

A 68-year-old man with exfoliative erythroderma: a diagnostic dilemma?

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ABSTRACT

Exfoliative erythroderma is an uncommon entity with guarded prognosis. It is characterized by generalized erythematous and exfoliative skin lesions, which affect over 80% of the body surface. The predisposing factors in adults include psoriasis, eczema (atopic, seborrheic, or contact), drug adverse effects, ichthyosis, cutaneous T-cell lymphoma, pityriasis rubra pilaris, Norwegian scabies, and Sézary syndrome. Our aim is to report a case study with conclusive clinical and histopathological data, emphasizing diagnosis challenges. We report the case of a 68-year-old man presenting with exfoliative erythroderma. He had a history of alcoholism, arterial hypertension, and plaque psoriasis, and he had rapidly reduced his daily oral corticosteroid dose. The patient's management included prednisone, methotrexate, hydroxyzine, loratadine, furosemide and diltiazem, in addition to topical care and nutritional support. After a period of clinical improvement, he had a recurrence of exfoliative erythroderma and died due to bacterial sepsis. The infectious agent that caused sepsis was a carbapenem-resistant strain of *Pseudomonas aeruginosa*. Because of frequent diagnosis challenges involving this uncommon and severe clinical entity, main features, predisposing factors, and precipitating factors should be highlighted to enhance the index of suspicion, which contributes to early diagnosis.

Key words. Dermatitis; exfoliative; erythroderma; erythema; psoriasis

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RESUMO

Homem de 68 anos com eritrodermia esfoliativa: um dilema diagnóstico?

A eritrodermia esfoliativa é uma entidade incomum com prognóstico reservado, caracterizada por lesões cutâneas eritematosas e esfoliativas generalizadas, que acometem mais de 80% da superfície corporal. As condições predisponentes em adultos incluem psoríase, eczema (atópico, seborréico ou de contato), efeitos adversos a drogas, ichtiose, linfoma cutâneo de células T, pitiríase rubra pilar, sarna norueguesa e síndrome de Sézary. O objetivo é relatar um caso de eritrodermia esfoliativa com dados clínicos e histopatológicos conclusivos, enfatizando-se dificuldades diagnósticas. Relata-se o caso de um homem de 68 anos com eritrodermia esfoliativa. Havia antecedente de alcoolismo, hipertensão arterial e psoríase em placas; e ele havia reduzido rapidamente a dose diária de corticosteroide oral. O tratamento do paciente incluiu prednisona, metotrexato, hidroxizina, loratadina, furosemida e diltiazem, além de cuidados locais e suporte nutricional. Após um período de melhora clínica, ele teve recorrência de eritrodermia esfoliativa e faleceu em virtude de septicemia bacteriana por *Pseudomonas aeruginosa* resistente a carbapenênicos. Por causa de frequentes dificuldades diagnósticas envolvendo essa entidade clínica incomum e grave, as principais características, condições predisponentes e fatores precipitantes devem ser ressaltados para aumentar o índice de suspeita, contribuindo para o diagnóstico precoce.

Palavras-chave. Dermatite esfoliativa; eritrodermia; eritema; psoríase.

INTRODUCTION

Exfoliative erythroderm is an uncommon entity with guarded prognosis, characterized by generalized erythematous and exfoliative skin lesions, which affect over than 80% of body surface.¹⁻⁵ In adults, previous psoriasis and eczema (atopic, seborrheic, or contact) constitute the main causes. Other predisposing conditions for exfoliative erythroderma include drug adverse effect, ichthyosis, cutaneous T-cell lymphoma, pityriasis rubra pilar, Norwegian scabies, and Sézary syndrome.¹⁻⁵

Detailed anamnesis is necessary to identify possible risk factors like infections, ingestion or topic use of medicines (e.g. anti-inflammatory, anti-hypertensive, sulfonamides, antibiotics, allopurinol, or carbamazepine).¹⁻⁵ Suspicious cases of exfoliative erythroderma must be confirmed by histopathology.¹⁻⁵ Systemic or oral corticosteroids, methotrexate, cyclosporine, infliximab and etanercept constitute the usual medicines to control episodes of exfoliative erythroderm associated with psoriasis.⁵ The main causes of death among patients with exfoliative erythroderm are septic and thromboembolic episodes.³

CASE REPORT

A 68-year-old man with antecedent of alcoholism, arterial hypertension and psoriasis was referred to Hospital das Forças Armadas, Brasília-DF, with erythematous, desquamative and itching lesions scattered on the trunk and upper extremities, which appeared after the abrupt taper of oral corticosteroid dose. These lesions had a rapid onset and affected almost all his body surface in less than a week. He was taking captopril to control hypertension and prednisone for plaque-type psoriasis. He denied personal and family history of atopy, photo-sensibility, as well as arthralgia.

