
- Patients with alopecia totalis or alopecia universalis
- Patients with known photosensitivity like having polymorphous light eruption, connective tissue diseases, porphyria or Xeroderma pigmentosum
- Pregnant or breast-feeding patients
- History of previous skin cancer.

Those patients in the excimer light therapy group were given the therapy twice a week, but not on consecutive days. The treatment was started at 300 mj/cm^2, and it was increased by 100 mj/cm^2 every visit. If erythema persisted for more than 2 days, the treatment was skipped until erythema was healed: and the previous dose was restarted. The end point was either 16 sittings or hair growth whichever was earlier.

Those of Intralesional Triamcinolone group was given Intralesional Triamcinolone 5 mg/ml every 3 weeks. Minoxidil group were given 5% topical Minoxidil and were advised to apply twice a day, 1 ml in each patch.

Those patients who were given treatments were taken photographs at the first visit prior to treatments after 2 months and then after 6 months and the photographs were compared. Those patients who achieved >50% hair regrowth were considered successful treatment.

RESULTS

A total of 100 patients were included in the study: 40 patients in Excimer light therapy group, 46 in triamcinolone group and 14 in Minoxidil group. The results of the study presented Tables 1 and 2. Clinical results of treatment with excimer light, triamcinolone and 5% minoxidil illustrate Figures 1 to 3.

DISCUSSION

Alopecia areata (AA) is a non-scarring, autoimmune, inflammatory, relapsing hair loss affecting the scalp and/or body. It is also known as Pelad or Area Celsi. It is commonly manifests as a sudden loss of hair in localized areas. In acute-phase AA, CD4+ and CD8+ T cells infiltrated in the juxta-follicular area. In chronic-phase AACD8+ T cells dominated the infiltrate around hair bulbs which contributes to the prolonged state of

Table 1: Results of the study according to number of lesions

Mode of treatment		
	>50% regrowth	
	Single	Multiple
Excimer	21/34 (61.76%)	1/6 (16.67%)
i/l Triamcinolone	23/30 (76.67%)	10/16 (62.5%)
Minoxidil	4/12 (33.33%)	0/2

Table 2: Results of the study according to the sites of the lesions

	>50% improvement				Both
	Scalp		Beard		
	Single	Multiple	Single	Multiple	
Excimer	22/32 (68.75%)	1/6 (16.67%)	0/7	0	0/1
Triamcinolone	22/25 (88%)	8/10 (80%)	1/5 (20%)	2/6 (33.33%)	0
Minoxidil	4/10 (40%)	0/1	0/2	0/1	0

Figure 1: (a) Patient treated with excimer light (pretreatment) (b) patient treated with excimer light (after 2 months) (c) Patient treated with excimer light (after 6 months)

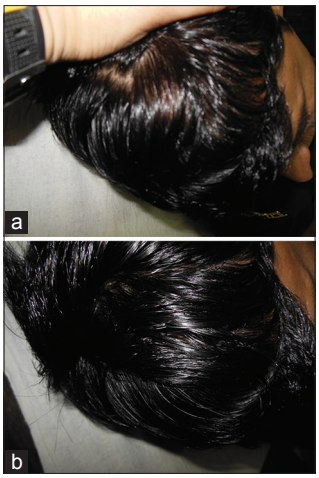

Figure 2: (a) Patient treated with triamcinolone (after 2 months) (b) Patient treated with triamcinolone (after 6 months)

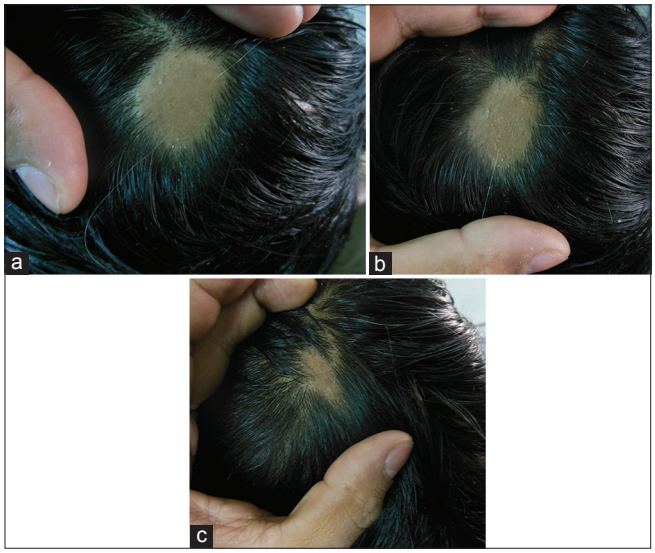

Figure 3: (a) Patient treated with 5% minoxidil (before treatment) (b) Patient treated with 5% minoxidil (after 2 months) (c) Patient treated with 5%minoxidil (after 6 months)

hair loss. It is postulated that the characteristic T cell "swarm of bees" infiltrate seen in alopecia areata is the result of T cells attracted to the hair follicle by NKG2D-activating ligands.

Triamcinolone acetonide is used most commonly with the concentrations vary from 2.5-10 mg/mL, the lowest concentration being used on the face. A concentration of 5 mg/mL is usually sufficient on the scalp. Less than 0.1 mL is injected per site, with approximately 1 cm between injection sites [7]. It is mainly used for its immunosuppressive effects. Hair-growth-stimulating effect of minoxidil is stimulation of PGE2 synthesis by activating prostaglandin-H synthase (PGHS)-1. Normally, 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. It also seems to have direct mitogenic effect on epidermal cells and also prolongs the survival time of keratinocytes [8].

The biologic events by which laser and light sources produce hair growth is unclear. Hypertrichosis is the result of follicles converting from telogen (the resting phase) to anagen (the active phase), or vellus follicles transforming into terminal follicles. Sunlight has been recognized as a promoter of hypertrichosis. Although the pathogenesis is unknown, evidence shows UV radiation may upregulate production of prostaglandin E2, an inflammatory mediator that is known to induce reversible eyelid hypertrichosis and to stimulate hair growth when applied topically on animal models [9].

In this study, 100 patients were included in the study. Among the excimer group, 21/32 (61.76%) with single patch and 1/6 (16.67%) with multiple patches achieved > 50% hair regrowth. Among Triamcinolone group, 23/30 (76.67%) with single patch and 10/16 (62.5%) with multiple patches achieved >50% hair regrowth. Among the Minoxidil group, 4/12 (33.33%) with single patch and none .i.e 0/2 with multiple patches achieved >50% regrowth. Regarding the sites of involvement, among those who achieved >50% regrowth, 22/32 (68.75%) had single patch on scalp, 1/6 (16.67%) had multiple patches on scalp. Among the triamcinolone group who achieved >50% regrowth, 22/25 (88%) had single patch on scalp, 8/10 (80%) had multiple patches on scalp, 1/5 (20%) had single patch on beard, 2/6 (33.33%) had multiple patches on beard. Among minoxidil group who achieved >50% regrowth, 4/10 (40%) had single patch on scalp, none among those who had multiple patches achieved successful results.

A study conducted on the efficacy of 308-nm excimer lamp for the treatment of alopecia areata by Ohtsuki A, et al showed that out 16 patients who completed the study , four (57%) of those with single AA showed re-growth involving more than 50% of lesional areas, while 2 (29%) showed regrowth involving less than 50% of lesional areas. Hair regrowth was documented in 86% of single AA patients. 6 patients (67%) with multiple patches showed re-growth involving more than 50% of lesional areas while two (22%) showed regrowth involving less than 50% of lesional areas [10]. Another study done by Al-Mutairi N, et al. on 308-nm

excimer laser for the treatment of alopecia areata on 42 patients, hair regrowth was observed in 41.5% of treated areas. Hair regrowth was noticed to begin to appear during the second month of therapy. No regrowth of hair was noted on the control patches. Laser therapy was administered twice a week for a maximum of 24 sessions. Apart from erythema at the treated sites, there were no significant adverse effects [11]. In our study, 21/32 (61.76%) with single patch and 1/6 (16.67%) with multiple patches achieved > 50% hair regrowth. Abell and Munro reported hair regrowth in 71% of patients with subtotal alopecia areata treated by triamcinolone acetonide injections and in 7% of a placebo group [12] while in our study, 23/30 (76.67%) with single patch and 10/16 (62.5%) with multiple patches achieved >50% hair regrowth.

In a placebo-controlled, double-blind study conducted by Price et al, although hair regrowth was observed in 63.6% and 35.7% of the minoxidil-treated and placebo groups respectively only 27% of the minoxidil-treated patients showed cosmetically acceptable hair regrowth [7], while in our study, 4/12 (33.33%) with single patch and none i.e 0/2 with multiple patches achieved >50% regrowth.

LACUNAE OF THE STUDY

It was not controlled study. Besides, the effects of duration of the disease and comorbidities (which could have some effects on the response of the treatments) were not included in the study.

CONCLUSION

Although all the three modalities of treatment are useful for treatment of alopecia areata, intralesional triamcinolone seems to be the most efficacious. Multiple patches were more resistant than single patch. Scalp response much better than beard, the reason being to explore further.

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patient for publication of this article and any accompanying images.

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Brief Report

A retrospective study of profile of leprosy patients in a District Hospital in North India

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ABSTRACT

Introduction: There is a high prevalence of leprosy in certain areas of our country. The main problem with leprosy is the prevalence of disability in untreated patients. **Aims:** To know the clinical profile of leprosy patients and to find out the risk factors for disabilities. **Methods:** A retrospective study of 10 years was conducted from April 2003 to March 2014 was conduced. **Results:** There were 137 MB (75.6%) and 44 PB (24.4%) cases. There were 35 (19.33%) MB patients with disability and 5 (2.76%) PB patients with disability. There were 5 cases (2.7%) with childhood leprosy. The percentage of defaulters was 9 (4.97%). The Patients were grade II disability were 19.4% and patients with grade I disability were 2.8%. Regarding the nerve involvement in leprosy, ulnar nerve was most commonly involved in 45 (24.86%) patients, lateral popliteal nerve in 20 (11.04%) patients, posterior tibial nerve in 15 (8.28%) patients and median nerve was involved in 12 (6.62%) patients. **Conclusions:** The multibacillary patients are more susceptible to neuritis as compared to the paucibacillary patients. The occurence of neuritis is a significant risk factor for disabilities in leprosy. Early diagnosis and treatment is important to reduce the load of infection.

Key words: Disability; prevalence; leprosy; grading; treatment; peripheral nerves; thickened

INTRODUCTION

Leprosy is a chronic infectious disease caused by mycobacteriae leprae. India has achieved elimination of leprosy with a national prevalence below 1/10,000. But due to lack of awareness about early diagnosis and treatment, there are many cases of disability still prevailing [1,2].

AIMS

1. To know the clinical profile of leprosy patients
2. To find out the patients with grade II disability
3. To find out the risk factors for disabilities
4. To find out the cases of childhood leprosy.

MATERIAL AND METHODS

A retrospective study of 10 years was conducted from April 2003 to March 2014 was conduced. The record of the patients was taken from the registers maintained. The registers had all the details about the dermatoneurological examination and WHO grading of disability. According to the WHO grading of disability: Grade 0- No disability due to leprosy; Grade I- Sensory impairment only; Grade II- Motor dysfunction and sequelae due to leprosy. All the thickened peripheral nerves were noted. The photographic record of the patients was also retrieved. The data including the age and sex of the patients, clinical profile and disability grading was tabulated and the data was analyzed statistically using chi square test.

RESULTS

The mean age of the patients was 25.85 years (Table 1). There were 139 (77.2%) males and 42 (18.9%) females. The male:female ratio was 3.3:1. There were 137 MB (75.6%) and 44 PB (24.4%) cases. There were 35 (19.33%) MB patients with disability

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(Fig. 1) and 5 (2.76%) PB patients with disability (Table 2). There were 5 cases (2.7%) with childhood leprosy (Fig. 2). The percentage of defaulters was 9 (4.97%). The percentage of Punjabi patients was 18.9% and non Punjabi patients was 81.7%. Patients were grade II disability (Fig. 3) were 19.4% and patients with grade I disability were 2.8%. Regarding the nerve involvement in leprosy, ulnar nerve was most commonly involved in 45 (24.86%) patients, lateral popliteal nerve in 20 (11.04%) patients, posterior tibial nerve in 15 (8.28%) patients and median nerve was involved in 12 (6.62%) patients (Table 3). A total of 11% patients had history of contact in the family and friends. The various risk factors for the development of disabilities were tabulated. Patients having multibacillary leprosy (75.69%) had high risk for development of deformities. Other risk factors for development of disability were: Old age (4.97%), patients with severe clinical disease (16.57%) and patients with neuritis (11.04%) (Table 4).

Table 1: Age distribution of patients

Sr no	Age distribution (years)	No of patients	Percentage
1	0 – 10	2	1.11
2	11 – 20	26	14.44
3	21 – 30	57	31.7
4	31 – 40	47	26.11
5	41 – 50	28	15.55
6	51 – 60	12	6.7
7	60	9	5

Table 2: Type of leprosy and disability

Sr no	Type of leprosy	No of patients	Percentage	Patients with disability	
				Number	Percentage
1	MB	137	75.6	35	19.33
2	PB	44	24.4	5	2.76

Table 3: Nerve involvement in leprosy

Sr no	Nerve involved	No of patients	Percentage
1	Ulnar nerve	45	24.86
2	Lateral popliteal nerve	20	11.04
3	Posterior tibial nerve	15	8.28
4	Median nerve	12	6.62

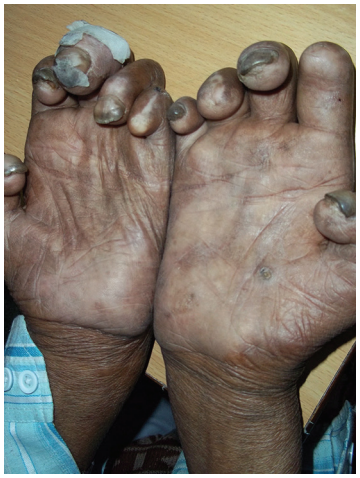

Figure 1: Claw hand in a 50 years old male

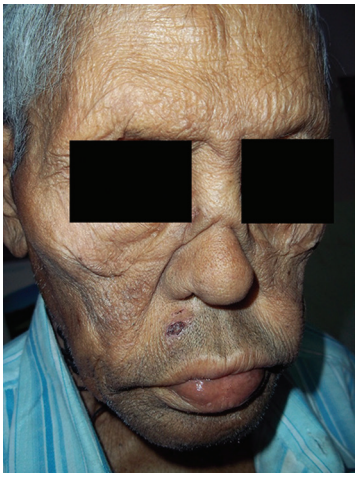

Figure 3: Facial deformity in a 78 years old male

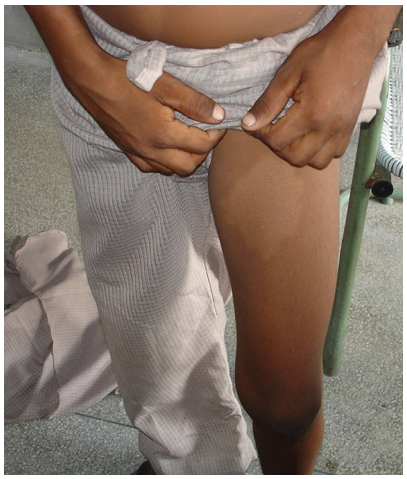

Figure 2: 12 years old child showing borderline tuberculoid leprosy

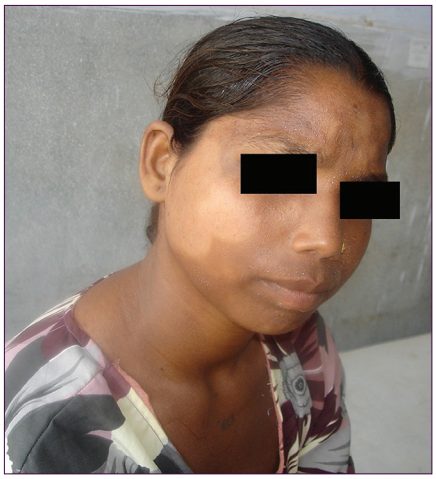

Figure 4: Borderline tuberculoid leprosy in a 26 years old female

Table 4: Risk factors for disability in leprosy

Sr no	Risk fctors	No of patients	Percentage
1	Patients with MB leprosy	137	75.69
2	Old patients	9	4.97
3	Patients with severe clinical disease	30	16.57
4	Patients with neuritis	20	11.04

DISCUSSION

The present study shows that more males were involved as compared to females which is not unusual as males have more exposure as compared to females who mostly stay indoors. It was also seen that multibacillary cases had higher chances of disability as compared to the paucibacillary cases (Fig. 4) as the patients with multibacillary leprosy required a long treatment and therefore some of the patients have poor compliance [3]. There were 2.7% cases of childhood leprosy in our study. With the decrease in the prevalence of leprosy in India, the number of childhood cases of leprosy have decreased significantly [4]. Contact tracing in leprosy is very important in leprosy and in our study 11% patients had history of contact in the family. India has achieved elimination of leprosy in 2005. Although elimination of leprosy has been achieved, still there are some high endemic zones in our country [5,6]. The main problem with leprosy is the development of impairments. The neurological sequelae are responsible for the stigma of leprosy as being a deforming disease.

Leprosy is a chronic granulomatous disease which mainly involves skin and peripheral nerves [7,8]. According to the WHO classification, leprosy is divided into MB or multibacillary leprosy and PB or paucibacillary leprosy depending upon the number of lesions. Several factors have been associated with disabilities in leprosy [9,10]. The main risk factors associated with disability in leprosy are patients having multibacillary leprosy, delay in the diagnosis of leprosy, old age, the extent of clinical disease and the presence of neuropathy. All the high risk patients with disabilities must be carefully followed up to prevent any further impairments [11,12].

CONCLUSIONS

To conclude, the multibacillary patients are more susceptible to neuritis as compared to the paucibacillary patients. The occurence of neuritis is a significant risk factor for disabilities in leprosy. Also, there are many other multiple factors causing disability in leprosy. Also, timely diagnosis and treatment is an important factor for the prevention of neural function impairment in leprosy. Early diagnosis and treatment is important to reduce the load of infection.

CONSENT

The examination of the patient was conducted according to the declaration of Helsinki principles.

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Brief Report

Zonun's regime (35% glycolic acid peel with microneedling followed by tretinoin 0.05% plus glycolic acid 12% application followed by salicylic acid 30% peeling) for treatment of acne scars: a pilot study

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ABSTRACT

Introduction: Acne scars are the result of inflammation within the dermis brought on by acne. The scar is created by the wound trying to heal itself resulting in too much collagen in one spot. Current treatment available are not much satisfactory. Microneedling injure the dermis, thereby stimulating collagen formation. Glycolic acid acts as vehicle for delivery of drugs to dermis: in addition to that, it also has a role in collagen induction. Tretinoin helps in collagen formation. Salicylic acid remodel the superficial skin after the treatment. **Material and Methods:** A total of 4 patients in which 3 out of 4 patient, grade 3 acne scars and 1 out of 4 had grade 2 scar were treated with the regime. After taking consent 35% Glycolic acid peeling was done followed by microneedling. From the next day 12% Glycolic acid plus 0.05% Tretinoin is applied once a day for 2 months. After 2 months 30% Salicylic acid peeling is done. Photographs were taken before treatment, after 1 month and after 2 months of completion of the therapy and compared. Objective assessment was done according to Global Acne Scarring Classification. **Result:** subjectively 2 patients reported excellent response and 2 patients reported good response. Objectively, all patients showed good to excellent response. **Conclusion:** Zonun's regime may be effective for treatment of acne scars.

Key words: Scars; Glycolic acid; Salicylic acid; Tretinoin; Microneedling

INTRODUCTION

Acne scars are the result of inflammation within the dermis secondary to acne. The scar is created by the wound trying to heal itself which results in excessive collagen in one spot. Post-acne facial scarring has a deep impact psychologically and the affected patient usually suffers from low self-esteem and many other psychological ill-effects because of this condition [1-3].

Facial scarring has always been a challenge to treat and there are different treatment options for the management of these scars. However, the majority of these treatment options have their limitations of either being marginally effective or else having considerable morbidity. Treatment options like laser resurfacing or dermabrasion that offer significant improvement in facial scars are invariably associated with considerable morbidity and downtime interference with the daily activities of the patient in the post-treatment period. On the other hand, treatments like microdermabrasion and non-ablative resurfacing with lasers that are associated with a minimal or no downtime, shows lesser efficacy than the traditional, ablative resurfacing techniques [1-4]. Monotherapy provides the benefits of exfoliation but may provide faster results and increased patient satisfaction when combined with superficial

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glycolic acid (alpha-hydroxy acid) peels because of the significant antiaging effects of glycolic acid peels [2–6].

There is still paucity in the current treatment available treatments for acne scars for which better and more satisfactory treatment is needed. At the same time, acne scar is not easy to treat and more aggressive treatment may be needed for better results.

MATERIALS AND METHODS

A Prospective pilot study was done on 4 patients, 1 with grade 2 acne scar and 3 with grade 3 acne scars; all were Fitzpatrick skin type 4; which was done at MBG Hospital Udaipur, Rajasthan. The patients with acne scar who have given consent for the treatment were included in the study. Patients with history of keloidal tendency, pregnant ladies, active acne and unco-operative patients were excluded from the study. Photographs were taken before treatment and then, 1 month and 2 months after completion of therapy .

On the first day, after draping the skin with spirit, followed by povidone iodine solution, 35% Glycolic acid peeling was done. Patients were asked to wash their face after 5 minutes. Then, Microneedling was done on the same day. Patients were asked to wash their face after 10 minutes. From 2nd day, 12% Glycolic acid plus 0.05% Tretinoin were applied daily at night for 2 months. The patients were given tab Vitamin C 500 mg daily. 35% Glycolic acid peeling plus Microneedling was repeated after 15 days. The patients were asked to use sunscreen on day time. Patients took oral antibiotics for 7 days after each microneedling to prevent infections.

After 2 months of completion of the therapy, the photographs were compared and assessed by two Dermatologists who were not involved in the study. Assessment was also done subjectively by asking the percentage of improvements from the patient. Objective assessment was also done according to Global Acne Scarring Classification.

RESULTS

After comparing serial photographs pretreatment, 1 month and 2 months after completion of the therapy, significant improvement was seen in all patients. Subjectively, 3/4 patients reported >70% improvements and ¼ reported 50-60% improvement. Objective assessment showed 2 out of 3 patients with grade 3 scars showed excellent response (shifting by 2 grades) and 1 out of 3 patients with grade 3 acne and 1 patient with grade 2 acne showed good response (shifting by 1 grade). Regarding the adverse effects, transient erythema was seen in all patients which was healed within 1-2 weeks.

DISCUSSION

Acne scars can cause emotional and psychosocial disturbance to the patient. Various modalities have been used for the treatment of acne scars like punch excision, subcision, peels, unfractionated and fractioned lasers and microneedling.

Glycolic acid is an alpha-hydroxy acid, which is soluble in alcohol. It is derived from fruit and milk sugars. Glycolic acid acts by thinning the stratum corneum, promoting epidermolysis and dispersing basal layer melanin. It increases dermal hyaluronic acid and collagen gene expression by increasing secretion of IL-6. Glycolic acid break the bonds and reach deeper into dermis. It acts as vehicle for delivery of the medication. It also helps in induction of collagen formation. By doing microneedling (a depth of 1.5 – 2 mm), skin develops multiple microbruises in the dermis that induces secretions of growth factors that finally results in collagen production. Histologically, thickening of skin and increase in new collagen and elastin fibers resulted. Tretinoin increases rate of shedding of skin and increasing growth of new skin, thereby causing faster scar reduction. Vitamin C also helps in collagen formation. Since Glycolic acid and tretinoin may cause photosensitivity, patients should use sunscreen on daytime. Saliylic acid is a beta hydroxy acid agent which removes intercellular lipids that are covalently linked to the cornified envelope surrounding cornified epithelioid cell .It helps in exfoliation of superficial layer of epidermis (keratolysis) as well as keratoplastic, and helps in reconstruction of skin surface [1-8].

A study conducted by Imran Majid on Microneedling therapy in atrophic facial scars on 36 patients showed that 34 patients achieved a reduction in the severity of their scarring by one or two grades. Subjectively, 29 patients reported the response as ‘excellent’ (7-10 on the 10-point scale), four patients reported the response as ‘good’ (score of 4-6) and only three patients reported the response as ‘poor’ (score of <4). The objective scoring showed 26 out of the total of 36 patients (72.2%) showed an excellent response to

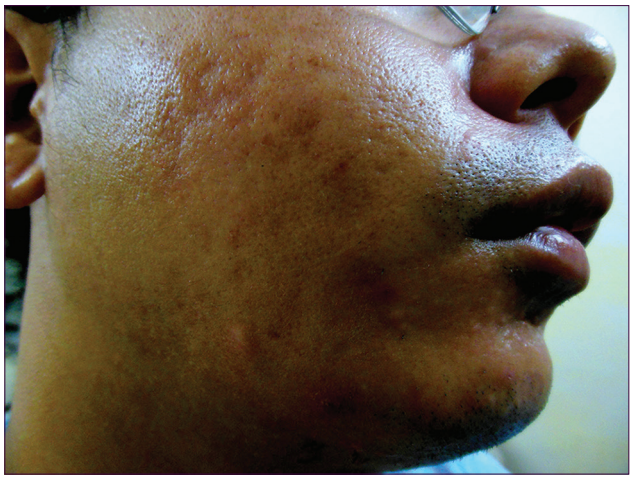

Figure 1: Pretreatment

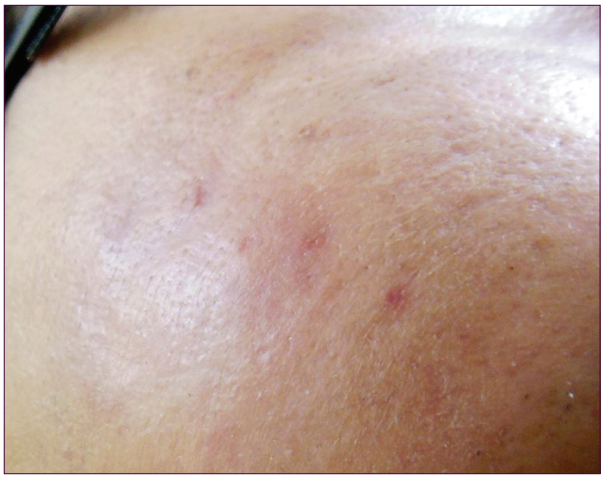

Figure 3: After 1 month

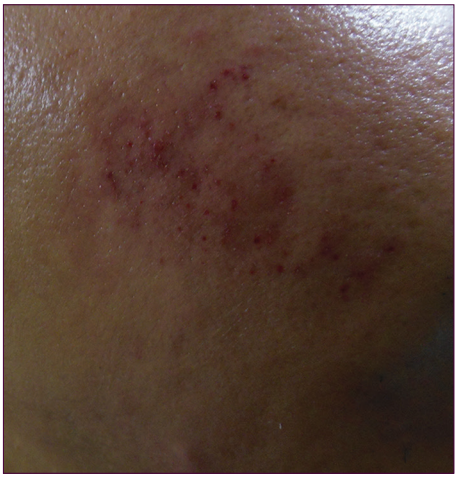

Figure 2: Immediate reaction

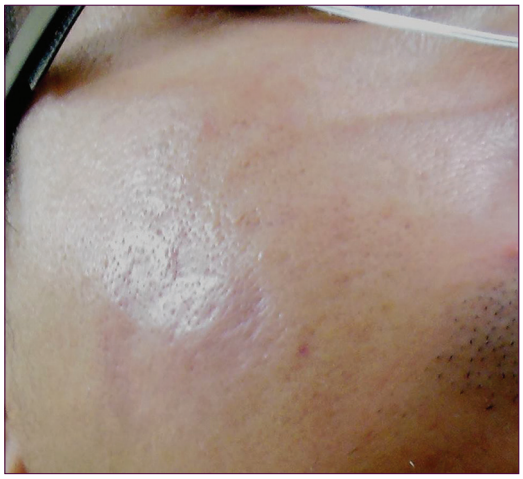

Figure 4: After 2 months

dermaroller treatment while six others achieved a good response (16.7%). Only four patients (11.1%) out of the total of 36 failed to show a significant response to treatment. A study conducted by the department of Dermatovenereology at the Sarajevo University Hospital centre on tretinoin for treatment of acne scars showed 79 % success rate [9].

Sharad J also evaluated Combination of microneedling and glycolic acid peels for the treatment of acne scars in dark skin in a way that the subjects were divided into two groups. The first group comprised of 30 patients in whom only microneedling was performed once in 6 weeks for five sessions. In the second group of 30 patients, a combination of microneedling and 35% GA. Thirty patients in the age group of 20-40 peels was carried out. Patients from both groups were evaluated on the basis of Echelle d'Evaluation clinique des Cicatrices d'acné classification. He found out that, there was significant improvement in superficial and moderately deep scars (grade 1-3). There was also improvement in skin texture, reduction in postacne pigmentation in the second group [10].

Another study conducted by Qian H. et al on treatment of acne scarring with fractional CO2 laser have showed that at the 12 months follow-up time period, 12.9% of the patients showed excellent improvement in their acne scars, while 38.71% noted good to fair results. The clinical response at the 12-month follow-up visit tended to be better than at the 3-month follow-up visit, but was not statistically significant. Four patients experienced post-treatment and transient PIH but three patients were noted to have prolonged erythema. There was no evidence hypopigmentation or worsening of the scarring in any of the study patients [11].

In study conducted by Kaminaka C. et al on Clinical evaluation of glycolic acid chemical peeling in patients with acne vulgaris: a randomized, double-blind,

placebo-controlled, split-face comparative study on 26 patients with moderate acne were treated with 40% GA (pH 2.0) on half of the face and placebo on the other half, performed five times at 2-week intervals showed statistically significant reductions in acne lesions at each time point from baseline values. There were statistically significant differences between the GA and placebo sides. The GA sides had better responses for noninflammatory lesions than for inflammatory lesions. In bioengineering measurements, sebum levels were statistically significantly reduced after the initiation of therapy on both sides at weeks 8 and 10, but there were no statistically significant differences between the two sides [12].

In this study, subjectively, the 2 patients reported excellent results (7-10 on 10 point scale), 2 patients reported good response (4-6). On objective assessment, 2 out of 3 patients (66.7%) with grade 3 acne scars were improved by two grades to grade 1 and were labelled as 'excellent' response. 1 (33.3%) out of 3 patients with grade 3 acne scars was improved by 1 grade to grade 2 and was labelled as 'good' response. 1 patient with grade 2 acne scar was improved to grade 1 and was labelled as 'good response'. Overall, all the patients showed good to excellent response. This therapy not only reconstruct the acne scars, it also seems to cause glowing of skin which made the patient more satisfied with the treatment.

The lacunae of the study is less number of patients to make better and more precise efficacy and safety of the regime and effects of skin type and gender differences in response of the treatment. Besides, there was no single patient with grade 4 acne scar.

CONCLUSION

The combination therapy (zonun's regime) may be effective treatment for treatment of acne scars. It also helps in glowing of skin in this study. Further study on more number of patients will be needed to get effects of skin type and gender differences, and also the influence of severity of acne scars, on response of the treatment. Further study on safety profile is also needed.

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patients for publication of this article and any accompanying images.

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Brief Report

Sweat control in male by the use of alunogen and cypripedium pubescens

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ABSTRACT

Aim of my study is to investigate upon the quality and quantity of the free fatty acids secreted by apocrine glands, as chief index to determine the real efficacy of a new model of antiperspirant-deodorant, that interferes directly with apocrine glands (by reducing drastically the secretion of free fatty acids) and indirectly with eccrine glands, by minimising the salted water secretion.

I created an innovative cosmetic formula that comprises the Alunogen, idest the heptadecahydrated form of aluminium sulphate, since the generic aluminium sulphate has been recently accused of the onset of the Alzheimer's disease, when penetrating the epidermis, although definitive scientific proof is difficult to establish due to the lack of longitudinal studies, and therefore could be banished in the very next future.

The formula comprises also the concrète of Cypripedium Pubescens (Lady's slipper) which contains, inter alia, the cypripedin, a quinine-analog, endowed by anticholinergic activities, that can be reputed useful as astringent agent with regards to eccrine glands, synergically to the action upon apocrine glands performed by alunogen.

I recruited 11 young men, 11 bricklayers that customarily have to work 9 hours pro day after the hot summer sun and assert without doubt to sweat copiously, in order to carry out my experience.

Key words: Alunogen; Cypripedium pubescens Aluminium; apocrine glands; valeric acid

INTRODUCTION

It is impossible to trace statistical data to clarify the phenomenon of human sweating: sex, race, age and psychological conditions represent a valuable variance in order to draw a precise profile.

It is well known that eccrine glands are deputed to secrete water and salts, principally sodium chloride and undergo the influence of adrenaline and similar molecules like scopolamine, elemycine, myristicine, the concrète of magnolia and all types of amphetamines and other natural or synthetic substances and therefore may by stimulated by anxiety, stress, fear, sexual appeal, and pain [1] and can be abstricted by the use of anticholinergics, meanwhile apocrine glands (large coil glands, retrievable only in certain districts of the body: axillae, nipples of the breast, ear canals, eyelids, wings of the nostril, perianal region and external genitalia [2] are responsible of the secretion of cholesterol (8.9 mg/cm2) and its salts (8.8 mg/cm2), waxes (21.2 mg/cm2), squalene (13.4 mg/cm2) and glycerides and free fatty acids and their esters (47.4 mg/cm2).

My attention is focused on the quality and quantity of free fatty acids secreted by apocrine glands, as chief index to determine the real efficacy of a new model of antiperspirant-deodorant, that interferes directly with apocrine glands (by reducing drastically the secretion of free fatty acids) and indirectly with eccrine glands, by minimising the salted water secretion.

Solovskaia, et al [3] referred that suggestive changes in the fatty acid composition of sweat lipid do occur in persons whose activity is associated with military service.

It must be stressed that when chemiosensiorial tests are carried out to investigate upon the pheromonal

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equipment of sweat in man or in woman, it is advisable that volunteers did not have sexual intercourses before undergoing the aforesaid tests, did not eat garlic or onion or cardamom or ginger or other spices, or drink alcohol or take drugs or smoke tobacco, since quantity and quality of free fatty acids may vary appreciably, during the activity of sweating.

Therefore, sweat represents a peculiar fingerprint of every person and so the main task of an antiperspirant is to reduce the percentage of the free fatty acids the same person secretes, without interfering with the quality that shall be always the same, provided that this person did not behave as I have already explained before.

Since time immemorial manifold salts of aluminium, zirconium, iron, zinc, chrome, hydragyrum and lead have been used as abstrictive agents with regards to human secretory glands, notwithstanding an avalanche of salts of rare metals can make up for the similar functions, like certain salts of Scandium, Yttrium, Lanthanum, Cerium, Praseodymium, Neodymium, Promethium, Samarium, Europium, Terbium, Holmium and Thulium [4].

Dermal-cosmetically speaking it is fully inconceivable the proposal of employ of these odd salts, but this stands for explaining that astringency of the apocrine glands can be evoked by a myriad of inorganic and organic substances.

The use of Pure Aluminium sulphate (that nowadays is obtained by the simple neutralization of sulphuric acid by aluminium hydroxide) has been recently indicted since traces of aluminium have been retrieved in the brain of Alzheimer's sufferers, which asserted they have been using antiperspirants based on rock alum for long time, albeit definitive scientific proof is difficult to establish due to the lack of longitudinal studies, as well as pushback from industries that use aluminium in their products [5-9].

Even if this is not the appropriate seat to speak about this concern, Aluminium is a neurotoxic metal and exposure to the metal, when dissolved in drinkable water or inhaled as dust, may be a factor in the aetiology of various neurodegenerative diseases such as Alzheimer's disease.

Objectively Aluminium is a risk in certain working environments, such as mines, where it can be found in water, people that work in factories where aluminium is applied during production processes may endure lung problems when they breathe in aluminium dust and can cause problems for kidney patients when it enters the body during kidney dialyses.

Occupational asthma has also been a problem in the pot rooms of aluminium smelters [10].

Anyway Nature provides other types of aluminium sulphates, e.g. alunogen, that is the heptadecahydrated form, that is paragenetic with gypsum, and may be found on the world market extremely easy.

Alunogen is completely natural, veins and lodes can be found in Cote du Rhone, Antofagasta (Chile), New Mexico, Pozzuoli and Isola d'Elba in Italy and is widely used and welcome in tanning of leather to prepare the hide, as a mordant for dyes, for clarifying turbid liquids, including post-storm treatment of lakes to precipitate contaminants, as a fire retardant in textile products as a hardener for photographic emulsions for films.

Moreover, Cypripedium pubescens (also known as Lady's slipper), the other ingredient I have inserted in my formulation, possesses a number of distinct therapeutic properties like soothing the nerves, such as headache, irritability, hallucination, hysteria, neuralgia, insomnia and even epilepsy, owing to its high percentage of valeric acid, that made it an excellent alternative for valerian, and is considered one of the most appreciated oneirogens by psychonauts [11,12].

It contains even cypripedin, a quinine-analog, endowed by anticholinergic activities, that can be reputed useful as astringent agent with regards to eccrine glands, synergically to the action upon apocrine glands performed by alunogen, even I did not insert this ingredient in the formula for this precise purpose, but for the presence of valeric acid, that could be supposed to show a feed-back action towards the valeric acid secreted by the apocrine glands, as it will be evident form the final results.

I have used for my study the concrète of Cypripedium Pubescens and the glycolic extract of the rootstock.

Among the manifold free fatty acids of sweat secreted by apocrine glands (which are manifold), I have selected, as principal indexes for my researches, the following ones:
Acid n-pentanoic
Acid n-hexanoic
Acid n-heptanoic

Acid iso-pentanoic
Acid n-octanoic
Acid 7-octenoic
Acid n-nonenoic
Acid n-decanoic
Acid n-undecanoic.

MATERIALS AND METHODS

We have selected 11 bricklayers that customarily have to work 9 hours pro day after the hot summer sun and assert without doubt to sweat copiously.

We prayed them to abide by some rules I dictated, in order not to alter results of investigations, and so they decided, in order to accomplish the target I promised to them, to cease to drink dark beer, eat garlic and spices for all the duration of the studies.

It is obvious that the individual that behaves routinarily (the same diet, the same habit of drinking and smoking or having sex intercourses) does not need to abide by this rule, since the quality of sweat must be reputed always the same, but not the quantity, whenever an antiperspirant is applied under his armpits and on his breast, during his habitual work effort.

They use to work from 8 a.m. till 5 p.m., so the first measurement of all the percentages of free acids secreted by their armpits has been carried out the day number 0.

At 5 p.m. of the day number 0, after their day's work, I prayed each volunteer to keep a 5X5 cm cotton pad soaked by isopropyl alcohol for 30 seconds underneath the right axilla, in order to record their habitual secretion of sweat free acids.

The pads were suddenly inserted in sealed phials and the phials numbered progressively, in order to have the following list:

Day 0 : A,B,C,D,E,F,G,H,I,L,M

At day number 1, at 7.30 a.m. all the volunteers were prayed to spray underneath their armpits my formulation and at 5 p.m., I repeated the same operation of day number 0 and inserted the relative pads in the appropriate phials, numbering those as follows:

Day 1: A,B,C,D,E,F,G,H,I,L,M

At day number 2, at 7.30 a.m. all the volunteers were prayed to spray underneath their armpits my formulation and at 5 p.m. of day number 2 and at 5 p.m. of day number 3, I repeated the same operation of day number 0 and inserted the relative pads in the appropriate phials, numbering those as follows:

Day 2: A.B.C.D.E.F.G.H.I.L.M
Day 3: A,B,C,D,E,F,G,H,I,L,M

At day number 4, at 7.30 a.m. all the volunteers were prayed to spray underneath their armpits my formulation and at 5 p.m. of day number 4 and at 5 p.m. of day number 5 and at the same hour of day number 6, I repeated the same operation of day number 0 and inserted the relative pads in the appropriate phials, numbering those as follows:

Day 4: A,B,C,D,E,F,G,H,I,L,M
Day 5: A,B,C,D,E,F,G,H,I,L,M
Day 6: A,B,C,D,E,F,G,H,I,L,M

Each afternoon I have the results scored by means of a Perkin Elmer 200 Series HPLC system and I plotted these, according to three series:
Series I: Protection 24 heurs
Series II : Protection 48 heurs
Series III : Protection 72 heurs (longue durée).

Here follows (Tab. I) where the initial scores for free acids secreted by the apocrine glands of the volunteers are recorded.

RESULTS AND DISCUSSIONS

The three following tables record the percentage of the real decreasing (measured by HPLC) of the single free fatty acids, secreted during sweating due to hard work under the summer sun, after 24, 48 and 72 hours (Tables 1-3).

