

## **Desquamative Erythroderma Associated to Urinary Tract Infection, Case Report**

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### **ABSTRACT**

Generalized exfoliative erythroderma is an inflammatory skin syndrome. The incidence in dermatological patients is 13 out of every 100,000 patients. Its etiology is multifactorial, so it is a challenge to identify them, among the most common causes are psoriasis, drug hypersensitivity and phototoxicity. Most of the time, the clinician is oriented to think of a direct relationship between the dermatological presentation and the consumption of medications, since it is the most published cause founded in the medical literature and indexed journals. The clinical case that we present, refers to a case of erythroderma associated to a systemic infection. So far there are three documented cases in this regard in medical databases such as PubMed <sup>[1, 2, 3]</sup>. Our report is unique in this sense, we present the clinical case of a woman in her seventh decade of life with a history of hyperuricemia and chronic eosinophilia syndrome, hospitalized for urosepsis that debuted as desquamative erythroderma.

**KEYWORDS:** Desquamative Erythroderma, DRESS syndrome, Urinary Tract Infection.

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### **INTRODUCTION**

Erythroderma, also known as generalized exfoliative dermatitis or exfoliative erythroderma, is an inflammatory skin syndrome characterized by scaling and erythema affecting >90% of the body surface <sup>[4]</sup>. This is a rare condition. A retrospective study conducted in China established that 13 out of every 100,000 dermatological patients present with erythroderma. Recently, a Portuguese retrospective study reported an incidence of 9.4 cases/years <sup>[4]</sup>. There is a predominance in males with a male-female ratio of 2-4:1, with an age range of 40 to 60 years <sup>[5, 6]</sup>.

Erythroderma has multiple etiologies and it is a challenge for the dermatologist to identify them. The most common are included in the acronym PALM (psoriasis, atopic dermatitis, lymphoproliferative, most due to lymphoma and medications) <sup>[5, 6]</sup>. The most common cause of erythroderma is psoriasis, representing 25-50% of cases <sup>[6]</sup>, the adverse reaction to drugs is described as the second most frequent cause, with antiepileptics and allopurinol being the drugs with the greatest capacity to trigger it <sup>[8]</sup>; Among rare presentations are those caused by systemic infections <sup>[5, 9]</sup>. The pathogenic mechanisms involved depends on the underlying cause,

which involves a wide variety of diseases and exogenous factors, including infections and medications <sup>[9]</sup>.

Early diagnosis and treatment are crucial to avoid complications associated with defects in thermoregulation and hemodynamic and metabolic instability <sup>[1]</sup>. Studies on prognosis are scarce and the results are inconsistent. In the first studies that were carried out, significant mortality secondary to complications were reported <sup>[4]</sup>. A recent retrospective population-based cohort study in Denmark found that 30.8% of patients with psoriatic erythroderma and 39.6% with erythroderma died in the first 3 years after hospital admission <sup>[4]</sup>.

### **CASE REPORT**

The case of a 66-year-old woman, housewife, resident of Xalapa, Veracruz, Mexico is presented. Her pathological history is diabetes mellitus diagnosed one year before, in treatment with Sitagliptin and Metformin; unspecified aortic anomaly diagnosed 4 years ago on treatment with Clopidogrel; idiopathic hypereosinophilia without follow-up treatment; Meniere's disease with a diagnosis of 4 years under management with diphenidol and flunarizine; and

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gastroesophageal reflux disease of 5 years under management with omeprazole.

A month and a half prior to his current condition, she received treatment with allopurinol 300 mg per day, due to a finding of hyperuricemia, which was suspended two weeks before the onset of dermatological symptoms. During this period, she had a repetitive urinary tract infection treated with ceftriaxone, for short periods of 7-10 days, in 3 occasions.

Her illness began with a fever of 100 ° F (38° C), rash on face and neck, accompanied by pruritus [Figure 1]. She was treated with injectable betamethasone (two doses) and chloramphenicol in eye drops, however, she did not have resolution of the symptoms and facial edema, eyelid edema and tearing were added. Subsequently she had respiratory distress, anterior chest pain in a scale of 8 out of 10, dysphagia and angioedema, for which she was hospitalized. During her stay in the emergency room, evidence of grade I septic shock was founded which responded to administration of crystalloid solutions and third-generation cephalosporin. Despite management with antihistamines, there was no improvement, with the dermal lesions progressing to generalized erythematous plaques that worsened, turning purplish throughout the body and ulcers in the mouth [Figure 2]. Upon her admission to the internal medicine department, she was already on the third day of antibiotic therapy and still had signs of a systemic inflammatory response. It was decided to escalate antibiotic therapy due to persistence of temperature rises and strong suspicion of urosepsis. Even without culture results, the use of carbapenem was chosen.