Before his admission, the hypothesis was psoriasis plus pellagra due to alcoholism, and blood tests showed (normal range = NR): glucose 114 mg/dL (NR = 70 - 99 mg/dL), albumin: 3.54 g/dL (NR = 3.5 - 5.2 g/dL), triglycerides: 144 mg/dL (NR < 150 mg/dL), total cholesterol: 164 mg/dL (NR < 200 mg/dL), HDL: 40 mg/dL (NR > 40 mg/dL), LDL: 95.2 mg/dL (NR < 130 mg/dL, VLDL: 28.8 mg/dL (NR < 40 mg/dL), and normal urinalysis.

On admission, he was eutrophic (body mass index: 23.7 kg/m²); blood pressure: 140/100 mmHg; pulse rate: 98 bpm; temperature: 36.6°C; there was neither lymph node enlargement nor visceromegaly. Confluent scaling plaques were scattered on his face, neck, trunk and limbs (Figure 1), and involved flexural areas, palms and soles. His clinical features were strongly suggestive of exfoliative erythroderma; worth of note was the absence of changes on



Figure 1. Confluent scaling plaques are disseminated on the trunk and limbs in a subject with exfoliative erythroderma.

the nails and mucous membranes. The electrocardiogram revealed signs of moderate left ventricle hypertrophy, and the image of chest radiography was normal. Remarkable laboratory findings were anemia, leukocytosis, eosinophilia and renal insufficiency (Table).

Skin biopsy studies supported the diagnosis of acute generalized exanthematic dermatosis due to severe erythrodermic psoriasis (Figure 2). There was irregular hyperplasia of epidermis,

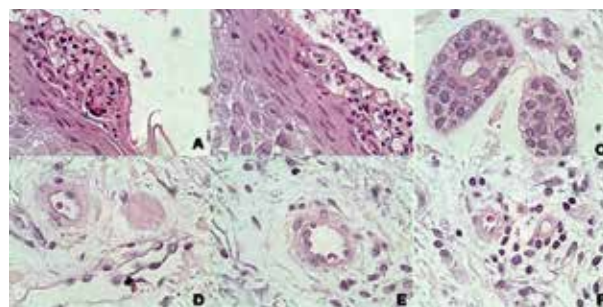


Figure 2. (A,B,C) Intracorneal Munro's microabscesses and spongiform micropustules of Kogoj in the superficial stratum spinosum, irregular hyperplasia of epidermis, hyperkeratosis and focal parakeratosis (D,E,F). Dilated tortuous vessels in the superficial derma, with lymphohistiocytic and eosinophilic perivascular infiltrates and edema. Hematoxylin and eosin; A and B 10x; C, D, E, and F 40x

Table. Laboratory data of a 68-year-old man with severe exfoliative erythroderma

PARAMETERS	ADMISSION	DAY 3	DAY 7	DAY 10	DAY 12	DAY 35	8 MONTHS*
Hemoglobin (g/L)	9.6	9.6	9.2	9.7	8.6	9.5	8.8
Hematocrit (%)	30.6	29.1	27.8	29	25.8	28.4	28.1
WBC ($\times 10^9/L$)	18.2	12	10.4	12.5	15.6	18	9.7
Eosinophils (%)	10	20	12	14	3	14	21
Lymphocytes (%)	16	6	13	12	25	6	9
Platelets ($\times 10^9/L$)	582	480	454	481	424	609	651
ESR (mm/hour)	60	Nd	51	63	48	47	Nd
US-CRP	Nd	4.9	6.7	6.7	Nd	0.9	23.8
Urea (mg/dL)	68.9	48.8	47.3	64.3	51.7	110.9	50
Creatinine (mg/dL)	1.7	1.5	1.6	1.5	1.4	1.6	2
Sodium (mEq/L)	141	138	138	138	136	132	136
Potassium (mEq/L)	4.6	4.7	4.2	4.3	4.2	4.8	5.1
Calcium (mg/dL)	Nd	9	8.6	Nd	9.5	9	9.5
Magnesium (mEq/L)	Nd	1.8	1.7	1.7	1.8	1.9	1.7
AST/ALT (U/L)	Nd	21.7/12.2	Nd	22.6/9.1	18.7/10.6	Nd	Nd