It is suggestive to remark that generally the valeric acid (n-heptanoic) decreases very significantly both after 24 hours and 48 hours, even though no valuable result is to be highlighted, for this acid, as far as the scores recorded after 72 hours are concerned, where the percentages of collapse of free fatty acids secretion is extremely scarce.

This is not the adequate seat to express the hypothesis of an odd feed back effect onto the glands with regards to the secretion of the same valeric acid,

Table 1: Scores of the initial quantities of free fatty acids (mg/5 cm² of skin) (day number 0)

	n-pentanoic	n-hexanoic	n-heptanoic	n-octanoic	n-nonenoic	Iso-heptanoic	n-decanoic	n-undecanoic	7-octenoic
A	5.2	7.4	14.1	2.0	4.1	3.6	4.4	9.1	8.2
B	4.1	8.3	11.2	5.9	3.2	4.3	6.1	5.3	9.7
C	6.2	6.6	13.1	3.8	5.3	2.4	7.1	6.7	9.1
D	2.2	9.3	14.0	5.1	3.8	6.6	3.2	7.1	8.7
E	4.3	7.1	12.8	3.3	5.1	6.2	4.3	8.6	6.4
F	3.4	9.2	11.0	5.5	4.2	3.3	2.7	10.1	9.2
G	2.8	7.6	16.3	4.4	4.1	6.2	3.3	5.7	10.0
H	6.1	6.6	13.5	3.2	3.4	4.8	5.7	7.9	11.1
I	5.4	5.1	16.3	2.1	3.2	4.1	6.6	7.4	8.7
L	4.6	7.1	12.2	4.5	4.3	5.1	5.2	3.6	11.9
M	6.2	5.1	14.0	2.0	6.1	1.7	8.2	4.3	11.5

Table 2: Scores of the quantities of free fatty acid (mg/5cm² of skin) at day number 1

	n-pentanoic	n-hexanoic	n-heptanoic	n-octanoic	n-nonenoic	Iso-heptanoic	n-decanoic	n-undecanoic	7-octenoic
A	3.3	5.2	8.0	2.0	3.1	2.9	3.5	7.3	5.6
B	2.4	7.7	6.1	4.4	2.4	4.1	4.3	2.5	6.7
C	1.2	5.5	5.7	4.4	4.1	1.9	6.3	4.6	6.8
D	2.1	4.3	5.2	3.8	2.7	1.8	2.2	5.4	6.2
E	3.2	6.7	4.8	1.1	3.2	4.4	2.6	5.6	3.4
F	2.5	7.4	6.9	3.1	2.8	1.1	1.9	8.2	6.5
G	1.1	5.4	10.4	2.7	3.1	4.7	2.5	4.4	8.6
H	3.5	4.2	5.9	1.5	2.7	2.7	3.1	5.6	8.4
I	4.1	3.6	8.0	4.6	1.1	3.2	4.1	5.8	6.4
L	3.1	6.6	5.2	2.9	0.9	2.7	3.8	4.6	10.1
M	5.1	3.7	6.4	2.4	2.9	1.8	5.6	2.9	8.9

Table 3: Scores of the quantities of free fatty acid (mg/5cm² of skin) at day number 3

	n-pentanoic	n-hexanoic	n-heptanoic	n-octanoic	n-nonenoic	Iso-heptanoic	n-decanoic	n-undecanoic	7-octenoic
A	4.4	6.5	11.1	1.4	3.3	2.7	2.9	7.8	6.6
B	3.8	7.2	9.6	3.9	2.5	2.7	4.9	4.7	6.8
C	5.4	4.6	7.9	2.8	4.1	1.9	6.1	5.3	7.2
D	1.8	7.7	6.9	4.1	2.8	4.9	2.4	5.8	6.6
E	3.1	5.8	10.0	2.9	4.5	5.0	3.3	6.2	7.1
F	2.8	7.7	8.9	2.5	3.4	2.8	1.9	8.4	7.4
G	1.7	6.3	13.3	3.7	3.7	5.2	2.9	4.4	8.5
H	5.3	5.3	10.1	2.6	2.7	3.9	2.7	6.6	10.1
I	4.4	4.7	10.0	1.1	2.4	3.8	4.9	6.1	7.2
L	3.9	4.2	9.8	3.6	3.7	4.1	4.5	2.9	9.8
M	4.8	2.6	8.1	1.7	5.2	0.9	7.3	2.5	10.3

that is contained in the Lady's slipper, even if it is advisable.

The volunteer F is a young red haired man and it is indicative to notice that after 48 hours the collapse of the free acids secreted by the apocrine glands is extremely feeble.

Meanwhile the volunteer E is a blond and blue eyed young man, for, the fact that the collapse of the valeric acid is less evident, could be imputed to his own phenotype.

The following tables are explanatory and descriptive, so that a statistical method to determine final data (e.g.: the Cramer-von-Mises's method) can result supervacaneous (Tables 4-7).

CONCLUSIONS

It can be confirmed the drastic efficacy of the cosmetic mix Alunogen-Lady's slipper must be reputed eminent when employed in antiperspirant-deodorant items destined to the protection 24 heurs, and significative when used in cosmetic items intended to cover a protection of 48 hours.

It is quite insufficient for the "longue durée" protection.

Table 4: Scores of the quantities of free fatty acid (mg/5cm² of skin) at day number 6

	n-pentanoic	n-hexanoic	n-heptanoic	n-octanoic	n-nonenoic	Iso-heptanoic	n-decanoic	n-undecanoic	7-octenoic
A	4.9	6.8	13.1	2.0	3.9	3.3	3.6	8.8	7.9
B	3.9	7.7	10.8	4.8	2.9	3.8	5.7	4.8	8.8
C	5.9	5.8	12.1	2.7	4.7	1.9	6.6	5.8	8.2
D	1.9	8.7	12.6	4.8	3.0	6.1	2.7	6.5	7.7
E	3.8	6.8	11.0	4.8	4.7	5.9	3.7	7.1	6.0
F	2.9	6.6	10.7	4.8	4.2	2.8	1.6	9.1	8.0
G	2.0	6.8	14.9	3.1	3.2	5.3	2.9	4.8	8.9
H	5.5	5.9	12.6	2.4	2.9	3.7	2.6	4.1	9.1
I	4.9	4.7	15.4	2.0	2.2	3.7	5.1	6.3	7.5
L	3.9	6.6	11.4	3.3	3.6	4.9	4.7	2.8	10.0
M	5.5	4.7	13.1	1.7	5.8	1.1	7.2	3.8	10.1

Table 5: Percentages of the collapse of the fatty acids from apocrine glands sweat after 24 hours (day number ONE)

	n-pentanoic	n-hexanoic	n-heptanoic	n-octanoic	n-nonenoic	Iso-heptanoic	n-decanoic	n-undecanoic	7-octenoic
A	37	29.8	43.3	100	24.4	19.5	20.5	19.8	31.8
B	41.3	7.3	43.3	25.5	25	4.7	29.6	52.9	31
C	80.66	16.7	56.5	88.5	59	20.9	11.3	31.5	25.5
D	4.6	53.8	60.3	100	29	72.8	69.1	19.5	28.8
E	25.6	5.64	96.2	96.6	37.3	29.1	39.6	35	46.9
F	46.5	19.6	37.3	43.7	33.4	96.7	29.7	18.9	29.4
G	60.8	29	36.2	39	8.9	24.2	24.3	22.9	14
H	42.7	36.4	56.3	53.2	20.6	43.8	45.7	29.2	24.4
I	24.1	29.5	51	78.1	65.7	22	37.9	21.3	26.5
L	32.7	49.3	57.3	35.6	79.1	47.1	27	87.9	15.2
M	17.8	27.3	47.55	88	52.5	89.5	31.8	32.6	26.7

Table 6: Percentages of the collapse of the fatty acids from apocrine glands sweat after 24 hours (day number THREE)

	n-pentanoic	n-hexanoic	n-heptanoic	n-octanoic	n-nonenoic	Iso-heptanoic	n-decanoic	n-undecanoic	7-octenoic
A	15.4	12.2	21.28	30	9.96	25	34.1	14.3	19.6
B	7.32	13.3	14.29	33.9	21.9	37.3	19.7	11.5	29.9
C	13	30.4	39.7	26.4	22.7	20.9	14.11	20.9	20.5
D	18.2	17.3	47.4	19.7	26.4	25.8	25	12.8	24.2
E	28	18.4	21.9	12.2	11.8	19.4	23.3	28	89
F	17.7	16.4	19.1	43.2	17.1	15.2	29.7	16.9	19.6
G	39.3	17.2	18.5	16	9.8	16.2	12.2	22.9	15
H	13.2	19.7	25.2	19	20.6	18.8	52.7	16.5	91
I	18.6	7.9	38.7	47.7	25	7.4	25.8	17.6	17.3
L	15.3	40.9	19.7	20	14	19.7	13.5	19.5	17.7
M	22.9	49.1	42.2	15	14.8	47.1	11	41.9	10.5

Table 7: Percentages of the collapse of the fatty acids from apocrine glands sweat after 24 hours (day number SIX)

	n-pentanoic	n-hexanoic	n-heptanoic	n-octanoic	n-nonenoic	Iso-heptanoic	n-decanoic	n-undecanoic	7-octenoic
A	5.8	8.2	7.2	nihil	4.9	8.4	18.2	3.3	3.7
B	4.9	7.3	3.6	18.5	9.4	11.7	6.6	9.5	9.3
C	4.9	12.2	7.7	29	11.4	20.9	7.5	13.5	9.9
D	13.7	6.5	10	5.9	7.9	4.9	14	17.5	6.3
E	11.7	4.3	14.1	5.9	7.9	4.9	14	17.5	6.3
F	14.8	28.7	3.7	12.8	nihil	15.2	40.8	9.1	6.3
G	28.4	10.6	8.6	29.6	22	14.6	12.2	39.3	11
H	9.9	10.7	6.7	25	9.4	23	54.4	48.2	18.1
I	9.3	7.9	5.6	4.8	31.3	9.8	22.8	14.9	13.8
L	15.3	7.1	6.6	26.7	16.3	4	9.7	22.3	16
M	11.3	7.9	6.5	15	5	35.3	13	11.7	12.2

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patient for publication of this article.

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Case Report

Videodermatoscopy of pearly penile papules. Case reports

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ABSTRACT

Pearly penile papules are harmless dermatological condition characterized by small dome-shaped to filiform skin-colored papules located in one to several rows along the sulcus or corona of the glans penis. We describe six male patients with pearly penile papules whose diagnosis was assisted by means of videodermatoscopy. All lesions showed a characteristic whitish pink cobblestone appearance arranged in one or several rows. Each papule contained central dotted or comma-like vessels and was surrounded by crescent-shaped whitish structures. Videodermatoscopy may assist the diagnosis of pearly penile papules and successfully differentiate them from genital warts and molluscum contagiosum.

Key words: Videodermatoscopy; pearly penile papules; genital warts; molluscum contagiosum

INTRODUCTION

Pearly penile papules (PPP) are harmless dermatological condition that may cause considerable discomfort and anxiety to male subjects [1,2]. They represent as small dome-shaped to filiform skin-colored papules located in one to several rows along the sulcus or corona of the glans penis [2-6]. The condition has been firstly described by Littre and Morgagni in 1700 however the term "pearly penile papules" has been introduced by Johnson and Baxter in 1964 [7]. PPP are considered a normal variant that is observed more frequently in uncircumcised males. Their incidence ranges from 8 to 48 %. PPP are noted most commonly in the second or third decades of life and they gradually may become less noticeable with increased age as well as after circumcision [2,8]. Diagnosis is made clinically and may be confirmed by performing histopathological examination. The observed thin-walled ectatic vessels in the dermis in association with a fibroblastic proliferation indicate angiofibroma. PPP are asymptomatic and require no therapy. At the request of patient they can be removed with cryotherapy, surgical excision, electrosurgery and laser therapy (carbon dioxide laser, pulsed dye laser, and Er: YAG laser). Topical application of podophyllin has been ineffective for PPP [2,9,10].

Most patients with PPP seek dermatological consultation because they are in doubt of a sexually transmitted disease. PPP are not associated with sexual activity but they quite often may be combined with infectious diseases such us genital warts and molluscum contagiosum. In that case the correct diagnosis is very important. It could be assisted by means of non-invasive dermatoscopy.

In the following report six cases of PPP whose diagnosis was assisted by means of videodermatoscopy are described.

CASE REPORT

Six uncircumcised men aged 16-50 years self-referred him to our dermatology clinic because they were in doubt of a sexually transmitted disease. All patients were clinically diagnosed with PPP based on the observation of various numbers of small pearly dome-shaped papules about 1 mm in width and length, which were arranged in 1-3 rows along the corona of the glans penis (Fig. 1). The papules were asymptomatic and had been present for several years. They were combined with genital warts in 2 patients (Figs 1C and E), and balanitis in 3 patients.

In the first two cases (Figs 1A and B) the irritation was related to physical trauma, whereas in the third case

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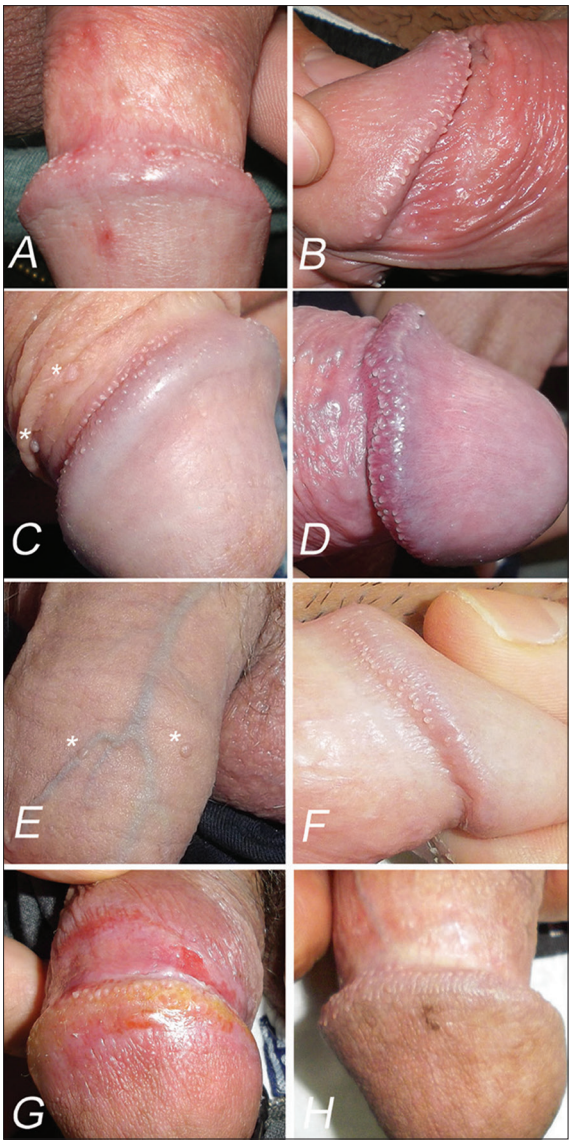

Figure 1: Clinical findings in male subjects: A-D, F, G. Small whitish papules oriented in a few rows on the corona of the penis of all patients; A, B, G. Redness and erosions of the preputium and glans in patients 1, 2 and 6; H. Patient 6 (G) after treatment; C, E. Genital warts in patients 3 and 4

(Fig. 1G) painful redness and erosions of the foreskin and glans were developed after self-application of topical podophylotoxin 0.5% solution.

Videodermatoscopy examination was performed using digital videomicroscope (DinoLite, AnMo, Taiwan) with magnification of x60 and x160, without and with oil immersion, and polarized light. PPP showed a characteristic whitish pink cobblestone appearance arranged in one or several rows.

Each papule contained central dotted or comma-like vessels and was surrounded by crescent-shaped

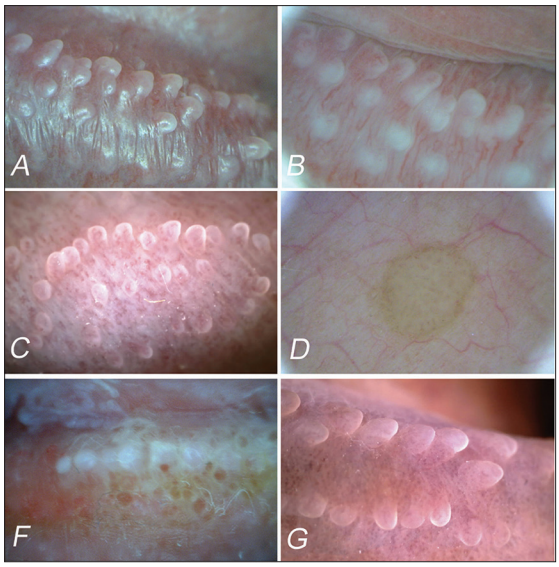

Figure 2: Dermatoscopic findings in male subjects: A-C, F, G. Small whitish pink cobblestone-like papules in a few rows with central dotted or comma-like vessels in each papule and surrounding whitish crescent-shape rim. D. Genital wart showing "mosaic-like" pattern consisting of a white reticular network surrounding dilated vessels. Magnification x60.

whitish structures (Figs 2A, B, C, F, and G). Balanitis was characterized by erythema and erosions (Fig. 2F). The dermoscopic findings of genital warts consisted of mosaic-like pattern with a white reticular network surrounding central dotted vessels (Fig. 2D).

All patients were informed about the benign character of PPP and specific treatment was not applied. Balanitis was treated with appropriate topical medications, and genital warts were destroyed with cryosurgery.

DISCUSSION

Videodermatoscopy (VD) is a modern non-invasive technique that allows in vivo visualization of the superficial skin structures with magnification ranging from x20 to x1000. It greatly improves the diagnostic accuracy not only for pigmented skin lesions, but also for many non-pigmented skin disorders.

Recently, the usefulness of VD for diagnosis, differential diagnosis and monitoring of ectoparasitic, infectious and inflammatory skin diseases has been documented [11].

A few reports about dermatoscopic findings of PPP exist until now [7,12-14]. Dermoscopically PPP are characterized by whitish pink cobblestone or grape-like papules arranged in a few rows and surrounded by crescent-shaped whitish structures. Each papilla

stands alone and shows central dotted, comma or hairpin-like vessels. The characteristic dermatoscopic findings may eliminate the necessity of biopsy and may help to differentiate PPP from other genital lesions such us genital warts and moluscum contagiosum [12-14].

Genital warts are papillomatous lesions in which multiple whitish projections with tapering ends arise from a common base (Fig. 3A). Dermatoscopic findings are described as "mosaic-like" pattern consisting of a white reticular network surrounding dilated vessels visible at higher magnification (Fig. 3B) [12-14].

Molluscum contagiosum is clinically characterized by dome-shaped, skin-colored, single or multiple papules with central depression (Fig. 3C). In small or early lesions native VD improves the visualization of central depression. Moreover, using oil immersion or polarized light multiple spherical, yellowish-white, amorphous structures with surrounding linear or branched vessels are observed (Fig. 3D) [13,15].

CONCLUSION

In this report we showed the characteristic dermatoscopic features that may assist the diagnosis of PPP and differentiate them from genital warts and molluscum contagiosum.

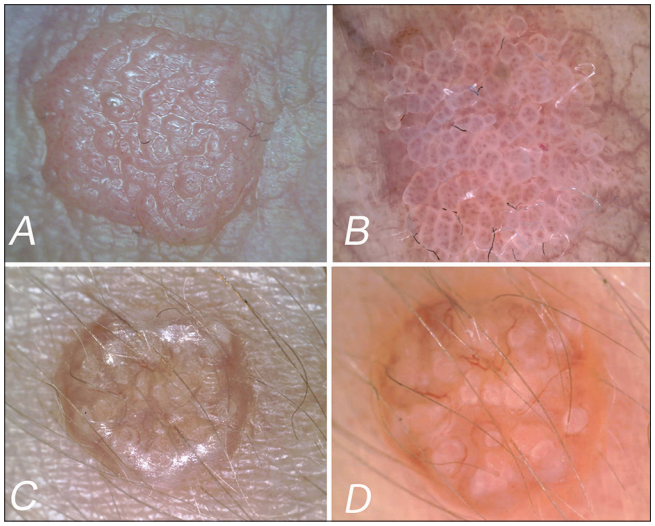

Figure 3: Clinical features of genital wart (A) and molluscum contagiosum (C); Dermatosopic features of genital wart (B) and molluscum contagiosum (D). Magnification x60.

Recognition of these specific features would enhance the accuracy and timeliness of diagnosis, help the choice of most appropriate therapeutic approach, and reduce anxiety. We recommend use of VD for diagnosis of penile lesions in the daily dermatological practice.

CONSENT

The examination of the patients was conducted according to the Declaration of Helsinki principles.

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Case Report

Acquired epidermodysplasia verruciformis in an HIV positive child. Report of a case

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ABSTRACT

Epidermodysplasia verruciformis (EV) is a rare genodermatosis whose main feature is a genetic predisposition to persistent skin infection by different serotypes of human papillomavirus (HPV). In recent years, an EV-like syndrome has been described in patients with impaired cell-mediated immunity, including patients with HIV.

We report the case of a teenage female patient with congenital infection with the human immunodeficiency virus (HIV), which has similar lesions to classical EV.

Keywords: Epidermodysplasia verruciformis; human papilloma virus; human immunodeficiency virus

INTRODUCTION

Epidermodysplasia verruciformis (EV) is a rare autosomal recessive genetic disorder, characterized by persistent skin infection by the human papillomavirus (HPV), because there is a greater genetic susceptibility to infection with certain oncogenic HPV subtypes [1,2]. The clinical appearance in patients with inherited and acquired immunodeficiencies is similar to those of classical EV symptoms.

It is proposed to call these acquired EV [1].

CASE REPORT

A 10-year-old female diagnosed at age 7 with human immunodeficiency virus (HIV), CD4 count = 765 cells/mm 3 and viral load (VL) of 58,842 copies at the time of diagnosis; initiation of antiretroviral therapy, aged 9, with CD4 count = 545 cells/mm 3 and CV = 132,589 copies.

Presented to the consult with white spots on neck progressively increasing in number and extending to arms, some of them tend to rise. Mycological study is negative. At that time a clinical diagnosis of flat warts is made, and receives several treatments including topical 20% urea and 35% trichloroacetic acid (TCA); imiquimod 7.5% 3 times/week; 0.025% retinoic acid 1 time/day; there was no improvement in the lesions.

At 13 years old returns to the consultation with the same lesions described above, to which are added warts on knees and toes. The patient reported no family history of consanguinity. On physical examination she presented numerous hypopigmented papules and plaques, with irregular and well defined borders, between 0,5-2 cm in diameter on forehead, neck, V-shaped neck line, back and upper limbs (Fig. 1). On knees and toes presented skin colored flat papules that were treated with electrocoagulation (Fig. 2).

Given several persistent treatments, it was decided to perform a skin biopsy.

Histopathology reports: epidermis with acanthosis with bulbous elongation of rete ridges, hyperkeratosis over acanthosis, absence of papillomatosis. Vacuolization of epidermal keratinocytes of superior layers. They show gray cytoplasm, enlarged nuclei, nuclear irregularity.

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These findings of enlarged cells in granular layer of grayish granular cytoplasm, enlarged and irregular nuclei, are indirect signs of HPV-EV infection in the skin (flat wart in the context of an EV) (Fig. 3).

With these data, the diagnosis of acquired epidermodysplasia verruciformis in a patient with vertical HIV transmission is made.

Prior to the study, patient agreed to the examination and biopsy and a legal representant signed the written consent after been informed about the procedure.

DISCUSSION

Epidermodysplasia verruciformis is a disease in which there is an increased genetic susceptibility to infection by certain subtypes of human papillomavirus (HPV-EV) viruses, such as subtypes 5 and 8 [2,3].

This disease can occur in all races, there is no sex predilection and is most common during childhood and puberty; age of onset is usually between 5 and 8 years old [4].

Initially the lesions are localized being only hypochromic scaly patches on the face and neck, similar to tinea versicolor. Over time they increase in number and tend to evolve to papules resembling flat warts from pink to brownish, sized a few millimeters, with a smooth surface. Subsequently they extend to the dorsum of the hands, forearms, knees, legs and feet. Mucous membranes are not affected [4,5].

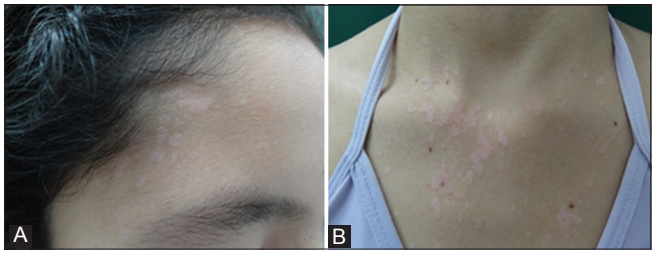

Figure 1: Dermatological features: hypopigmented papules and plaques with irregular and well defined margins, between 0.5 and 2 cm in diameter, distributed in forehead (A) and V neckline and chest (B)

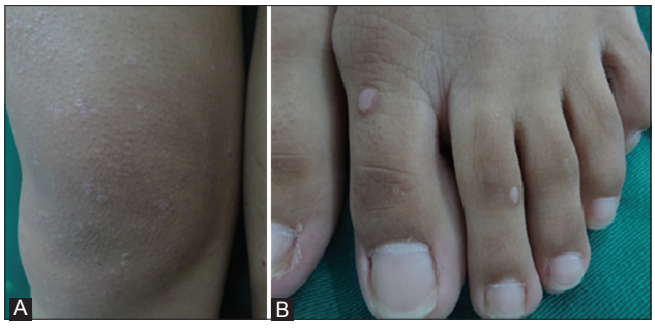

Figure 2: Dermatological clinic: skin-colored flat papules on knees (A) and dorsum of toes (B)

In highest sun exposed areas such as the face, especially the forehead, V neckline and back of hands erythematous plaques arise, become keratotic and prone to erosion and in the third decade of life can evolve into Bowen's disease or squamous epithelioma [4].

The EV has a pathognomonic histological and ultrastructural features. Hypergranulosis, acanthosis and hyperkeratosis, and large clear cell nests extending from one level to the granulosa suprabasal layer, mainly at the level of the rete ridges. Cells have large, clear and lumpy cytoplasm, thick cytoplasmic membrane without intercellular bridges and a core with a central vacuole. These cells are the result of viral cytopathic effects and were described by Rueda, in 1967, who called them epidermodisplastic cells [6].

In the last decade there have been some cases of acquired EV associated with immunosuppression states such as renal transplantation, graft versus host disease, systemic lupus erythematosus and HIV infection [1,7].

In the HIV carrier population, men and women are affected in the same proportion. It has been observed that it is more frequent in younger patients with

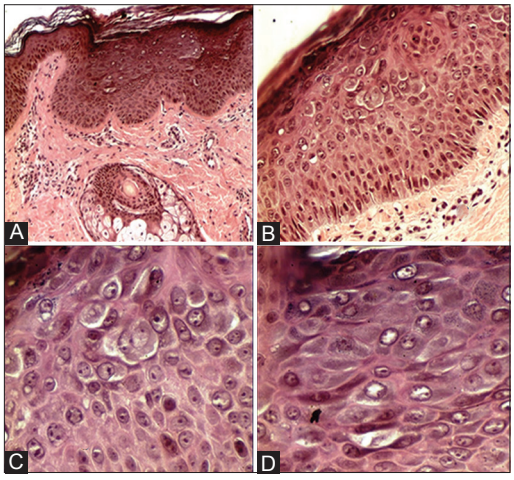

Figure 3: Histopathology. a. Epidermis with acanthosis, bulbous elongation of rete ridges, hyperkeratosis over the acanthosis, absence of papillomatosis (HE 4X). b. Vacuolization of epidermal keratinocytes (HE 20X). c, d. The keratinocytes show gray cytoplasm, enlarged nuclei, nuclear irregularity (HE 40X). These findings are indirect signs of HPV-EV infection in the skin (flat wart in the context of an EV)

congenital HIV infection because they were probably infected with HPV before developing a good state of cellular immunity [7].

Classical EV results from a deficiency in cell-mediated immunity and genetic susceptibility to HPV-EV. This results in a natural inhibition of cytotoxic mechanisms against infection by HPV keratinocytes, leading to the development of skin lesions.

It is likely that patients infected with HIV have an acquired deficiency of the secondary cell mediated immunity to chronic infection and untreated HIV.

Patients with vertical HIV transmission probably have their first HPV infection in early childhood when their cell mediated immune system has already been infected with HIV, while adults who have been infected with HIV have strengthened immune mechanisms against HPV infection, which develops in childhood while their immune system is still intact. This could explain why EV is not as common in HIV-infected adults as it is in HIV MTCT adults [3,8].

According to the literature, the progression of skin lesions appears to be influenced by the immune status of the patient, by the viral phenotype and sun exposure, and its evolution to malignancy, particularly squamous cell carcinoma, is described in up to 30-60% of patients. [3,7]. On EV lesions carcinomas may appear, mainly epidermoid, Bowen's disease (squamous cell carcinoma in situ), basal and some premalignant lesions such as actinic keratoses [9].

Currently there is no specific or effective treatment for EV, the management of patients includes preventive measures such as genetic counseling, photoprotection and monitoring of symptoms for proper identification of premalignant and malignant lesions. Sunscreens are recommended to avoid direct exposure to UV radiation, since constant exposure tends to increase the risk of malignancy. Topical and systemic retinoids, in combination with with vitamin D analogs (calcipotriol) and alpha interferon are used. 5-fluorouracil has also been used for the treatment of precancerous lesions. Other treatments options include photodynamic therapy, immunotherapy and surgical treatment of premalignant and malignant lesions [10].

CONCLUSIONS

1. The absence of affected family members or history of consanguinity in the case presented, and the fact that it appears in the context of a state of immunodeficiency leads to the diagnosis of Acquired Epidermodysplasia Verruciformis.
2. It is important to establish a proper diagnosis in patients with lesions resembling flat warts and that are refractory to treatment.
3. The gold standard for diagnosis is histopahology, although in this case no HPV serotypes have been identified, there were indirect histological signs of HPV-EV serotypes infection that all dermatopathologists should know.
4. This patients should undergone lifetime monitoring due the high risk of developing premalignant and malignant lesions.

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. A legal representant signed the written consent for the publication of this article and any accompanying images.

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Case Report

Dermatophytic blepharitis due to *Microsporum gypseum*. An adult variety of *Tinea faciei* with dermatophytoma

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ABSTRACT

Tinea faciei, is a facial superficial mycosis. The most frequent etiological agents are *Microsporum canis*, *Trichophyton rubrum* and *T. tonsurans*. We report a 40 year-old woman, with an eight days history of an erythematous plaque on her superior right eyelid. Hyphae and dermatophytoma were easily visualized in KOH examination, and *Microsporum gypseum* was isolated.

Key words: *Tinea*; *Microsporum gypseum*; dermatophytoma; blepharitis

INTRODUCTION

Tinea (ringworm) is a superficial dermatophytosis, first described by the Greeks and Romans. The etiology are well known fungal agents of the genus *Trichophyton*, *Microsporum* and *Epidermophyton* [1].

Tinea faciei occurs primarily in pediatric patients and also in the second and fourth decades of life, usually with animal contact, predominantly in tropical regions and it is considered a variety of *tinea corporis*.

Microsporum gypseum is the most important geophilic dermatophyte with fast growth of light brown, powdery colonies and under the microscope, with fusiform blunt tips macroconidia, with less than six septa and thick walls [1].

Long septate or arthrosporated filaments can be observed with potassium hydroxide and dimethyl sulfoxide (KOH - DMSO) or chlorazol black. It is sometimes possible to show masses of hyaline filaments with presence or absence of spores, known as dermatophytomas. This phenomenon may hinder the effects of antifungal treatments; and it also has been reported, especially in onychomycosis [1].

CASE REPORT

A 40 year old female from southwest Guatemala, denying previous animal contact, presented with an 8 days history, of an ill-defined 3.5 × 2.5 cm erythematous scaly plaque with irregular borders on her right superior eyelid, and intense pruritus. She received irregular treatment with oral terbinafine for one week without improvement (Fig. 1).

KOH-DMSO showed hyaline hyphae and clusters of filaments (dermatophytoma). Culture in Sabouraud agar with cycloheximide and chloramphenicol (quadruplicate), after 3 weeks revealed a flattened colony, with beige and powdery surface, suggestive of

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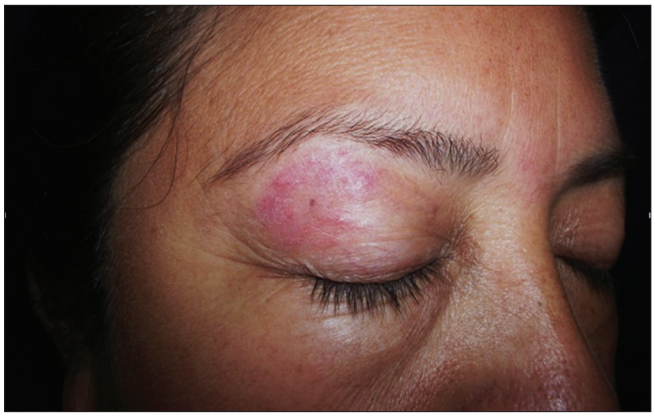

Figure 1: Clinical presentation (erythematous plaque of superior right eyelid)

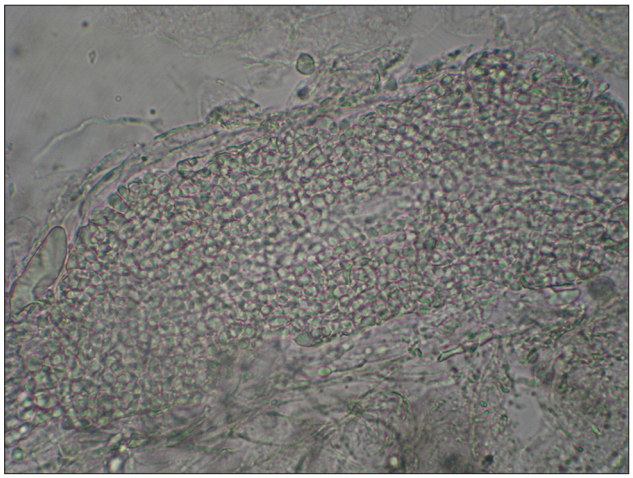

Figure 2: Dermatophytoma (KOH _ DMSO examination)

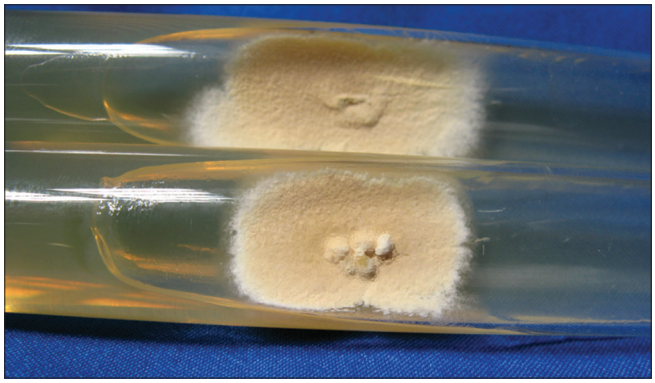

Figure 3: Powdery flattened surface colony, suggestive of *M. gypseum*

Microsporum gypseum (Figs 2 and 3). It was confirmed by direct microscopic examination with lactophenol cotton blue, showing fusiform blunt-topped macroconidia, each one with six septa and scant hyaline mycelium (Fig. 4).

The patient was treated with topical terbinafine, with complete resolution within two weeks.

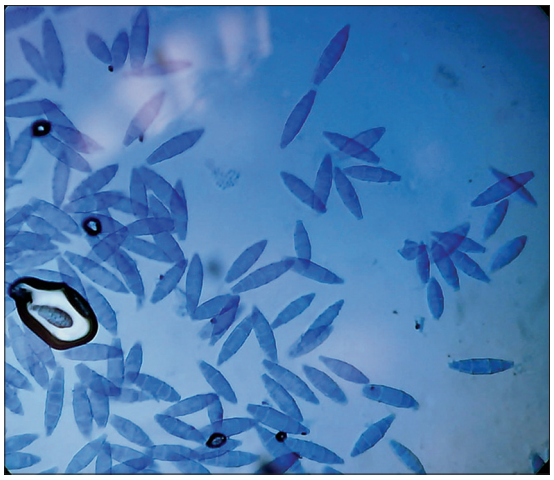

Figure 4: Fusiform blunt – topped microconidia (lactophenol cotton blue)

DISCUSSION

Tinea faciei may represent up to 20% of *tinea corporis* (which predominates on the trunk and limbs) [2], and is characterized by pruritic erythematous scaly lesions with annular centrifugal growth, but sometimes it may vary in its morphology [2].

Dermatophytomas are defined as a conglomerate of hyphae with or without spores; first described by Roberts and Evans [3], as a subungual microscopic phenomenon.

Martinez et al. in previous studies, indicated that this phenomenon predisposes to a poor response to treatment with oral antifungal agents, so it requires a combination therapy (oral-topical), to obtain clinical remission [4].

It is important to emphasize the absence of onychomycosis or any other fungal skin infections that could predispose to *tinea faciei*, as it has been reported in some of these cases, with a direct relationship with any superficial mycosis [5,6].

In some studies, like the one conducted by Romano et al., it is mentioned that the mean average age of *tinea faciei* is 27 [7], while Aste et al. reported that is more common from 36 to 45 years of age, as well as in pediatric patients, which is consistent with our report [2,8].

Probably in our case, the irregular previous treatment with oral terbinafine could be related to the development of dermatophytoma, as a defense mechanism against the antifungal agent [4].

The main causative agents of *Tinea faciei* are *Trichophyton rubrum*, *M. canis* and *T. tonsurans*, which may vary according to geographical region [2], so, in our case, the development of *Microsporum gypseum* is rare among the most frequent species.

According to a previous epidemiological study conducted in Guatemala by Martínez et al., the most common etiologic agent was *M. gypseum* in *Tinea faciei*, in 9 of 15 cases (60%) [4]. However, the results of this case series, reveal the dermatophyte condition in other areas such as the nose, chin and malar region [4], so our case, could be regarded as an exceptional case of fungal blepharitis by *M. gypseum* in Guatemala, which is an agent easily isolated from soil [9] and infection occurs from direct contact with infected animals [10].

Microsporum gypseum is an agent infrequently isolated. It has been identified in an epidemiological study by Bhagra in Brazil, in 71 cases over 30 years and in some microepidemics reported in Ivory Coast, England, Colombia and Brazil. Lavalle et al. identified this agent in Mexico in 41 cases from 11,148 dermatophyte isolates over a period of 45 years [9,10]. Infrequent manifestations in immunocompromised HIV-infected patients have been described such as subungual hyperkeratosis, *facial tinea incognito* and cerebral mycosis.

Because of its location and morphology (a single lesion) this could be considered within the clinical range described as "mini-*tinea*", caused precisely by *Microsporum gypseum*, and informed by Lavalle et al. in 2002, where the most frequent location were the face and folds (27%), possibly because in these areas the accumulation of dust is more feasible; it also occurred on the scalp (22%), trunk (12.5%) and hands (10%) [9].

According to Lin et al., the most widely used treatments include the group of azoles and topical allylamines, according to the extent of the disease, which may require the use of oral treatment in disseminated forms [2].

In *tinea* associated with dermatophytoma, the best results have been observed with combination of oral and topical antifungal treatments; the most widely used are oral terbinafine and topical 2% ketoconazole [4].

In our case, treatment with topical terbinafine for two weeks, achieve remission of the disease, and the previous poor antifungal oral treatment probably led to the formation of dermatophytoma.

CONCLUSION

Tinea faciei may represent up to 20% of cases of *tinea corporis*, especially in tropical regions, and is characterized by lesions with variable morphology, so it is necessary to confirm the diagnosis by KOH-DMSO, which could highlight the presence of dermatophytoma, since biofilms or this structure, predispose to a poor response with oral antifungal agents.

In previous studies in Guatemala, *Microsporum gypseum* has been identified as the causative agent of *tinea faciei*, however this is the first case of dermatophytic blepharitis with dermatophytoma due to this agent.

CONSENT

The examination of patient is conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patient for publication of this article.

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Case Report

Exfoliative Cheilitis a male patient – a case report

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ABSTRACT

Introduction: Exfoliative cheilitis, one of a spectrum of diseases that affect the vermilion border of the lips, is uncommon and has no known cause. It is a chronic superficial inflammatory disorder of the vermilion borders of the lips characterized by persistent scaling; it can be a difficult condition to manage. The diagnosis is now restricted to those few patients whose lesions cannot be attributed to other causes, such as contact sensitization or light. **Case Report**: We present a 17 year-old male presented to the out clinic in Baghdad with the chief complaint of a persistent scaly on his lower lips. The patient reported that the skin over the lip thickened gradually over a 3 days period and subsequently became loose, causing discomfort. Once he peeled away the loosened layer, a new layer began to form again. **Conclusion:** The lack of specific treatment makes exfoliative cheilitis a chronic disease that radically affects a person's life. The aim of this paper is to describe a case of recurrent exfoliative cheilitis successfully treated with intralesional corticosteroids and to present possible hypotheses as to the cause.