Laboratory studies highlight hypereosinophilia that causes leukocytosis and elevation of acute phase reactants (VSG and PCR); the general urine examination with a cloudy yellow appearance, presence of nitrites, countless leukocytes and abundant bacteria; complete blood count reported absence of anemia and leukocytosis due to eosinophilia; blood chemistry with elevated nitrogen levels which normalized after hydration, liver function tests without significant alterations, serum immunoglobulin E was measured with a value of 1.46 IU/ml, which was within normal parameters [Chart 1].

After 48 hours of treatment with carbapenem, the lesions disappeared by ninety percent, reducing to peeling and light itching in a period of 72 hours [Figure 3].

### DISCUSSION

There is scarce evidence of the association between desquamative erythroderma and systemic infections as a triggering factor; of the reported cases, this condition has been associated with infections such as Covid-19, endocarditis and herpes viruses.

In 2007, a case of exfoliative erythroderma and infectious dermatitis was reported in an infant infected with human T lymphotropic virus type I (HTLV I) whose diagnosis was confirmed by PCR. The infant presented with acute, severe, generalized eczema, exfoliation and severe erythroderma that led to acute protein malnutrition and recurrent staphylococcal

infections, which did not respond to treatment, since his second month of life. Immunodeficiencies of other origin and other causes of erythroderma were ruled out. Histopathology and clinical evolution studies yielded the diagnosis of infectious dermatitis associated to HTLV-I [3].

In 2020, a case of a 45-year-old homeless addicted male was reported in which he presented a second flare of psoriatic erythroderma and positive PCR test for COVID 19. His first attack occurred two months earlier, when he was screened for SARS-CoV-2 before admission which all evaluations showed negative results. The patient was treated and relatively controlled with cyclosporine and therefore he was discharged. During this interval, he not only discontinued his medication, but also became SARS-CoV-2 positive. It seems that both factors participated in flare of his erythroderma [2].

Erythrodermic psoriasis is a rare subtype of psoriasis vulgaris that presents with diffuse erythema and scaling over more than 75% of the body surface. In 2022, it was present a case of a 57-year-old man who was admitted for a diffuse erythematodesquamative rash that covered the entire body, with associated subjective fevers. Skin biopsy revealed erythrodermic psoriasis and blood cultures were positive for methicillin-susceptible *Staphylococcus aureus*. The echocardiogram revealed vegetation of the mitral valve. Clinical improvement was achieved with the administration of intravenous antibiotics and topical corticosteroids without the use of immunomodulators [1].

The main etiology associated with erythroderma is due to the administration of drugs such as allopurinol, the same medication involved in our patient's history, so the main differential diagnosis made was hypersensitivity associated with drugs and DRESS syndrome (drug reaction with eosinophilia and systemic symptoms: Drug reaction with eosinophilia and systemic symptoms).

Given the diagnostic doubt with the differential diagnoses, it was necessary to rule out that the lesions were due to an allergic reaction of hypersensitivity to medications, so a study of total IgE and eosinophil count was performed, supporting the ruling out of allergic process, associated especially IgE or Th2 mediated [10].

In 2012, the case of a patient with desquamative erythroderma and eosinophilia, with a diagnosis of allopurinol hypersensitivity syndrome, was presented. In this process of autoimmune dysregulation, the subsequent appearance of autoimmune symptoms after asymptomatic periods was described. Perhaps the patient's underlying disease could be considered a risk factor for the development of hypersensitivity syndrome [11].

In our case, the IgE result was within normal parameters and although eosinophilia was reported, it is important to consider that the patient already had a history of eosinophilia more than 6 months prior to her diagnosis, which could have been a predisposing factor for erythroderma and not associated with it.

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In DRESS syndrome, hypersensitivity can begin 2 to 8 weeks after exposure to the pharmacological agent [12], presenting facial edema and purpuric lesions in regions with stasis, half of the patients present discrete mucous involvement, being the oral presentation the most commonly affected [12]. To rule out this syndrome, organic involvement (hepatitis, pneumonitis or nephritis) must be evaluated based on laboratory studies with a total eosinophil count > 700.