*Death. WBC: leukocytes. ESR: erythrocyte sedimentation rate. US-CRP: ultra-sensitive C-reactive protein. AST/ALT: aspartate aminotransferase/alanine aminotransferase. Nd: not done. Abnormal data are showed in italic.

hyperkeratosis with focal parakeratosis and apoptotic keratinocytes; moreover, neutrophilic pustules (Munro's abscesses) and spongiform pustules of Kogoj were found in the stratum corneum and in the superficial stratum spinosum. Superficial derma showed edema, vasodilation and congestion, with lymphohistiocytic and eosinophilic perivascular infiltrates. Initially, he evolved with worsening and dissemination of the skin changes, and development of pitting edema in the lower limbs.

His treatment schedule included prednisone, methotrexate (12.5 mg/week), hydroxyzine (25 mg/day), loratadine (10 mg/day), topical care (antiseptic baths, keratolytics and emollients), vitamin supplements and nutritional support, furosemide and diltiazem (instead of captopril). During hospitalization, the patient presented with respiratory symptoms and chest radiography images of inflammatory infiltrate on the right lung, which was successfully treated by levofloxacin. An acute episode of gouty arthritis (uric acid: 8.1 mg/dL (NR = 3.4 - 7.0 mg/dL) affecting the left wrist was rapidly controlled by nonsteroidal anti-inflammatory drugs. His general improvement was gradually achieved, and the erythematous desquamation of the skin completely subsided without any remarkable sequel 35 days after his hospital admission.

After hospital discharge, he was referred to specialized outpatient surveillance. A new episode of exfoliative erythroderma flared up seven months later, and he received clinical, nutritional and intensive care support during three weeks. Notwithstanding, his death occurred following a severe bacterial sepsis, which was unresponsive to treatment.

DISCUSSION

Exfoliative erythroderma constitutes a severe and uncommon condition, with high morbidity and mortality rates.¹⁻⁵ This entity predominantly affects male individuals over 40 years of age, with a skin disease.¹⁻⁵ We report the occurrence of exfoliative erythroderma after rapid tapering of oral corticosteroid used to treat psoriasis in a 68-year-old

Brazilian man with antecedent of alcoholism and arterial hypertension. With diagnosis of plaque-type psoriasis, he was under treatment with prednisone in other service.

Fernandes *et al* performed a study about erythroderma in 170 Brazilian patients aging from 30 to 80 years, 92 (54.1%) male.² Previous skin diseases were found in 99: 58.23% of the cases, mainly psoriasis (66: 66.7%), contact eczema (18: 18.2%), and atopic eczema (7: 7.1%); followed by seborrheic eczema, ichthyosis, Norwegian scabies and pityriasis rubra pilar. Other causes included drug adverse effect (37: 21.8%) and cutaneous T-cell lymphoma (18: 10.6%); while in 16 patients (9.4%) the origin was not established. Many of our findings are in accordance with the data of that study, like male gender, psoriasis, pruritus, lower limb edema, anemia, high erythrocyte sedimentation rate, leukocytosis, and eosinophilia. Nevertheless, lymph node enlargement, lymphocytosis, hypoalbuminemia, elevated aminotransferases, and Sézary cells were not observed in the patient here reported.² Another Brazilian study about exfoliative dermatitis involved 58 patients with mean age of 56.9 years, and 37 (63.8%) were male.⁴ Previous skin diseases were found in 33: 56.9% of the cases, and the main causes were psoriasis (11: 33.3%), contact eczema (9: 27.3%) and seborrheic eczema (5: 15.1%), in addition to atopic eczema, ichthyosis and pityriasis rubra pilar. Drug side effect caused 11 (19%) of the cases, and the cause was unclear in 14 patients (24.1%). Similar to our findings, the most common laboratory changes were anemia, leukocytosis, eosinophilia and renal failure; otherwise, hypoalbuminemia occurred in 37% of those cases.⁴ Recently, Hawilo *et al* reported a retrospective study of 60 Tunisian patients with psoriatic erythroderma; the mean age of the patients was 53.7 years, 46 were male (76.7%) and 47 (78.3%) of the individuals had an antecedent of psoriasis as follows: plaque psoriasis (40 cases, 85.1%), scalp psoriasis (5 cases, 10.6%), and palmoplantar keratoderma (2 cases, 4.3%).³ Therefore, in 13 (21.7%) of the patients, erythroderma was the first manifestation of disease; phenomenon that can pose more diagnosis challenges,³ with consequent under/misdiagnosis. There could be an additional concern in