Key words: Exfoliative cheilitis; testosterone; sustanon; corticosteroid

INTRODUCTION

The definition of the vermilion as the transition area between the skin and the mucous membrane (*semimucosa*) was introduced for the first time by Jean Darier, a French dermatologist, in the 19th century [1].

The term cheilitis is understood as referring to an inflammatory process that affects the lips, either the cutaneous section or the contiguous semi-mucosal area called the vermilion (the lips in the common use of the term), and the mucosal section of the internal lip [2]. Cheilitis is classified into various types: angular cheilitis, actinic cheilitis, contact cheilitis, plasma cell cheilitis, cheilitis glandularis, cheilitis granulomatosa, exfoliative cheilitis and factitious chelitis. Lip lesions can be manifestations of systemic diseases, a localized expression of dermatologic diseases or a localized condition of the lips. In most cases, a good history, thorough clinical examination and relevant investigations will help the clinician arrive at a diagnosis [3].

Exfoliative Cheilitis (EC) is defined as a chronic inflammatory disorder of the vermillion border of the lips, which is characterized by the persistent formation of scales and crusts [4].

It is characterized by unremitting production and desquamation of thick scales of keratin. Crusts may be attributed to self induced trauma such as repetitive biting, picking or licking of the lips. Underlying stress or psychiatric conditions may cause or exacerbate exfoliative cheilitis which regress with psychotherapy and anxiolytic-antidepressant treatment. This condition is disabling as it causes cosmetic disfigurement and also affects daily activities such as chewing and speaking. The lack of specific treatment makes exfoliative cheilitis a chronic disease [5].

The recurrent exfoliation leaves a temporarily erythematous and tender surface. The lips are chronically inflamed and covered with crusts that from time to time tend to desquamate, leaving a glazed surface on which new crusts form. Fissures may be present, and there may

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be burning, tenderness, and some pain. The lower lip is more often involved, with the inflammation limited to the vermilion part [6].

Most cases occur in girls or young women, and the majorities have personality disorders [7].

Etiology and pathogenesis are unknown, although some cases may be factitious. Chronic lip biting, picking, sucking or unconscious licking of the lips may be the underlying mechanism for trauma and scaling [8].

CASE REPORT

A healthy 17-year-old man, unmarried, high school student of Arab descent complained of one year and six months history of chronic dry scaling lesion of the lower lip. The main chief was aesthetic compromising. The patient reported that the skin over the lip thickened gradually over a 3 days period and subsequently became loose, causing discomfort. Desquamation was followed immediately by the formation of new scales which became thick within days. Once he peeled away the loosened layer, a new layer began to form again.

Past medical history disclosed painful, right hemiscrotum in November 2012, and was referred to an endocrinologist after presenting to his general practitioner with diagnosis of male hypogonadism. He had no history of hypothalamic, pituitary, or testicular disorders. Physical examination was unremarkable. Biochemical investigations confirmed the presence of hypogonadism with slightly depressed testosterone levels, for which no cause (including Klinefelter syndrome) was identified.

He was then put by endocrinologist on injectable sustanon-250 mg, one injection every three weeks, in total two injections. In December he was also put on injectable sustanon-250 mg one injection every four weeks, in total four injections. Three months later, the patient returned to his general practitioner, complaining of cheilitis of the lower lip and exacerbation of preexisting acne vulgaris and he was referred to dermatologist.

Initially, there had been a tingling sensation but pain, ulceration, fissuring and bleeding were denied. He denied excessive licking or biting of the lips, and he denied skin, conjunctival and genital lesions and the patient could not identify a specific initiating cause. There was no history of any mucocutaneous problem. The family history for atopic diseases in the patient and his family was negative.

He had no symptoms of gastrointestinal disturbances or other relevant medical conditions. No member of his family had a similar condition and no use of new creams, toothpaste or cosmetic items around the lips before the problem began.

The results of a general examination revealed young man who weighed 70 kg. He had no fever and looked generally well. Examination of his head and neck revealed no palpable cervical lymph nodes. Intraoral examination showed good oral hygiene.

The patient had consulted several dental practitioners and dermatologists; Ketoconazole cream was prescribed for treatment of the fungal contaminant, but no change was noted, as was the application of Fucidin cream topically. The patient was prescribed mild topical corticosteroid this improved his condition somewhat, but did not resolve it completely. Our patient's condition was also resistant to topical tacrolimus.

DERMATOLOGICAL CONDITION

Examination revealed small, thick, white-coloured scales of the vermilion zone at two sites one in the left and the other on the right of the middle site of the lower lip. The adjacent skin and labial mucosa were not affected. Lesions characteristic of acne vulgaris were visible on the skin of the chin, cheeks, forehead with papules, and comedones (Fig. 1).

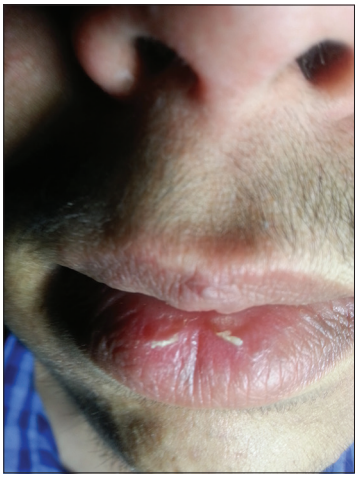

Figure 1: Scaling and crusting of lips including vermilion border

INVESTIGATION AND DIAGNOSIS

The results of a battery of tests, including complete blood work, general urine examination, liver function tests, a Mantoux test and chest radiograph showed no abnormalities. Vermilion swabbing for bacteriological examination was negative. Fungal culture for fungal examination was also negative. No antibodies against herpes simplex virus (anti-HSV1, HSV2 in the classes IgM and IgG) were found in blood serum. The concentration of vitamin B12, zinc was normal. FSH, LH, testosterone in blood serum was normal at the present time. Ultrasound examination of the abdominal cavity and scrotal ultrasound showed no deviations from the normal. Inflammatory bowel conditions were also ruled out after consultation with a gastroenterologist. Patient refused biopsy.

The overall findings suggested a diagnosis of exfoliative cheilitis. A diagnosis of exfoliative cheilitis was made based on the history and the clinical findings.

TREATMENT

Intralesional corticosteroid was successful treatment and he has not had a relapse in three months. No adverse effects from intralesional corticosteroids were noted in this patient (Fig. 2).

DISCUSSION

Clinicians knowledge of the clinical course of this disease is important for accurate diagnosis. This report records in detail the clinical progress of the disease over a period of 3 days.

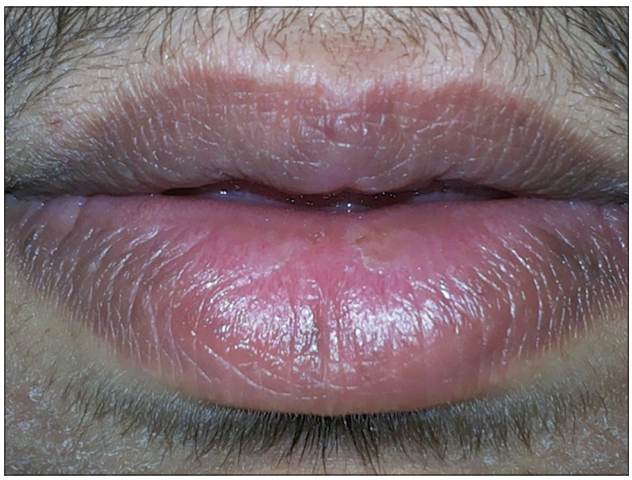

Figure 2: Marked improvement following intralesional corticosteroids.

Daley and Gupta [9] and Brooke [10] reported a similar cyclical pattern of disease activity. Brooke mentioned a 5-day period for completion of the whole cycle. Our patient claimed that the hyperkeratotic plaque developed and became loose over a period of 3 days.

Our patient had no factitious activity. In fact, he took particular care to avoid pain and bleeding when moving his lips. However, the possibility of Munchausen's syndrome cannot be ruled out in those cases in which the patient does not give any indication of factitious activity when questioned or observed [11].

Raede and others [12] discussed the possibility of cheilocandidosis. The authors achieved successful resolution of such lesions with antifungal therapy. However, for people who have no specific predisposing factors, such as our patient *Candida* could not be isolated from the lesion nor did the condition respond to antifungal therapy.

Oral sepsis has also been implicated as a cause of exfoliative cheilitis because it has resolved after implementation of good oral hygiene [13]. Our patient had very good oral hygiene.

Management of exfoliative cheilitis is difficult but it has responded to treatment with reassurance, topical steroids, psychotherapy and tranquillizers. Some cases can resolve spontaneously [14]. The few reported cases in literature describe therapeutics limitations of topic and systemic steroids, antibiotics, keratolytic agents, sunscreen and cryotherapy. Antifungal agents can be administered to patients in whom there is secondary fungal infection but it does not prevent the formation of keratin scales [15]. Medication with anti-depressants was helpful in the case of a 16-year-old male with persistent crusting of the lips with the diagnosis of exfoliative cheilitis [16]. Our patient's condition was resistant to emollients, life-style changes, and different topical treatment as mentioned before; only intralesional corticosteroid has successfully cleared the lesions.

Although androgens have no direct anabolic effect on the epidermis, they may modulate keratinocyte maturation. Several authors reported increased speed of epidermis proliferation after testosterone treatments [17].

Transdermal testosterone-replacement therapy is associated with a variety of skin reactions, mainly erythema or pruritus, which are more common with

patches than with gel preparations. Intramuscular injections of testosterone can cause local pain, soreness, bruising, erythema, swelling, nodules, or furuncles. [18]. Acne, oily skin, increased body hair, and flushing have also been observed [19].

It was also reported a case of hyperpigmentation and acanthosis nigricans in the same patient due to testosterone injections [20].

In our patient, the probable cause of the disease was due to testosterone injection. In our patient, significant improvement in scaling was seen with intralesional corticosteroids therapy without any recurrence till date.

CONCLUSION

Exfoliative cheilitis is a benign but often cosmetically unsightly condition. It predominantly affects both sexes under 30 years of age and typically follows a cyclical course. No appropriate treatment has been identified for this condition because the cause remains unclear; although some cases, such as our case, may be initiated by testosterone. This case highlights the fact that exfoliative cheilitis is may be secondary to drug such as testosterone injection and intralesional corticosteroids can be used as therapeutic option in such affected patients.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The examination of patients is conducted according to the Declaration of Helsinki principles. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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Case Report

Recurrent lupus miliaris disseminatus faciei: A case report

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ABSTRACT

Lupus miliaris disseminatus faciei (LMDF) is a granulomatous eruption characterized by monomorphic, reddish-brown papules and nodules predominantly localized on the face. A 43 years old lady presented with multiple, painful, papulo-pustules over face 6 years back. Biopsy showed showed large foci of suppurative granulomatous dermatitis with a large central area of suppuration surrounded by histiocytes and occasional giant cells. Epidermis is not disrupted. Perifollicular and perivascular lymphocytic infiltrates were also seen. The lesions were healed with atrophic scars. She is now presented with multiple asymptomatic papules over bilateral periorbital regions of the face.

Key words: Lupus miliaris disseminatus faciei (LMDF), tuberculosis, rosacea, Demodex folliculorum

INTRODUCTION

Lupus miliaris disseminatus faciei (LMDF) is a granulomatous eruption characterized by monomorphic, reddish-brown papules and nodules predominantly localized on the face [1-3]. Earlier, it was thought to be a hypersensitivity reaction to tuberculosis, but a conclusive relationship to tuberculosis has not been established. Now a days, it is considered to be a variant of rosacea. Extrafacial manifestations can also be seen which may affect the axilla, shoulders, arms, hands, groins and leg. Tuberculin test and culture for Mycobacteria are usually negative [1-4]. Scarring is the primary complication.Recurrence is not common as far as our knowledge is concern after checking pubmeds and few dermatological journals. We hereby report a case of recurrent LMDF [2-5].

CASE REPORT

A 43 years old lady presented with multiple, painful, papulo-pustules over face 6 years back (Fig. 1 and 2). There was no history of cough, chest pain, hemoptysis, weight loss, fever, photosensitivity, flushing. Patient denied history of aggravation with spicy foods. She had undergone skin punch biopsy which showed large foci of suppurative granulomatous dermatitis with a large central area of suppuration surrounded by histiocytes and occasional giant cells. Epidermis is not disrupted. Perifollicular and perivascular lymphocytic infiltrates were also seen (Fig. 4).The features seems to be consistent with Lupus Miliasis Disseminatus faciei (LMDF). She was treated with Cap. Tetracyclines 500 mg QID, Tab. Dapsone 100mg OD and Fusidic acid ointment. Response to the treatment was seen after 3months of starting therapy. Due to slow response, patient was not satisfied and Tab. Azithromycin pulse (Azithromycin 500mg OD for 3 days followed, after Azithromycin off days for 10 days, by 3 days course of same dose of Azithromycin). was added to the treatment after 7 months. 1 month after Azithromycin pulse was started, the papulo-pustular lesions completely subsided and the patient left the treatment by herself. The lesions were healed with atrophic scars. There was no recurrence until November 2013, when she started developing multiple asymptomatic papules over bilateral periorbital regions of the face. The morphology and the distribution was more or less same as before except that it was in a less severe form. The photograph of the active phase of the second episode could not be taken as it was not so severe that she neglected as far as possible. Besides, she had some problem in transportation as she came from some far off village. By the time she came, only few lesions were present. However, he atrophic scars from previous

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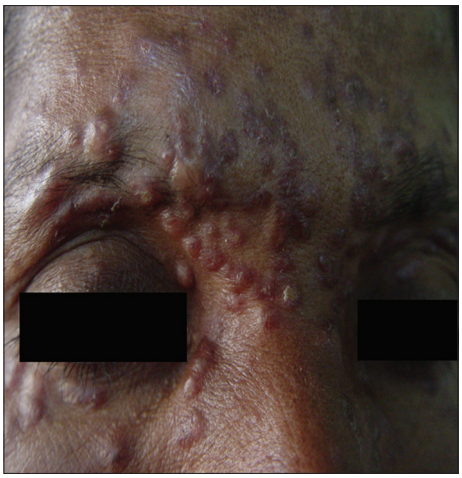

Figure1: Periocular lesions of previous episode

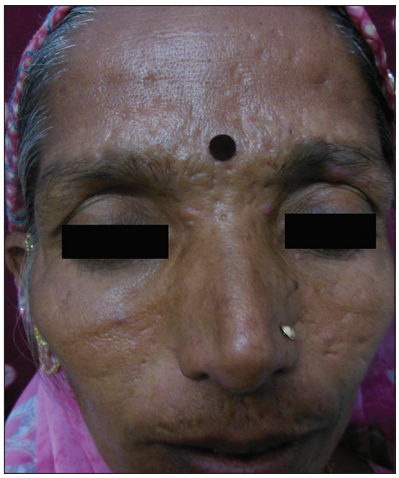

Figure 3: Current episode (after healing)

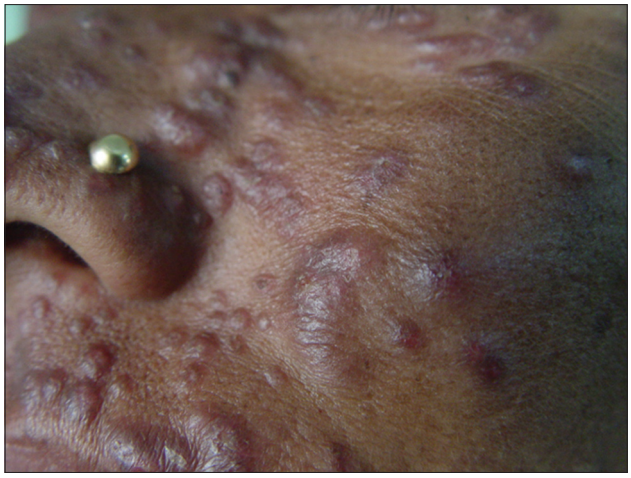

Figure 2: Perioral and cheeks of previous episode

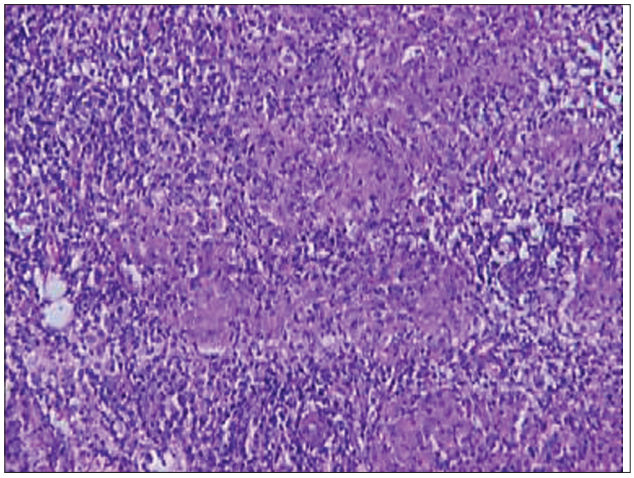

Figure 4: Histopathology. Suppurative granulomatous dermatitis with a large central area of suppuration surrounded by histiocytes and occasional giant cells. Epidermis is not disrupted. Perifollicular and perivascular lymphocytic infiltrates

episode were also present (Fig. 3). Unfortunately, she refused biopsy this time to confirm the recurrence. However, by clinically, It seems to be same as before and it is more or less proved to be recurrence.

The patient's informed consent was obtained.

Prior to the study, patient gave written consent to the examination and biopsy after having been informed about the procedure.

DISCUSSION

LMDF was first described in 1903 as an eruption consisting of groups of discrete dull red-brown papules tending to form pustules with spontaneous involution over several weeks, healing with scars [1-6]. It affects only skin [3-5]. Originally, LMDF was considered to be a variant of lupus vulgaris or a tuberculid, since the histological features show granulomatous-type inflammation and caseation necrosis [5-7]. However, there has been no evidence to date supporting a link with tuberculosis. Therefore, acne agminata and facial idiopathic granuloma with regressive evolution have replaced the term LMDF in some parts of the world [2-6]. Some authors suggested that LMDF is a reaction to Demodex folliculorum but the association has not been confirmed [5]. Others suggested that LMDF is a granulomatous reaction to hair follicle destruction or ruptured epidermal cyst [1-6]. The etiopathogenesis of LMDF is currently unknown. Originally, LMDF was thought to be a "tuberculid," i.e., a condition related to tuberculosis because of its histopathologic features resembling this infection (epithelioid cell granuloma with central necrosis) [6-9]. However, bacteriological cultures from LMDF lesions

failed to reveal bacilli and studies using the more sensitive polymerase chain reaction failed to detect Mycobacterium tuberculosis DNA. Therefore, the tuberculous origin of LMDF is no more accepted. Based on the fact that the granulomatous reaction frequently develops in the vicinity of a ruptured hair follicle, it has been hypothesized that LMDF is an expression of an immune response to the pilosebaceous units [5-9]. According to this hypothesis, damage to the hair-follicle epithelium (occurring in the early stage) releases follicular antigens that trigger an autoimmune reaction directed against hair-follicles [2-7]. Other authors consider LMDF to be a variant of granulomatous rosacea on the basis of the localization of the lesions in the midface and the pathological changes, which may be similar to those seen in granulomatous rosacea. However, several clinicopathological differences exist between rosacea and LMDF [4-8]. The former runs a more chronic course than LMDF. Extrafacial involement may occur in LMDF [8]. Patients do not report flushing and the disease is not worsened by alcohol or spicy food intake. Contrary to rosacea, LMDF lesions do not contain Demodex mites and they are more resistant to treatment and heal with scarring [5-7,10-12].

The treatment is unsatisfactory. The response to tetracyclines and retinoids (isotretinoin) is variable. Some repots of tetracyclines with isoniazide have been coming up. Some reports of effectiveness of dapsone are also seen [1,11,12]. Recently, Nonablative fractionated laser resurfacing and 1450-nm Diode Laser are reported to give promising results [13,14].

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patient for publication of this article.

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Case Report

Monilethrix - Case report of a rare disease

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ABSTRACT

Monilethrix is a rare genetic disorder of hair characterized by beaded appearance of the hair shaft leading to hair fragility and patchy dystrophic alopecia. In this disorder, the hair shaft has alternate widenings (nodes) and constrictions (internodes) that lead to fracture of hair shaft and varying degree of alopecia. We report an eight year old Kashmiri boy who presented with diffuse hair loss since infancy. As monilethrix is a rare disease entity which prompted us to report this case.

Key words: Alopecia; beaded appearance; hair fragility; monilethrix

INTRODUCTION

The word Monilethrix is derived from Latin 'monile' meaning 'necklace' and the Greek 'thrix' meaing 'hair'. It's a structural hair shaft disorder characterized by a beaded appearance due to the presence of elliptical or fusiform nodes which have a diameter of normal hair. These nodes are medullated and separated by areas of constrictions called as internodes which lack medulla. These unmedullated internodes are the sites of hair breakage leading to dystrophic alopecia [1]. The first case of monilethrix was described by Walter Smith in 1879. However, the term 'monilethrix' was coined by Radcliff Crocker [2]. Monilethrix is transmitted as an autosomal dominant trait with high penetrance but variable expressivity. However, there are sporadic cases of autosomal recessive inheritance reported for this disease [3].

CASE REPORT

An 8-year-old male child born of a nonconsanguineous marriage presented to us in the outpatient department (OPD) with a chief complaint of diffuse hair loss since seven months of his age. There is increased fragility and inability to grow long hair over the scalp. He had normal hair initially after which it got replaced with short and sparse hair. The parents revealed that the hair broke when it reached a certain length of few centimeters. There was no such history in any of his family members.

Macroscopic inspection of the scalp showed sparse short stubby hair of few centimeters in length with no signs of scarring (Fig.1). The nape of the neck showed multiple prominent horny follicular papules with hair emerging from the summit of these papules. His eyebrows and eyelashes were normal. On light microscopic examination hair shafts revealed the characteristic alternating fusiform or spindle shaped swellings (nodes) and constrictions (internodes) which confirmed the diagnosis of monilethrix in our patient.

Developmental examination of the child was normal. His mental and physical growth was normal. There was no nail, dental, sweat gland, otorhinolaryngological or other systemic abnormality. Routine laboratory screening was unremarkable. His serum copper and ceruloplasmin levels were normal.

DISCUSSION

The cause of monilethrix remains unclear. Several Genetic studies have suggested that monilethrix

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is likely caused by a hair keratin mutation. Some researchers have suggested mutations in the human hair basic keratins hHb1 and hHb6 in this disorder [4]. The most common mutation is the E413K mutation in hHb6 [5]. Autosomal dominant monilethrix is caused by mutations in hair keratin genes KRT81, KRT83, or KRT86, whereas in autosomal recessive form, mutations in the desmoglein-4 gene (DSG4) have been reported [6]. Defects in the cortical keratins lead to wrinkling of the cells at the internodes and make them susceptible to fracture while at nodes, the growth is normal [7].

Monilethrix occurs mainly on the scalp which can be widespread or circumscribed. The eyelashes, eyebrows, axillary, pubic, and limb hair are affected occasionally. The increased fragility of the hair shaft to premature weathering results in its inability to attain a normal length. The condition persists throughout life but may resolve spontaneously in some cases [2,8]. Monilethrix is usually associated with keratosis pilaris presenting as horny keratotic papules. In our case there were also keratotic horny papules on the nape of the neck but the skin biopsy was not taken.

The diagnosis of monilethrix can be confirmed on light microscopy which shows alternating wider elliptical nodes and narrower internodes. At the fragile internodes, There is premature weathering and breakage. Transmission microscopy of the internode showes deviation in the axis of the macrofibrils within the cortical cells and disorganized globular inter-macrofibrillar cystine rich material. Dermoscopy can be used as a rapid diagnostic tool for monilethrix which may show hair shafts with uniform spindle shaped nodes and intermittent constrictions (internodes); hairs bent at multiple locations in a regular fashion and a tendency to shaft fracture at the sites of constrictions [9,10]. However, in our case dermoscopy was not done due to the unavailability of the same as the case was diagnosed in a peripheral hospital.

There is no specific treatment for this condition. Avoiding trauma is the primary goal in managing this condition. The various activities which cause an increased susceptibility to fracture of the hair shafts including dyeing, bleaching, curling, etc. should be avoided. Some improvement has been reported with griseofulvin, iron supplementation, oral retinoids and topical minoxidil in isolated cases [11,12].

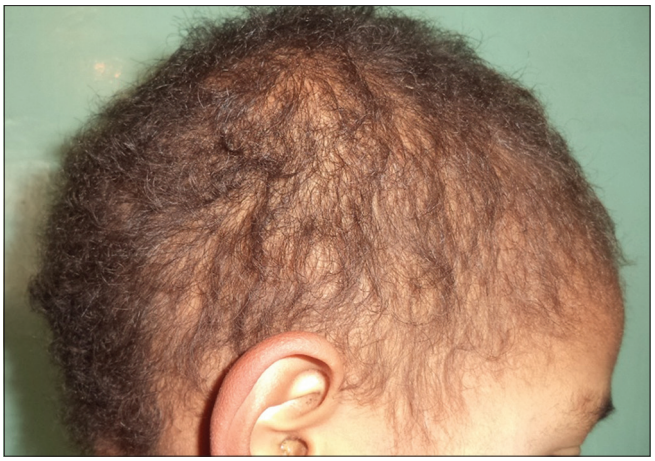

Figure 1: Monilethrix in an 8 year old boy. There is sparse short stubby hair of few centimeters in length over the whole scalp

Though, there are many reports of use of minoxidil in monilethrix but the improvement seems to be temporary and reversible. Rossi et al treated four cases of monilethrix with topical minoxidil 2%. The dosage was kept 1 ml day and night for a duration of one year. There was an increase of normal hair shafts after one year. They concluded that topical minoxidil 2% can be a good therapeutic option for Monilethrix [13].

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patient's caregivers for publication of this case report and any accompanying images.

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NASZA DERMATOLOGIA Online
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Case Report

Late onset 'en coup de sabre' following trauma: Rare presentation of a rare disease

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ABSTRACT

En coup de sabre (linear scleroderma of face) is a rare type of morphea (localized scleroderma) involving fronto-parietal area of the forehead and scalp. Many triggering factors have been implicated in the development of morphea like trauma, immobilization, bacille Calmette–Guérin (BCG) vaccination, injections of vitamin K, mechanical compression from clothing, etc. Linear scleroderma primarily affects the pediatric population, with 67% of patients diagnosed before 18 years of age. In this article, we describe a case of 26 year old female who presented with a three months history of brownish indurated plaque of skin on the frontal and forehead regions of the head. The patient gave a history of trauma at the same site six years back. The diagnosis of morphea was made clinically supported by histopathological features of the skin biopsy. Her neurological examination was normal. ANA was negative. Brain MRI didn't reveal any abnormality. She was treated with topical tacrolimus 0.1% ointment. The late onset en coup de sabre is a rare presentation and hence reported.

Key words: En coup de sabre; localized scleroderma; morphea; trauma

INTRODUCTION

Scleroderma is a connective tissue disorder of unknown etiology which is characterized by increased collagen production leading to the thickening and hardening of skin and other organs. It encompasses a spectrum ranging from localized scleroderma (LS) at one end to the systemic sclerosis (SSc) at the other extreme [1]. The localized form, also known as morphea, is characterized predominantly by the involvement of the skin; occasionally involving the underlying muscles with sparing of internal organs [2]. The exact cause of morphea is unknown, but several triggering factors have been mentioned in the literature which include trauma, immobilization, bacille Calmette–Guérin (BCG) vaccination, injections of vitamin K, mechanical compression from clothing, etc [3, 4]. Clinically, LS is subdivided into five types: plaque, linear, en coup de sabre, generalized and pansclerotic [5]. Linear scleroderma of en coup de sabre is a rare subset of LS. The typical presentation affects fronto-parietal region of the head, and the mean age of onset is around 13 years [1]. Here we present a late onset en coup de sabre in a 26 year old female who developed it at the site of trauma after six years.

CASE REPORT

A 26 year female, unmarried, presented to us in the outpatient department (OPD) with a chief complaint of dermatosis affecting her frontal and forehead regions of the head for the last three months. The disease began as a discrete area of erythema and progressed steadily forming indurated plaques. The surface became smooth and shiny. There is history of trauma at the same site six years before and she related this dermatosis to the trauma. There is no history of weakness of face. There is no history of seizures, headache or weakness of any body parts. The patient denied any systemic complaints.

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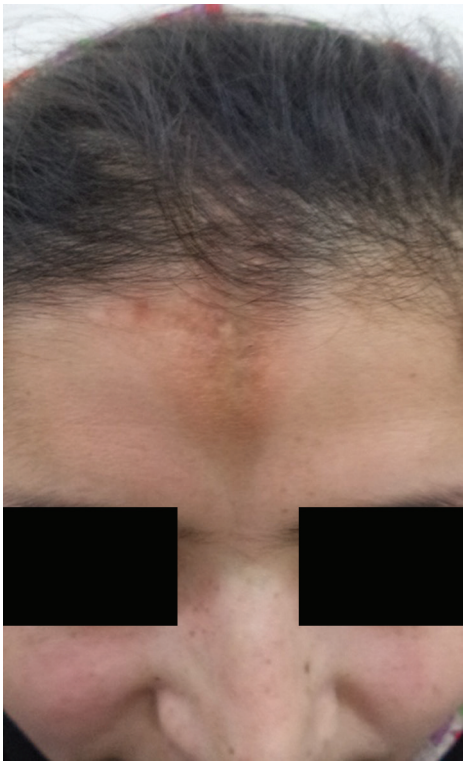

Figure 1: En coup de sabre following trauma in a 26 year old female. Brownish hyperpigmented indurated plaque with areas of atrophy

She didn't give any history of sequential colour changes of digits on exposure to the cold. Physical examination revealed a well defined, brownish hyper pigmented, indurated plaque present on the frontal and forehead regions of the head reaching to the glabellar region close to the midline in a vertical fashion (Fig. 1). The plaque showed areas of atrophy at some places. Neurological examination didn't reveal any abnormality. ANA was negative. MRI brain didn't show any abnormal findings. Skin biopsy on histopathological examination showed atrophy of the epidermis, a dermal and subcutaneous perivascular infiltrate of lymphocytes and plasma cells and thickened and closely packed dense bundles of collagen with sparse adnexal structures. The diagnosis of en coup de sabre was made based on the patient's history, a suggestive clinical examination and further supported by histopathological findings. She was prescribed topical tacrolimus 0.1% ointment to be applied twice daily on the affected area. After two months of treatment, the induration and the pigmentation of the lesion improved.

The written consent for the examination and biospy was obtained from the patient after having been informed about the procedure.

DISCUSSION

Scleroderma connotes a spectrum of disorders characterized by thickening and/or hardening of the skin and fibrosis of the tissues involved. It has been divided into localized and systemic forms. The localized form, also known as morphea, is characterized by predominant skin involvement, with occasional involvement of subjacent muscles. However, it usually spares the internal organs [5]. Linear scleroderma, a type of localized scleroderma, is unique in the sense that it primarily affects the children. Sixty seven percent (67%) of the patients of linear scleroderma are diagnosed before 18 years of age. Linear scleroderma frequently occurs on the limbs but sometimes may involve frontoparietal area of the forehead and scalp; where it is referred to as linear scleroderma en coup de sabre, as the skin lesions resemble to the stroke of a sabre (sword) [6]. The pathogenesis of skin lesions in LS, en coup de sabre and systemic sclerosis seems to be similar, though the exact mechanism is not fully clear [3]. The primary target in LS seems to be vasculature which is supported by clinical and pathological findings [6]. Early skin biopsies have revealed endothelial cell damage preceding the development of fibrosis by months to years. Later, Increase in the vascular permeability is associated with mononuclear cell infiltrate which further leads to perivascular inflammatory cell infiltrates, thickening of intima of vessels, and consequent narrowing of vascular lumina [7]. The inciting event for causing damage to the microvasculature remains elusive. However, antecedent trauma as initial event has been observed in pediatric population [8]. But in older age group, trauma as a precipitating factor has been rarely reported which makes our case a rare presentation.

En coup de sabre has been associated with a number of neurological abnormalities and is usually preceded by the development of skin lesions months to years. Central nervous system (CNS) involvement is usually not correlated with the cutaneous disease activity and may present years after skin lesions. Neurological manifestations in en coup de sabre are varied which include headache, epilepsy, movement disorders, focal neurological deficits and intellectual deterioration [9]. However, in our case there was no neurological involvement seen clinically. In addition, MRI Brain didn't show any CNS involvement as well. However, a meticulous follow up of the patient is

being taken to diagnose any incipient neurological involvement at the earliest.

The treatment of morphea has been updated. The various therapeutic options described in the literature include phototherapy, Imiquimod, topical tacrolimus, calcipotriol in combination with betamethasone dipropionate, methotrexate in combination with systemic steroids, D-penicillamine, cyclosporine, mycophenolate mofetil, photophoresis, etc [10]. In our case, the patient was prescribed topical tacrolimus 0.1% ointment twice daily. After a follow up of two months, the plaque showed reduction in skin thickening, induration and hyperpigmentation.

CONCLUSION

The authors conclude that 'en coup de sabre' can present with a late onset in adults and can follow trauma after many years. Hence, a periodic follow up is recommended in such cases to diagnose any CNS involvement at the earliest.

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patient for publication of this article and any accompanying images.

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Case Report

Ledderhose disease: A case report with palmar fibromatosis, keloid and partial response to oral retinod

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ABSTRACT

Ledderhose disease is a rare hyperproliferative disorder of fibrous tissue. We present the case of a 40-year-old man who presented with bilateral plantar fibromatosis, dupuytren contracture and keloid, with partial response to oral acitretin.

Key words: Ledderhose disease; plantar fibromatosis; dupuytren contracture

INTRODUCTION

Plantar fibromatosis or ledderhose disease is a rare hyperproliferative disorder of fibrous tissue [1], occurring over the medial sole of the foot with tendency for local recurrence but do not metastasize [2]. Patient described in this report is a man with bilateral plantar fibromatosis, dupuytren contracture and keloid, with partial response to oral Acitretin.

CASE REPORT

A 40-years-old hospital employer man referred to our clinic with multiple painful nodules in plantar surface of his feet (Figs 1A-D), in spring 2013.

20 years ago (1994) he noticed stiffness and flexion deformity in the third finger of his right hand. The patient underwent two surgical operations with the diagnosis of dupuytren contracture. Six years later (2002) slow growing nodule appeared in plantar surface of his left foot, and it was gradually progressive with a dull ache type of pain. Initial management consisted of a skin biopsy of this foot lesion which led to the confirmation of scar tissue, then a surgery performed and report of pathology, confirmed the previous diagnose. A few months later lesion recurred again at the site of operation on left sole and additionally the same nodules occurred in right sole (Figs 1A-D). The lesions were painful, somewhat preventing him from working. On examination, there were multiple skin colour to violaceous firm nodules with sharp margin and scale-crust on some of them in plantar, medial and latral aspect of his feet (Figs 1A-D). The size of biggest nodule on right sole was 2.5*2.9 cm and 3.5*3.0 cm on left sole. No flexion contracture of toes or neurovascular deficits was noted. Motion of the feet was within the normal range. Also he had a scar of dupuytren contracture surgery in right hand and two keloides in his chest and shoulder (Fig. 2). The patient reported no history of any diseases such as diabetes, seizure, trauma and he did not consume alcohol. Also there was no family history of similar lesions.

Laboratory data such as CBC/ESR/FBS/renal and liver function tests were normal. Pathology slides reviewed again and in microscopy the epidermis revealed hyperkeratosis, hypergranulosis and irregular acanthosis. In the dermis, there was proliferation of bland looking spindle shaped fibroblasts arranged vertically, within dense collagenous stroma suggestive of fibromatosis (Figs 3A-C).

Prior to the study, patient gave written consent to the examination and biopsy after having been informed about the procedure.

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MRI of lesions revealed small masses without invasion to muscle or tendon sheets (Fig. 4).

To management, we recommended him to change his job and suggested him not to stand for long time any more. Then prescribed the patient Acitretin 20 mg/day.

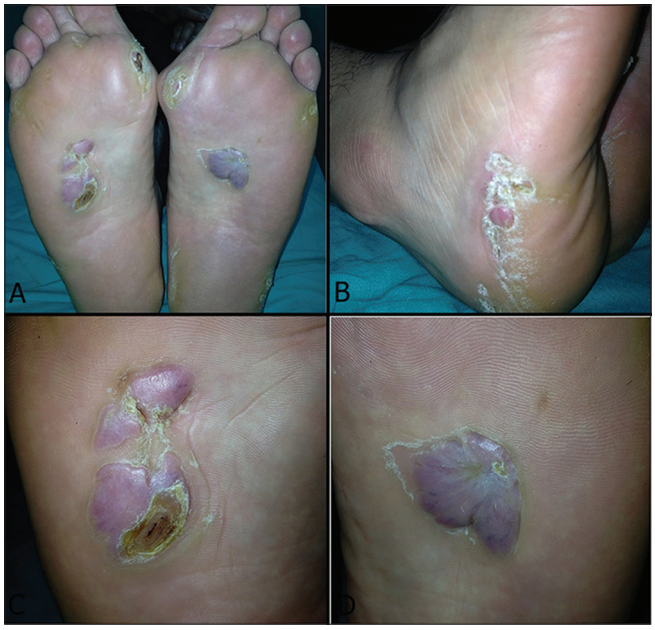

Figure 1: (A and D) The patient presents with multiple firm nodules on sole of both feet

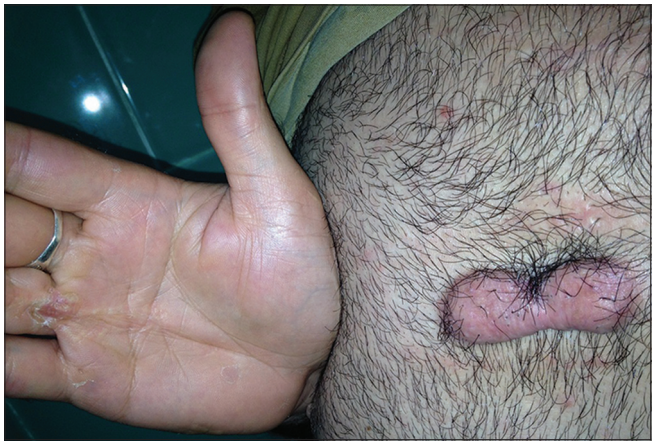

Figure 2: Scar of dupuytren contracture surgery and keloid in his chest

He consumed Acitretin for two months and stopped it for a month. However, the patient's symptoms, including pain reduced a lot and some of the nodules became flat and smaller in size (The dimensions of biggest nodule on right sole were 2.5*2.7 cm and 3.5*2.6 cm on left sole). In addition scales and crusts disappeared significantly (Figs 5A,B and 6A,B).

The patient's informed consent was obtained.

DISCUSSION

Fibromatoses are a family of fibroblastic proliferation sharing similar histology, an infiltrative pattern of growth and a tendency to recur after excision [2]. In general the superficial types are less aggressive than deep ones (such as desmoid) [3]. Plantar fibromatosis (ledderhose disease), palmar fibromatosis (Dupuytren contracture), penile fibromatosis (Peyronie's disease) and knuckle pads are benign superficial neoplastic proliferation of fibroblasts and/or myofibroblasts. Patients with palmar fibromatosis have additional areas of plantar fibromatosis in 5% to 20% of cases and penile fibromatosis in 2% to 4% of cases [4]. Recently, Trybus et al. reported an association rate of 14.85% of Ledderhose in 101 cases of Dupuytren contracture [5]. An increased incidence of knuckle pads has been observed [6,7]. Plantar fibromatosis occurs less frequently than palmar lesions with incidence of 0.23% [8].

Ledderhose disease, described in 1897, characterized by one or more slow growing nodules, most often on the medial half of the mid foot. Most lesions are asymptomatic and if they invade the adjacent structures they become painful. The pain increased by prolonged standing or walking and rarely produces contracture [9]. Nodules may be multiple in 33% of cases [10]. The condition affect any age but more often in younger age group, most often age 30 [11,12] and men are affected twice as often as females. Bilateral involvement is seen in 20-50% of cases [13,14].

