MANAGEMENT OF ERYTHRODERMA AND TWO CLINICAL CASE PRESENTATIONS

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Summary:

Erythroderma is a severe skin condition characterized by a generalized erythematous rash covering more than 90% of the skin surface. It is associated with various underlying dermatological and systemic conditions. Diagnosis involves a comprehensive medical history, clinical examination and laboratory investigations. Erythroderma can be caused by the exacerbation of pre-existing skin conditions (e.g. psoriasis or atopic dermatitis) or by a drug hypersensitivity reaction, among other etiologies. In severe cases, it requires inpatient management to prevent complications such as dehydration, electrolyte imbalances and infections.

Treatment includes addressing the underlying cause, supportive measures like fluid resuscitation and symptomatic relief using topical corticosteroids and antihistamines. Early diagnosis and targeted treatment are crucial for reducing the mortality and morbidity associated with this dermatological emergency.

***Key words**: erythroderma, exfoliative dermatitis, erythema.*

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Introduction

Erythroderma, also known as exfoliative dermatitis, is a clinical presentation of various dermatological pathologies, as well as systemic conditions. It is defined as a generalized or nearly generalized erythematous rash that involves more than 90% of the skin surface, associating varying degrees of descuamation.

Exfoliative dermatitis is most commonly attributed to the exacerbation of pre-existing inflammatory skin conditions (psoriasis, atopic dermatitis, contact dermatitis), underlying neoplasms (cutanous T-cell lymphoma) and adverse drug reactions. Other known etiologies are solid malignant tumors, inflammatory diseases and infections[1].

Studies have generally shown a male predominance in the epidemiology of erythroderma, with a male to female ratio of 2:1-4:1 and an age range of patients between 41 and 60 years, excluding pediatric patients[2][3]. Early diagnosis of the underlying pathology and targeted treatment, combined with the supportive management of erythroderma, can reduce the mortality and morbidity associated with this condition.

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Etiology

Erythroderma is a clinical manifestation reported in severe forms of a wide range of pathologies, which can be broadly categorized into: congenital, infections, inflammatory, immunobulous, neoplastic, iatrogenic and idiopathic (**Table 1.**). Most commonly, erythroderma is caused by the exacerbation of pre-existing dermatoses, such as psoriasis vulgaris or atopic dermatitis [4]. The triggers for erythroderma in these cases are often the sudden withdrawal of systemic corticosteroid therapy, the maintanance therapy or photothereapy-induced burns[5].

Adverse drug reactions are another common etiology of erythroderma. A wide range of drugs have been reported to be associated with erythroderma, including penicilins, sulfona-mides, carbamazepine, allopurinol and phenytoin (**Table2.**). Various patterns of adverse drug reactions , ranging from macopapular eruptions to drug reaction with eosinophilia and systemic symptoms (DRESS) or toxic epidermal necrolysis, can manifest with erythroderma[6][7].

Management

Erythroderma is dermatological emergency and the severe cases require inpatient management and careful monitoring. The initial assesement of the patient should include the following:

- Comprehensive medical history, focusing on previously diagnosed dermatological diseases and drug administration;
- Complete clinical examination, including blood pressure and body temperature monitoring;
- Discontinuation of any drug that is not essential;
- Complete blood work, assesing the electrolyte balance[8].

Patients should be placed in an optimal environment (30 to 32 degrees Celsius) to prevent hypothermia resulted from heat loss through de skin[9].

Hypovolemia resulted from transepidermal water loss requires fluid resuscitation with crystalloid solutions (500 ml bolus in under 15 minutes) and monitoring of laboratory investigations to address any electrolyte imbalance that may need correction.

If the patient exhibits signs of secondary bacterial skin infection, local cultures are recommended in order to start systemic antibiotic therapy .

Skin barrier function can be improved with wet compresses and emollients. For the symptomatic treatment of skin inflammation and pruritus, low to medium-potency topical corticosteroids can be applied 2-3 times a day.

Oral first-generation antihistamines can relieve pruritus (e.g. hiphenhydramine 25-50 mg p.o. every 4-6 hours).