the present case study regarding the previous use of captopril, because this drug may be a rare precipitant factor for exfoliative erythroderma in individuals with psoriasis.^{2,3} Although such hypothesis could not be ruled out entirely, our patient was taking captopril for decades with no adverse effect; moreover, exfoliative erythroderma flared up after the rapid tapering of prednisone. Stopping local or oral corticosteroid has been an usual triggering factor for psoriatic erythroderma.^{3,6} On day 10 of admission, our patient presented classical features of acute gout in the right hallux, following the elevation of serum uric acid to 8.1 mg/dL (normal level: ≤ 7 mg/dL). Signs and symptoms rapidly subsided after a short course of oral NSAID, and uric acid lowering. Because of renal impairment, drug dosage was adjusted according to creatinine clearance. Although the diagnosis of gouty arthritis seemed clinically characterized in the present case, histopathological confirmation is lacking because of the risk-benefits of invasive procedures; in fact, there was no clinical or imaging data to support the possibility of psoriatic arthritis. Our patient had the dry form of exfoliative erythroderma,³ without mucous changes or deformities on nails or joints.⁵ Moreover, skin lesions involved flexural areas as well as palms and soles. Therefore, hypotheses like papuloerythroderma of Ofuji and osteoarthropathic psoriasis were ruled out.^{1,5} Interestingly, Liu *et al* (2009) described the first case of coexistent tophaceous gout, erythrodermic psoriasis and psoriatic arthritis in a 59-year-old man without alcohol abuse, and speculated that urate crystal deposits in the skin could play a role in erythrodermic psoriasis.⁶ Previous diagnosis of psoriasis, the rapid tapering of corticosteroid, clinical features, the Munro's microabscesses and Kogoj's pustules

characterized erythrodermic psoriasis in our patient.^{3,7-9} He improved with clinical management and was referred to specialized surveillance; however, he suffered further recurrence of exfoliative erythroderma, which was followed by unresponsive sepsis and death. Hawilo *et al* found 15% of recurrences; sepsis and thromboembolism were causes of death.³

In conclusion, exfoliative erythroderma is a clinical syndrome with guarded prognosis and most of cases are due to previous skin diseases; moreover, it often constitutes a diagnosis challenge and the prognosis is under influence of potential risk factors. Based on early clinical suspicion, three simultaneous biopsies must be performed to confirm the diagnosis. ✦

REFERENCES

1. Altiner A, Chu J, Patel R, Latkowski JA, Schaffer J, Sanders S. Erythroderma of unknown etiology. *Dermatol Online J.* 2011;17:6.
2. Fernandes NC, Pereira FSM, Maceira JP, Cuzzi T, Dresch TFLR, Araújo PP. Eritrodermia: estudo clínico-laboratorial e histopatológico de 170 casos. *An Bras Dermatol.* 2008;83:526-32.
3. Hawilo A, Zaraq I, Benmously R, Mebazaa A, El Euch D, Mokni M, et al. Erythrodermic psoriasis: epidemiological clinical and therapeutic features about 60 cases. *Tunis Med.* 2011;89:841-7.
4. Kondo RN, Gon AS, Minelli L, Mendes MF, Pontello R. Dermatite exfoliativa: estudo clínico-etiológico de 58 casos. *An Bras Dermatol.* 2006;81:233-7.
5. Teran CG, Teran-Escalera CN, Balderrama C. A severe case of erythrodermic psoriasis associated with advanced nail and joint manifestations: a case report. *J Med Case Rep.* 2010;4:179.
6. Liu M, Li J-H, Li B, Xiao T, Chen H-D. Coexisting gout, erythrodermic psoriasis and psoriatic arthritis. *Eur J Dermatol.* 2009;19:184-5.
7. Ayala F. Clinical presentation of psoriasis. *Reumatismo.* 2007;59(Suppl 1):40-5.
8. De Rosa G, Mignogna C. The histopathology of psoriasis. *Reumatismo.* 2007;59(Suppl 1):46-8.
9. Lisi P. Differential diagnosis of psoriasis. *Reumatismo.* 2007;59(Suppl 1):56-60.