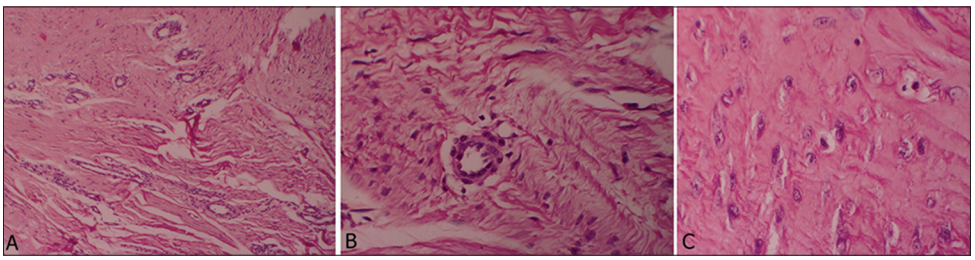

Figure 3: (A-C) Histopathology. Proliferation of bland looking spindle shaped fibroblasts arranged vertically, within dense collagenous stroma

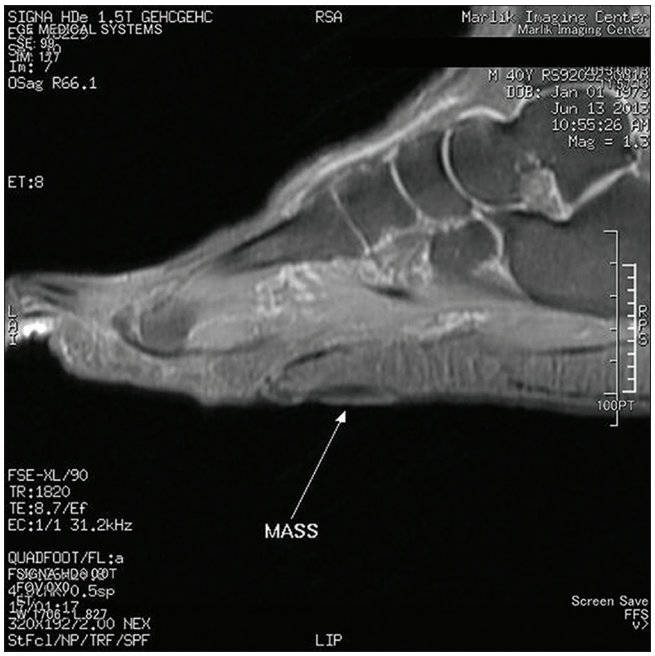

Figure 4: Magnetic Resonance Imaging. Small masses without invasion to muscle or tendon sheets

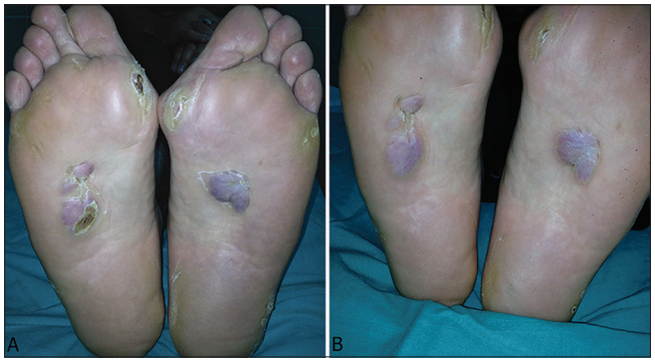

Figure 5: (A) Sole lesions before treatment (left side) and after treatment (right side)

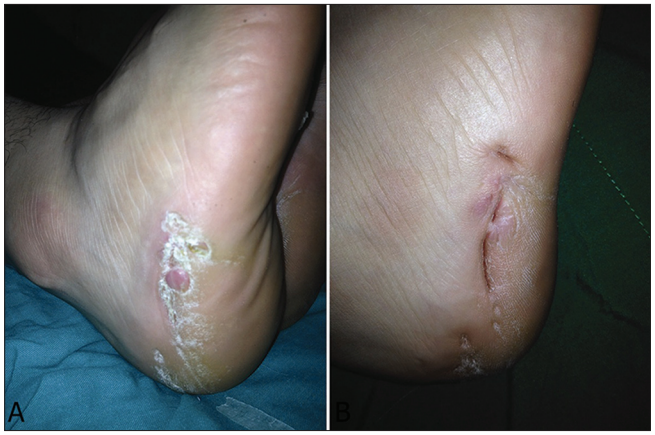

Figure 6: Lateral lesions before treatment (left side) and after treatment (right side)

The etiology of ledderhose disease remains unknown but genetic predisposition as well as repeated trauma is thought to play a role in its pathogenesis [9]. Some association with diabetes, alcoholic liver disease and epilepsy have been described [2]. Our case had none of these associations or predisposing factors, also he didn't indicate any family history of fibromatosis. Radiographs are frequently normal in Ledderhose disease, since the lesion is not encapsulated. Evaluation is most commonly performed with ultrasound and MRI. MRI is an excellent, non invasive method for delineating the extent of the lesion and planning surgical treatment [15], as it showed no invasion to muscle and tendon sheet in our patient.

In asymptomatic patients conservative managements such as footwear modification may be helpful [13]. For those suffering from pain of large lesions which cause disability, excision of the lesion with total fasciectomy is desirable with the lowest incidence of recurrence [16]. Kan and Hovius reported no recurrence after graft repair in two brothers, with a long term follow up, ranging from 14-25 years [17].

Adjuvant radiotherapy decreases the rate of recurrences but should be used selectively because of its side effects [18]. High-energy focused extracorporeal shockwave therapy reduces pain in plantar fibromatosis [19].

There are no specific medical treatment for plantar fibromatosis, other than symptomatic relief and supportive measures. In the other hand, Viera et al reported that retinoic acid and other vitamin A derivatives produce a marked reduction in human fibroblast proliferation by interfering with DNA synthesis in vitro. Retinoids also exhibit an inhibitory effect on TGF-β1-induced type I collagen gene expression in human fibroblasts [20].Furthermore the proliferation and activity of cultured fibroblast cells and type III collagen synthesis are inhibited as the concentration of retinoids are increased in the medium [21]. Etretinate, free acid of etretinate and 13-cis retinoic acid(RA),reduce type IV collagen synthesis in vitro, the largest decrease being found with free acid of etretinate and 13-cis-RA [22].

So with regard to the results of a two monthes course of oral Acitretin in our case and above mentioned data, it may be a worth trying medical opportunity in cases, who deny surgery, with multiple surgical failure, or are not good candidate for surgery. However, these results require confirmation in future studies.

CONSENT

The examination of the patients was conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patient for publication of this article and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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Case Report

Reactive erythema multiforme as atypical manifestation of leprosy. Case report

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ABSTRACT

The clinical course of leprosy is often interrupted by reactions, which are acute inflammatory episodes that can be classified as type I or type II. Type II reactions may occur as skin lesions resembling erythema multiforme (EM), which conventionally has been associated mainly with existing drug allergies or viral infections. However, differential diagnostic criteria of the different causal agents of multiform erythema remain controversial. We present an unusual case of a male patient whose first manifestation of leprosy has been a type II reaction, multiform erythema support.

Key words: Leprosy; erythema multiforme; reactional State

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Case Report

Eritema multiforme reaccional como manifestación atípica de lepra. Reporte de caso

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RESUMEN

El curso clínico de la Lepra se interrumpe a menudo por reacciones lepromatosas, que son episodios inflamatorios agudos que pueden ser clasificados como de tipo I o de tipo II. Las reacciones de tipo II pueden presentarse como lesiones cutáneas que se asemejan al eritema exudativo multiforme (EEM), el cual clásicamente ha sido asociado principalmente con alergias a medicamentos o infecciones virales preexistentes. Sin embargo, los criterios diagnósticos diferenciales de los diversos agentes causales de EEM siguen siendo controvertidos. Presentamos el caso atípico de un paciente masculino, cuya primera manifestación de Lepra ha sido un eritema exudativo multiforme reaccional.

Palabras claves: Lepra; eritema multiforme; estado reaccional

INTRODUCCIÓN

La Lepra es una enfermedad infecciosa crónica causada por el bacilo intracelular obligado *Mycobacterium leprae*. Aunque ha disminuido la incidencia de esta enfermedad, no lo ha hecho tanto como se esperaba, a pesar de la introducción de la poliquimioterapia (rifampicina, dapsona y clofazimina) por la Organización Mundial de Salud (OMS) hace tres décadas. Esto ha llevado a que siga siendo un importante problema de salud pública en numerosos países subdesarrollados [1,2]. En Paraguay, según datos del Programa Nacional de Control de Lepra en el año 2013 se reportaron 408 casos nuevos, lo que corresponde a una tasa de 6,11 casos por 100.000 habitantes; además se reportó, una tasa de prevalencia de 0,76 casos por 10.000 habitantes [2].

El curso crónico de la Lepra, se interrumpe a menudo por reacciones, que son respuestas inflamatorias agudas que pueden ocurrir antes, durante o después de la poliquimioterapia.

El riesgo estimado de que un paciente con Lepra experimente al menos un episodio de reacción puede ser tan alto como 60% en pacientes multibacilares (MB) sometidos a poliquimioterapia (PQT), según algunas series (Nery et al. 1998) [3]. Estas reacciones han sido clasificadas como:

- Reacción Tipo I: caracterizada por la reactivación de lesiones antiguas y la aparición de nuevas lesiones que presentan placas eritematosas infiltradas, y que están frecuentemente acompañadas por daño neural. Afecta a pacientes con las formas Borderline de la Lepra. Las reacciones que se desplazan hacia el polo tuberculoide se llaman de ascenso (o reacción reversal). Las reacciones que se desplazan hacia el polo lepromatoso se llaman de descenso. Ambas son efecto de la hipersensibilidad retardada (en la clasificación de Gell y Coombs corresponden a la reacción de tipo IV) [1]. La reacción de tipo 1 se origina por el aumento de la respuesta inmunitaria mediada por células contra los antígenos de *M. leprae*, con mayor expresión de citocinas del patrón Th1, como la IL-1β, TNFα e INFγ [4].

How to cite this article: Re Domínguez ML, Di Martino Ortiz B, Rodríguez Masi M, Knopfelmacher Domínguez O, de Lezcano LB. Eritema multiforme reaccional como manifestación atípica de lepra. Reporte de caso. Our Dermatol Online. 2014;6(1):56-61.

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- Reacción Tipo II: que incluyen al Eritema Nodoso Leproso (ENL), Eritema Multiforme y al Fenómeno de Lucio. Estas reacciones ocurren más frecuentemente en Hansen Lepromatoso (HL) y con menor incidencia en Hansen Borderline Lepromatoso (HBL), en pacientes con o sin tratamiento y se deben a la formación de complejos inmunes antígeno-anticuerpo que se depositan en los tejidos produciendo respuestas inflamatorias agudas en piel, nervios y órganos, y está mediada por la liberación de TNFα y las IL6, IL8 y IL10. En la clasificación de Gell y Coombs corresponde a las reacciones de tipo III [1,3,4].

En los casos de ENL, aparecen nódulos cutáneos eritematosos dolorosos, asociados con síntomas sistémicos inflamatorios, incluyendo fiebre, malestar general, anorexia, iritis, orquitis, linfadenopatía y generalmente neuritis [1,5].

Aunque las lesiones necróticas a veces se han observado en las reacciones de tipo II, pocos casos de eritema multiforme se informaron como estado reaccional de la Lepra [1].

EM se ha observado en relación con muchas otras enfermedades, incluyendo infecciones por el virus del herpes, *chlamydia* y con el uso de fármacos; tal es así que esta entidad, sigue siendo idiopática en al menos el 35% de los pacientes afectados. Varias lesiones, tales como máculas, pápulas, vesículas y ampollas, están presentes, pero la lesión denominada "en diana o en blanco de tiro" es la característica principal del EM [1].

Las reacciones de tipo 1 y de tipo 2 se pueden presentar hasta en 30% y 20% de los pacientes con enfermedad de Hansen, respectivamente.

Las reacciones son la principal causa de daño neural en la lepra y producen anestesia y deformidades permanentes en las manos y en los pies [4].

CASO CLÍNICO

Varón, 41 años, militar, procedente de medio urbano del Paraguay, sin patologías de base conocidas con cuadro de tres meses de evolución de lesiones sobre elevadas violáceas en todo el cuerpo, en ocasiones dolorosas y que cursa con episodios de sensación febril y de lesiones de contenido líquido claro que drenan espontáneamente. Al examen físico se observa una dermatosis diseminada a tórax, abdomen y extremidades, constituida por placas redondeadas eritematovioláceas, de entre 1 y 3 cm de diámetro, de bordes regulares y límites difusos, algunas exulceradas, otras con costras hemáticas y otras centradas por ampollas de contenido líquido blanquecino, en blanco de tiro (Figs. 1 y 2). Se observa también infiltración de lóbulos de ambas orejas (Fig. 3). Sensibilidades táctil y térmica conservadas.

Hemograma, glicemia, hepatograma y perfil renal normales. Baciloscopía positiva (4+) para BAAR (linfa cutánea del lóbulo de la oreja).

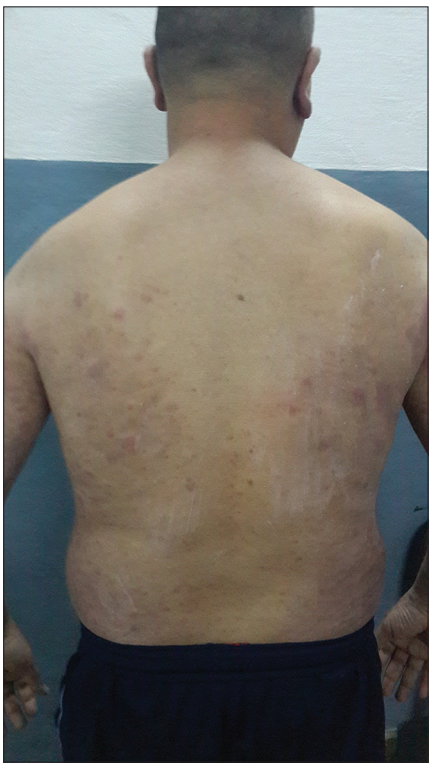

Figure 1: Clínica. Placas redondeadas infiltradas eritematovioláceas, de entre 1 y 3 cm de diámetro, de bordes regulares y límites difusos, que asientan en tórax

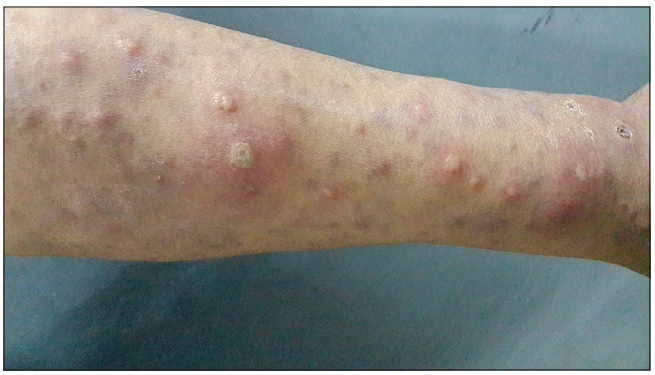

Figure 2: Clínica. Placas redondeadas infiltradas eritematosas, de entre 1 y 3 cm de diámetro, de bordes irregulares y límites difusos, algunas exulceradas, otras centradas por ampollas de contenido blanquecino, en blanco de tiro que asientan en antebrazos

A la histopatología se observa ampolla subcórnea de contenido fibrino leucocitario, infiltrado dérmico superficial y profundo, constituido por histiocitos espumosos de disposición perivascular, perineural y perifolicular, acompañado de un denso infiltrado neutrofílico sobreimpuesto. Se ven además imágenes de vasculitis leucocitoclástica (necrosis fibrinoide e infiltrado neutrofílico intraparietal). Coloración de Ziehl Neelsen positiva para BAAR (4+, bacilos fragmentados) (Figs 4AB y 5ABC).

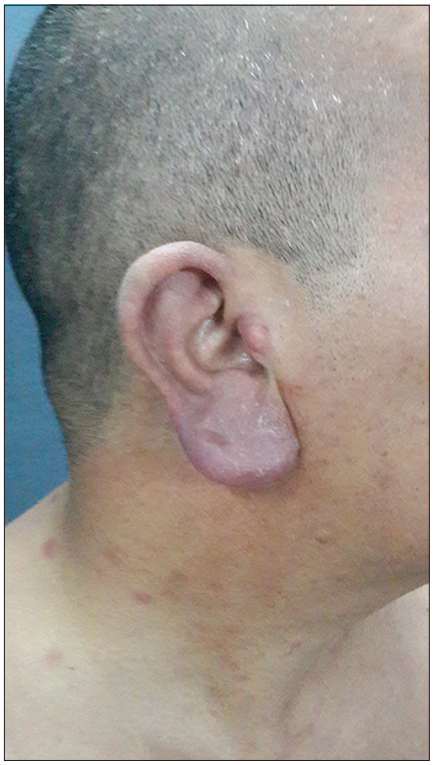

Figure 3: Clínica. Pápulas de 5 a 8 mm eritematosas en región cervical. Infiltración de lóbulo de la oreja

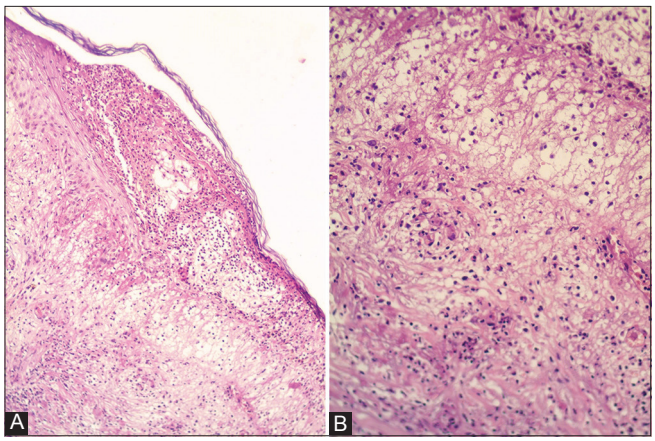

Figure 4: Histopatología. A. Ampolla subcórnea de contenido fibrino leucocitario (HE 4X). B. A mayor aumento (HE 20X)

Diagnóstico final: Eritema Exudativo Multiforme Reaccional.

Se inicia tratamiento según esquema multibacilar de la OMS (Rifampicina, Clofazimina y Dapsona) e Ibuprofeno con buena evolución de las lesiones.

Se obtuvo el consentimiento informado del paciente.

Antes del estudio, el paciente dio consentimiento escrito para el examen y la biopsia, tras haber sido informado sobre el mismo y el objetivo de éste.

DISCUSSIÓN

El EM es una variante poco frecuente de la reacción Lepromatosa de tipo II, que se presenta mayoritariamente como pápulas y placas eritematosas en blanco de tiro centradas por ampollas; casi invariablemente se caracteriza por vasculitis de los vasos sanguíneos pequeños, daño endotelial, depósito de fibrina, y extravasación de glóbulos rojos [3,5].

En un estudio realizado por Miranda A., et al en Brasil [1], de 600 casos de reacciones lepromatosas de tipo II, 27 correspondían a EM, lo que representa una frecuencia de 4,5%; de entre éstos, 8 pacientes (30%) presentaron lesiones de EM como como la primera manifestación de la lepra; once pacientes (40%) se encontraban realizando tratamiento PQT y 8 pacientes

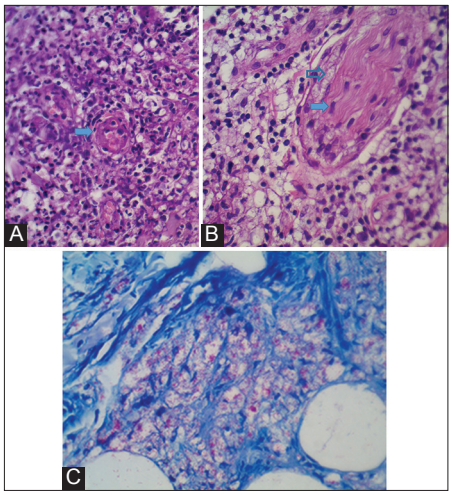

Figure 5: Histopatología. A. Infiltrado dérmico superficial y profundo, constituido por histiocitos espumosos, acompañado de un denso infiltrado neutrofílico sobreimpuesto. Necrosis fibrinoide de la pared vascular e infiltrado neutrofílico intraparietal (flecha) (HE40X). B. Infiltrado dérmico de histiocitos espumosos perineural (el nervio se halla señalizado con una flecha y el infiltrado que irrumpe en él con una flecha hueca) (HE 40ª). C. BAAR 4+, bacilos fragmentados (ZN 40X)

(30%) desarrollaron EM después del alta. Dieciocho pacientes (66,6%) presentaron lesiones típicas vesico-ampollares, mientras que los otros pacientes diagnosticados se presentan con diversas lesiones cutáneas eritematosas en forma de placas, pápulas y úlceras. En el caso de nuestro paciente, se presenta el EM como debut de la Lepra, manifestándose con las típicas lesiones vesicoampollares y en blanco de tiro.

En cuanto a los hallazgos histopatológicos de las lesiones de EM reaccional, se describen leve a moderado engrosamiento de la epidermis, ligera espongiosis y exocitosis, variable cantidad de células apoptóticas, ampollas intra epidérmicas, edema en dermis superficial en asociación con infiltrado celular de linfocitos, neutrófilos y macrófagos espumosos conteniendo bacilos fragmentados, que van desde numerosos en los pacientes no tratados, y escasos en los pacientes que ya recibieron algún tratamiento. Los haces de nervios invariablemente exhiben una serie de cambios histológicos, en particular el engrosamiento del perineuro, infiltración por células inflamatorias y la presencia de BAAR [1,6,7].

En la serie de Miranda A., et al [1], los cambios vasculares fueron evidentes en todos los casos, encontrándose angiogénesis (85,1%), dilatación de vasos (81,4%), congestión de linfáticos (66,6%), células inflamatorias (predominantemente linfocitos) invadiendo la pared (88.8%), interrupción de la capa elástica dentro de las arteriolas (50%), presencia de leucocitos polimorfonucleares circundante a los vasos (96,2%), oclusión de la luz por células endoteliales hipertróficas o fibrina (51,8%) y BAAR dentro de la pared (37%).

Estos cambios vasculares observados en las lesiones EM son similares a los descritos en la hipodermis dentro de las lesiones de ENL y sugieren que los micro vasos dérmicos (principalmente capilares y vénulas) representan objetivos pertinentes en las lesiones de EM y de ENL durante la patogénesis de la lepra y podrían representar variantes de reacciones de tipo II provocados por las variaciones de un mecanismo patogénico común [1,6,7].

La histopatología de nuestro caso, concuerda casi con la totalidad de los hallazgos anátomo patológicos antes mencionados, siendo diagnósticos la ampolla subcórnea, el infiltrado de histiocitos espumosos a los que se les sobre imponen neutrófilos, la infiltración neural, la imagen de vasculitis leucocitoclástica y la presencia de BAAR en su forma fragmentada.

Existen publicaciones que plantean que las reacciones vasculonecróticas de la Lepra constituyen un espectro de reacción, encontrándose en un polo el fenómeno de Lucio y en el otro el Eritema Nodoso Lepromatoso necrótico [8].

La frecuencia a nivel mundial de las reacciones varía considerablemente, pero entre un 25-50% de pacientes tendrán reacciones en algún momento durante el curso de su enfermedad [9]. Alrededor del 50% de los pacientes con HL y 25% de los pacientes con HBL tendrán reacciones de tipo 2 antes del inicio de la terapia multidrogas [10].

En un estudio realizado en Paraguay en dos centros dermatológicos de referencia en un período de 7 años, de un total de 256 pacientes con diagnóstico de Lepra, 79 presentaron leprorreacciones, lo que constituye el 31%; predominando en el sexo masculino, siendo la franja etaria más afectada la comprendida entre los 20 y 60 años; el índice bacilar predominante fue alto (3 - 4+). La forma clínica en la que se observó el mayor número de reacciones fue la de HL con el 74% de los casos, siendo la forma más frecuente la reacción de tipo 2, y dentro de ésta, el ENL puro 67% de los casos. En dicha serie el EM puro representaba sólo el 3,8% de los casos reaccionales [11]. En otra serie realizada en Paraguay durante un período de 10 años, de 250 pacientes con diagnóstico de lepra, el 30,4% presentó algún episodio reaccional, siendo el más frecuente, la reacción tipo 2, y dentro de ésta el eritema nodoso leproso [12].

CONCLUSIÓN

El eritema multiforme es considerado una variante poco frecuente de la reacción Lepromatosa de tipo II, cuya identificación recaerá casi exclusivamente en el dermatólogo, por lo que resulta imperioso tenerlo presente de tal forma a no retrasar el diagnóstico de Lepra y del estado reaccional, lo cual es crucial para prevenir las discapacidades causadas por la afectación neural que acompañan a estos episodios.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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Case Report

Angiocentric lymphomatoid papulosis in a child: uncommon benign clinical entity with malignant histology

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ABSTRACT

Lymphomatoid papulosis (LyP) is a rare form of chronic inflammatory skin disease with histologic features of a malignant lymphoma.It presents clinically with history of recurrent crops of pruritic papules that occur on the trunk and limbs that resolve spontaneously. We report an unusual case of angiocentric LyP in a 4 year old child and review the literature.

Key words: Lymphomatoid papulosis; child; cutaneous lymphoma

INTRODUCTION

The term lymphomatoid papulosis originally was used by Macaulay in 1968 to describe "a self-healing rhythmical paradoxical eruption, histologically malignant but clinically benign" [1]. Awareness of this entity is important as the histological features may result in a mistaken diagnosis of malignant lymphoma, if clinical picture is not taken into account. Follow-up is essential as it can progress to malignant lymphoma in a subset of patients.

CASE REPORT

A 4 year old male child presented with itchy erythematous and skin colored papules over trunk, upper and lower limbs of 3 months duration (Fig. 1). There were few excoriated papules. The child did not have genital or web space lesions. There was no history of prior viral infection, drug intake etc. A clinical diagnosis of prurigo simplex was considered and a skin biopsy was taken. Histopathological examination revealed wedge shaped superficial and deep aggregates of atypical lymphoid cells with hyperchromatic nuclei and scanty cytoplasm, along with few mononuclear Reed Sternberg like cells with prominent nucleoli, admixed with plasma cells and histiocytes. Folliculotropism of the lymphoid cells was noted (Figs 2 and 3). Angiocentric infiltration around dermal blood vessels with necrosis of blood vessel wall was seen (Fig. 4). The lymphoid cells were predominantly CD 3 positive with admixed CD 20 positive cells, while the large atypical cells stained positive for CD 3 and CD30 (Fig. 5). A diagnosis of Lymphomatoid papulosis was made based on the clinical and histopathological features.

The patient's informed consent was obtained. Prior to the study, patient gave written consent to the examination and biopsy after having been informed about the procedure.

DISCUSSION

Lymphomatoid papulosis (LyP) is a chronic inflammatory skin disease which can histologically be mistaken for malignant lymphoma. It presents clinically with recurrent crops of itchy papules that occur on the trunk and legs that heal spontaneously over 1-2 months leaving slightly depressed oval scars.

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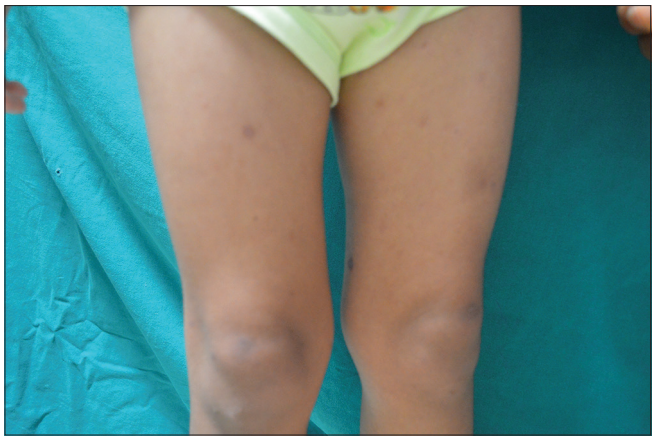

Figure 1: Clinical picture showing multiple resolving erythematous papules on the legs

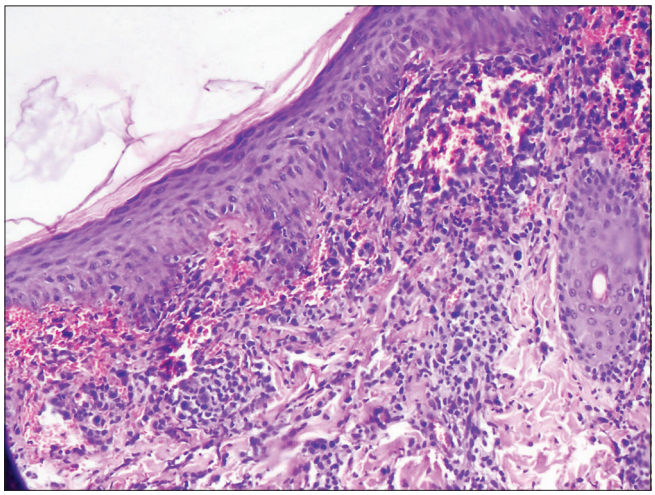

Figure 2: Wedge shaped superficial and deep diffuse and perivascular inflammatory infiltrate. H&E 200X

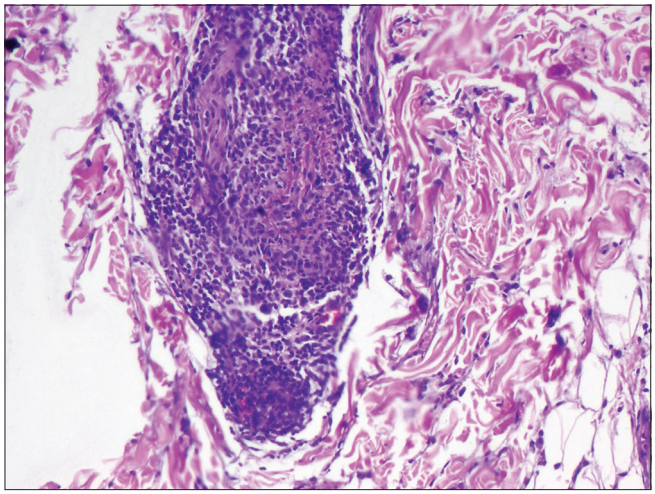

Figure 3: Angiocentric infiltration by lymphoid cells with fibrinoid necrosis of vessel wall. H&E, 200X

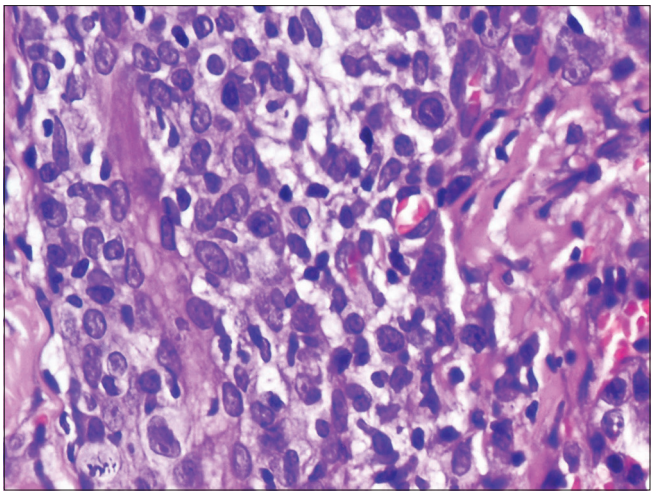

Figure 4: High power pictute showing large atypical lymphoid cells, and occasional mitosis. H&E, 400X

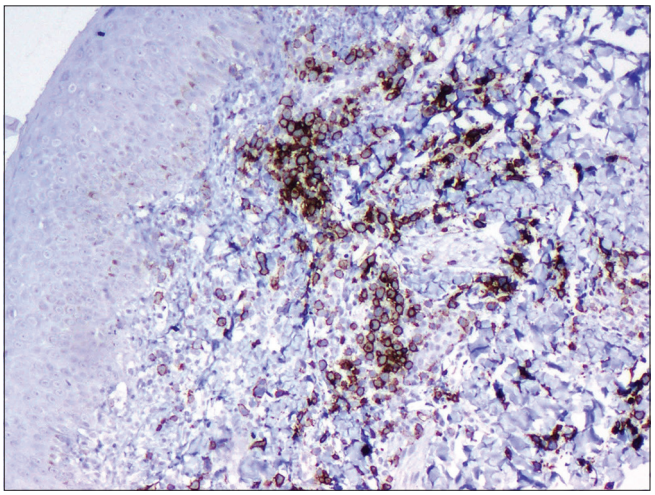

Figure 5: CD30 positivity among large atypical lymphoid cells. IHC, 200X

LyP was previously considered to be a pseudolymphomatous inflammatory process, because of the typical waxing and waning clinical course. However, World Health Organization—European Organization for Research and Treatment of Cancer (WHO-EORTC) classification, during the consensus meetings in 2003-2004 grouped lymphomatoid papulosis among the indolent cutaneous T-cell lymphomas [2]. The rationale behind classifying lymphomatoid papulosis as a cutaneous lymphoma is because of its association with other malignant lymphoproliferative disorders. Some experts consider this entity as chronic skin disease rather than a true malignancy because of its spontaneous resolution and benign clinical course.

Lymphomatoid papulosis belongs to the spectrum of CD30 (Ki-1)–positive cutaneous lymphoproliferative diseases ($CD30^+$ LPDs).This group includes lymphomatoid papulosis, primary cutaneous anaplastic

large cell lymphoma (pcALCL), and borderline CD30+ lesions [3].

The prevalence of lymphomatoid papulosis is estimated to be 1.2-1.9 cases per million population in the United States. It can develop at any age, but the peak incidence is in the fifth decade. LyP may rarely occur in children [4]. About 10-20% of LyP is thought to be associated with malignant lymphoma (ALCL, Hodgkin's disease, or Mycosis Fungoides) prior to, concurrent with, or subsequent to the diagnosis of lymphomatoid papulosis [5,6]. The etiology of lymphomatoid papulosis is not clear. There is debate about the nature of LyP,whether it is a benign or malignant condition. Histologically, it has features resembling malignant lymphoma; however, its clinical course manifested by recurrent, self-healing lesions suggests a benign nature.

Histopathologically, LyP is characterized by wedge shaped inflammatory infiltrate extending to the deep dermis or superficial subcutaneous tissue, and is further divided into subtypes based on morphologic features and immunohistochemistry. LyP Type A shows wedge-shaped, superficial and deep infiltrate of CD 30+atypical lymphoid cells, that resemble Reed Sternberg's cells along with small lymphocytes, often, plasma cells, neutrophils, and eosinophils. No epidermotropism is seen is seen in this subtype. LyP Type B is characterized by perivascular or band like dermal infiltrate of small to medium sized lymphocytes with cerebriform nuclei which are CD30+ or CD 30-, with epidermotropism, resembling Mycosis fungoides. LyP Type C shows monotonous population of CD 30+ large atypical cells with fewer inflammatory cells, and resembles ALCL. LyP Type D is a variant that histologically simulates an aggressive epidermotropic CD8 positive T-cell lymphoma. This cytotoxic variant of LyP may be histopathologically indistinguishable from primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma, and may be the source of pitfalls in the diagnosis and classification. A type E variant with clinical and histologic manifestations simulating highly aggressive angiocentric and angiodestructive T cell lymphoma has been described [7,8]. Patients present with a few papulonodular lesions that rapidly evolve to large ulcerations covered by a hemorrhagic and necrotic crust.However, our patient showed lymphomatoid papulosis, with angiocentric lymphoid infiltrate, but presented clinically with papular lesions, that regressed in 4 weeks.

Several inflammatory and reactive disorders like viral infection, drug eruption, arthropod bite reaction may contain a significant number of CD30+ cells and mimic lymphomatoid papulosis clinically or histologically [3]. Clinicopathologic correlation is hence necessary to establish an accurate diagnosis and to differentiate LyP from ALCL, Mycosis fungoides and Hodgkin's lymphoma and other inflammatory mimics.

Various therapeutic options are available to treat LyP, with methotrexate being the treatment of choice. Others include PUVA, potent topical steroids, interferon and topical mechlorethamine.

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles.

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Case Report

Cutaneous metastases from primary carcinomas of unknown origin. Contribution with 3 cases and brief review

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ABSTRACT

Metastases of unknown primary site occurs in about 5-10% of patients diagnosed with cancer. Usually appear after diagnosis of the primary cancer, but may be the first clinical sign of a tumor of unknown origin or the first sign of relapse of cancer. Cancer treatment is based on the recognition of the primary neoplasm, which raise diagnostic and therapeutic challenges. Skin biopsy should be considered in newly emerging lesions in cancer patients in addition to those lesions of sudden onset that are slow to heal, prone to bleeding or vascular appearance, that are not resolved with appropriate treatment. We present three cases of cutaneous metastases as the first manifestation, from which the primary tumor was found.

Key words: Cutaneous metastasis; metastatic renal cell carcinoma; immunohistochemistry

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Case Report

Metástasis cutáneas de carcinomas primarios de origen desconocido. Aporte de 3 casos y breve revisión

Silvia Mancía[1], Beatríz Di Martino Ortiz[1], Tatiana Moreno[1], Lourdes Rodríguez[1], Romina Contreras[1], Julio Recalde[1], Mirtha Rodríguez[1], Oilda Knopfelmacher[1], Lourdes Bolla de Lezcano[1], Hugo Boggino[2]

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RESUMEN

Las metástasis de origen primario desconocido ocurren en alrededor de un 5-10 % de los enfermos diagnosticados de cáncer. Habitualmente aparecen tras el diagnóstico del cáncer primario, pero pueden ser el primer signo clínico de un tumor de origen desconocido o la primera señal de recaída de un paciente oncológico. El tratamiento del cáncer se fundamenta en el reconocimiento de la neoplasia primaria, por lo que plantean grandes retos diagnósticos y terapéuticos. La biopsia cutánea debe ser considerada en lesiones de reciente aparición en pacientes oncológicos además de en aquellas lesiones de instauración brusca, que tardan en curar, con tendencia al sangrado o con apariencia vascular, que no se resuelven con tratamiento adecuado. Presentamos tres casos de metástasis cutáneas como primera manifestación, a partir de las cuales fue hallado el tumor primario.

Palabras clave: Metástasis cutánea; carcinoma renal metastásico; inmunohistoquímica

INTRODUCCIÓN

La piel y las mucosas pueden expresar manifestaciones de malignidad interna principalmente bajo dos formas, como paraneoplasia o como metástasis, por lo que el dermatólogo debe estar familiarizado con este tipo de hallazgos [1]. La presencia de metástasis es una de las características de los tumores malignos que amenaza la vida del paciente, e implica indefectiblemente la existencia de un proceso sistémico.

Las metástasis cutáneas (MC) son el resultado de la infiltración de la piel por proliferaciones de células procedentes de tumores malignos situados a distancia. La detección temprana de la mayoría de las metástasis requiere de pruebas complementarias sofisticadas; por el contrario, las MC son fácilmente observables en una exploración física dirigida y cuidadosa en la mayoría de los casos. Hasta un tercio de las MC se diagnostican de forma previa o simultánea al tumor de origen, por ello el papel del dermatólogo para establecer una sospecha clínica adecuada es esencial. Su reconocimiento clínico precoz es imprescindible, pues puede permitir el diagnóstico de un tumor maligno primario no previamente conocido, poner de manifiesto la diseminación de un tumor primario ya conocido, o ser un signo precoz de recurrencia tumoral de un tumor maligno en aparente remisión. Por tanto, el diagnóstico de las MC puede suponer un cambio en la estadificación de la enfermedad tumoral, con implicaciones terapéuticas y pronósticas. Su presencia, a menudo, varía drásticamente la actitud terapéutica, especialmente cuando las metástasis implican la persistencia de una neoplasia en aparente remisión, además permite obtener fácilmente muestras de tumor que pueden ser de utilidad para analizar la sensibilidad del tumor primario a tratamientos específicos. Algunos tumores parecen tener predilección por metastatizar en

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áreas específicas. El reconocimiento de estos patrones puede ser útil para dirigir la búsqueda de un tumor subyacente no conocido [2].

CASOS CLÍNICOS

CASO N°1

Varón, 49 años, soltero, carpintero, procedente de medio urbano del Paraguay (Sudamérica) que consulta por lesiones sobre elevadas rojas de 1 mes de evolución en frente, mentón y cuero cabelludo, con crecimiento progresivo, sangrado frecuente y dolor, sin fiebre, pérdida de peso u otro síntoma.

Antecedentes patológicos personales: Hipertenso en tratamiento con enalapril y lesiones blandas, no adheridas a planos profundos en hipodermis, compatibles clínicamente con lipomas, en tronco y miembros.

Examen Físico: Dermatosis constituida por tumoración eritemato violácea de límites netos, bordes regulares, superficie lobulada, con costras hemáticas, de 2 cm de diámetro en frente y tumoración eritematosa, ulcerada, 1 cm de diámetro en mentón (Figs 1A y 1B).

Laboratorio: Hemograma, glicemia, urea, creatinina, perfil hepático: normales. Colesterol total: 264mg/dl, Colesterol HDL: 38mg/dl, Colesterol LDL: 71mg/dl, Triglicéridos: 273mg/dl.

Ecografía de partes blandas: Nódulo de la cara, antero inferior izquierdo: Posible granuloma inflamatorio con vascularización aumentada.

Diagnósticos clínicos presuntivos: Queratoacantoma, Cuerno cutáneo, Granuloma piógeno.