If the undelying condition is identified, targeted treatment for the condition will be added to the initial treatment regimen. If an adverse drug reaction is the most likely diagnosis, all medication that is not necessary should be discontinued and the patient should undergo systemic corticosteroid treatment. Patients who present with an exacerbation of pre-existing psoriasis vulgaris require specific therapies, including methotrexate or cyclosporine. If a diagnosis of atopic dermatitis is suspected, the patient should be administered immunosuppressant or immunomodulatory drugs, such as cyclosporine, methotrexate or azathioprine. The patients diagnosed with Sezary syndrome may require therapies that target the circulating Sezary cells, such as systemic retinoids, methotrexate, histone deacetylase inhibitors and mogamulizumab. In patients with idiopathic erythroderma who do not respond to topical treatments, systemic corticosteroids or other immunosuppressive agents are recommended. Systemic corticosteroid therapy is preferred due to its faster onset of the therapeutic effect (e.g. prednisone 0,5-1mg/kg per day for 7-10 days with a maximum daily dose of 60 mg) with slow tapering to avoid rebound adverse reactions. Patients should be closely monitored due to the increased risk of complications such as hypertension, hyperglicemia and an elevated risk of infection. If there are any contraindications for initial systemic corticosteroid therapy, the use of cyclosporine (4-5 mg/kg per day) or methotrexate (10-20 mg per week) is recommended.

By controlling the underlying condition and avoiding triggering factors, relapses can be prevented. The most common triggering factor in

Table 1.Etiologies associated with erythroderma

- **Congenital:**
  - Ichtyosis (e.g. CHILD syndrome, IFAP syndrome, X-linked ichtyosis, autosomal recessive lamellar ichtyosis, Harlequin ichtyosis)
  - Immunodeficiencies (e.g. Omenn syndrome, hyper-igE syndrome)
  - Metabolic syndromes (e.g. congenital enteropathic anhidrosis)
- **Inflammatory:**
  - Psoriasis vulgaris
  - Atopic dermatitis
  - Pityriasis rubra pilaris
  - Lichen planus
  - Seborrheic dermatitis
- **Infectious:**
  - Staphylococcus scalded skin syndrome
  - Scabies
  - Toxic shock syndrome
  - HIV
- **Autoimmune bullous diseases:**
  - Pemphigus foliaceus
  - Pemphigus vulgaris
  - Bullous pemphigoid
- **Neoplastic:**
  - Cutaneus T-cell lymphoma/ Sezary syndrome
  - B-cell lymphoma
  - Leukemia
  - Hematological or solid malignancies (e.g. ovarian, renal, hepatic, pulmonary)
- **Iatrogenic (drug-induced):**
  - Drug reaction with eosinophilia and systemic symptoms(DRESS)
  - Stevens-Johnson syndrome
  - Toxic epidermal necrolysis
  - Acute generalized exanthematous pustulosis(AGEP)
- **Others:**
  - Cutaneous mastocytosis
  - Hypereosiniphilic syndrome
  - Sunburn
- **Idiopathic (30%)**

Table 2. The most common drugs involved in the etiology of erythroderma

- Antibiotics(penicillin, vancomycin, streptomycin, trimethoprim/sulfamethoxazole)
- Anticonvulsants (carbamazepine, phenobarbital, phenytoin)
- Antimalarials (hydroxychloroquine)
- NSAIDs (piroxicam, diclofenac, naproxen)
- Proton pump inhibitors
- JAK inhibitors(imatinib)
- Retinoids
- Otheres: isoniazid, sulfasalazine, thalidomide, erythropoietin, dapsone

patients with psoriasis and atopic dermatitis is the discontinuation of corticosteroid therapy or other immunosuppressive agents. Drug hypersensitivity reactions typically improve 2-6 weeks after the withdrawal of the triggering medication.[10].

Case presentation 1

We describe the clinical case of a 56-year-old man diagnosed with psoriasis vulgaris one year before admission to the clinic. He presented with a nearly generalized erythematous rash, covering >90% of the skin surface, intensely pruritic and accompanied by mild scaling, evolving over the past two weeks.