For the diagnosis, at least three of the following criteria are required:

- Causal relationship between the administration of the medication and the manifestation of the adverse reaction.
- Acute skin rash.
- Involvement of at least one internal organ.
- Lymphadenopathy in at least two different sites.
- Lymphocytosis and eosinophilia or thrombocytopenia.
- Fever of more than 100° F (38° C)

Although our patient had an acute skin rash and hypereosinophilia, the diagnosis of DRESS was not made since there was no evidence of target organ involvement or lymphadenopathy; Drug-induced erythroderma resolves

within a period of two to six weeks after stopping the administration of the causative drug in contrast, in DRESS syndrome it may require months [5]. In this case, the patient had SIRS (systemic insufficiency respiratory syndrome) associated with the onset of symptoms, so an infectious focus was sought, finding it in the urinary tract, antibiotic administration was started and the lesions disappeared after 48 hours [12].

### CONCLUSIONS

This report details the case of a patient with desquamative erythroderma, exposing the association to an infectious process as a trigger, in this case a urinary tract infection. An extensive analysis is made of the differential diagnoses and the various etiologies of this condition, emphasizing a good history considering the association with infections, where the priority of management is the resolution of the infection, as was the case in this case, where the skin lesions resolved after 72 hours from the start of antibiotic treatment. We consider that eosinophilia was a chronic history, so its role in the case is related as a predisposing factor and not as a diagnostic criterion of the current condition.

### ATACHMENT



**Figure 1. Edema and erythema, facial and neck.**



**Figure 2. Multiple confluent scaly erythematous plaques on extremities.**

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Figure 3. Disappearance of erythematous plaques, with evolution to peeling on the face and ex

Chart 1. Laboratory tests upon admission with reference values.

| LAB RESULTS  |  | REFERENCE RANGE      |
|--|--|----------------------|
| <b>BLOOD CHEMISTRY</b>   |  |                      |
| Glucose  | 190 ng/ml  | 70.0 - 110.0 ng/ml   |
| Serum urea   | 66 mg/dl   | 15.0 - 39.0 mg/dl    |
| Urea nitrogen  | 30.84 mg/dl  | 7.0 - 20.0 mg/dl     |
| Serum creatinine   | 1.6 mg/dl  | 0.40 - 1.50 mg/dl    |
| <b>SERUM ELECTROLYTES</b>  |  |                      |
| Sodium   | 129 mmol/l   | 136.0 - 145.0 mmol/l |
| Potassium  | 4.7 mmol/l   | 3.50 - 5.30 mmol/l   |
| Chlorine   | 96 mmo/l   | 98.0 - 107.0 mmol/l  |
| <b>LIVER FUNCTION TESTS</b>  |  |                      |
| ALT  | 71 u/l   | 30 - 65 u/l          |
| AST  | 38 u/l   | 6 - 37 u/l           |
| GGT  | 127 u/l  | 5 - 40 u/l           |
| DHL  | 498 u/l  | 105 - 333 u/l        |
| <b>INMUNOGLOBULIN</b>  |  |                      |
| Inmunoglobulin E   | 1.46 ui/ml   | 1.0 - 183.0 ui/ml    |
| <b>HEMATIC BIOMETRY</b>  |  |                      |
| Hemoglobin   | 15.80 g/dl   | 12.0 - 16.0 g/dl     |
| Medium corpuscular volume  | 87 fl  | 76.0 - 96.0 fl       |
| Average hemoglobin concentration   | 27.8 g/dl  | 27.0 - 32.0 g/dl     |
| Platelets  | 219 miles/ul   | 150 - 400 miles/ul   |
| Leukocytes   | 17.73 mile/ul  | 4.0 - 10.0 miles/ul  |
| Eosinophils  | 9.80 miles/ul  | 0.0 - 0.5 miles/ul   |
| Lymphocytes  | 3.46 miles/ul  | 1.0 - 4.0 miles/ul   |
| Neutrophils  | 7.12 miles/ul  | 1.5 - 7.5 miles/ul   |
| Monocytes  | 1.23 miles/ul  | 0.15 - 0.7 miles/ul  |
| VSG  | 20mm/hr  | 0 - 20 mg/dl         |
| PCR  | 22.63 mg/dl  | <0.3 mg/dl           |
| <b>PERIPHERAL BLOOD SLIM</b>   |  |                      |
| Neutrophils 32%, Lymphocytes 11%, Monocytes 2%, Eosinophils 54%, basophils 0%, bands 1%. Dysplastic eosinophils. |  |                      |
| <b>GENERAL URINE EXAMINATION</b>   |  |                      |
| Chemical test  | Density 1.020, PH 5, Leukocytes 500 leu/uL, Nitrites positive, ketones 15 s/u, proteins 75 mg/dl, hemoglobin 250 ery/ul, cloudy appearance |                      |
| Urinary sediment   | Countless leukocytes, countless erythrocytes, epithelial cells +++, very abundant bacteria.  |                      |

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