Anatomía Patológica: Proliferación dérmica de células claras (Figs 2A y 2B) las cuales son positivas para EMA, vimentina, CD10, AE1, AE3 y negativas para e-cadherina, CK7, CK20, CD34, CD68, S100 y RCC.

Diagnóstico final: Metástasis cutánea de carcinoma renal a células claras

Evolución: Se interna al paciente en Clínica Médica para completar estudios y tratamiento. Se realiza Tomografía axial computarizada con contraste de cráneo, cuello, tórax, abdomen y pelvis donde se constata masa renal derecha (Fig. 3). Es evaluado por oncología y se plantea inicio de la quimioterapia.

CASO N° 2

Varón, 70 años, con lesiones tipo granos rojizos de 2 meses de evolución en región supra labial, asintomáticos, que aumentan de tamaño, pérdida de peso y tos con expectoración blanquecina de varios meses de evolución.

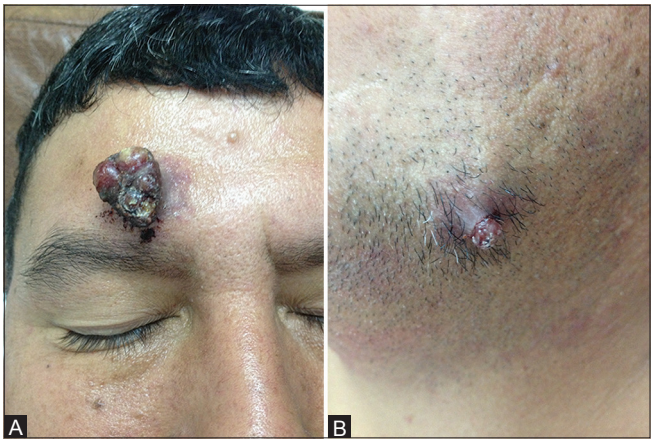

Figura 1: Caso Nº 1. Clínica. A. Tumoración eritematoviolácea de límites netos, bordes regulares, superficie lobulada, con costras hemáticas, de 2 cm de diámetro en frente. B. Tumoración eritematosa, ulcerada, 1 cm de diámetro en mentón

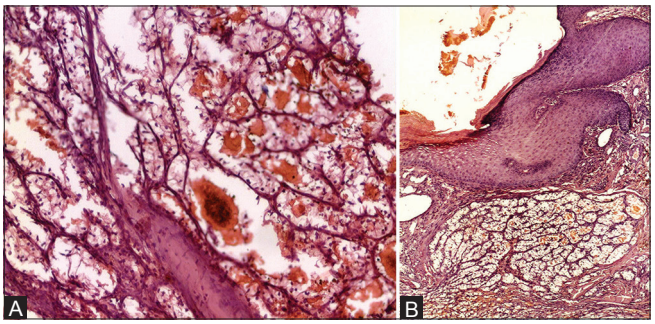

Figura 2: Caso Nº 1. Histopatología. A. Proliferación dérmica de células claras. B. A mayor aumento, detalle de las células claras

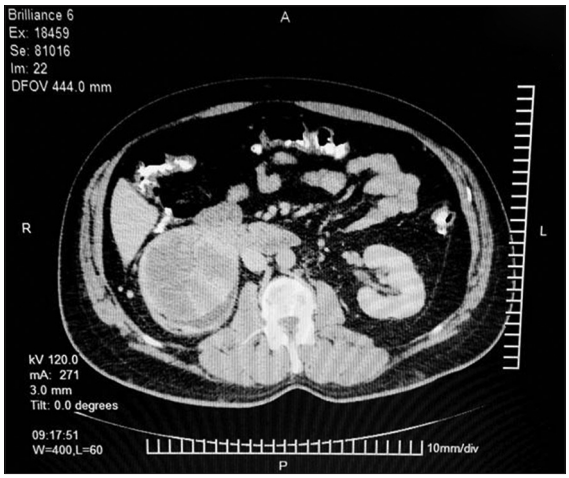

Figura 3: Caso Nº 1. Tomografía axial computarizada con contraste. Se constata masa renal derecha

Examen Físico: dos lesiones tumorales eritematosas, redondeadas, bien delimitadas, de consistencia sólido-dura, la mayor de aproximadamente 3 cm de diámetro, la menor de aproximadamente 1,5 cm de diámetro, localizadas en región supra labial derecha y surco nasogeniano izquierdo respectivamente (Figs 4A y 4B) y adenomegalias en región cervical y supraclavicular derechas.

Se procede a la biopsia de piel en la que se observa un área de infiltración dérmica por una neoplasia maligna indiferenciada de estirpe epitelial, con algunas células indiferenciadas conformando estructuras tipo organoide y con infiltración en fila india (Figs 5A y 5B).

Se solicitan radiografía y tomografía de tórax, donde se observa una imagen redondeada en región parahiliar derecha sugestiva de un proceso expansivo pulmonar (Figs 6A y 6B).

Diagnóstico final: Metástasis cutánea de adenocarcinoma pulmonar

Se deriva el paciente al servicio de oncología donde se inicia tratamiento quimioterápico paliativo

CASO N° 3

Mujer, 64 años, pápulo nódulo de 1 año de evolución, de crecimiento progresivo en la región mamaria derecha, que se acompaña de intenso y continuo prurito.

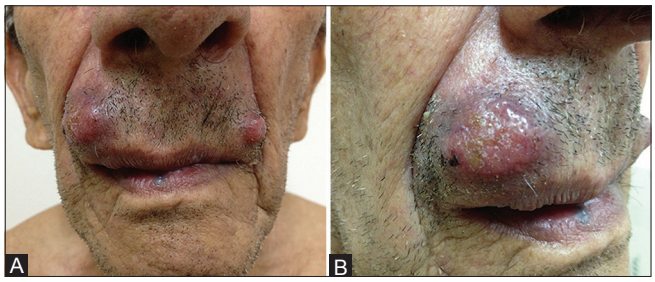

Figura 4: Caso Nº 2. Clínica. A. Lesiones tumorales localizadas en región supralabial derecha y surco nasogeniano izquierdo. B. A mayor detalle

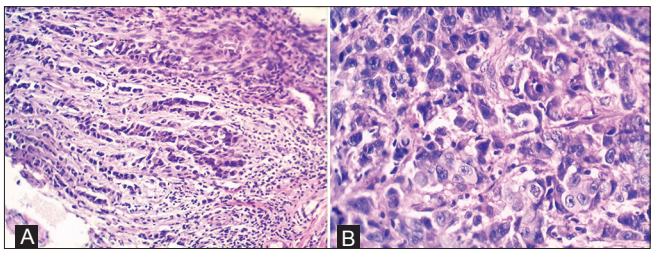

Figura 5: Caso Nº 2. Histopatología. A. Infiltración dérmica por una neoplasia maligna indiferenciada de estirpe epitelial que infiltra en forma de fila india. B. Y también remeda estructuras organoides

Examen Físico: placa eritematosa mal delimitada sobre la región de pezón y aréola de mama derecha, indurada, infiltrada (esclerodermiforme), que se extiende a piel adyacente (Figs 7A y 7B) sin signos inflamatorios.

Auxiliares de diagnóstico: Ecografía mamaria: Ausencia de imágenes nodulares, sólidas o quísticas. Discreto borramiento del tejido celular subcutáneo en la mama derecha, y un espesamiento de la piel (7mm) en las áreas periareolares del mismo lado. Se observa fina colección de líquido no cuantificable en la región retroareolar derecha, región axilar aparentemente libre. Regiones pectorales libres.

Se toma Biopsia de piel y la *Anatomía Patológica* informa: infiltración dérmica por una neoplasia maligna moderadamente diferenciada que forma luces glandulares y es mucosecretante (adenocarcinoma moderadamente diferenciado). No se observan invasiones linfáticas ni de la epidermis (Figs 8A y 8B).

Diagnóstico final: Metástasis cutánea de adenocarcinoma mamario

Los pacientes firmaron el consentimiento informado para la realizacion de las biopsias y obtencion de fotos.

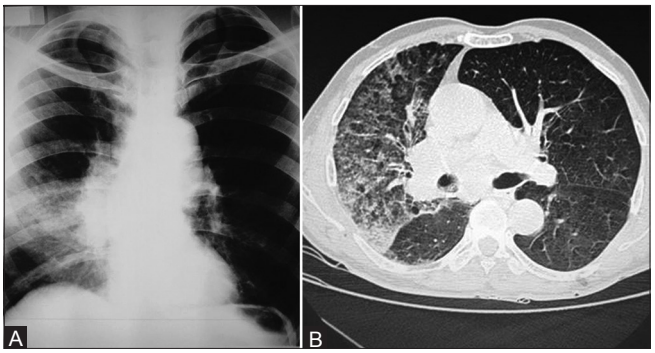

Figura 6: Caso Nº 2. Imágenes. A. Radiografía de tórax con imagen radioopaca redondeada en región parahiliar derecha. B. Tomografía computarizada de alta resolución de tórax con imagen hiperdensa redondeada en región parahiliar derecha

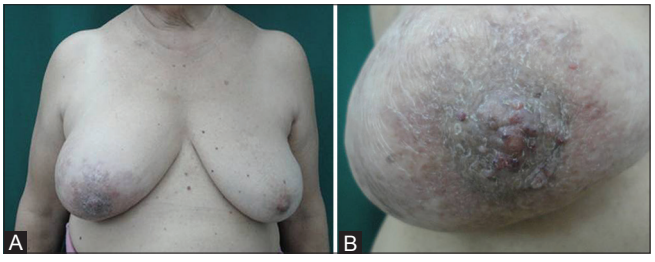

Figura 7: Caso Nº 3. Clínica. A. Placa eritematosa sobre la región de pezón y aréola de mama derecha.B. Mayor aumento de la dermatosis

COMENTARIOS

La frecuencia de metástasis cutáneas de una neoplasia se estima actualmente entre el 0.2 - 9%. Cualquier tumor tiene la capacidad de metastatizar a la piel [2,3,4,5,6,7,8]. Generalmente se trata de tumores primarios conocidos y se correlaciona con los tipos más frecuentes de cánceres primarios en cada sexo, el carcinoma de mama en la mujer y el de pulmón en el varón. En el caso de metástasis cutáneas de origen primario desconocido, el tumor es identificado en tan sólo un 27% de los casos antes del fallecimiento del paciente, en el 57% en la autopsia y en el 16% restante no se logra encontrar el origen primario ni aun mediante exámenes *post mortem*. La mayoría de los estudios han revelado que son los cánceres de pulmón y páncreas los primarios que más comúnmente se presentan inicialmente como cáncer de origen desconocido (COD).

Las metástasis cutáneas tienen un importante valor pronóstico dado que reducen sustancialmente la supervivencia [3,4,6,9].

La búsqueda del tumor primario debe constar de: historia clínica y un examen físico minucioso, exámenes de laboratorio completos, radiografía de tórax, TAC de abdomen y pelvis, tomografía por emisión de positrones (*PET scan*) y, mamografías en la mujer. La TAC sólo identifica el 10-35% de los COD, pero pone de manifiesto otros focos metastásicos [3,4].

El análisis anatomopatológico tiene una misión fundamental en la evaluación del COD a través de estudios histológicos e inmunohistoquímicos. Proporciona una orientación imprescindible, con el fin de clasificar subgrupos e identificar aquellos individuos para los que hay tratamiento eficaz. La anatomía patológica permite por un lado una aproximación diagnóstica hacia ciertos tumores concretos como linfomas, melanomas, sarcomas o tumor de células germinales, y por otro lado la agrupación del resto de los pacientes en cuatro categorías histopatológicas: neoplasias pobremente diferenciadas (5%), carcinoma de células escamosas (5%), adenocarcinomas bien o moderadamente diferenciados (60%) y carcinomas y adenocarcinomas pobremente diferenciados (30%) [4].

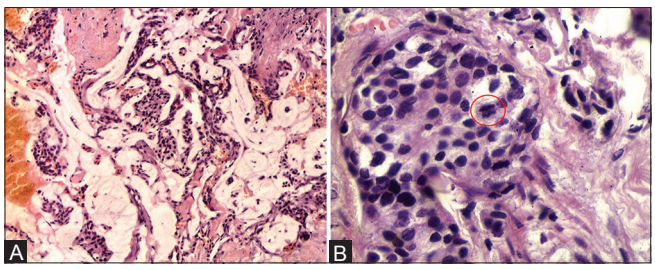

Figura 8: Caso Nº 3. Histopatología. A. Neoplasia epitelial que forma luces glandulares y produce grandes pools de moco. B. Estructuras glandulares. Una mitosis (en círculo)

Cada grupo presenta características diagnósticas, terapéuticas y pronósticas específicas. Tan sólo en las neoplasias poco diferenciadas es preciso añadir a las técnicas de inmunohistoquímica, la microscopía electrónica y el análisis citogenético. El adenocarcinoma bien o moderadamente diferenciado constituye un 60% de COD y suele tratarse generalmente de pacientes de edad media con enfermedad diseminada en el momento del diagnóstico [4].

Se considera que las localizaciones más frecuentes del tumor primario son el aparato digestivo (especialmente páncreas y árbol biliar) y el pulmón[5]. Las metástasis se localizan con mayor frecuencia en hígado, pulmón, ganglios linfáticos y hueso y muy excepcionalmente en la piel. A pesar del desarrollo de la quimioterapia en estos últimos años, se trata de una enfermedad altamente agresiva y de muy mal pronóstico, con supervivencias que oscilan entre 5-12 meses y con una mortalidad superior al 70% durante el primer año del diagnóstico [4].

La frecuencia de metástasis cutáneas es extremadamente baja, a pesar del gran tamaño de la superficie corporal y de la riqueza de vasos sanguíneos y linfáticos. Las vías de implantación de las células metastásicas en la piel son la linfática, la sanguínea, por contigüidad y la implantación por procedimientos quirúrgicos [4].

En cuanto a la semiología, pueden ser:

- nodulares,
- subcutáneas (pueden simular lesiones benignas como lipomas o quistes cutáneos),
- angiomatosas, principalmente en los carcinomas renales, pulmonares y en los coriocarcinomas,
- esclerodermiformes (la alopecia neoplásica en cuero cabelludo que puede confundirse con la alopecia cicatricial, y el carcinoma en coraza por un carcinoma mamario),
- inflamatorias, y
- eczematiformes.

Las metástasis inflamatorias, que en ocasiones semejan celulitis son generalmente procedentes de cánceres de mama, aunque también pueden aparecer si el origen

es pancreático, rectal, pulmonar u ovárico [10-14]. El denominador común responsable de las características clínicas de las lesiones es la infiltración por parte de las células neoplásicas de los vasos linfáticos dérmicos, lo cual produce clínicamente lesiones infiltradas eritematosas que semejan procesos infecciosos agudos como erisipela o celulitis [10].

Se han descrito recordando patologías benignas como eritema anular, condilomas, herpes zóster [15] quistes epidérmicos, chancros y úlceras venosas, además de lesiones cutáneas primarias a modo de queratoacantomas, carcinomas epidermoides o basocelulares [3,4].

Las metástasis de carcinomas renales pueden semejar un sarcoma de Kaposi o un granuloma piogénico [3].

El carcinoma de células transicionales y el carcinoma de próstata pueden semejar un chancro.

Ocasionalmente los adenocarcinomas metastáticos se pueden desarrollar dentro de nevus melanocíticos, generalmente en relación a carcinomas de estómago y mama. Pueden aparecer también en el seno de otras erupciones cutáneas o sobre cicatrices quirúrgicas por implantación directa y sobre localizaciones radiadas [3,4].

Las metástasis cutáneas tienden a aparecer en proximidad al tumor primario. El cuero cabelludo, el ombligo, la pared torácica y el abdomen son las localizaciones más frecuentes para las metástasis. En el 75% de los varones las metástasis afectan al cuero cabelludo, cuello, tórax y abdomen. En el 75% de las mujeres aparecen en el tórax y abdomen. Cuando se consideran los dos sexos en conjunto, el carcinoma colorrectal es la neoplasia visceral más frecuente [3].

Dentro del diagnóstico diferencial siempre se deben considerar los tumores anexiales.

El 60% de las metástasis cutáneas son adenocarcinomas y el 15% son carcinomas escamosos. Son con frecuencia menos diferenciadas que el tumor primario y pueden perder algunas de sus características inmunotintoriales.

Los adenocarcinomas de colon, pancreáticos y de vesícula suelen ser tumores bien diferenciados semejantes al primario.

Los adenocarcinomas que con mayor frecuencia producen metástasis son la mama, el tracto gastrointestinal y el pulmón [3-5].

El carcinoma renal es el más frecuente de los productores de metástasis de células claras, pero las metástasis de pulmón, hígado, ovario, endometrio, cérvix y vagina también pueden mostrar células claras.

Las metástasis de carcinoma escamoso suelen proceder de primarios pulmonares y tumores de cavidad oral y esófago. Otros primarios menos frecuentes son los de cervix uterino, pene y otros primarios cutáneos.

Las CK7 y CK20 distinguen los adenocarcinomas pulmonares y colorrectales en hasta un 95% de los casos, mostrando hasta un 75% de los carcinomas colorrectales un perfil CK7-/CK20+ y la mayoría de los adenocarcinomas pulmonares mostrando el patrón inverso (CK7+/CK20-). Los cánceres de mama muestran un patrón de citoqueratinas semejante al pulmón [3,16,17,1].El carcinoma renal muestra positividad para la CK7 en un 28% de los casos. La mayor parte de los carcinomas de próstata son negativos para CK7 y CK20. La CK20 es expresada en carcinomas colorrectales, uroteliales y en carcinomas de células de Merkel. El resumen de estos hallazgos se expone en la tab. 1.

Las CK5/6 se emplean como marcadores de diferenciación escamosa.

La correlación clínica junto con las exploraciones radiológicas, la localización de la lesión y el examen anatomopatológico son esenciales.

Los carcinomas renales son los que con mayor frecuencia dan metástasis cutáneas como primera manifestación. Son más frecuentes en cabeza y cuello, debido a la ausencia de válvulas en las venas de la columna vertebral. Generalmente aparecen como nódulos cutáneos únicos o múltiples bien delimitados, color carne, violáceos o azulados con prominente vascularidad. Sus metástasis se caracterizan por grupos de células claras, rellenas de lípidos y glucógeno, de morfología poliédrica, con el núcleo central, formando glándulas, con distribución a modo de cordones, alvéolos y formaciones tubulares, acompañado de una red vascular con extravasación de hematíes y hemosiderina [3].

Células claras semejantes pueden metastatizar a piel procedentes de pulmón, hígado, ovario, endometrio, cérvix o vagina. El marcador de carcinoma renal es un anticuerpo contra un antígeno del túbulo proximal, siendo positivos en un 80% de los casos [3,19]. Las metástasis cutáneas confieren un grave

Tabla 1: Expresión de citoqueratina 7 y 20 y orientación sobre posible localización del tumor primario (Chu *et al.* Histopathology 2002; 40: 403)

CK7+ CK20+	CK7– CK20+
Mucinoso de ovario 90%	Adenocarcinoma colorrectal 80%
Células transicionales 65%	Carcinoma de células de Merkel 70%
Adenocarcinoma de páncreas 65%	Adenocarcinoma gástrico 35%
Colangiocarcinoma 65%	
Adenocarcinoma gástrico 40%	
CK7+ CK20–	**CK7– CK20–**
Ovario no mucinoso 100%	Adrenal 100%
Tiroides los tres tipos 100%	Células germinales 95%
Mama 90%	Próstata 85%
Adenocarcinoma de pulmón 90%	Hepatocarcinoma 80%
Endometrioide de útero 85%	Adenocarcinoma renal 80%
Mesotelioma 65%	Carcinoide pulmonar e intestinal 80%
Células transicionales 35%	Microcítico y escamoso de pulmón 75%
Adenocarcinoma de páncreas 30%	Escamoso de esófago 70%
Colangiocarcinoma 30%	Escamoso de cabeza y cuello 70%
	Mesotelioma 35%

pronóstico, diferentes estudios establecen una media de supervivencia de 3 a 6 meses, con escasas diferencias respecto a si las lesiones son únicas o múltiples [20].

CONCLUSIÓN

1. Tan sólo un 2% de las neoplasias internas se manifiestan inicialmente con metástasis cutáneas.
2. Suelen aparecer en estadios avanzados de la enfermedad y se consideran de un pronóstico infausto.
3. En nuestro caso los carcinomas renal, pulmonar y de mama fueron diagnosticados a partir de las metástasis cutáneas.
4. Las metástasis de los carcinomas renales pueden simular un granuloma piogénico, por lo que la enseñanza del caso radica en la importancia de remitir a estudio patológico toda lesión de reciente aparición en pacientes oncológicos o no, en aquellas lesiones de instauración brusca que tardan en curar, con tendencia al sangrado o con apariencia vascular, que no se resuelven con tratamiento adecuado.
5. La biopsia de piel es un método accesible, rápido y útil, proporciona valiosa información del tumor primario, su origen y estirpe, y confirma su progresión o recurrencia.

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Case Report

Cervical carcinoma with skin metastasis – Case report

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ABSTRACT

Although cervical carcinoma is common, cutaneous metastasis is rare. In advanced disease, metastases may be present in the adnexa, abdomen, lungs, bone, liver and lymph nodes or. elsewhere. Cutaneous metastasis is uncommon. Unusual sites of metastasies seems to be skin, brain, heart and spleen. In this case, a 45 years old female was diagnosed to have squamous cell carcinoma of cervix on february 2013, who took radiotherapy treatment presented with cutaneous metastasis after a year. She received 4400 cGy/22 fractions of Extended Beam radiotherapy, followed by 4 doses of 700 cGy Cavity Radiotherapy (Brachytherapy). She completed her treatment on march, 6, 2013 with complete remission, without any complication. She was considered cured by the oncologists until after a year when she presented with cutaneous metastasis, which was proven with skin biopsy. The case is reported as this kind of case seems to be rare as far as our knowledge is concerned.

Key words: Cervical cancer; metastasis; extended beam radiotherapy; human papillomavirus; papanicolaou smear

INTRODUCTION

The incidence of metastasis to the skin from visceral cancer is less than 10% (0.7–9.0%) [1]. Cutaneous metastasis in women mainly arises from breast, ovary, and colon cancer. Patients with cervical carcinoma are at risk for local invasion and metastasis, most often to the lungs, bone, liver and lymph nodes [2]. However, Cervical cancer rarely metastasizes to the skin; this occurs in < 2% (0.7% to 1.3%) of patients [3]. Patients with cutaneous metastatic disease may present at the time of diagnosis or up to 10 years later [4]. Unusual metastases also occur in some patients. Patients with skin metastases are sally preterminal particularly when the primary is the lung where the time between appearance of the metastasis and death is between 1.5 and 2.6 months. In patients with carcinoma of the esophagus, the time from diagnosis to death is 4.3 months, on the average. However, metastases to the skin from primary malignant tumors involving the colon, bladder, kidney, and ovary do not necessarily represent preterminal events. The time form diagnosis to death varies from 7.3 months in carcinoma of the ovary to 12.7 months in carcinomas of the kidney. Cervical cancers can also spread locally through the angiolymphatic apparatus and very rarely metastasize to the brain [5,6]. The intracranial metastasis is a late event and a sign of poor prognosis. Even meatstasis to spleen, breasts, heart and bones (especially tibia) have also been reported so far [7-10]. Therefore, it is important to establish the primary source, the extent of the metastatic lesions and devise treatment programs that are appropriate to the pattern of the metastasis and the primary diagnosis [11].

CASE REPORT

A 45 years old female was diagnosed to have squamous cell carcinoma of cervix on February 2013. She received 4400 cGy/22 fractions of Extended Beam radiotherapy followed by 4 doses of 700 cGy Cavity Radiotherapy (Brachytherapy). She completed her treatment on march, 6, 2013 with complete remission, without any complication. She had no symptom until january, 2014, when she suddenly developed multiple, asymptomatic, rapidly progressive ulceroproliferative lesion over the perigenital areas, associated with occasional bleeding from the lesion (Figs 1 and 2). She also complained of menorrhagia, and oedema over bilateral thighs. Skin biopsy was taken from the skin lesion and was diagnosed

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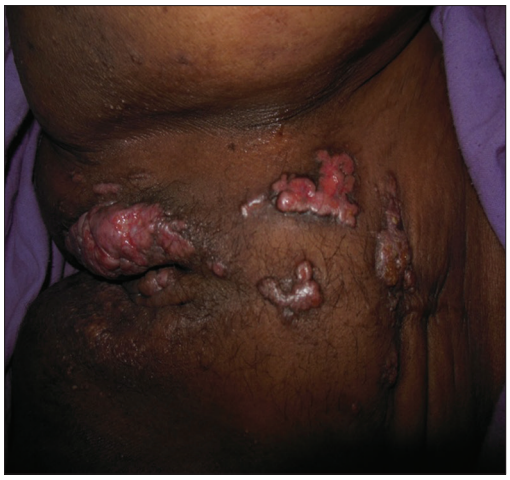

Figure 1: Patient with cevical carcima metastasized to skin

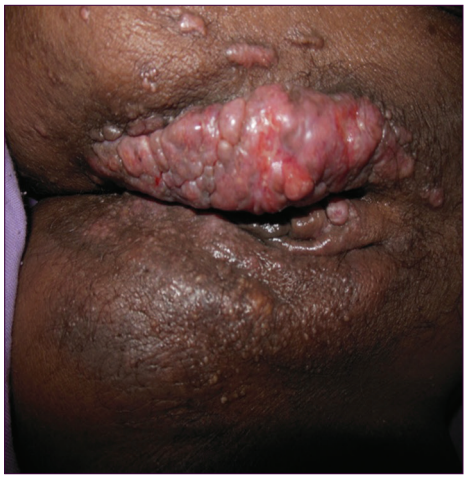

Figure 2: Patient with cervical carcimo metastasized to skin (closer view)

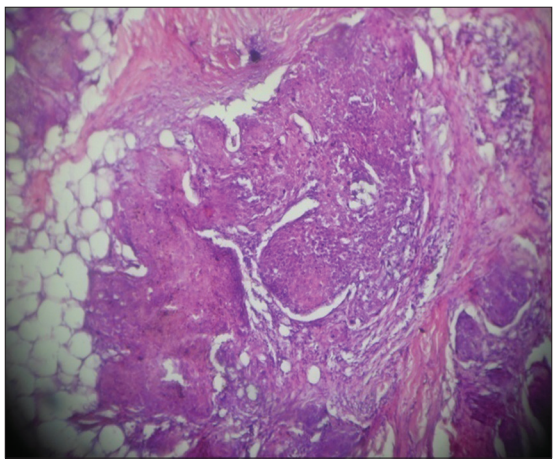

Figure 3: Hisptopathological features of the same patient (sample taken from skin lesion). Squamous invasion of dermis, replacing and damaging normal dermal architecture, infiltrating upto subcutis

to be Squamous cell carcinoma, infiltrating dermis and subcutaneous tissues (Figure 3).

The patient's informed consent was obtained.

Prior to the study, patient gave written consent to the examination and biopsy after having been informed about the procedure and aim of the study.

DISCUSSION

Cervical cancer is a malignant neoplasm arising from cells originating in the cervix uteri. Abnormal vaginal bleedingis one of the most common presentation, but in some cases there may be no obvious symptoms until the cancer has progressed to an advanced stage. Human papillomavirus (HPV) infection appears to be involved in the development of almost all cases (>90%) of cervical cancer. The cervical carcinoma may be classified based on hitology as follows: squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma, small cell carcinoma, neuroendocrine tumour, glassy cell carcinoma, villoglandular adenocarcinoma [4,12]. Most cervical cancers are squamous cell carcinomas that are arising from the squamous (flattened) epithelial cells that line the cervix. Adenocarcinoma seems to be the second most common type. Rarely, cancer can arise in other types of cells in the cervix [6]. The early stages of cervical cancer may be completely asymptomatic. Vaginal bleeding, contact bleeding, or (rarely) a vaginal mass may indicate the presence of malignancy. Also, moderate pain during sexual intercourse and vaginal discharge are symptoms of cervical cancer. Symptoms of advanced cervical cancer may include: loss of appetite, weight loss, fatigue, pelvic pain, back pain, leg pain, swollen legs, heavy bleeding from the vagina, bone fractures, and/or (rarely) leakage of urine or faeces from the vagina. In advanced disease, metastases may be present in the adnexa, abdomen, lungs, bone, liver and lymph nodes or. Elsewhere [13]. Cutaneous metastasis is uncommon. Unusual sites of metastasies seems to be skin, brain, heart and spleen. Papanicolaou smear should include rescreening programs and fluid-based technology. Once cervical cancer is diagnosed, clinical staging takes place. Protein markers for detection of recurrence and vaccines for prevention of cervical cancer are under investigation. In the past few years, researchers have introduced several new cervical cytology technologies that attempt to increase the sensitivity and decrease the false-negative rate of the conventional screening methodology. Two automated rescreening devices are presently labeled by the U.S. Food and Drug Administration: the AutoPap 300 QC (NeoPath,

Redmond, Wash) and the PapNet (Neuromedical Systems, Suffern, N.Y.). Both are intended to identify possible false-negative results in previously manually screened Pap smears [14]. Wentz and Reagan divided cervical squamous carcinomas into three cell types: large cell keratinizing, large cell nonkeratinizing, and small cell [13]. Large cell keratinizing squamous carcinoma is characterized by sheets and nests of cells with abundant cytoplasm, large pleomorphic nuclei and inconspicuous nucleoli. Keratin pearls and intercellular bridges are evident. Mitotic figures are noted occasionally, and the growth pattern is largely infiltrative [15]. Large cell nonkeratinizing squamous carcinoma has large cells of similar size and shape. The cytoplasm is moderate in amount, eosinophilic to amphophilic, some having individual cell keratinization with distinct cell borders. By definition keratin pearl formation should be absent. Nucleoli are prominent and mitotic figures are common. The invasive edge is often smooth [16]. Small cell squamous carcinoma is characterized by loosely cohesive nests and sheets of small to medium sized cells with hyperchromatic nuclei, scant cytoplasm and small nucleoli. Keratinization is minimal or absent, and mitotic figures are abundant. The nuclear chromatin is finely to coarsely granular, and small nucleoli are often evident. Crush artifact and nuclear smudging are not prominent. The nuclear cytoplasmic ratio is lower than small cell anaplastic carcinoma. The cell borders are also more distinct. Rare cytoplasmic keratinization also belies the squamous nature of the lesion [15,16]. Early-stage tumors can be managed with cone biopsy or simple hysterectomy. But the problem with any surgical procedure is, although rare, the incisional site metastasis can bea complication of cervical carcinoma especially of the squamous type [10]. Higher stage tumors can be treated surgically or with radiotherapy. Advanced metastatic disease may respond to radiation therapy and concurrent chemotherapy.

To conclude, let us look into some management in a precise manner. Stage 0: Carcinoma in situ (stage 0) is treated with local ablative or excisional measures such as cryosurgery, laser ablation, and loop excision; surgical removal is preferred. Stage IA1: The treatment of choice for stage IA1 disease is surgery; total hysterectomy, radical hysterectomy, and conization are accepted procedures. Stage IA2, IB, or IIA: Combined external beam radiation with brachytherapy and radical hysterectomy with bilateral pelvic lymphadenectomy for patients with stage IB or IIA disease; radical vaginal trachelectomy with pelvic lymph node dissection is appropriate for fertility preservation in women with stage IA2 disease and those with stage IB1 disease whose lesions are 2 cm or smaller Stage IIB, III, or IVA: Cisplatin-based chemotherapy with radiation is the standard of care. Stage IVB and recurrent cancer: Individualized therapy is used on a palliative basis; radiation therapy is used alone for control of bleeding and pain; systemic chemotherapy is used for disseminated disease [17].

In conclusion, although cervical carcinoma is a common disease, its metastasis to the skin is a rare entity. Even after diagnosis, its treatment especially surgical intervention seems to be risky as the incision site itself may lead to further metastasis.

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patient for publication of this article.

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Case Report

Mycosis fungoides: The great imitator

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ABSTRACT

Introduction: Mycosis fungoides although a cutaneous T-Cell lymphoma can immitate many dermatological disorders. A 60 year old man presented to our hospital with generalized annular plaques, few with verrucous surface. The annular lesions imitated Psoriasis, Tinea, Syphilis and the diagnosis was in dilemma. Histopathology gave the light and path to diagnosis. **Case report:** A 60 year old man presented with complains of erythematous scaly lesions since 20 year, Lesions were initially flat and erythematous which later became ulcerated, crusted and painful. H/O exacerbation and remission was present. **Conclusions:** Mycosis Fungoides is a great imitator both clinically and histopathologically. We are presenting a case report of patient with Mycosis Fungoides, Stage IIA.

Key words: Cutaneous T cell lymphoma; lymphoma; NB-UVB

INTRODUCTION

In the ocean of similar dermatological manifestations it is very important to keep an eye of eagle to diagnose a case. A patient presenting as chronic plaques psoriasis, which on investigation turned out to be Mycosis Fungoides.

CASE REPORT

A 60 year old man presented with multiple erythematous scaly plaques with ulcerations all over the body since 20 years. There was history of exacerbation and remission. Patient was treated by various doctors on the lines of Psoriasis and Tinea corporis without any improvement in patient condition. No history of recurrent fever or weight loss.

Mucocutaneous examination

Multiple erythematous scaly plaques with circinate margins present over extremities and trunk with ulcerations (Figs 1A and B). Hyperpigmented patches were present over the trunk in bathing trunk pattern (Fig. 2).

Multiple verrucous plaques present over the palms with ulceration and over dorsal aspect of feet (Figs 3A and B). Auspitz sign was negative. Lymph nodes.

Left inguinal lymph nodes enlarged approx 1 × 1 cm, soft and mobile with no dermopathic changes.

The patient's informed consent was obtained.

INVESTIGATIONS

Complete blood count, Liver function test, Renal function test-were within normal limits. Peripheral Smear - Normal blood picture, no evidence of Sezary cells. KOH MOUNT - Negative for fungal filaments; V.D.R.L - Negative; H.I.V-I AND II – Negative; CT and M.R.I was advised but was deferred as the patient was not affordable. FNAC - Negative for atypical lymphoid cells.

SKIN BIOPSY - Showed moderately dense superficial perivascular patchy lichenoid infiltrate of lymphocytes with mild spongiosis within the epidermis. The epidermis shows slight psoriasiform hyperplasia and infiltration by numerous large lymphocytes without much spongiosis. The stratum corneum shows elongated mounds of parakeratosis. Several lymphocytes are aligned along the basal layer in toy soldier pattern. The papillary dermis shows thickening of collagen bundles that appear wiry.

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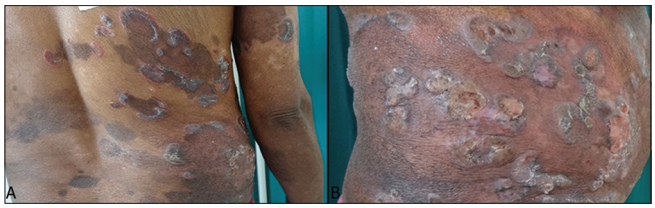

Figure 1: (A and B) Multiple erythematous annular plaques with hyperpigmented patches and ulcerations

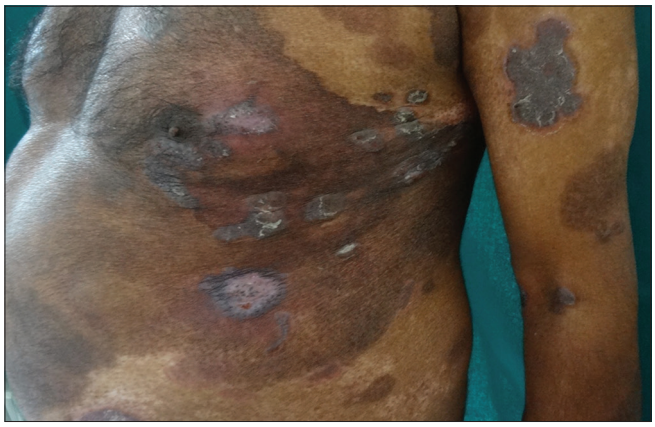

Figure 2: Hyperpigmented patches were present over the trunk in bathing trunk pattern

The above features are suggestive of plaque type of mycosis fungoides (Figs 4A and B).

Prior to the study, every patient gave written consent to the examination and biopsy after having been informed about the procedure.

Differential diagnosis

1. Tinea Corporis
2. Chronic Plaques Psoriasis
3. Secondary Syphilis
4. Mycosis fungoides

Treatment

Patient was started on radiation therapy (NB-UVB), with topical steroids.

Outcome and follow-up

The lesion stopped spreading and improved but the patient was lost for the follow up.

DISCUSSION

Mycosis fungoides (MF) and the Sezary syndrome are a group of extranodal non-Hodgkin's lymphomas

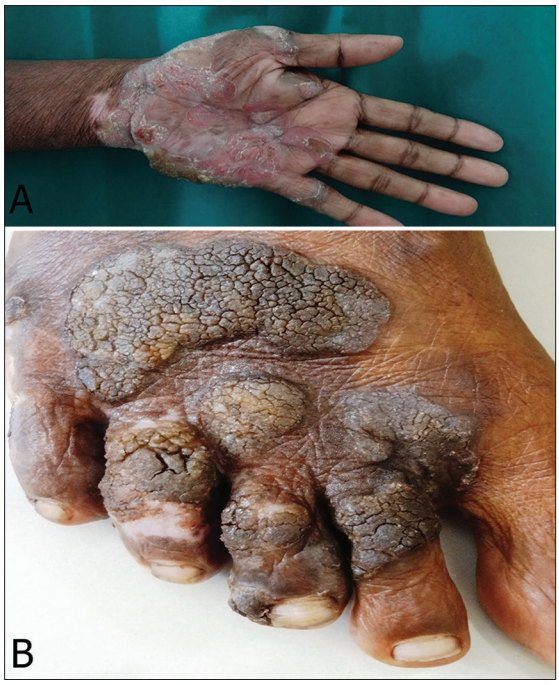

Figure 3: (A and B) Multiple verrucous plaques were present over the palms and dorsal aspect of feet

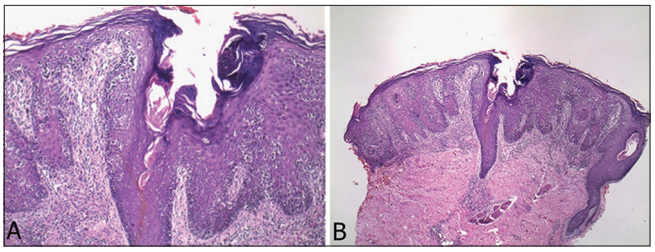

Figure 4: (A, B) Histopathological pictures showing moderately dense superficial perivascular patchy lichenoid infiltrate of lymphocytes with mild spongiosis within the epidermis. The epidermis shows slight psoriasiform hyperplasia and infiltration by numerous large lymphocytes without much spongiosis. The stratum corneum shows elongated mounds of parakeratosis. Several lymphocytes are aligned along the basal layer in toy soldier pattern. The papillary dermis shows thickening of collagen bundles that appear wiry

of T-cell origin with primary cutaneous involvement. The group differs from other primary cutaneous T-cell lymphomas (CTCL) by its unique clinical features and histopathology [1].

In its early stages, it mimics many common benign dermatoses, and hence a definitive diagnosis can be delayed. The affected T cells are of CD4+ phenotype with loss of CD7 (pan-T-cell antigen) and demonstrate T-cell receptor (TCR) rearrangement. The prognosis of patients with MF is highly dependent on the extent and type of skin involvement. The initial cutaneous presentation of MF can be patches, plaques, tumors, or erythroderma. Patients who present with limited patch/

plaque disease have good prognosis with an overall long-term survival that is similar to the expected survival of a matched control population whereas Patients with hypopigmented mycosis fungoides (HMF) present at a younger age in contrast to those with classic MF [2].

Patients presenting with limited or generalized patch/plaque type disease without peripheral lymphadenopathy can rarely exhibit extracutaneous involvement. Therefore, the staging evaluation differs for patients with MF compared to patients with other non-Hodgkin's lymphomas. Patients with tumorous or erythrodermic type of skin involvement have a less favorable prognosis, while those presenting with extracutaneous disease have a poor prognosis. Myriad of therapeutic options are available for patients with MF and the Sezary syndrome.

Selection of a specific treatment plan is based primarily on the clinical stage of the disease.

Variants and subtypes

Folliculotropic mycosis fungoides - occurs in adults and men are most commonly affected. Presents as grouped erythematous follicular papules, acneiform lesions with severe pruritis, indurated plaques and rarely it is associated with non-scarring alopecia. Characteristic lesions are hairless infiltrated plaques.

Pagetiod Reticulosis-Localized types is characterized by presence of a single asymptomatic, psoriasiform, hyperkeratotic or circinate plaques on the extremities. Granulomatous Slack. Skin-occurs mostly in adult men. The flexure shows area of pendulous lax skin associated with Hogkins Lymphoma has been reported [3].