From the patient's history we note the presence for 3 years of an erythematous-squamous plaque with a diameter of 3-4 cm on the back, confirmed through histopathological examination as psoriasis vulgaris in 2002. Two weeks prior to admission he developed an erythematous rash localized on the scalp and forehead, for which he received topical antifungical treatment. A biopsy was taken for histopathological examination, confirming the diagnosis of psoriasis vulgaris. The rash became generalized over the following weeks, involving the whole body surface, despide the topical corticosteroid treatment. The patient also reported flu-like symptoms a few weeks before for which he was administered nonsteroidal antiinflammatory drugs.

During the clinical examination at the time of admission no significant changes are observed. The skin examination reveals a nearly generalized erythematous rash, covering >90% of the skin surface, intensely pruritic and accompanied by mild scaling. There are no changed noted in the mucous membranes. (**Fig. 1,2,3,4**).

Laboratory investigations did not reveal significant changes, except for elevated LDH levels (813 U/L) and total IgE levels (497.6 UI/ml). Despide these altered parameters, the patient does not meet the diagnostic criteria for atopic dermatitis. Following the clinical examination, medical history and previous histopathological examination, the diagnosis of erythroderma was established, most likely caused by the exacerbation of preexisting psoriasis vulgaris.

Case presentation 2

We present the case of a 67-year-old female patient with chronic myeloid leukemia, undergoing treatment with imatinib 400 mg per day for approximately 2 months. She presents with a generalized erythematous rash involving >90% of the skin surface, associated with mild scaling and intense pruritus, evolving for two weeks.

From the patient's medical history, she reports the onset of lesions on the trunk with a rapid involvement of the whole body associated with intense itching (**Fig. 5,6**). Laboratory tests, including liver and kidney function tests, did not reveal significant changes .

Considering the patient's medical history, the complete clinical examination and the results of the laboratory tests, the diagnosis of erythroderma due to imatinib administration was established as a grade 3 adverse drug reaction. Imatinib therapy was discontinued and the patient started treatment with methylprednisolone (0,5 mg/kg/day) tapered over several weeks, along with the application of wet compresses and local emollients. After one week of treatment, the evolution was favorable with improvement of the rash and itching, achieving complete remission after 4 weeks. The patient was changed to an alternative oncological medication and remains under observation by the hematology department.

Discussions

Erythroderma manifests as generealized erythema accompanied by scales and it is a clinical presentation caused by numerous pathologies. Diagnosing the underlying etiology and initiating targeted treatment in overall management remains the key element in the management of erythroderma, reducing the mortality rate of the disease, which is reported to be between 18-64% [8].

Erythroderma represents a dermatological emergency due to the severe complications that can occur as the result of the loss of the skin barrier function. The loss of skin integrity leads to dehydration, which can result in acute kidney injury, electrolyte imbalance and hypoalbuminemia associated with edema. The fluctuation in body temperature (hypothermia/hyperthermia)