Staging

Various types of staging systems are done for Mycosis Fungoides. Two important once are TNM staging (Table 1) and Bunn and lambert system (Table 2) which involves clinical findings like body surface area involved, lymph node status and erythroderma. Staging of Mycosis Fungoide makes it easier to prognosticate and to make a treatment plan.

Differential diagnosis

The differential diagnosis with Tinea corporis was ruled out on the basis of KOH mount as it was negative. Seconadry syphilis was ruled out by V.D.R.L negativity. There was no histopathological correlation with Chronic plaque psoriasis and there is no evidence that early aggressive systemic therapy is preferable to conservative therapy in the management of limited disease. Anticonvulsants such as carbamazepine, phenytoin, phenobarbital and valproic acid are the major offenders [4]. Out of these Carbamazepine induced pseudo-MF is the common one [5,6]. Drugs like Gleevec, protein tyrosine kinase inhibitor used in the treatment of chronic myelogenous leukemia, melanoma and gastrointestinal stromal tumor are also implicated [7].

Treatment

Topical therapy is the main stay of treatment for patch/plaque type without extracutaneous involvement, whereas chemotherapy and other aggressive systemic regimens are reserved for recalcitrant disease or extracutaneous involvement [8]. Various treatment modalities (Table 3) are available for treatment of

Table 1: Stages of Mycosis Fungoides. TNMB Classification of Mycosis Fungoides and Sezary Syndrome

TNMB Classification of Mycosis Fungoides and Sezary Syndrome	
T (skin)	
TI	Limited patch/plaque (involving<10% of total skin surface)
T2	Generalized patch/plaque (involving>10% of total skin surface)
T3	Tumor(s)
T4	Erythroderma
N (lymph node)	
N0	No enlarged lymph nodes
N1	Enlarged lymph nodes, histologically uninvolved
N2	Enlarged lymph nodes, histologically involved (nodal architecture unaffected)
N3	Enlarged lymph nodes, histologically involved (nodal architecture effaced)
M (viscera)	
M0	No visceral involvement
M1	Visceral involvement
B (blood)	
B0	No circulating atypical (Sezary) cells or <5% of lymphocytes
B1	Low blood tumor burden (>5% of lymphocytes are Sezary cells, but not B2)
B2	High blood tumor burden (1000/mL Sezary cells+positive clone)

Table 2: Stages of Mycosis Fungoides. Bunn and Lambert system

Bunn and lambert system	Clinical findings	Tumor-node-metastasis stage
IA	<10% BSA patch/plaque	T1 N0
IB	>10% BSA patch/plaque	T2 N0
IIA	Patch or plaque with palpable nodes without histological involvement	T1/2 N1
IIB	Cutaneous tumours with or without palpable nodes	T3 N0/1
III	Erythroderma with or without palpable nodes	T4 N0/1
IVA	Non-palpable or palpable nodes with histological involvement	T-any N2/3
IVB	Visceral involvement	T-any N-any M1

Table 3: Treatment of mycosis fungoides/Sezary syndrome

Stage	First line	Second line	Experimental	Not suitable
IA	Skin-directed therapy or no therapy	Skin-directed therapy or no therapy	Bexarotene gel	Chemotherapy
IB	Skin-directed therapy	α-Interferon+PUVA, Total skin electron beam	Denileukin Diftitox, Bexarotene	Chemotherapy
IIA	Skin-directed therapy	α-Interferon+PUVA, Total skin electron beam	Denileukin Diftitox, Bexarotene	Chemotherapy
IIB	Radiotherapy/total skin electron beam, chemotherapy	α-Interferon, Denileukin Diftitox, Bexarotene	Autologous PBSCT, mini-allograft	Cyclosporin
III	PUVA +α interferon,Extracorporeal photopheresis +α Interferon, methotrexate	Total skin electron beam, Bexarotene, Denileukin, Diftitox, chemotherapy, Alemtuzumab	Autologous PBSCT, mini-allograft	Cyclosporin
IV A	Radiotherapy/Total skin electron beam, chemotherapy	α-Interferon, Denileukin Diftitox, Alemtuzumab, Bexarotene	Autologous PBSCT, mini-allograft	Cyclosporin
IV B	Radiotherapy, chemotherapy	Palliative therapy	Mini-allograft	-

Abbrevations: PBSCT - Peripheral blood stem cell transplant; PUVA - Psoralen ultraviolet A; Skin-directed therapy including topical Emollients, Steroids, Mechlorethamine, Carmustine, Bexarotene gel, UVB/PUVA, Superficial Radiotherapy. Stage III includes Sezary syndrome, although some casesare seen in stage IVA. ECP is ideal for those patients with peripheral blood involvement. (From the joint BAD and UKCLG guidelines for Primary CTCL)

Mycosis Fungoides. Our patient was treated with topical steroids and Radiation therapy in the form of NB-UVB which led to improvement of lesions.

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The examination of patients is conducted according to the Declaration of Helsinki principles.

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Review Article

Hepatitis B and skin: review

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ABSTRACT

Hepatitis B virus (HBV) infection and its complications have become a global health problem. The spectrum of HBV infection ranges from asymptomatic carrier state to chronic hepatitis. It is usually preceded by constitutional symptoms. It has a wide range of dermatological manifestations. This review includes the pathogenesis along with the pathophysiology with their clinical significance and overview of the treatment.

Key words: Hepatitis B; Concomitant infection; Re-infection; steatorrhea

Hepatitis B virus (HBVDNA virus), a double-shelled virion (surface and core), is a member of the hepadnavirus family, classified as hepadnavirus type-1. It is a partially single stranded, partially double-stranded. The spectrum of HBV infection ranges from asymptomatic carrier state to chronic hepatitis, which may progress to cirrhosis and end-stage liver disease. It is estimated that 15-40% of people with chronic HBV will progress to cirrhosis [1,2].

EPIDEMIOLOGY

Hepatitis B virus (HBV)infection and its complications have become a global health problem. Approximately 400 million people are chronic HBV carriers worldwide.

Age

The severity of a hepatitis B virus (HBV)infection seems to be related with age. Fortunately, majority (around 95%)of adults and older children who are infected with HBV clear the virus within four months after they get infected. The rest progress to chronic state. Chronic infection with HBV is more common in infants and children. Around ninety percent of infants who are infected with hepatitis B during delivery are expected to become chronically infected with the virus [1-4].

Serotypes and genotypes

Genotype A is most commonly found in the US, Africa, India and Europe. Genotype B and C are most commonly found in Asia and US. Genotype D is most commonly found in Southern Europe, Turkey, India and US. Type E is most commonly found in West and Southern Africa. Type F is most commonly found in Central and South America. Genotype G is found in France and US. Type H is most commonly found in Central and South America and US [1-6].

TRANSMISSION

Hepatitis B can be transmitted sexually, through injection drug use, during delivery of an infant and through other types of blood exposure, fomites (toothbrushes, razors, etc). HBV can remain infectious outside of the body for up to seven days [2-9].

HIGH RISKS GROUP

High risks group includes people with multiple sex partners, previously infected with STD, homosexual men, people who have a sexual partner with hepatitis, people who are addicted to injection drugs or who have partners who use them, people who share a household with someone chronically infected with hepatitis, Health care workers, Dialysis patients, patients with

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HCV and HIV infections and patient who is taking immunosuppressive or cytotoxic therapy [2-9].

PATHOGENESIS

The mechanism of extrahepatic syndromes seen with chronic viral hepatitis appears to be immune-mediated, including deposition of circulating immune complexes, induction of local immune complex formation by viral antigens, reaction with tissue antigens by viral-induced auto antibodies or direct viral reaction to extrahepatic tissue sites [7-11].

Concomitant infection

Hepatitis D (HDV) can occur only with a concomitant hepatitis B infection, because HDV uses the HBV surface antigen to form a capsid. Co-infection with hepatitis D increases the risk of liver cirrhosis and liver cancer [7-11].

Reactivation

Hepatitis B virus DNA persists in the body after infection and in some people the disease recurs. Reactivation is seen in following alcohol or drug use, people with impaired immunity, Males with baseline ALT of 200 UL/L are three times more likely to develop a reactivation than people with lower levels, people who undergo chemotherapy have a higher risk, Immunosuppressive drugs favor increased HBV replication while inhibiting cytotoxic T cell function. Although those with detectable HBs Ag in their blood are at the greatest risk, those with only antibodies to the core antigen are also at risk [4-11].

CLINICAL FEATURES

The incubation period of Hepatitis B is 30– 180 days (mean 60 – 90 days).

Dermatological signs and symptoms [12-22]

1. **Jaundice**
   This is yellow discolouration of sclera ad/or skin due to deposition of bilirubin. Jaundice is usually visible in the sclera or skin when the serum bilirubin value is >43 mol/L (2.5 mg/dL).
2. **Pruritus**
   This is due to deposition of bile salts and toxins which are not metabolized due to impaired liver function. It tends to be generalized, but worse on the hands and feet. Although the severity of pruritus is not directly associated with the level of bile salts and toxic substances, lowering bile salt levels can mitigate symptoms.
3. **Spider angiomas**
   Spider angiomas or spider nevi, are collections of dilated blood vessels near the surface of the skin. They appear as slightly raised, small, reddish spots from which fine lines radiate outward, giving them a spider-like appearance.
4. **Bier spots**
   Bier spots are small, irregularly shaped, hypopigmented patches on the arms and legs. They are likely due to venous stasis associated with functional damage to the small vessels of the skin.
5. **Paper-money skin**
   Paper-money skin (or "dollar-paper" markings) describes the condition in which the upper trunk is covered with many randomly scattered, needle-thin superficial capillaries. It often occurs in association with spider angiomas.
6. **Palmer erythema**
   It occur anywhere on the palm and fingers but is most common on the hypothenar eminence. It can occur in a number of liver conditions but most often with cirrhosis.
7. **Xanthelasma**
   It is a localized cholesterol deposit beneath the skin, often presents as a painless, yellowish, soft plaque with well-defined borders, which may enlarge over the course of weeks. Several liver diseases can lead to various forms of secondary dyslipoproteinemia leading to this condition.
8. **Bleeding, petechiae and bruising**
   Liver disease can cause hypersplenism and thrombocytopenia and decrease in clotting factors. These may present purpura, bleeding gums and easy bruising and bleeding, even with minor trauma.
9. **Hyperpigmentation of the skin**
   It may accompany cirrhosis.
10. **Dupuytren contracture**
    Dupuytren contracture is characterized by progressive fibrosis and thickening of tendons in the palmar fascia, the connective tissue that lies beneath the skin of the palms. It is seen in cirrhosis. The reason behind this is still to explore.
11. **Disseminated superficial porokeratosis**
    Both humoral and cell-mediated immune responses are impaired in liver disease which favors development of porokeratosis. These lesions can

transform into squamous cell carcinoma.

12. **Granuloma annulare**
    It is not only associated with hepatitis B infection, is also reported with hepatitis B vaccination [17,18].
13. **Lichenoid eruption**
    Although this is not directly associated with Hepatitis B infection, it is reported to be associated with hepatitis B vaccination [19,20].
14. **Alopecia**
    Alopecia is also reported to be associated with both HBV and HCV infections [21].
15. Other reported associated skin diseases are Giannoti-crosti syndrome, serum sickness, urticaria and angioedema, EM-Like lesions and Polyarteritis Nodosa.
16. **Hair changes**
    Patients with hepatocellular dysfunction may develop hair-thinning or hair loss.
17. **Nail changes**
    Nail changes are seen such as clubbing, leukonychia (whitening), or onycholysis, Terry's nail, affecting the nails of the hands and feet.

Extra hepatic sites

Hepatitis B may affects extra hepatic sites, including lymph nodes, bone marrow, circulating lymphocytes, spleen, and pancreas [23-26].

Constitutional symptoms

Approximately 70% of people who become infected with hepatitis B will show some symptoms, usually within three months of infection and may include jaundice (yellowing of the skin/whites of the eyes), fatigue, abdominal pain, loss of appetite, nausea, vomiting, joint pain, low grade fever and flu-like symptoms. In general, children are less likely to experience symptoms than adults [3-7,12-17,23-26].

INVESTIGATIONS

Blood

Neutropenia and lymphopenia are transient and are followed by a relative lymphocytosis. Atypical lymphocytes (varying between 2 and 20%)are common during the acute phase. Blood sugar should be checked as prolonged nausea and vomiting, inadequate carbohydrate intake and poor hepatic glycogen reserves may contribute to hypoglycaemia. The serum aminotransferases aspartate aminotransferase (AST) and ALT (previously designated SGOT and SGPT) show a variable increase during the prodromal phase of acute viral hepatitis and precede the rise in bilirubin level. The acute level of these enzymes, however, does not correlate well with the degree of liver cell damage. Mild elevation of the gamma globulin is common during acute viral hepatitis. Serum alkaline phosphatase may be normal or only mildly elevated, while a fall in serum albumin is uncommon. Measurement of the prothrombin time (PT)is important in patients with acute viral hepatitis, for a prolonged value may reflect a severe hepatic synthetic defect, signify extensive hepatocellular necrosis, and indicate a worse prognosis [14-16,23].

Stool and urine examination

May be done as mild and transient steatorrhea as well as slight microscopic hematuria and minimal proteinuria are seen in some patients[14,15].

Serology

1. **Serum IgG and IgM levels**
   They are elevated in viral hepatitis. IgM reflects acute infection. During the acute phase of viral hepatitis, antibodies to smooth muscle and other cell constituents may be present and low titers of rheumatoid factor, nuclear antibody and heterophil antibody can also be foundoccasionally [14,23-27].
2. **Antibodies to LKM**
   They may be positive in case of Hepatitis D.
3. **HBsAg**
   A diagnosis of HBV infection may be made by detection of HBs Ag in serum. The titer of HBsAg bears an inverse with the degree of liver cell damage [14,15,23-27].
4. **IgM anti-HBc**
   The levels of HBs Ag may be too low to be detected during acute HBV infection, even with contemporary, highly sensitive immunoassays. In such cases, the diagnosis can be made by detection of IgM anti-HBc [14,15,23-27].
5. **HbeAg**
   It is an indicator of relative infectivity. HBeAg testing is indicated primarily during follow-up of chronic infection because HBeAg is invariably present during early acute hepatitis B [14,15,23-27].
6. **Anti-HBs**
   This is rarely detectable in the presence of HBsAg in patients with acute hepatitis B, but 10–20% of persons with chronic HBV infection may harbor

low-level anti-HBs. It has no recognized clinical significance. After immunization with hepatitis B vaccine, which consists of HBsAg alone, anti-HBs is the only serologic marker to appear [14,15,23-27].

7. **PCR assay**
   PCR assay can detect as few as 10 or 100 virions/mL. The commercially available PCR assay is the most useful, with highest sensitivity (5–10 IU/mL)and the largest dynamic range (10^0–10^9 IU/mL). With increased sensitivity, amplification assays remain reactive well below the threshold for infectivity and liver injury [14,15,23-27].

TREATMENT

Most cases of typical acute viral hepatitis do not require specific treatment.

Pruritus

It is very resistant to therapy. Cholestyramine at a starting dose of 4 g/day, gradually increased to 24 g/day in two doses at mealtimes. If the pruritus does not respond adequately to cholestyramine or the patient cannot tolerate the drug, then the antituberculosis drug rifampin can be tried. Rifampin promotes metabolism of endogenous pruritogens and has been effective against cholestatic pruritus when started at 150 mg/day and increased up to 600 mg/day, depending on the clinical response. Third-line drug therapies include opioid antagonists such as naltrex one and nalmefene. Plasmapheresis can be considered if drug therapy fails. The other options include antioxidant treatment, light therapy and even Liver transplantation for intractable pruritis when all other options failed [27-32].

Fulminant hepatitis

The goal of therapy is to support the patient by maintenance of fluid balance, support of circulation and respiration, control of bleeding, correction of hypoglycemia and treatment of other complications. Protein intake should be restricted. Oral lactulose or neomycin may be administered. Glucocorticoid, exchange transfusion, plasmapheresis, human cross-circulation, porcine liver cross-perfusion, hemoperfusion and extracorporeal liver-assist devices have not been proven to enhance survival. The prophylactic antibiotic coverage improves survival. Orthotopic liver transplantation shows excellent results in patients with fulminant hepatitis [27-32].

Pharmacological therapy

The drugs which have been approved for treatment of chronic hepatitis includes injectable interferon (IFN) and oral agents such as lamivudine, adefovir dipivoxil, entecavir, telbivudine and tenofovir [27-32].

Lamivudine

The nucleoside analogues approved, the dideoxynucleoside lamivudine, inhibits reverse transcriptase activity of both HIV and HBV and is a potent and effective agent for patients with chronic hepatitis B. The daily doses of 100 mg for 48–52 weeks suppressed HBV DNA by a median of approximately 5.5 log10 copies/mL and to undetectable levels, as measured by PCR amplification assays [27-32].

Interferon

IFN- was the first approved therapy for chronic hepatitis B. It is no longer used to treat hepatitis B. For immunocompetent adults with HBeAg-reactive chronic hepatitis, a 16-week course of IFN given subcutaneously at a daily dose of 5 million units, or three times a week at a dose of 10 million units, results in a loss of HBeAg and hybridization-detectable HBV DNA (i.e. a reduction to levels below 105 –106 virions/mL)in 30% of patients, with a concomitant improvement in liver histology. Seroconversion from HBeAg to anti-HBe occurs in approximately 20 [27-32].

Adefovir Dipivoxil

The oral dose of 10 mg per day of Acyclic nucleotide analogue Adefovir dipivoxil, the prodrug of adefovir, reduces HBV DNA by approximately 3.5–4 log10 copies/mL, with resulted in histologic improvement in 2/3rd, normalization of ALT in 3/4th and suppression of HBV DNA to PCR-undetectable levels in ½ to 2/3rd of the patients [27-32].

Pegylated Interferon

In HBeAg-reactive chronic hepatitis B, comparative studies were done, one with PEG IFN- 2b, 100 g weekly for 32 weeks, then 50 g weekly for another 20 weeks for a total of 52 weeks; compared with combination PEG IFN with oral lamivudine; and the other was on PEG IFN- 2a, 180 g weekly for 48, compared with lamivudine monotherapy and combination PEG IFN plus lamivudine. Although the combination of PEG

IFN and lamivudine was superior at the end of therapy in one or more serologic, virologic or biochemical outcomes, neither the combination arm (in both studies) nor the lamivudine monotherapy arm (in the PEG IFN- 2a trial) demonstrated any benefit compared to the PEG IFN monotherapy arms 6 months after therapy [27-32].

Entecavir

Entecavir, an oral cyclopentyl guanosine analogue polymerase inhibitor, (the most potent of the HBV antivirals so far according to most of the studies), is not only just as well tolerated as lamivudine, with a dose of 0.5 mg daily orally, also effective against lamivudine-resistant HBV infection. It has had an excellent safety profile; doses need not be reduced in patients with reduced creatinine clearance. Entecavir has low-level antiviral activity against HIV and should not be used as monotherapy to treat HBV infection in HIVHBV co-infected persons [27-32].

Telbivudine

Telbivudine, a cytosine analogue with oral daily dose of 600 mg, appears to be similar in efficacy to entecavir; however it is slightly less potent in suppressing HBV DNA. Although it is well tolerated, it is associated with a low frequency of asymptomatic creatine kinase elevations and with a very low frequency of peripheral neuropathy; frequency of administration should be reduced for patients with impaired creatinine clearance [27-32].

Tenofovir

Tenofovir disoproxil fumarate, an acyclic nucleotide analogue and potent antiretroviral agent used to treat HIV infection, with an oral once-daily dose of 300 mg for 48 weeks, is similar to adefovir but more potent in suppressing HBV DNA and inducing HBeAg responses (according to most of the studies). It seems to be highly active against both wild-type and lamivudine-resistant HBV and active in patients whose response to adefovir is slow and/or limited [27-32].

PREVENTION

Passive immunoprophylaxis

This is done either with standard Immunoglobulins, containing modest levels of anti-HBs or hepatitis B immunoglobulin (HBIG), containing high-titer anti-HBs [27-32].

Active immunization

These includes

1. Purified, noninfectious 22-nm spherical forms of HBsAg derived from the plasma of healthy HBsAg carriers
2. Plasma-derived vaccine, supplanted by a genetically engineered vaccine derived from recombinant yeast, consisting of HBsAg particles that are nonglycosylated but are otherwise indistinguishable from natural HbsAg.

Pre-exposure prophylaxis

It is indicated for health workers exposed to blood; hemodialysis patients and staff; residents and staff of custodial institutions for the developmentally handicapped; injection drug users; inmates of long-term correctional facilities; persons with multiple sexual partners; persons such as hemophiliacs who require long-term, high-volume therapy with blood derivatives; household and sexual contacts of HBsAg carriers; persons living in or travelling extensively in endemic areas; unvaccinated children under the age of 18; unvaccinated children who are immigrants from endemic countries [27-32].

Dose

Three IM (deltoid, not gluteal)injections of hepatitis B vaccine are recommended at 0, 1 and 6 months. Pregnancy is not a contraindication to vaccination.

Precautions

To reduce the risk of sexual transmission, it is important to use condoms every time you have sex. Avoiding sharing personal items that may have become contaminated with blood, such as toothbrushes or razor blades, is also essential. HBV can remain infectious outside of the body for up to seven days, so it is important always wear gloves when cleaning up blood - even if it has dried. A 1:10 solution of bleach and water can be used to kill the virus on most surfaces [27-32].

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Review Article

Alopecia areata: medical treatments

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ABSTRACT

Alopecia areata (AA) is a non-scarring, autoimmune, inflammatory, relapsing hair loss affecting the scalp and/or body. In acute-phase AA, CD4+ and CD8+ T cells infiltrated in the juxta-follicular area. In chronic-phase AACD8+ T cells dominated the infiltrate around hair bulbs which contributes to the prolonged state of hair loss. Treatments include mainly corticosteroids, topical irritants, minoxidil, cytotoxic drugs and biologicals. This review highlights mainly the pathomechanism and pathology, classifications and associated diseases with regard to their importance for current and future treatment.

Key words: Alopecia areata; Pelade; Area Celsi; NKG2D-activating ligands

INTRODUCTION

Alopecia areata (AA) is a non-scarring, autoimmune, inflammatory, relapsing hair loss affecting the scalp and/or body. It is also known as Pelade or Area Celsi. It is commonly manifests as a sudden loss of hair in localized areas [1-3].

PATHOMECHANISM

In acute-phase AA, CD4+ and CD8+ T cells infiltrated in the juxta-follicular area. In chronic-phase AACD8+ T cells dominated the infiltrate around hair bulbs which contributes to the prolonged state of hair loss. It is postulated that the characteristic T cell "swarm of bees" infiltrate seen in alopecia areata is the result of T cells attracted to the hair follicle by NKG2D-activating ligands [1-5,7-9,11-14,19,20].

Alopecia areata may be associated with HLA-DQ3, DQ7, DR4 and DR11, Thyroid dysfunctions, Psychological problems, Atopy, Pernicious anemia, infections, including H. pylori, Vitamin D deficiency, autoimmune polyglandular syndrome type 1 (APS1), Immune thrombocytopenia and alopecia areata. Coexistence of psoriasis and alopecia areata with trachyonychia in Turner Syndrome has also been reported. Interferon alpha-2b and ribavirin therapy, possibly due to the collapse of hair follicle immune privilege [1-5,7-9,11-14,15,17,19,20].

HISTOLOGY

The early stage of AA is characterized by the presence of CD^{+4} and CD^{+8} T lymphocytic infiltration in the peribulbar region. The late stage is characterized by numerous miniaturized hair follicles [1-3].

CLASSIFICATIONS

Based on sites and extend of AA:

1. Diffuse Alopecia areata: When hair lost more diffusely over the whole scalp.
2. Alopecia areata multilocularis: shows multiple areas of hair loss.
3. Alopecia monolocularis: when hair loss is only in one spot which may be in anywhere of the scalp of the head.
4. Alopecia areata barbae: when the disease is only limited only in the beard.
5. Alopecia areata totalis: When patient loss all his hair.
6. Alopecia areata universalis: When hair is lost from all the body including the public hair.

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Based on pattern of AA:
1. Restricted to scalp - Patchy, Ophiasis, Sisapho, Reticulate, Diffuse, Subtotal and Alopecia totalis
2. Generalized
3. Alopecia universalis

Based on Ikeda's type:
1. Atopic type
2. Autoimmune type
3. Prehypertensive type
4. Common type

The poor prognostic indicators include early age of onset, extensive (>50%)scalp involvements, loss of eyebrows and eyelashes, Alopecia totalis, Alopecia universalis, recurrent episode, Patterns: ophiasis, sisaphio, reticular, Nail changes: pits, onychodystrophy, onycholysis, anonychia. Associated systemic disorder: Atopy, hypertension, connective tissue disorders, associated genetic disorder: Down syndrome, Patchy regrowth of terminal hairs within the patch, Family history of AA and MIF-173*C gene are also associated with poor prognosis [1-3].

TREATMENTS

Topical treatments

(A). Corticosteroids

This can be given by either intralesional injections or topical application.

Intralesional steroids - Triamcinolone acetonide is used most commonly with the concentrations vary from 2.5-10 mg/mL, the lowest concentration being used on the face. A concentration of 5 mg/mL is usually sufficient on the scalp. Less than 0.1 mL is injected per site, with approximately 1 cm between injection sites, administered every 4-6 weeks. The dverse effects mostly seen are pain during injection and minimal transient atrophy [1-3,6,8].

Topical steroids

It is useful in children who cannot tolerate injections. The adverse effects commonly seen include local folliculitis (most common), telangiectasia and local atrophy [1-3,6,8].

B. Topical immunotherapy

It is based on the principle of induction and periodic elicitation of an allergic contact dermatitis by topical application of potent contact allergens. Regarding the mechanism of action, antigenic competition has been hypothesized. The introduction of a second antigen can initiate a new infiltrate containing T-suppressor cells and suppressor macrophages that may modify the pre existing infiltrate and allow regrowth [1-3].

The commonly used agents squaric acid dibutylester (SADBE), diphencyprone (DPCP) and Dinitrochlorobenzene (DNCB). Both SADBE and DPCP appear to be equally effective. Acetone-based solutions usually are preferred because they evaporate quickly; allow patients to wear a hat or wig immediately after treatment. Quick drying also decreases the chances of dissemination to other body parts by contact. Treatment is provided weekly. The patient first is sensitized directly on the scalp with a 2% concentration on a small area (2 cm).The following week, a low concentration (0.0001%)is applied. The concentration is increased slowly every week as needed until a mild tolerable allergic contact dermatitis is elicited (Many concentrations are available that achieve this goal).Treating only half of the head allows the physician to use the untreated half as a control. Once regrowth occurs on the treated half, treatment can be applied to the entire scalp. If regrowth initially occurs on both sides, spontaneous remission is likely, although treatment cannot be excluded as the cause. Initial regrowth may be seen at 12-24 weeks. Once cosmetically acceptable regrowth is achieved, the treatment can be tapered gradually. Maintenance treatment is needed as almost all patients relapse if the treatment is discontinued [1-3].

Precaution

1. Avoid severe contact dermatitis.
2. Patients are advised to avoid light exposure on the scalp for 48 hours because light degrades the chemical.
3. Patients also are advised not to wash the scalp for 48 hours.

The adverse effects include mild contact dermatitis (redness, scaling, itching)which is desireable, cervical lymphadenopathy, Urticaria and pigment changes. Vitiligo developed on the application site. Transient leukoderma on a distant untreated area has been reported. Hyperpigmentation, Confetti-type dyschromia (ie, hyperpigmentation, hypopigmentation) has been described as an adverse effect of DPCP Erythema multiforme–like eruptions [1-3].

C. Anthralin

The concentrations varied from 0.2-1%. The exact mechanism is unknown. Most likely, it creates inflammation by generating free radicals, which have antiproliferative and immunosuppressive actions. Irritant contact dermatitis, pruritus, erythema, scaling, folliculitis, local pyoderma and regional lymphadenopathy are the main adverse effects [1-3].

D. Minoxidil

Minoxidil appears to be effective in the treatment of alopecia areata. Response rates in that group vary from 8-45%. Little benefit in patients with alopecia totalis or alopecia universalis. Maximum of 25 drops are applied twice per day, usually 1ml per site. Initial regrowth of hair can be seen within 12 weeks. Continued application is needed to achieve cosmetically acceptable regrowth.

The Hair-growth-stimulating effect of minoxidil is stimulation of PGE2 synthesis by activating prostaglandin-H synthase (PGHS)-1. Normally, 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. It also seems to have direct mitogenic effect on epidermal cells and also prolongs the survival time of keratinocytes [1-3].

It is usually is well tolerated. Some adverse effects include distant hypertrichosis (5%)and irritation (7%)[1-3].

E. Topical garlic

Although it may not be effective as monotherapy, one study which analyzed the effect of a combination of topical garlic gel and betamethasone valerate ointment in alopecia areata in a double-blind study found the combination useful in majority of the patients with a statistically significant difference between the treatment and control groups [1-3].

F. Topical retinoids:

Among topical retinoids, tretinoin and bexarotene have been used. Irritation of the skin is a very common side effect. The efficacy is doubtful [1-3].

G. Prostaglandin analogs:

Agents usually used are Latanoprost and Bimatoprost. Prostaglandin receptor (EP)3 and EP4 mRNA are expressed in the dermal papilla cells and the outer-root-sheath cells located in the hair bulb region. In the telogen phase, the signals for both EP3 and EP4 mRNA disappear. Re expression of EP3 and EP4 mRNA and induction of cyclooxygenase (COX)-2 mRNA leads to development and regrowth of the hair follicles. Changes in hair appearance is seen with regard to increased in number, length, thickness, curvature and pigmentation [1-3,5,9,10].

H. New immunomodulatory therapies

The aims of this therapy include a fall in the number of pathogenic T-cells, slowing down T-cell activation, Change a type 1 cytokine response to a type 2 response and to impede activities of inflammatory cytokines [17,18].

1. Tacrolimus

The mechanism includes inhibiting calcineurin, thereby inhibiting both T-lymphocytes signal transduction and IL-2 Transcription, preventing cytokines (such as TNF-alpha and IFN-gamma)from activating the T-cells. Topical application of tacrolimus induces anagen during the telogen phase and stimulates hair growth [4,17,18].

2. Pimecrolimus

It is derived from Ascomycin. This agent is highly skin specific anti-inflammatory agent. Pimecrolimus gets lodged into macrophilin-12 and holds back Calcineurin. This, in turn, hinders the synthesis of the inflammatory cytokines IL-2 and IFN-gamma. Hence, neither the mast cells nor the T-cells are activated. It fails to target the T-cells involved in alopecia areata owing to its thick, greasy quality, the cream fails to penetrate deeper into the inner layers of skin [17,18].

3. Topical cyclosporine

This drug acts by inhibiting Calcineurin, which in turn slows down IL-2 production and limits CD4 lymphocyte cell activity. It poorly penetrates the skin. To overcome this hurdle, a heptamer of arginine-conjugated formulation of CsA (joined with a pH-sensitive linker)with an enhanced power to penetrate the skin has been developed of late. This hyperactive form of Cyclosporine penetrates full skin thickness (even subcutaneous fat).

SYSTEMIC TREATMENTS

A. Psoralen plus UV-A

Both systemic and topical PUVA therapies have been used. The number of treatments required for

regrowth varies between 20-40 treatments in most cases with the initial response rate varies from 20-73%. The relapse rat is high, around 50-88% which is usually seen within a few months mean 4-8 months after treatment is stopped. The adverse effects include burning sensation and increased risk of skin cancer [7,11,13].

B. Prednisone

Systemic steroids seems to be effective via their immunosuppressive effects. With this therapy, the rate of regrowth varies greatly (27-89%). Although the initial regrowth appears promising, the prednisone dose necessary to maintain cosmetic growth usually must be high enough that adverse effects are inevitable. The adverse effects include diabetes, weight gain, hypertension, psychological changes, osteoporosis, suppression of the adrenocorticotropic axes, striae, acne, hypertrichosis and purpura [1-3,6,8].

C. Cyclosporine

Cosmetically acceptable regrowth is seen with doses of 3- 6 mg/kg/day in most of the studies. Unfortunately, relapse is also seen within 3 months of discontinuation of cyclosporine. There is no evidence which indicate that CsA can prevent hair loss during an active episode [1-3].

E. Interferon

This agent is used intralesionally with a dose interferon alfa-2 (1.5 million IU, 3 times per wk for 3 wk). Few studies had been conducted with unsatisfactory results [1-3].

F. Dapsone

Dapsone is usually used at a dose of 50 mg twice per day or 100 mg OD. Although dapsone showed some efficacy in few studies, the high incidence of adverse effects rendered it unacceptable [1-3].

G. Methotrexate

Alopecia areata responded well to methotrexate, with or without systemic corticosteroids. Regrowth greater than 50% was observed in more than 60% of patients in some studies with the therapeutic dose ranges from 10-25 mg/week. Relapse rate is around 30%. One should not forget that this agent can also cause both anagen and tellogen effluvium [1-3,8].

H. Sulfasalazine:

It is administered orally, usually as enteric coated tablets to minimize the gastrointestinal side effects. It is started at a lower dose, usually in the range of 500 mg twice daily and then the dose is gradually increased to 1 g three times a day. Sulfasalazine helps in alopecia areata because it causes inhibitions of T cell proliferation, Natural killer cell activity, antibody production, secretion of interleukin (IL)-2, IL-1, TNF- and IFN-gamma and even IL-6.The adverse effects include gastrointestinal distress, liver toxicity and haematological side effects [1-3,12].

I. Azathioprine:

It has immunosuppressive effect on circulating lymphocytes as well as Langerhan cells. It is usually used with a dose of 50mg BD/100 mg per day[1-3,14].

J. Oral zinc sulphate

Serum zinc levels have been found to be lower in patients with alopecia areata than in control population [15,16].

K. Antimalarials

The agents used for this are Plaquenil and Hydroxychloroquine. Anti - inflammation action is because of their T cell suppression [1-3].

L. Other treatment modalities

These include nitrogen mustard, massage and relaxation, isoprinosine and aromatherapy.

NEW DRUGS

A. FDA-approved JAK inhibitors

They are used as 0.5% cream for topical application.

1. Ruxolitinib

It blocks the NKGD-activating ligand and NKG2D receptor interaction, halst activated T cells and modifies of the inflammatory cytokine network[1-3,20].

2. Tofacitinib

It inhibits the Janus kinase 3 (JAK-3)enzyme located along the IL-15 signaling pathway. Regowth of hair can be seen within 12 weeks. The drug's effect is long-lasting, as the new hair persisted for several months after stopping treatment in Mouse model [1-3,20].

B. Biologicals

The efficacy of all biologicals for treatment of alopecia is, so far, unsatisfactory in most of the studies. The mechanism of action of these biological agents includes four basic strategies: Reduction of pathogenic T cells, Inhibition of cell activation, Immune deviation and Blocking the activity of inflammatory cytokines [17,18].

CURRENT BIOLOGIC AGENTS IN USE

1. Etanercept

It is a human fusion protein that inhibits the inflammatory cytokine TNF- a [17,18].

2. Infliximab

It is a chimerical (mouse/human)antibody protein which inhibits the inflammatory cytokine TNF- alpha [17,18].

3. Efalizumab

This is a humanized monoclonal antibody that has several effects with potential therapeutic benefit in alopecia areata. It binds CD11a, a component of LFA-1 that binds to ICAM-1 on APCs and thus it interrupts the co-stimulatory signals. It also blocks T cell adhesion to endothelial cells and T cell migration (trafficking) into inflamed tissues [17,18].

4. Alefacept

It is a fusion protein that induces apoptosis in T cells expressing high levels of CD2. It also blocks the LFA-3/CD2 interaction necessary for the activation and proliferation of T-cells by binding to CD2 on T-cells [17,18].

New biologicals

(b) Abatacept
This agent is a CTLA4Ig is a fusion protein that blocks CD80/86 (B7)co-stimulation binding with CD2 and is being suggested as a potential treatment for alopecia areata. [17,18].

(c) Anakinra
This is an interleukin-1 (IL-1)receptor antagonist. The usual dosage is 100 mg s.c OD. Dose reduction to 100 mg s.c. every other day should be considered in patients with severe renal impairment [17,18].

(d) Rituximab, a chimeric monoclonal antibody against the protein CD20

(e) adalimumab

(f) Fontolizumab (anti-IFNgamma)

Future possible treatments

1. Interleukin injections or the administration of their cDNA sequences. This can inhibit the entry of inflammatory cells into the skin and hair follicles.
2. Blocking of the production or increasing the tolerance of lymphocyte clones reactive for hair follicle antigen epitope.
3. Blocking the antigen presentation and costimulation by antigen presenting.
4. Prevention of migration of inflammatory cells from activation sites to the follicle and skin, even after activation of the lymphocytes. The targets include CD44v10 and other activated cell surface markers. These treatment modes may be used as a cure as well as a preventive measure in the case of individuals predisposed to alopecia areata.
5. The effect of PTHrP is to stimulate and accelerate the hair cycle. So, PTHagonists would be expected to promote hair growth.
6. Dealing with the disease (after the hair follicle inflammation has already set in)by inhibiting or modulating the expression of the targeted antigens in the anagen phase hair follicles, masking of the expression of these threatened antigens, modification of the harmful antigen expression, caused by inflammation and prevention of expressions of MHC antigens in the hair follicles.
7. Blocking the NKGD-activating ligand and NKG2D receptor interaction.
8. To target the mechanism by which the inflammatory cells adversely affect hair follicle growth. This includes Fas-Fas ligand interaction, prevention of granzyme and perforin action, oxygen radical neutralization and alteration of the cytokine receptor and cytokine environment [1-3,19,20].

As far as the author's experience, conventional therapy like intralesional steroid injection is more effective than newer treatment like targeted phototherapy. The results of unpublished data of efficacy of excimer light therapy is not satisfactory. Immunosuppressant like Methotrexate is effective for extensive cases, but side effects should always be considered. Biologicals like Tacrolimus is not satisfactory.

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Clinical Image

Ulcerated Cutaneous Leishmaniasis

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CLINICAL CASE

This is a case of a twenty-nine year old male patient who was referred to our dermatology service with an ulcerative lesion of the left cheek of approximately 4 cm, circular, with well-defined borders and a clean base of granulation tissue, as well as 2 ulcerated nodular lesions (Fig. 1). The rest of the physical exam was within normal limits.

Family and personal history were noncontributory. The lesion on the left cheek first appeared two and a half months earlier, with a "clay-like appearance", which he tended to scratch often. Gradually the lesion reached its current state, for which he sought treatment with an outside dermatologist. Presumptive diagnosis was deep fungal infection versus cutaneous leishmaniasis, and biopsy of the lesion showed a granulomatous process with negative Fite, PAS, and Gomori trichome stain. The patient was then referred to our dermatology service. Differential diagnosis included ulcerated cutaneous leishmaniasis, cutaneous lymphoma, and pyoderma gangrenosum. Upon further questioning, the patient claimed to have recently visited his homeland, Chisec Coban, which is an area in Guatemala that is endemic for leishmaniasis. We performed a microscopic examination of the lesion with Giemsa stain, obtained by skin scraping, was negative and another biopsy for histologic examination, along with fungal and bacterial culture. Histologic examination of the second biopsy again showed a granulomatous process highly suspicious for Leishmaniasis. More specifically, the lesion showed an epidermis with hyperkeratosis and parakeratosis with areas of plasma cells and neutrophils. Irregular acanthosis with thick rete ridges, some of them fused, with moderate spongiosis. From the papillary dermis to the deep reticular dermis, a dense diffuse inflammatory infiltrate consisting of histiocytes, lymphocytes, neutrophils, plasma cells and occasional eosinophils. Giemsa, periodic acid- Schiff (PAS) and Kinyoun were negative. The patient was sent to the Section of Parasitology of the National Laboratory of Health Leishmaniasis Unit confirmed the diagnosis of leishmaniasis with a scraping of the lesion examined with Giemsa stain, and the patient was started on intralesional and intramuscular glucantime 20, which led to complete healing of the lesion (Fig. 2).

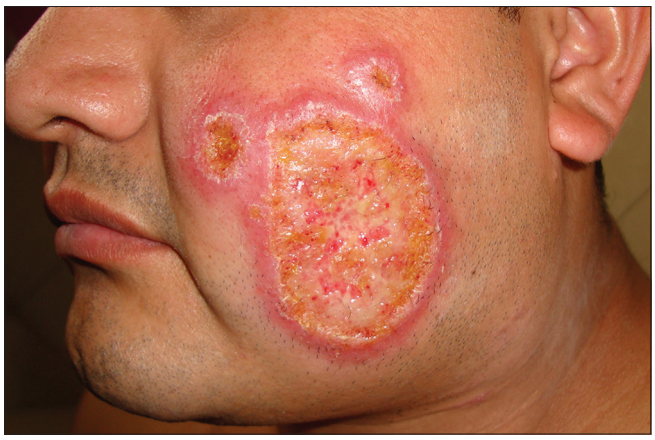

Figure 1: Large Ulcer with clean base, well-defined erythematous borders and two nodular, ulcerated, satellite lesions

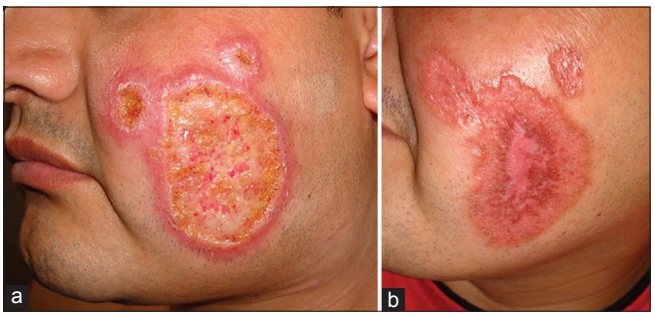

Figure 2: Pre and post treatment with Glucantime. a: Cutaneous Lesions before treatment. b: One month after treatment

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DISCUSSION

Cutaneous Leishmaniasis is a parasitic disease endemic to much of Latin America, and is caused by the species *L. braziliensis*, *L. mexicana*, *L. panamensis*/*L. guyanensis*, among others. The organism is transmitted by the bite of an infected female sandfly of the genera Phlebotomus or Lutzmyia, with lesions typically located on exposed areas of the body [1]. Manifestations may include single or multiple localized cutaneous ulcers, or diffuse cutaneous lesions with possible mucosal involvement, typically caused by L. Mexicana. Cutaneous lesions may consist of ulcers, reddish-brown, firm, infiltrative nodules, or verrucous plaques that may or may not ulcerate [2-5]. Along with a history of travel to an endemic area, the following are useful for the diagnosis of cutaneous leishmaniasis: microscopic analysis of skin scrapings revealing amastigotes, punch biopsy with tissue-impression smears, and needle aspiration of tissue fluid from the margin of a lesion with culture of the fluid to isolate the organism and identify the species [3]. Although lesions may heal spontaneously within 12-18 months, topical medications such as paromomycin sulfate 15% plus methylbenzethonium chloride 12%, ketoconazole cream under occlusion, cryotherapy, local heat, photodynamic therapy, laser ablation, and 100 ml intralesional sodium stibogluconate antimony are often used to avoid significant scarring of exposed areas, especially the face. Five milliliters of intralesional Antimony n-methyl glutamine (Glucantime) is often used in Central and South America due to local availability and efficacy [2,4]. Insecticides and pyrethroid-impregnated curtains are useful to prevent cutaneous leishmaniasis [3]. In Guatemala, the endemic areas for leishmaniasis are Peten, Huehuetenango, El Quiche, Alta Verapaz, and Izabal, and the most important area is Peten, with 80 percent of the cases (Fig. 3) [6].

Figure 3: Areas endemic for leishmaniasis in Guatemala

CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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NASZA DERMATOLOGIA Online
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Clinical Image

Tender erythematous papule on the face

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A 36 year old male visited our dermatological outpatient department (OPD) with a chief complaint of a raised reddish skin lesion on the left side of the face for the last one month. There is history of local discomfort associated with the lesion. The patient denied any history of trauma at the affected site. On physical examination, there was an erythematous papule around 1 cm in diameter present on the left side of the face 2-3 cm below the left lower eyelid (Fig. 1). It was firm in consistency and exquisitely tender. The summit of the papule was relatively harder and was the site of maximum tenderness. After manipulating the lesion in the minor operation theatre, a glass fragment of the size 9-10 mm × 2-3 mm was removed from the lesion (Figs 2A-B, and 3). A diagnosis of foreign body reaction to the glass was made. The affected skin at the lesional site was irrigated with normal saline. The patient was prescribed topical fluticasone plus mupirocin ointment and oral antibiotics in the form of Amoxycillin and clavulanic acid 625 mg thrice a day for one week. The lesion regressed completely in 2-3 weeks.

Foreign body granuloma is a reaction pattern to either endogenous materials (hair shafts, keratin, cholesterol, etc.) or exogenous substances (suture material, glass, oil droplets, wooden material,

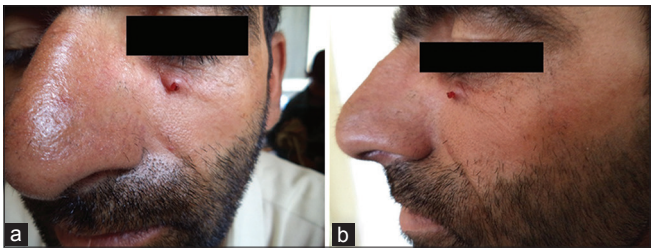

Figure 2: (A) Glass slit projecting out from the top of the erythematous papule (frontal view); (B) 2-3 mm of glass slit clearly visible coming out from the summit of the papule (lateral view)

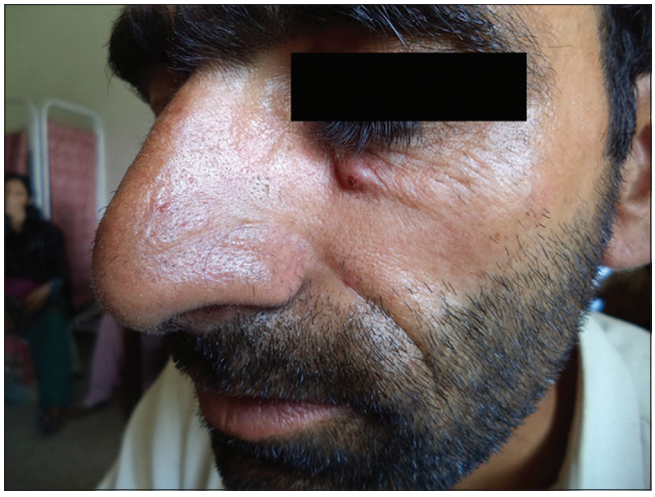

Figure 1: An erythematous papule on left side of the face

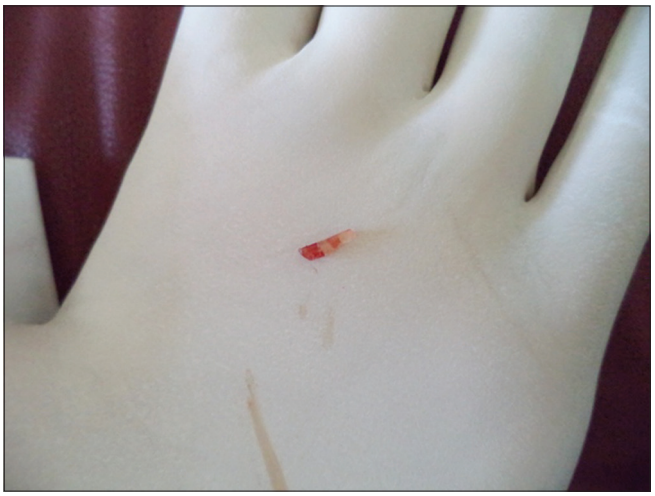

Figure 3: Glass foreign body which has caused the foreign body reaction (9-10 mm × 2-3 mm)

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metals, silica, etc.) which are immunologically inert. Soft tissue foreign bodies mostly occur secondary to some abrasive or penetrating trauma. These can lead to discomfort, delayed wound healing, deformity, localized and systemic infections [1-3]. A number of different types of foreign bodies elicit a granulomatous response which clinically present as erythematous brown or purple papules, plaques or nodules.

With the passage of time such lesions often become harder due to fibrosis. Retained foreign bodies can lead to bacterial infection while the vegetative foreign bodies have been reported to cause fungal infection [4].

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patient for publication of this article and any accompanying images.

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NASZA DERMATOLOGIA Online
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Clinical Image

Pilar leiomyoma

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A 30 years old man presented to our dermatology clinic with complaint of multiple firm tender red brown masses on his leg (Figure 1). We did an excisional biopsy. Under high power examination there were interwoven bundles of spindle cells. The nuclei were elongated with blunt ends (cigar shape), so the patient was diagnosed with pilar leiomyoma (Figure 2). We recommended him to use gabapentin for pain relief.

The patient's informed consent was obtained.

Prior to the study, patient gave written consent to the examination and biopsy after having been informed about the procedure.

Pilar leiomyoma is a benign smooth muscle tumor arising from the arrectores pili muscles associated with the hair follicles of the skin [1]. They usually occur as multiple firm dermal nodules located on the extremities and trunk. Leiomyomas usually develop during adolescence or early adult life [2]. Tumours can be painful from compression of cutaneous nerves or because of fibre contraction within the tumour in case of cold weather or emotional stress [3]. The treatment of solitary leiomyoma is surgical excision. In case of multiple leiomyomas, surgery can be done for lesions, which are large and painful. The aim of medical line of treatment is relieving pain. Various drugs have been tried with variable results [4], calcium channel blockers like nifedepine, a-adrenoreceptor blockers (phenoxybenzamine), nitrates, analgesics, antidepressants, and gabapentin. CO2-laser ablation has shown good results [5].

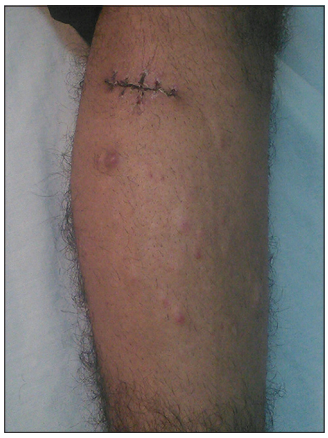

Figure 1: Multiple firm red brown masses on the leg

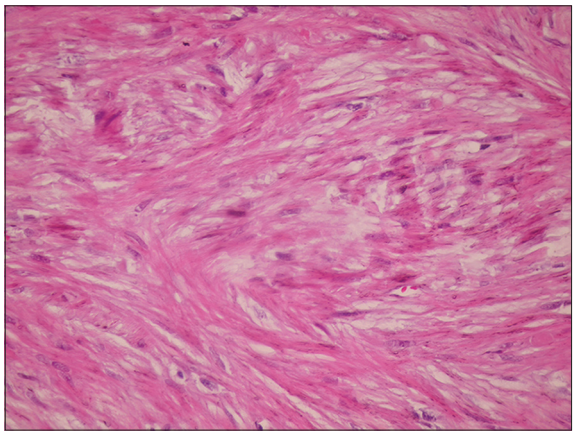

Figure 2: Interwoven bundles of spindle cells with cigar shape nuclei

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NASZA DERMATOLOGIA Online
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Clinical Image

Case of Mistaken Identity: Pyogenic granuloma of chin is actually a draining dental fistula

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A 27 year old PHD student had an asymptomatic, slightly hemorrhagic, somewhat pedunculated skin mass of his chin (Figure 1) surgically excised more than 3 times approximately 4 years earlier. A biopsy of the second recurrence showed the mass to be pyogenic granuloma. It recurred a 4th time but he could not afford further physician care so he grew a beard to hide the mass. After graduation and employment at a university he sought treatment of numerous cariously destroyed teeth (Figure 2). An anterior mandibular radiograph reveals considerable but painless destruction of 3 of his lower incisors (Figure 3). The dentist concluded at the chin lesion was actually granulation tissue at the opening of a draining dental fistula from the lower incisors. Endodontic treatment of the affected teeth resulted in healing with new bone formation around the roots as well as reduction in size of the chin mass. A small excision of the mass was performed by a dermatologist with no recurrence at 3 years of follow-up.

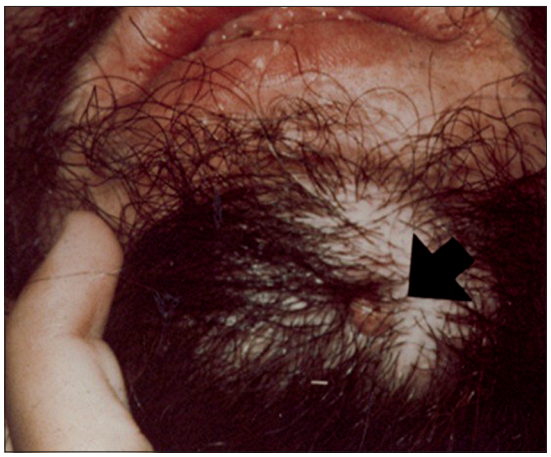

Figure 1: At examination the dentist found a painless, somewhat lobulated soft tissue mass within the beard on his chin; the mass had been present at least 4 years without change and an early biopsy showed granulation tissue

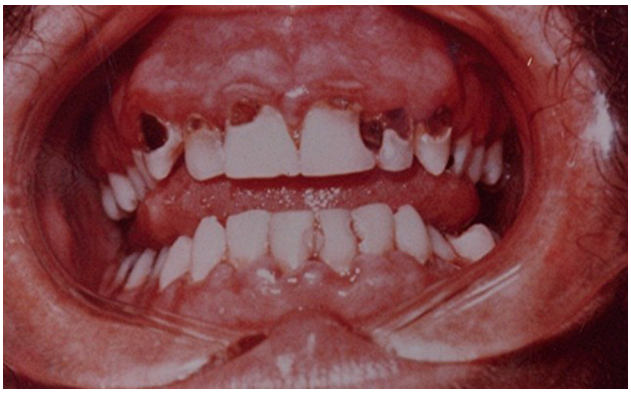

Figure 2: Numerous, often large, carious lesions were present in multiple teeth, with inflammatory enlargement of the anterior mandibular gingiva; the patient seldom brushed his teeth

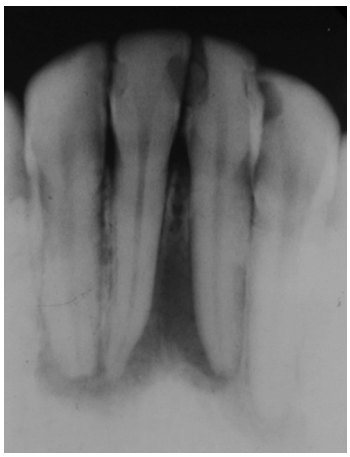

Figure 3: Three mandibular incisors show periapical radiolucency, with vertical bone destruction along the entire root surface of one, associated with drainage into the overlying inflamed gingiva; all three incisors were nonviable according to electric pulp testing

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CONSENT

The examination of patients is conducted according to the Declaration of Helsinki principles.

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NASZA DERMATOLOGIA Online
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Letter to the Editor

Diagnostic pitfall of localized lentigo accompanied by post-inflammatory pigmentation on the palm with a several-month history

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Sir,

When dermatologists see acquired and well-circumscribed pigmented macules on the palm, dorsal hand or forearm of the elderly, they tend to consider blue nevus, hematoma, nevus cell nevus and malignant melanoma as differential diagnoses [1]. We herein described the very rare case of localized lentigo accompanied by post-inflammatory pigmentation in a patient who has been treated for palmoplanter pustulosis for a long time. This eruption mimicked some kinds of lentiginous lesion and it was difficult to diagnose clinically.

A 59-year-old female was referred to our hospital with a pigmented macule on her left palm. She had been to the family doctor for treatment of palmoplanter pustulosis by topical steroid ointment application for several years. According to the history-taking interview, she said that the lesion had appeared 5 months before referral to our hospital as a tiny pigmented macule and had gradually enlarged during those 5 months (Fig. 1a). In clinical appearance, the macule was dark brown to black, well-demarcated, flat, round and 3 x 4 mm in size. Dermoscopic examination showed homogenous brownish pigmentation; however, the parallel ridge or furrow pattern that is commonly observed in acral lentiginous lesions was not apparent (Fig. 1b). Histopathological findings with hematoxylin-eosin staining showed acanthosis and spongiosis in the epidermis, liquefaction degeneration at the dermal-epidermal junction and scattered melanophages in the superficial dermis (Fig. 2a). Neither aggregation

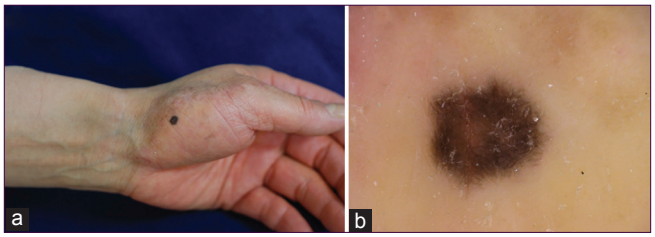

Figure 1: Clinical manifestations. a. The macule is brown to dark black, well-demarcated, flat, round and 3 x 4 mm in size. b. Dermoscopy of the macule shows homogenous brownish pigmentation without the parallel ridge or furrow pattern that is commonly observed in acral lentiginous lesion

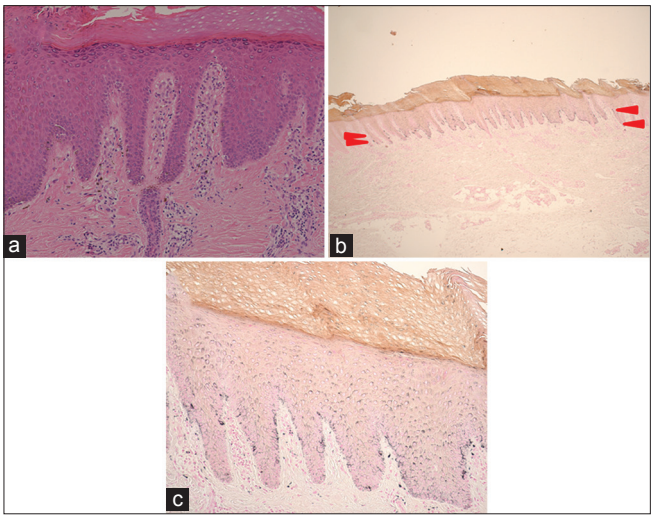

Figure 2: Histopathological findings. a. Histology of the macule shows acanthosis, spongiosis, liquefaction degeneration, basal melanosis and some melanophages in the superficial dermis (Hematoxylin and eosin stain; x100). b. Fontana-Masson staining revealed the melanin granules to be in the epidermis at full-thickness, and the melanin granules were distributed with a clear boundary on the bilateral side. Red arrowhead shows the edge of melanin-granules distribution. (Fontana-Masson; x20). c. A number of melanin granules are distributed on top of the nuclei in the prickle cell layer (Fontana-Masson; x100).

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of melanocytes in the epidermis nor proliferation of dermal melanocytes was observed, nor there no subcutaneous bleeding. Fontana-Masson staining revealed the melanin granules to be in the epidermis at full-thickness, and the melanin granules were distributed with a clear boundary on the bilateral side (Fig. 2b, red arrowhead). Notably, in the prickle layer, a number of melanin granules were distributed on top of the nuclei (Fig. 2c). From these findings, we finally made the diagnosis as lentigo accompanied by post-inflammatory pigmentation.

Prior to the study, patient gave written consent to the examination and biopsy after having been informed about the procedure.

It is very difficult to define correct diagnosis in the case of dissociation among present illness, dermoscopic and histological findings. Our initial diagnosis was blue nevus. However, the dermoscopic findings were inconsistent with typical blue nevus, which has homogeneous blue pigmentation and a bluish-white structure [2,3]. Furthermore, the histologic features included a lack of the dermal melanocytes that are typically seen in blue nevus.

Fontana-Masson staining revealed a distinctive distribution of melanin granules in the upper portion of epidermis, which was very similar to those seen in lentigo and in sun-damaged skin [4]. We were easily able to find incontinentia pigmenti histologica due to the liquefaction degeneration.

In this case, although the cause of the localized pigmentation is unclear, the homogenous brownish pattern in dermoscopy, interestingly, may be due to a combination of melanin deposition in the epidermis and the aggregation of dermal melanophages.

In conclusion, it is noteworthy that we must keep this pathological condition in mind when we encounter a well-circumscribed pigmented lesion in a patient who has been treated for inflammatory diseases such as palmoplanter pustulosis, dishydrotic eczema and the like.

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. The patient has provided permission to publish these features of her case and the identity of the patient has been protected.

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NASZA DERMATOLOGIA Online
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Letter to the Editor

Post Herpes zoster dermatome/s – A therapeutic ground for cutaneous T-cell lymphoma (CTCL) & Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN)

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The term isotopic response was coined by Wolf et al. in 1995 to describe the occurrence of a new skin disease at the site of a previous, unrelated and already healed cutaneous disorder [1]. Dermatome/s that have been infected by herpes zoster virus become breading sites for a subsequent development of heterogeneous skin disorders, the occurrence of which generate the well-defined 'Wolf's post-herpetic isotopic response' [2,3].

Alongside the large number of cases of post-herpetic isotopic response, there are also few reports of generalized skin disorders which spared exactly the cutaneous areas that had been subjected to herpes zoster virus infection [4]. These peculiar observations, apparently pave the way to introduce a new entity called isotopic nonresponse (Wolf's post-herpetic isotopic nonresponse') [3,4].

So far only four cases have been described in medical literature that could be categorized under Wolf's post-herpetic isotopic nonresponse' related to post herpetic dermatome sparing cutaneous T-cell lymphoma (CTCL) and Stevens–Johnson syndrome/ toxic epidermal necrolysis (SJS/TEN) (Table 1) [5-7].

Immune reactions associated with CTCL

CTCL is characterized by the accumulation and clonal proliferation of malignant, epidermotrophic, CD4+/ CD45ro+ (Helper/Memory) T lymphocytes that interact with keratinocyte within the lesion. These keratinocytes are atypical in that they express ICAM-1 plus MHC-11. They also produce increased amount vascular permeability and increase the effectiveness of other keratinocytes attractants for lymphocytes, such as IL-8. Thus, these lesional keratinocytes have an enhanced ability to interact with epidermotrophic, malignant T lymphocytes, which tend to produce a T helper-2 cell cytokine profile [8].

There is evidence that CTCL cells may home to the epidermis as a result of their interaction with LC (an immature member of the dendritic cell lineage). Dendritic cells (OKT6+, now CD1a+) were interspersed among the dermal and epidermal infiltrates of CTCL has been described by Chu et al [9]. Various other researchers have shown that epidermotropic lymphocytes are closely associated with LCs [10,11].

Immune reactions associated with SJS/TEN

SJS/TEN is categorized as a cytoplasmic immune reaction targeted at the destruction of keratinocytes expressing foreign antigens. In both erythema multiforme and TEN, epidermal keratinoytes express intercellular adhesion molecule-1 (ICAM-1) and major histocompatibility complex-1 (MHC-1) antigens [10]. Cytotoxic T lymphocytes (mainly CD8) expressing the skin homing receptor and cutaneous lymphocyte antigen is the major effector cell in this process. It has been proposed that drug or their metabolites act as haptens, and drug-specific CD 8 cells secrete interferon-gamma which facilitate keratinocytes antigenic to produce tumour necrosis factor-alpha (TNF α), Fas ligand (FaSL), interleukin-6 (IL-6) and IL-10. TNF-alfa up-regulates expression of MHC-1 and MHC-11 molecules, which increase exposure of keratinocytes to

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Table 1: Summary of the reported cases relevant to Wolf's post-herpetic isotopic nonresponse sparing CTCL & SJS/TEN

Case no.	Age & sex of patient	Herpes Zoster affected dermatome	Interval between Herpes zoster and	Second cutaneous disease	Site involved (sparing site)
1.Twersky et al 2004. [5]	58 Male	Left T8	3 weeks	Cutaneous T cell lymphoma	Left side abdomen
2. Kannangara et al 2008 [6]	62 Male	Left C3–C4	3 months	Cutaneous T cell lymphoma	Left upper arm & anterior chest
3. Kannangara et al 2008 [6]	53 Female	Left V1, V2	2 months	SJS-TEN	Left upper face
4. Tenea D 2010. [7]	39 Female	Right T8-T9	4 weeks	SJS	Right lower abdomen

cytotoxic T cells (CTLS) [12]. Cytotoxic T lymphocytes can induce apoptosis through perforin/granzyme caspase cascade leads to cell destruction [13,14].

Proposed mechanisms of post herpetic dermatome/s sparing TEN/SJS & CLCL

One possible mechanism states that Immunohistochemistry of the previous zoster lesion showed a notable reduction in LC in the area clinically spared by the CTCL. If an LC-Tcell interaction is essential to proliferation of the lymphomatous cell line perhaps the decrease in LC in the previous herpes zoster dermatome leads to less epidermotropism of CTCL to the local area concern [6].

The second proposed theory is that down-regulation of MHC-1, MHC-11 and ICAM-1 expression in HZV-infected keratinocytes has been proved [15]. Thus, the reduction or inhibition of ICAM-1 expression on keratinocytes by HZV most probably attenuates the keratinocytes to function as antigen-presenting cells and inhibit its role in LFA-1/ICAM- 1-mediated T-cell response. This down-regulation would have probably prevented the SJS-TEN and CTCL involving on previously HZV-affected area [6].

Considering existing facts I would like to state that Post Herpes Zoster dermatome/s eventually behave as a therapeutic ground for dermatosis like CTCL and SJS/TEN. As clinicians we should emphasize more weight on this unique phenomenon and encourage researches who are engaging in discovery of new pharmaceuticals for these two serious skin diseases to turn eyes to proposed mechanism for this skin reaction.

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NASZA DERMATOLOGIA Online
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Letter to the Editor

Perforating metastatic melanoma

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Sir,

We describe a case of metastatic malignant melanoma on the thigh with comedo-like appearance, which histologically showed elimination of tumor cells.

A 70 year-old man was diagnosed with a nodular type malignant melanoma involving the lower back with satellite lesions (stage IIIB, T4b N2c M0, Breslow's tumor thickness; 10.3 mm, Clark's level; IV) (Fig. 1a). Sentinel lymph node evaluation was not performed. Three months after the excision of the primary melanoma with a 2-cm margin, skin metastasis appeared on his right inguinal region. Physical examination an additional month later revealed a firm, black-colored 5-mm sized nodule with crusts on the surface on the right thigh, with surrounding subcutaneous induration (Fig. 1b). Dermatoscopic examination found that keratins at the surface of the central lesion and a blue-white veil at the periphery. Histological examination of a totally removed nodule showed a small, symmetric and well-circumscribed lesion composed of nests of numerous atypical melanocytes in the dermis (Fig. 1c). Those atypical cells were positively stained with Melan-A, HMB45 and S-100. Tumor cells were located in abutment with and also within the epidermis. Nests of atypical melanocytes were confined to the crusts and perforated the skin surface (Fig. 1d). Treatment with chemotherapy was not implemented because the patient refused aggressive treatments. Six months after the onset of skin metastasis, he died of respiratory failure.

The patient's informed consent was obtained.

Prior to the study, patient gave written consent to the examination and biopsy after having been informed about the procedure.

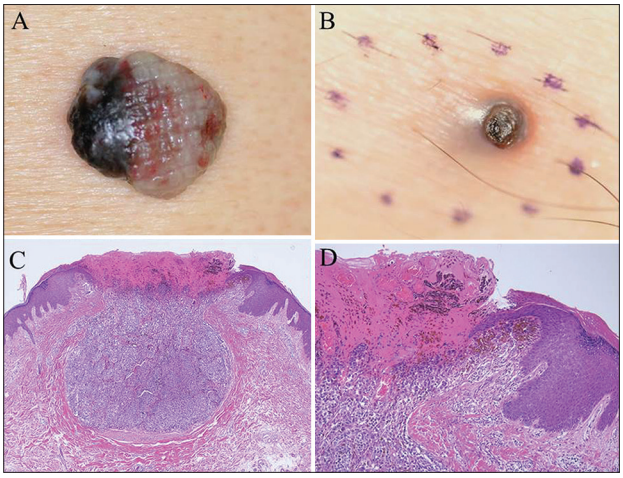

Figure 1: (a) Clinical appearance of a primary melanoma on the lower back. (b) Clinical appearance of a metastatic melanoma on the right thigh. (c) The histopathological view showing a perforating metastatic melanoma. (Hematoxylin-eosin stain, x 40). (d) Atypical melanocytes in irregulary shaped nests within epidermis and crusts perforated to the skin surface (Hematoxylin-eosin stain, x 100)

The most interesting feature in this case is the elimination of metastatic skin tumor masses through the epidermis. An epidermotropic growth pattern is an uncommon feature in malignant skin neoplasms, and tumor cell invasion in the epidermis is extremely rare in cutaneous metastatic tumors [1]. In our case, metastatic tumor cells were located in abutment with and also within the epidermis, which may lead to the clinical manifestations of superficial ulceration and crusts. The mechanism of epidermotropism in cutaneous metastasis still remains unknown; however, affinity of tumor cells with keratinocytes is speculated, possibly *via* adhesion molecules. Alternatively, epidermotropism in cutaneous metastases may be related to transepidermal elimination. Transepidermal elimination is a mechanism whereby foreign or altered constituents can be removed from the dermis through a channel that facilitates extrusion without gross

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disturbance of epidermal integrity. Transepidermal elimination of malignant tumor cells has been reported in the primary lesions of malignant melanoma [2,3]. By contrast, in our case we could not find any indication of elimination of tumor cells through the epidermis in the primary lesion. The presence of tumor cells in abutment with the epidermis, or infiltration of tumor cells into the epidermis, may trigger transepidermal elimination of tumor cells. In a strict meaning, our case did not show transepidermal elimination, and thus we prefer to use the term of perforating melanoma.

CONSENT

The examination of patient is conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patient for publication of this article.

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NASZA DERMATOLOGIA Online
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Letter to the Editor

Follicular pityriasis versicolor-Rare variant of a common dermatological disease

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Sir,

Pityriasis versicolor is a superficial fungal infection of the skin caused by yeast of the genus *Malassezia*. It is characterized by hypopigmented or hyperpigmented macules and patches usually involving the trunk [1]. The variants of pityriasis versicolor include hypochromic, hyperchromic, combination of hypo-hyperchromic, erythematous, circinate, atrophic and acral [2-4]. However, the follicular variant of pityriasis versicolor has been rarely reported. In this article we describe a young female with the follicular variety of this common skin disease.

CASE REPORT

A 30 year old female presented with a one month history of multiple light brownish colored macules over the neck, trunk and proximal limbs. It was associated with mild pruritis. She denied any previous history of similar complaints. On examination, there were multiple light brownish macules present in a follicular distribution over neck, chest, abdomen, back, proximal arms and thighs (Figs 1 and 2). On stretching the affected skin, the scaling became prominent showing the positive Zireli's sign. Hair, nail and mucous membranes were normal. KOH examination of skin scrapings showed the presence of multiple short hyphae and spores confirming fungal infection. A skin biopsy from the lesion over back showed small 2-4 μm spores in the horny layer of the epidermis. The dermis contained mild inflammatory infiltrate. The adnexal structures including the hair follicles were unremarkable.

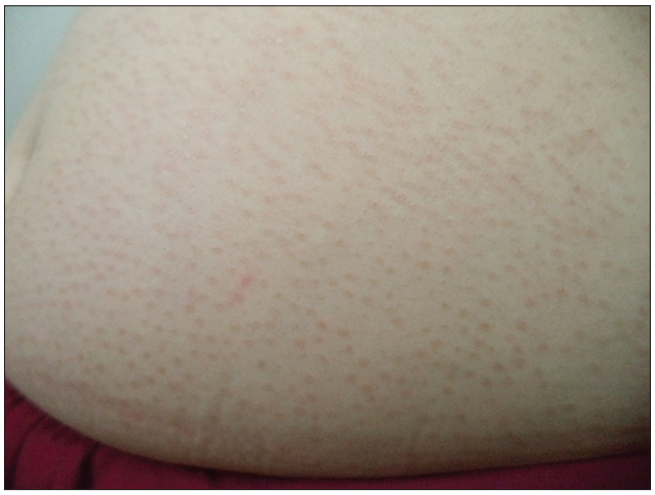

Figure 1: Multiple light brownish macules in a perifollicular distribution over abdomen

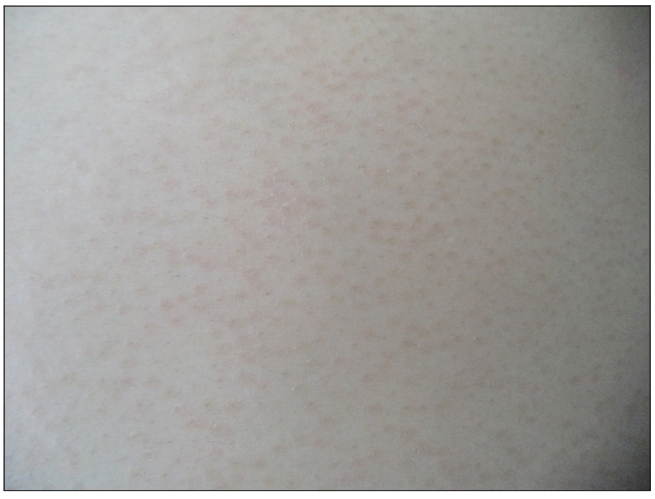

Figure 2: Close view of follicular macules of pityriasis versicolor

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A written consent for the examination and biospy was obtained from the patient after having been informed about the procedure.

She was treated with topical sertaconazole 2% cream twice daily and oral fluconazole 400mg weekly for two weeks. After four weeks she was free of skin lesions.

DISCUSSION

Currently *Malassezia globosa* and *Malassezia furfur* are the predominant species implicated in pityriasis versicolor [5]. Various species of genus *Malassezia* are among the normal flora of yeast on human skin. In most cases it is the shift in the relationship between the resident yeast flora and the human skin which presents clinically as pityriasis versicolor. Clinically patients present with well defined discrete or confluent macules characterized by fine branny scaling which can be made prominent by stretching the skin [1]. The various clinical variants of pityriasis versicolor that have been described include hypochromic, hyperchromic, combination of hypochromic and hyperchromic, erythematous, circinate, acral, atrophic, etc. but follicular type has rarely been reported [2-4]. Framil VMS et al in a study of 102 patients of pityriasis versicolor from Brazil reported only one case of follicular variety [2]. The present case was reported due to the rarity of this clinical variant. The various treatment options for pityriasis versicolor include topical azole antifungals, 2.5% selenium sulphide in a detergent base, terbinafine 1% cream, 20% sodium hyposulphite solution, etc. The systemic antifungals which are effective in pityriasis versicolor include fluconazole, ketoconazole, itraconazole, etc. [1]. Our case also responded well to the topical azole (sertaconazole) together with oral fluconazole.

CONSENT

The examination of the patient was conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patient for publication of this article and any accompanying images.

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NASZA DERMATOLOGIA Online
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Letter to the Editor

Sebaceous hyperplasia in neonates and adults

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Sir,

Sebaceous hyperplasia is a common benign proliferation of the sebaceous glands seen during the first weeks of life and in middle-aged and elderly people. Clinical picture is quite different in neonatal period compared to adulthood.

In neonate the lesions are small, tiny yellow papules distributed on the nose [1].

Sebaceous hyperplasia is a quite common finding in neonatal period, being reported in 894 (89.4%) neonates, with a slight predominance of males vs. females: 1.08/1in a recent Australian survey [2].

Sebum secretion is high in neonates probably induced by maternal androgen: dehydroepiandrosterone transferred trans-placental [1].

It is also named "the miniature puberty of the newborn" along with vaginal bleeding in infant girls and neonatal acne (Fig. 1).

Sebaceous hyperplasia is a benign finding and spontaneously resolves with time. No evaluation is needed and no treatment is necessary. Reassurance of the family members is of great importance.

In adults soft, yellow papules with central umbilication are noticed not only on the face (particularly on the forehead), also on the genitalia, areola, chest [3] (Fig. 2).

In adults variable treatment methods have been tried for esthetic reasons: electrodessication, light lasers, applications of acids and photodynamic therapy with deceivable results and sometimes scars. Despite numerous séances of therapy rapid recurrences have been noted, explained at least partially, by the lack of penetrance of treatment, only superficial layers are treated [1].

Figure 1: Neonatal sebaceous hyperplasia

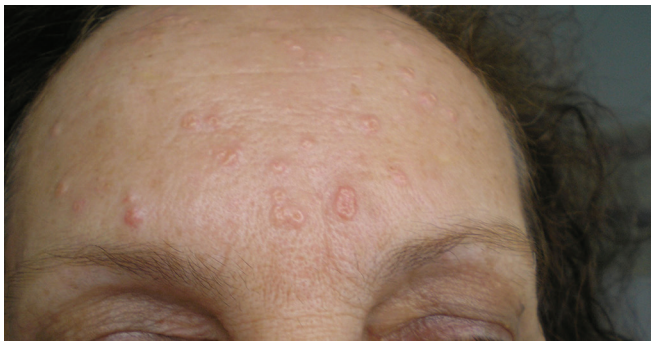

Figure 2: Adult sebaceous hyperplasia

No abnormal levels of hormones have been proved in patients with sebaceous hyperplasia regardless the age.

In elderly persons sebaceous hyperplasia is induced by reduced androgen levels followed by a secondary

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diminish of cellular turnover [1,2]. Higher sensitivity of the sebaceous cells to androgens would be a trigger to cellular proliferation especially in genital area [4].

Skin biopsy is not necessary; diagnostic is purely clinic, although histological report would confirm a lobular array of well-differentiated mature sebaceous lobules.

Neonatal sebaceous gland hyperplasia is a frequent clinical observation, different from adult form that requires no treatment, no surveillance and no prediction to evolution to later form of the disease (Tab. 1).

Table 1: Differences between neonatal and adult form of sebaceous hyperplasia

	Neonatal sebaceous gland hyperplasia	Adult sebaceous gland hyperplasia
Age of onset	First weeks of life	Middle age-elderly persons
Gender: Males/females	1.08/1	?
Sites of lesions	Nose	Forehead , genitalia, areola, chest
Androgen levels	High	Low/normal with a high sensitivity of receptors
Evolution	Spontaneously remission within weeks	Progressive evolution without treatment

CONSENT

The examination of the patients was conducted according to the Declaration of Helsinki principles. Written informed consent was obtained from the patients for publication of this article and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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NASZA DERMATOLOGIA Online
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Letter to the Editor

Homonyms in medicine: A perspective

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In linguistics, a homonym is, in the strict sense, one of a group of words that share spelling and pronunciation but may have different meanings. Thus homonyms are simultaneously homographs (words that share the same spelling, regardless of their pronunciation) and homophones (words that share the same pronunciation, regardless of their spelling) [1].

One can find easily a name in medicine which be perceived as 2 different meanings [2]. Table 1, list few examples, and Table 2 [2-6], focus on few eponyms which can be misunderstood as related to countries.

Acronyms might be considered a major source for homonyms. Acronyms such as CHILD, CLOVE, KID, LEOPARD, NAME, and POEM might cause confusion to the patient as to the relation to the other meanings of these acronyms [7]. CLOVE syndrome stands for (congenital lipomatous overgrowth, vascular malformations, and epidermal nevus) [8].

The Eponyms are the most common type of medical names which may cause confusion with other names, inside and outside medical field [1]. A previous paper in this journal highlighted on this issue1. From which I am copying the following segment; Similar name might be thought for and confused with another person, for example verrucous carcinoma of Ackerman is named after Lauren Vedder Ackerman (1905-1993) and not, A. Bernard Ackerman (1936-2008).

One may see also identical names for 2 different eponyms.

For examples "Sjögren" in "Sjögren's syndrome" (Sicca syndrome), is named after Henrik Samuel Conrad Sjögren (1899-1986), Swedish ophthalmologist. Whereas, "Sjögren", in "Sjögren-Larsson syndrome", is named after, Karl Gustaf Torsten Sjögren (1896-1974), Swedish physician, psychiatrist and inheritance researcher.

Similarly, "Stewart" in "Stewart-Treves syndrome", (a malignancy that arises within chronic lymphedema), is different from the one in "Stewart-Bluefarb syndrome". The latter is a type of acroangiodermatitis which was described independently by Stewart as well as by Bluefarb and Adams on the legs of patients with arterio-venous malformations. The term, pseudo-Kaposi sarcoma, is generally used synonymously with acroangiodermatitis of Mali, but is a broader term and includes both acroangiodermatitis of Mali and Stewart-Bluefarb syndrome.

As one more example, there are 2 "Bart's" in the eponyms of dermatology. Dr Bruce J Bart, who is behind "Bart syndrome", and Dr Robert Bart, who was one of the men behind "Bart-Pumphrey syndrome". "Look-alike or sound-alike" eponyms are not rare. This is because there is extensive list of eponyms bearing the name of the same scientist.

Hutchinson's sign, for example which can be seen both in subungual melanoma and ophthalmic herpes zoster. In such situations it is better to be more specific by adding the site of involvement when mentioning the sign, e.g., Hutchinson's nail sign [9-10].

Warning

Medical practitioners should be vigilant about the homonyms in medicine in order to protect the safety of the patient. Care should be taken in spelling and pronunciation of medical terms to prevent any possible mistakes.

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Table I: Few examples of Homonyms in medicine

The term	The first meaning	The second meaning
Calculus	Kidney stone.	Name of heel bone.
Dermatome	An Area of skin that send sensory information to spinal cord.	Surgical instrument used to make shallow, continuous cut during skin grafting.
"Down" syndrome (Trisomy 21)	From higher to lower.	John Langdon Haydon Down (1828-1896) was a British physician. He described the syndrome in 1866.
"Hunter" syndrome (mucopolysaccharidosis Type II, a lysosomal storage disease)	A person who hunts.	Charles A. Hunter (1873-1955), who first described it in 1917.
Hutchinson's sign	Pigmentation of the proximal nail fold as a sign of subungual melanoma.	Vesicles on the tip of the nose as indicator of ophthalmic zoster.
Pelvis	Funnel-shaped area in kidney.	Hip bones with sacrum and coccyx.
"Sweet" syndrome	Having the taste of sugar.	Dr Robert Douglas Sweet, who first described it 1964.

Table 2: Few eponyms who can be misunderstood as related to countries

Eponyms who can be misunderstood as related to countries	Remarks
Acroangiodermatitis of Mali [2]	Named for Dr Mali, who reported it in 1965. He described it in 18 patients having mauve coloredmacules and papules predominantly over the extensor surface of feet with underlying chronic venous insufficiency.
Cronkhite-Canada syndrome [3]	It is a rare disease characterized by diffuse polyposis of the gastrointestinal tract, diarrhea, weight loss, abdominal pain, cutaneous hyperpigmentation, dystrophic changes of fingernails, and alopecia). It was first described in 1955 by the American internist Leonard Wolsey Cronkhite and the American radiologist Wilma Jeanne Canada in the New England Journal of Medicine.
German syndrome [4,5]	It is, one of the "arthrogryposis" hypotonia syndromes, was named after German who withother authors reported the condition for the first time in 1975.
Poland anomaly [6]	It is a pectoral muscle hypoplasia/aplasia variably associated with ipsilateral thoracic and/or upper limb anomalies. Named for Sir Alfred Poland (1822-1872), who was a19th-century British surgeon.

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Letter to the Editor

Sutures in dermatosurgery

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Sir,

Sutures are a very important component of dermatosurgery. During the three years post graduate curriculum in dermatology, hardly any kind of dermatosurgery or aesthetic dermatology is taught. Aesthetic dermatology is usually not practiced in the medical colleges. But their are some basic surgical techniques, which every dermatologist ought to know. The technique of closing wounds by means of needle and thread is several thousand years old [1]. The history of surgical sutures can be traced back to ancient Egypt where a number of surgical techniques involving sutures were used. There are two types of sutures: Absorbable and Non absorbable. The absorbable sutures include: Polyglactin, Polydiaxonone, PGA and Catgut. The nonabsorbable sutures include nylon, silk and polypropylene [2]. The size of the suture refers to the diameter of the suture strand. The more the zeroes characterizing the suture size, the smaller the resultant strand diameter. The smaller the suture, the lesser the tensile strength of the strand [3]. The suture size ranges from 7 to 11-0.

- Size 7 is largest
- Size 11-0 is smallest
- Size 7-0 approximately corresponds to the thickness of human hair.

The classification of the sutures is as follows:

- Absorbable/Non-Absorbable - Absorbable Sutures are those which undergo degradation in tissues, losing their tensile strength within 60 days. Non-Absorbable Sutures are those which are not digested by body enzymes or hydrolyzed in body tissue.
- Natural/Synthetic – Natural sutures includes gut, chromic gut, silk and collagen. Synthetic sutures includes nylon, polypropylene and stainless steel sutures.
- Braided/Monofilament- Monofilament is a single strand of material [4]. It is less resistance as it passes through the tissues. It causes less tissue reaction and less tissue drag but it has less knot security. It also resists bacterial harboring compared to braided suture. One should avoid using multifilament on the skin as it can harbor bacteria. Braided sutures are multifilament sutures that consist of several filaments or strands, twisted or braided together [5]. They have greater tensile strength and more pliability and flexibility. It causes more tissue reaction and more tissue drag but it has more knot security.
- Antibacterial Sutures: These are effective against S. aureus and S. epidermidis which are most common for device infections. They have ability to withstand manufacturing process. These do not negatively alter suture properties and have the ability to maintain antibacterial activity on the suture for a clinically relevant duration [6,7]. Coated polyglactin 910 (available as vicryl rapide) sutures with triclosan exhibit antibacterial activity on the suture in vitro against methicillin-sensitive and resistant S. aureus and S. epidermidis.

The various absorbable sutures are: Catgut, chromic catgut,vicryl and dexon.

Non absorbable sutures includes: Silk, prolene, nylon and Dacron.

DISCUSSION

Catgut has been used as a surgical suture since the 19th century. These days catgut is used as an absorbable suture world wide. Catgut is prepared from animal connective tissue and continues to play a major role in wound closure world wide [8].

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Suturing technique, the type of diameter of suture material, the type of surgical needle, the design of the surgical knot are essential factors for achieving optimizing wound healing. Tensile strength is an important quality when determining which suture materials are appropriate for specific situations. Therefore selection of suture materials should be based on the goals of the surgical procedure. There are two types of sutures, absorbable and non absorbable sutures. Sutures of biological origin like plain and chromic catgut are gradually digested by enzymes in the tissue, whereas absorbable sutures fabricated from synthetic materials like polyglycolic acid are hydrolyzed via the kreb's cycle. When using gut (plain or chromic)sutures, it is recommended to soak the package in warm water. This will remove the kinks and straighten the suture. Vicryl is an absorbable suture and is most commonly used while suturing in layers. Non absorbable sutures are made from natural or synthetic material. Silk has been the most commonly used material for skin suturing [9]. Silk is easy to handle but it has some disadvantages as it is a multifilament thread and it demonstrates wick effect which pulls bacteria and fluids into the wound site. Other nonabsorbable sutures include nylon, polyester, polyethylene.

The ideal suture should have the following characteristics:

- Sterile
- Easy to handle
- Resistant to infection
- High tensile strength
- Favorable absorption profile
- Uniform diameter and size

There are various types of natural and synthetic sutures:

- Catgut/chromic catgut – It is made of submucosa of small intestines.It is a multifilament and it breaks down by phagocytosis.Inflammatory reaction ic common with this suture.The plain catgut dissolves within 3 – 5 days and chromic catgut dissolves within 10-15 days.
- Vicryl (Polyglactin 910)– It is a braided synthetic absorbable suture which is stronger than catgut and retains strength for 3 weeks. It is broken down by enzymes and not by phagocytosis and the breakdown products inhibit bacterial growth. Its main advantage is that it can be used in contaminated wounds unlike other multifilaments.
- PDS (Polydioxine)- It is a synthetic absorbable suture with very good tensile strength which lasts months [10]. It is a monofilament which is absorbed completely by 182 days.
- Nylon – It is a synthetic suture. It can be mono or multifilament. It has a very less tissue reaction but poor knot security.
  Polypropylene – Also called prolene, it is a monofilament which is synthetic and does not lose strength over time. It has a good knot security and very little tissue reaction.
- Stainless steel suture – It is a monofilament and is the strongest of all the sutures. It has great knot security, very little tissue reaction and it does not harbor bacteria. Its main disadvantage is that it is difficult to handle and it can cut through the tissues.
- Skin staples – These are expensive but easy to put and have very little tissue reaction. The only disadvantage with the staples is that a special tool is required to remove it.

Regarding the knot strength, generally four throws are given for more than 90% knot security. If less throws are put, they are more likely to untie itself. Stainless steel sutures are an exception which require only two throws. The completed knot must be tight, firm, and tied so that slippage will not occur. To avoid wicking of bacteria, knot should not be placed in incision lines. Knots should be small and the ends cut short (2-3 mm). Excessive tension to finer gauge materials should be avoided as breakage may occur. Jerking motion should be avoided as it may break the suture. Crushing or crimping of suture materials should be avoided by not using hemostats or needle holders on them except on the free end for tying. Suture should not be tied too tightly as tissue necrosis may occur. Sutures should be removed in 7 to 10 days to prevent epithelialization or wicking about the suture.

CONCLUSIONS

To conclude, suturing is a surgical technique and is governed by the basic principles of aseptic techniques. Adequate knowledge about the size and type of sutures is very important for doing any type of dermatosurgery procedure.

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Historical Article

Eponyms related to genetic disorders associated with gingival enlargement: Part II

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There are genetic disorders associated with gingival enlargement. In our part I, we reviewed the eponyms linked to Hereditary Gingival Fibromatosis (HGF) [1]. In this part II of this review, we are going to shed some light on eponyms linked to groups of genetic disorders which may feature gingival enlargement (Table I) [2-15].

Table 1: Eponyms related to genetic disorders associated with gingival enlargment

Eponyms related to genetic disorders associated with gingival enlargement	Remarks
Anderson – Fabry Disease [2,3]	Also known as Fabry disease, angiokeratoma corporis diffusum and alpha-galactosidase A defi-ciency. It is a rare X-linked lysosomal storage disease, which can cause a wide range of systemic symptoms. The disease is named for Johannes Fabry (1860-1930), (Fig. 1). who was a German dermatologist. And William Anderson (1842-1900), (Fig. 2), who was an English surgeon and dermatologist. In this disease the angiokeratomas may also involve the oral mucous membrane and the gingiva. Histologically, angiokeratoma of the gingiva shows ceramide inclusions not only in the connective tissue, but also in the oral epithelial cells
Goltz syndrome [4,5]	This is another name for, focal dermal hypoplasia. Also called Goltz-Gorlin syndrome. It is a rare syndrome and may result in multisystem disorders. Robert William Goltz, (Fig. 3), is an American dermatologist, born 1923. Robert James Gorlin (1923-2006), (Fig. 4), was an American oral pathologist and geneticist. Partial anodontia is the characteristic dental feature. Other oral manifestations include lip papillomas, gingival enlargement and hypoplastic teeth. Histopathologic features showed deposits of fat cells or adipose tissue in the dermis
Hunter syndrome [6]	Also known as Mucopolysaccharidosis II. It is a rare, X-linked disease caused by a deficiency of the lysosomal enzyme iduronate-2-sulfatase, which catalyses a step in the catabolism of glycosaminoglycans. The glycosaminoglycans accumulate within tissues affecting multiple organs and physiologic systems. The clinical manifestations include neurologic involvement, severe airways obstruction, skeletal deformities and cardiomyopathy. Hunter syndrome presents the same oral manifestations as Hurler syndrome.Hunter syndrome is named after physician Charles A. Hunter (1873-1955), who first described it in 1917. Born in Scotland, Hunter emigrated to Canada and had a medical practice in Winnipeg, Manitoba
Hurler syndrome [7-9]	This is another name for Mucopolysaccharidosis type I (MPS I). It is one of the most frequent lysosomal storage diseases. It has a high morbidity and mortality, causing in many cases severe neurological and somatic damage in the first years of life. MPS I involves a broad spectrum of clinical symptoms and can be divided into three clinical subtypes: Hurler, Hurler/Scheie, and Scheie syndromes. Scheie syndrome is considered a less severe version of Hurler syndrome. Gingival hyperplasia is a common feature in Hurler syndrome.Other intraoral features include macroglossia, spaced hypoplastic peg-shaped teeth with retarded eruption. Gertrud Hurler (1889-1965), (Fig. 5), was a German Pediatrician and a Medical practitioner. Harold Glendon Scheie (1909-1990), (Fig. 6), was an American Ophthalmologist
Klippel-Trenaunay Syndrome (KTS) [10]	It is an uncommon mesodermal phakomatosis characterized by a triad of cutaneous and visceral hemangiomas, venous varicosities and soft tissue or bone hypertrophy. It was first described, in 1900, by French physicians Maurice Klippel (1858-1942) and Paul Trénaunay. Frederick Parkes Weber (1863-1962), (Fig. 7), who was an English dermatologist described cases in 1907 and 1918 that were similar but not identical to those described by Klippel and Trénaunay. KTS may be associated with many oral abnormalities such as gingival enlargement, gingival capillary hemangiomas, gingival fibroma, gingival fibromatosis, gingival hyperplasia, high arched palate, unilateral hypertrophy, or increase in size of periodontal tissues, tongue capillary hemangiomas and unilateral macroglossia

Contd...

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Table 1: continued...

Eponyms related to genetic disorders associated with gingival enlargement	Remarks
Maroteaux-Lamy Syndrome [11]	This is another name for Mucopolysaccharidosis VI (MPS VI). It is an inheritable, clinically heterogeneous lysosomal storage disorder that develops due to a deficiency in the arylsulfatase B (ASB) enzyme. This deficiency impairs the stepwise degradation of glycosaminoglycans (GAGs) resulting in the accumulation of partially degraded GAGs in tissues and organs throughout the body. The oral findings include short or stubby, malformed, peg-shaped, poorly formed and calcified teeth with delayed eruption and gingival hyperplasia. It is named after Pierre Maroteaux (1926-), (Fig. 8), and his mentor Maurice Emil Joseph Lamy (1895-1975), both French physicians
Menkes Kinky hair Disease [12]	It is a very rare X-chromosome disorder affecting copper metabolism. Menkes et al. in 1962, first described the disease in a family of English-Irish descent living in New York, who presented by early retardation in growth, peculiar hair, and focal cerebral and cerebellar degeneration. The disease leads to psychomotor retardation, pili torti, pallor, seizures and death in infancy or early childhood The oral findings include delayed dentition and gingival hyperplasia. The disease is named after John Hans Menkes (1928-2008) (Fig. 9). Menkes, was born in Vienna. In 1939, following the German annexation of Austria, the family fled Austria and immigrated to the USA via Ireland. Menkes was then eleven years old. Menkes, son and grandson of physicians, followedthefamilytraditionandstudiedmedicine, despitehiswishtobecomeajournalist. Menkes became head of pediatric neurology at the Johns Hopkins Hospital and later at the University of California, Los Angele (UCLA)
Niemann - Pick disease [13]	This disease is a form of sphingolipidosis, which in turn, are included in the larger family of lysosomal storage diseases (LSDs). Oral findings include thick lips, macroglossia and widely spaced teeth. Gingival enlargement is not considered a constant feature. Albert Niemann (1880-1921), who was a German physician published the first description of what is now known as Niemann-Pick disease, type A, in 1914. Ludwig Pick (1868-1944), (Fig. 10), who was a German pathologist described the pathology of the disease in a series of papers in the 1930s
Sly syndrome [14]	This is another name for Mucopolysaccharidosis Type VII. It is an autosomal recessive lysosomal storage disease characterized by a deficiency of the enzyme β-glucuronidase, a lysosomal enzyme. Sly syndrome belongs to a group of disorders known as mucopolysaccharidoses, which are lysosomal storage diseases. The oral features include mainly thickening of the alveolar ridges and rarely gingival hyperplasia. It was named after its discoverer William S. Sly (1932-), (Fig. 11), an American Biochemist, in 1969 who has spent nearly his entire academic career at Saint Louis University
Sturge Weber syndrome [10]	It is a rare sporadic condition of mesodermal phakomatosis, characterized by purple-colored flat cutaneous cranial (face) hemangiomas (most commonly along the trigeminal nerve), glaucoma and vascular lesions in the ipsilateral brain and meninges. One of its features is unilateral vascular hyperplasia of oral mucosa and gingiva. It is named for William Allen Sturge (1850-1919), (Fig. 12), who was an English physician and Frederick Parkes Weber (1863-1962), (Fig. 7), who was an English dermatologist
Wilson syndrome [15]	Wilson disease (WD) is a genetic disorder with copper metabolism disturbances leading to copper accumulation in many organs with their secondary damage. It is caused by mutation in the ATP7B gene on chromosome 13, which encodes ATP-ase 7B involved in copper transport. It is characterized by multiple small red papules of the lips, gingival enlargement, early onset periodontitis, and repeated oral candidiasis. Enamel hypoplasia is the characteristic dental feature. Wilson's disease is named after Samuel Alexander Kinnier Wilson (1878-1937) (Fig. 13), the British neurologist who first described the condition in 1912. Kayser-Fleischer rings (KF rings) are dark rings that appear to encircle the iris of the eye. They are due to copper deposition in Descemet's membrane as a result of this disease. They are named after Dr. Bernhard Kayser (1869-1954) and Dr. Bruno Fleischer (1874-1965), (Fig. 14), the German doctors who first described them in 1902 and 1903. Initially thought to be due to the accumulation of silver, they were first demonstrated to contain copper in 1934

Figure 1: Johannes Fabry (1860-1930)

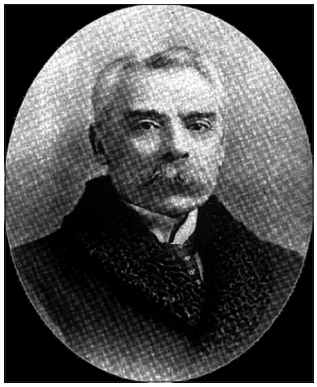

Figure 2: William Anderson (1842-1900)

Figure 3: Robert William Goltz

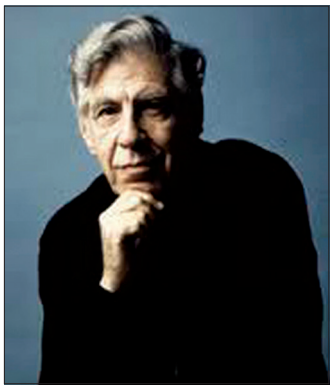

Figure 4: Robert James Gorlin (1923-2006)

Figure 5: Gertrud Hurler (1889–1965)

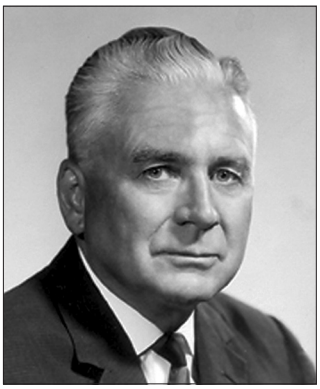

Figure 6: Harold Glendon Scheie (1909-1990)

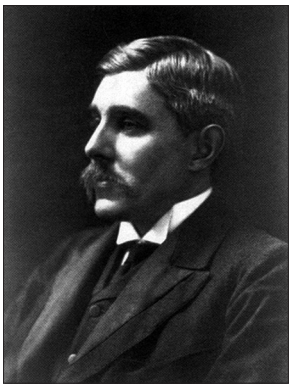

Figure 7: Frederick Parkes Weber (1863-1962)

Figure 8: Pierre Maroteaux (1926-)

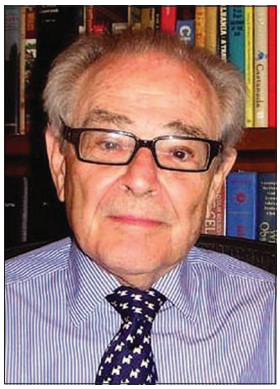

Figure 9: John Hans Menkes (1928-2008). Reprinted with permission from Neurology Today, an official publication of the American Academy of Neurology

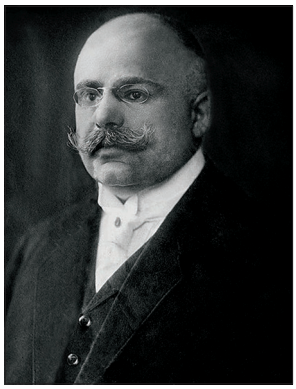

Figure 10: Ludwig Pick (1868-1944)

Figure 11: William S. Sly

Figure 12: William Allen Sturge (1850-1919)

Figure 13: Samuel Alexander Kinnier Wilson (1878-1937)

Figure 14: Bruno Fleischer (1874-1965)

These groups include lysosomal storage disorders, vascular disorders and syndromes characterized by the presence of characteristic dental abnormalities.

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NASZA DERMATOLOGIA Online
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Historical Article

Dermatology Eponyms – sign –Lexicon (O)

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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 (O) and other. The symptoms and their synonyms, and those who have described this symptom or phenomenon.

Key words: Eponyms; skin diseases; sign; phenomenon

OBLATEN SIGN (THE LAST HÄUTSCHEN SIGN)

In Psoriasis. Last little piece of skin. If all scale is removed, a most, thin, translucent layer of skin covering the lesion is revealed. The lesion remains dry until this last level is reached [1].

OIL DROP (SPOT) SIGN

Nails with pitting, onycholysis, subungual hyperkeratosis, irregular and brown nail bed discoloration in Psoriasis [2].

Psoriasis can affect the nails and produces a variety of changes in the appearance of finger and toe nails. These changes include pitting of the nails (pinhead-sized depressions in the nail is seen in 70% with nail psoriasis), whitening of the nail, small areas of bleeding from capillaries under the nail, yellow-reddish discoloration of the nails known as the oil drop or salmon spot, thickening of the skin under the nail (subungual hyperkeratosis), loosening and separation of the nail (onycholysis), and crumbling of the nail [3,4].

OMNIBUS SIGN

Eyebrow alopecia in secondary syphilis (Fig. 1)- this phenomenon was known to French syphilologists at the turn of the century as Pautrier's signed'omnibus, "the omnibus sign," or the sign which could be seen by a glance at a patient in an omnibus— from the sidewalk [5].

LUCIEN-MARIE PAUTRIER

French dermatologist, 1876-1959 (Fig. 2). He commenced his medical studies in Marseille but transferred to Paris where he was influenced towards dermatology by Emile Leredde and became a

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dermatologist with Louis-Anne-Jean Brocq at the Hôpital Saint-Louis.

His thesis in 1903 on "Atypical Cutaneous Tuberculosis," an imposing 350 page document, attracted the attention of Ferdinand-Jean Darier with Pautrier's demonstrations and clear patient presentation.

He joined the army at the outbreak of the first World War and became a medical officer to a field artillery regiment. He was awarded the Croix de Guerre for bravery under fire and became a Chevalier de la Légion d'Honneur in 1916, finally becoming Grand Officer. Towards the end of the war he established a centre for investigation of skin and venereal disease in Bourges, in the département Cher in Central France.

When the war ended and the Alsace once more became a part of France, he was appointed professor of dermatology at Strasbourg and there rapidly built up a national and worldwide reputation which attracted students from all over the world. When the second World War commenced he was repatriated to Claivive in the Dordogne, but in 1942 he was invited to take the chair of dermatology in Lausanne, Switzerland, when professor Edwin Ramel died.

At the end of the war he returned to Strasbourg, but two years later retired, occupying himself with his great loves of art and music. He was a close friend of the Romanian violinist Georges Enesco, known for his interpretation of Bach and his work in Romanian style. He founded a society of the Friends of Music in Strasbourg and was largely responsible for the 21st Festival of Music in that city. He founded the Society of Friends of the avant-garde cinema and finally whilst he was president of the Friendly Society of the University of Strasburg he managed to find the necessary funds to create a centre for research in experimental surgery [6,7].

JEAN ALFRED FOURNIER

French dermatologist, 1832-1914 (Fig. 3). He specialized in the study of venereal disease. As a young man he served as an interne at the Hôpital du Midi as an understudy to Philippe Ricord. In 1863 he became médecine des hôpitaux, and from 1867 worked with Augustin Grisolle at the Hôtel-Dieu de Paris. In 1876 he was appointed chef de service at the Hôpital Saint-Louis, later becoming a member of the Académie de Médecine (1880).

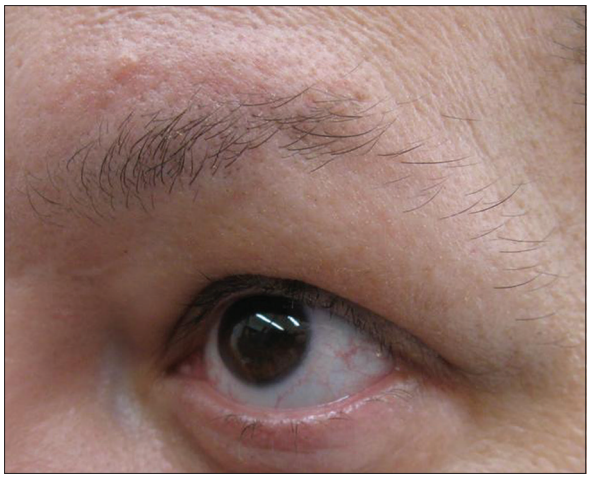

Figure 1: Omnibus sign

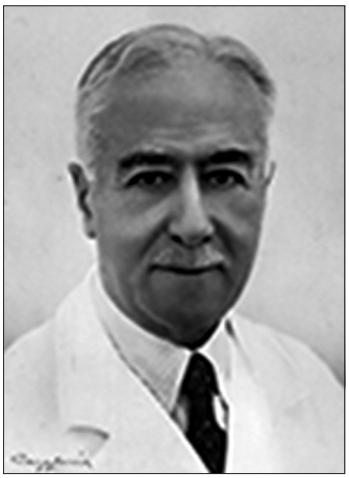

Figure 2: Lucien-Marie Pautrier

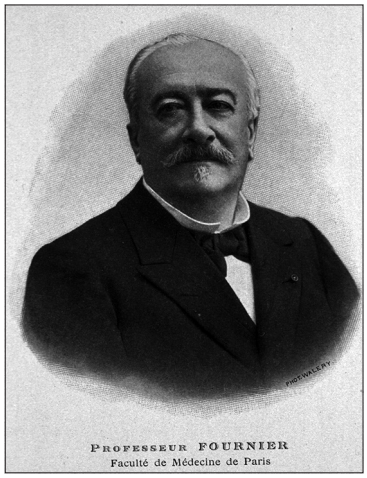

Figure 3: Jean Alfred Fournier

His main contribution to medical science was the study of congenital syphilis, of which he provided a description of in 1883. In his numerous publications he stressed the importance of syphilis being the cause

of degenerative diseases. In addition, he founded an organization called the Société Française de Prophylaxie Sanitaire et Morale.

His name is associated with the following three medical terms:

Fournier's gangrene: Gangrene caused by infection of the scrotum and usually associated with diabetes. Although the condition is named after Fournier, it was first described by a physician named Baurienne in 1764.

Fournier's sign: Scars on the mouth following the healing of lesions in congenital syphilis.

Fournier's tibia: Fusiform thickening and anterior bowing of the tibia in congenital syphilis.

Along with his study of venereal disease, Fournier was also a medical historian, republishing works by erstwhile physicians that included Girolamo Fracastoro, Giovanni de Vigo and Jacques de Béthencourt. [6,8].

ORKIN SIGN

Cerebriform dermal nevus in pseudocutis verticis gyrata [9,10]. The possible malignant degeneration of this disease, which can also be described as "cerebriform intradermal nevus".

OSLER'S SIGN

1. Blue black pigmentation in the sclera near insertion of rectus muscle in patients who have Alkaptonuria (Endogenous ochronosis) [11].
2. Small, painful, erythematous swellings in the skin of the hands and feet in malignant endocarditis (Figs 4a and b). Also known as Osler's nodes [12].

SIR WILIAM OSLER, BARONET

Canadian physician, 1849-1919 (Fig. 5). He played a key role in transforming the organization and curriculum of medical education, emphasizing the importance of clinical experience.

He began to study arts at Trinity College, Toronto, but decided that the church was not for him and entered the Toronto Medical School in 1868. He subsequently transferred to McGill University in Montreal, Quebec, where he took his medical degree in 1872. During the following two years he visited medical centres in London, Berlin, Leipzig, and Vienna, spending the longest period at University College, London, in the physiology laboratory of John Burdon-Sanderson, who was making experimental physiology pre-eminent in medical education.

Osler returned to Canada and began general practice in Dundas, Ontario, but was soon appointed lecturer in the institutes of medicine at McGill University, Montreal. He became professor there in 1875. A year later he became pathologist to the Montreal General Hospital and in 1878 physician to that hospital.

In 1888 Osler accepted an invitation to be the first professor of medicine in the new Johns Hopkins University Medical School in Baltimore. It was here that he established himself as the most outstanding medical educator of his time, and commenced the modern era as we know it today.

In 1873 Osler demonstrated that hitherto unidentified bodies in the blood were in fact the third kind of

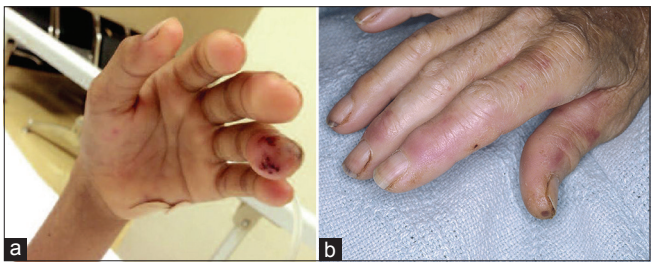

Figure 4: (a) Osler's sign. From Dr Chiam Keng Hoong z Hospital Sultanah Bahiyah Alor Setar, Malaysia (b) Osler's sign

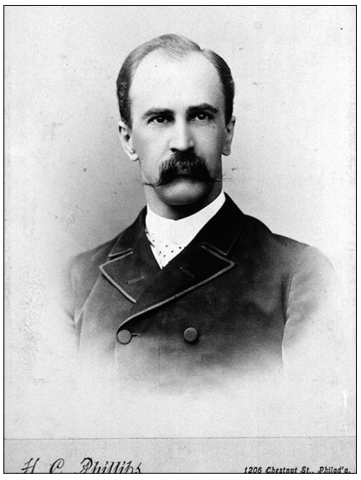

Figure 5: Sir Wiliam Osler, Baronet

blood corpuscles, which were later named the blood platelets. These corpuscles had been observed before, but no one before Osler had studied them so thoroughly [13,14].

Osler lent his name to a number of diseases, signs and symptoms, as well as to a number of buildings that have been named for him.

Osler's sign; Osler's nodes; Rendu-Osler-Weber disease (also known as hereditary hemorrhagic telangiectasia); Osler-Vaquez disease (also known as Polycythemia vera); Osler-Libman-Sacks syndrome; Osler's filaria; Osler's manoeuvre; Osler's rule; Osler's syndrome; Osler's triad: association of pneumonia, endocarditis, and meningitis; Sphryanura osleri.

OCCULTA HAIR SIGN

The tuft of hair found over a spina bifida (Figs 6 – 7a, b) [15].

OGLE'S SIGN

Decrease in the sense of smell as leukoderma spreads [16]. Also called anosmia.

WILLIAM OGLE

British physician, and lecturer on physiology at St. George's Hospital, 1827-1912 [17].

OIL FEVER SIGN

Fever and encephalitis caused by the mosquito-borne zoonotic Bunyaviridae viral Tahyna fever [18].

OMSK SIGN, [RUSSIA]

Flu symptoms, then encephalitis including deafness. Caused by the tick-borne zoonotic Omsk hemorrhagic fever virus [19].

OPALESCENT SIGN

Violet colored teeth that have an opalescent iridescence (Fig. 8a-d). A sign of dentinogenesis imperfecta. This sign when found in a patient with blue sclerae indicates the presence of osteogenesis imperfecta. Also known as brittle bone disease [20].

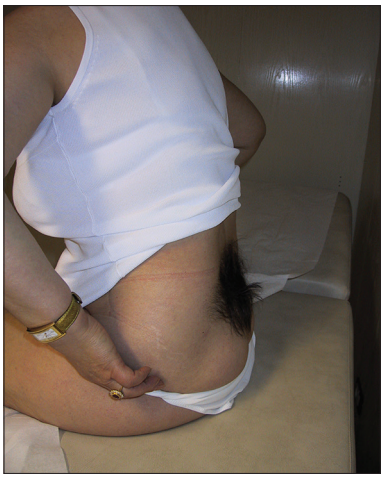

Figure 6: Occulta Hair sign. Courtesy dr. Stefano Boriani, Unit of Oncologic and Degenerative Spine Surgery, from the archives of Rizzoli Institute, Bologna, Italy

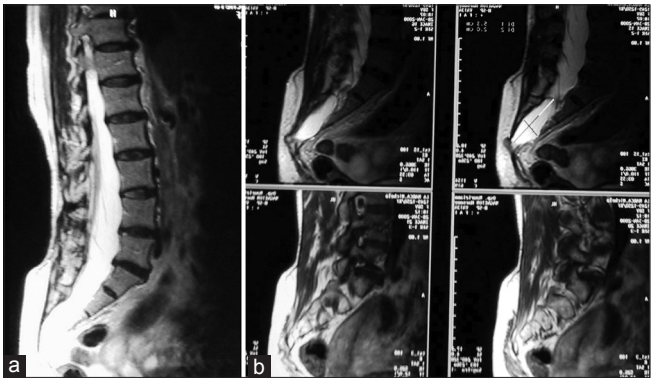

Figure 7: (a) Occulta Hair sign. Courtesy dr. Stefano Boriani, Unit of Oncologic and Degenerative Spine Surgery, from the archives of Rizzoli Institute, Bologna, Italy (b) Occulta Hair sign. Courtesy dr. Stefano Boriani, Unit of Oncologic and Degenerative Spine Surgery, from the archives of Rizzoli Institute, Bologna, Italy

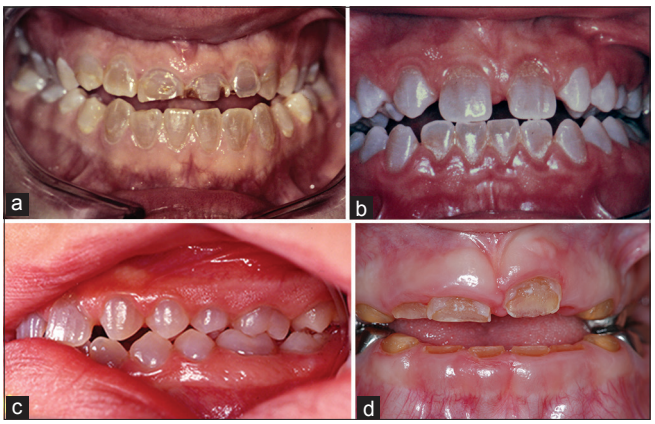

Figure 8: (a-d) Opalescent sign. A sign of dentinogenesis imperfecta

OPERCULUM SIGN

Acute inflammation of the gingival tissue partially covering an incompletely erupted tooth. Often involves

trismus and severe pain. Operculum is Latin for little lid as it correctly describes the flap of tissue. Also known as acute pericoronitis [21].

ORANGE-PEEL SIGN

A sign for distinguishing lipoma: on compressing the tumor between the thumb and forefinger, it will be perceived that the skin overlying the mass is irregularly dimpled by the downward traction of the vertical trabeculae [22]. Also used to determine breast inflammation. Called also signe de peau d'orange [23].

ORF SIGN

"Orf" is name given to a skin condition in humans caused by the same parapoxvirus. The infection in humans is named orf; alternative synonymns are contagious ecthyma or contagious pustular dermatitis (Figs 9a - c).

Chronic (weeks to months), poorly healing exudative papules, develop most commonly on the hands and arms.

The virus is acquired by direct contact with exudates from sheep or goats with clinical lesions [24,25].

ORIENTAL EYEWORM SIGN

Conjunctivitis caused by the zoonotic Thelazia roundworm infecting the orbital cavities and associated tissues [26].

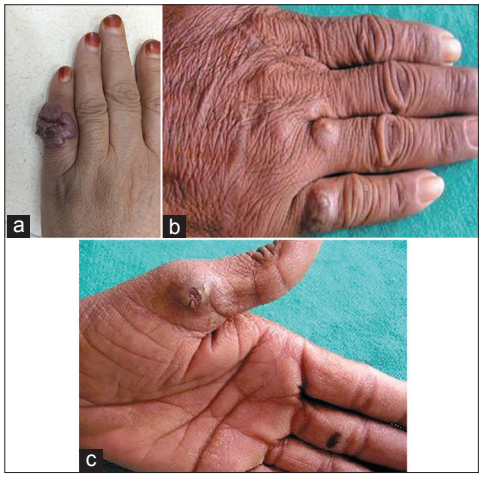

Figure 9: (a-c) Orf sign

LOUIS-JOSEPH ALCIDE RAILLIET

French veterinarian and helminthologist, 1852-1930. Professor at the Veterinary School of Alfort, he received the Legion of Honor. He is considered one of the founders of modern parasitology. He chaired the Zoological Society of France in 1891. He was a member of the Academy of Medicine.

Railliet's name is honoured by several genera: Raillietia (Acari), Raillietina (Cestodes), Raillietascaris, Raillietnema and Raillietstrongylus (Nematodes), Raillietiella (Pentastomida), et the Acari family Raillietiidae.

Numerous species were named after Railliet, such as Amidostomum raillieti, Angiocaulus raillieti, Aspidodera raillieti, Conoweberia raillieti, Eucoleus raillieti, Haemostrongylus raillieti, Henryella raillieti, Onchocerca raillieti, Protostrongylus raillieti, Quasiamidostomum raillieti, and Thominx raillieti (Nematodes), Coccidium raillieti and Eimeria raillieti (Coccidia), Dibothriocephalus raillieti, Hilmylepis raillieti, Ichthyotoenia raillieti, Sparganum raillieti, and Synthetocaulus raillieti (Cestodes).

All these animals are parasites, named in honour of Railliet by other parasitologists [27].

ALBERT-JOSEPH-LUCIEN HENRY

Ouch-ouch sign

Chills, muscle aches, the loss of the ability to smell, headache, fever, skeletal damage, with respiratory and renal failure. Indications of cadmium poisoning. Can be associated with mining, industrial wastes, fertilizers, smoking cigarettes, and smoking marijuana that has been grow in soils containing high levels of the soft toxic metal. Known as the cadmium blues and in Japan as the itai-itai disease [28].

Oxalic sign

Burning pains in mouth and throat with vomit containing white lumps of mucous and altered brown or black blood. Stains on skin and mucous membranes appear white or brown and stains clothing brown or orange. A sign of poisoning with oxalic acid. Also known as Lemon Salt sign and Sorrel Salt sign [29].

Oyster blister sign

Bullous skin lesions, severe diarrhea and dehydration, with high mortality rate. Caused by the zoonotic vibriosis diseases contained in raw oysters, mussels, crabs, and shrimp [30].

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NASZA DERMATOLOGIA Online
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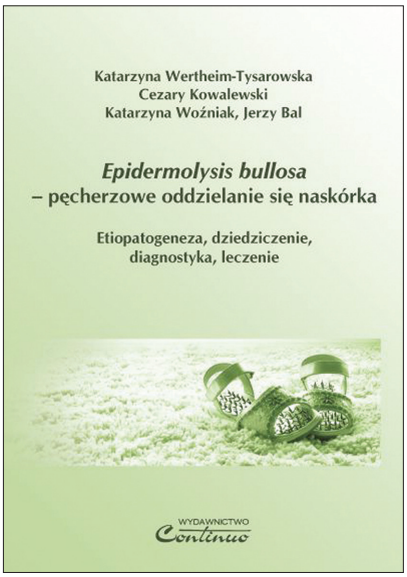
Book Review

Epidermolysis bullosa – pęcherzowe oddzielanie się naskórka. Etiopatogeneza, dziedziczenie, diagnostyka, leczenie

Epidermolysis bullosa. Etiopathogenesis, inheritance, diagnosis, treatment



Katarzyna Wertheim-Tysarowska, Cezary Kowalewski, Katarzyna Woźniak, Jerzy Bal

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Epidermolysis bullosa jest chorobą genetycznie uwarunkowaną, zaliczaną do tzw. chorób sierocych. Szacuje się, że różnych chorób tego typu jest ponad 6000. Mimo, że częstość ich występowania nie jest wysoka, stanowią w krajach wysoko rozwiniętych ogromny problem diagnostyczny, terapeutyczny i psychospołeczny. Stąd też potrzeba badań nad ich patologią, jak również upowszechniania wiedzy zarówno wśród lekarzy, jak i chorych oraz ich rodzin.

Monografia "*Epidermolysis bullosa* – pęcherzowe oddzielanie się naskórka. Etiopatogeneza, dziedziczenie, diagnostyka, leczenie" to pierwsze na polskim rynku wydawniczym źródło wiedzy dotyczące tej choroby, napisane przez naukowców oraz klinicystów z wieloletnim doświadczeniem w takich specjalnościach jak dermatologia i genetyka.

Autorzy w sposób przystępny i bogato ilustrowany przedstawiają aspekty kliniczne, diagnostyczno-genetyczne oraz terapeutyczne *epidermolysis bullosa*. Monografia kierowana jest do szerokiego grona odbiorców, w tym studentów kierunków biomedycznych, praktykujących lekarzy różnych specjalności oraz osób bez wykształcenia medycznego, pragnących pogłębić swoją wiedzę dotyczącą tej choroby.

Epidermolysis bullosa is a disease caused by an inherited genetic condition, that belongs to the so-called orphan diseases. It is estimated that there are more than 6000 various diseases of this type. Although their incidence is not high, they pose a huge diagnostic, therapeutic and psychosocial problem in developed countries. Hence there is a need for research on the pathology, as well as the dissemination of knowledge among both physicians and patients and their families.

Monograph "*Epidermolysis bullosa*. Etiopathogenesis, inheritance, diagnosis, treatment" is the first on the Polish market source of knowledge about the disease, written by researchers and clinicians with years of experience in specialties such as dermatology and genetics.

The authors in a popular and richly illustrated way show both the clinical, diagnostic, genetic and therapeutic features of *epidermolysis bullosa*. The monograph is addressed to a wide audience, including biomedical students, practitioners of various specialties and people with no medical training who wish to deepen their knowledge about the disease.

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