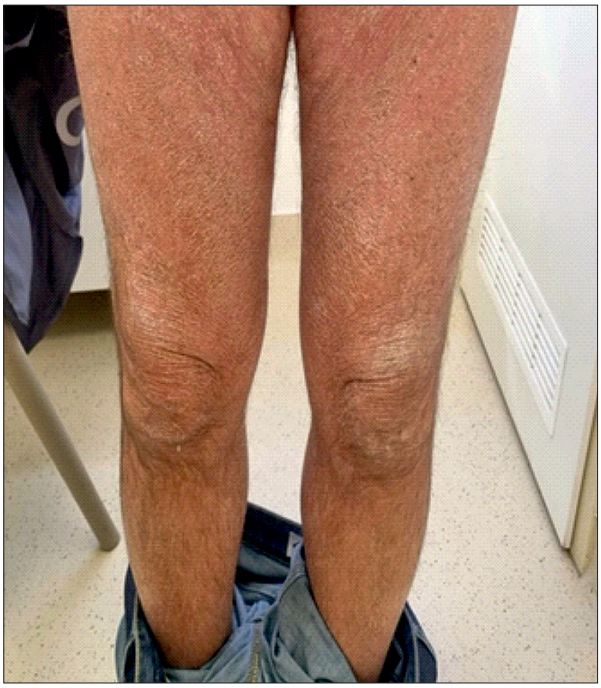

Figure 1. Erythematous-squamous rash on the lower limbs

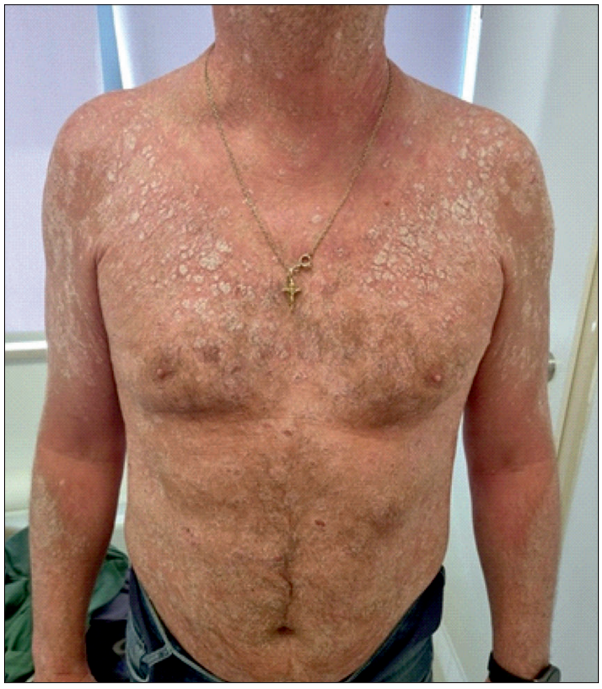

Figure 2. Erythematous-squamous rash on the upper lims, chest and abdomen

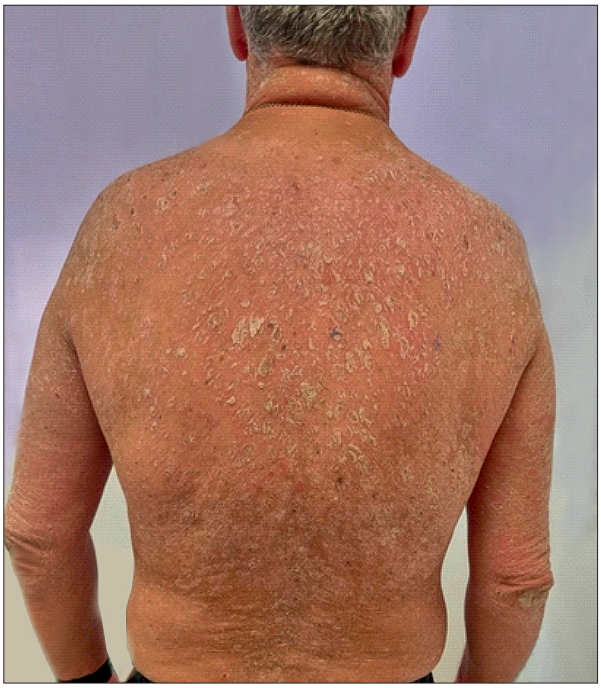

Figure 3. Erythematous-squamous rash on the back and upper limbs

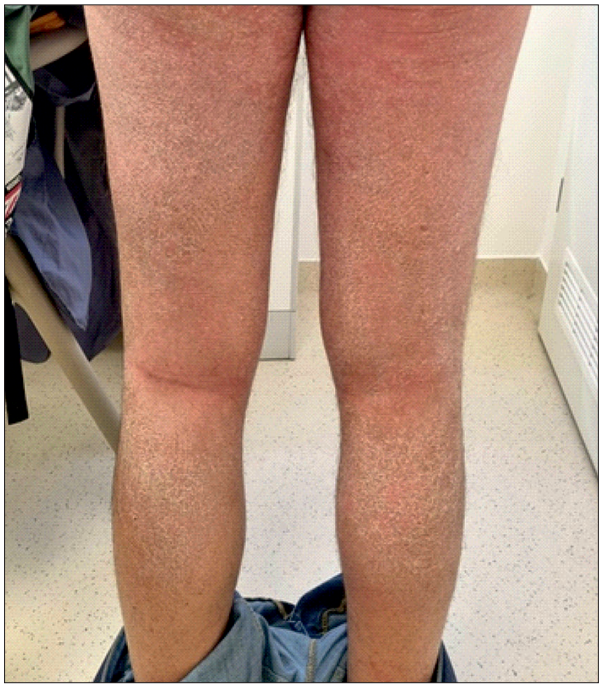

Figure 4. Erythematous-squamous rash on the lower limbs

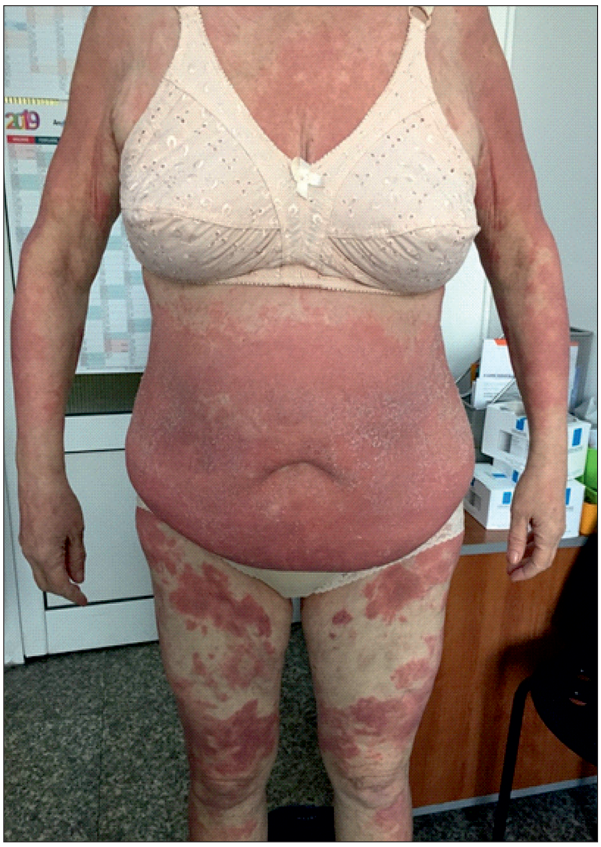

Figure 5. Generalized erythematous-squamous rash

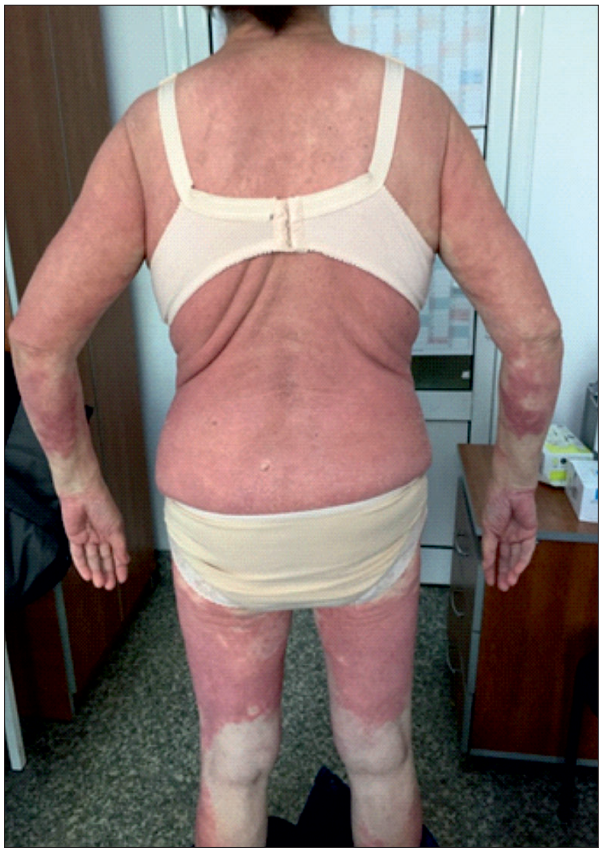

Figure 6. Generalized erythematous-squamous rash

leads to peripheral vasodilatation, potentially causing heart failure. Due to the impairment of the skin barrier, patients have an increased susceptability to systemic infections, increased catabolism and a risk of hyperglicemia .

The management of erythroderma involves a detailed medical history and a comprehensive medical examination. Any pre-existing skin pathologies, the onset of symptoms, associated systemic symptoms, the history of recently administered medication and possible exposure to allergens should be highlighted. Immediate management includes fluid resuscitation to regulate hemodynamic imbalance, systemic antibiotics to combat infection and maintaining optimal body temperature.

Conclusions

Erythroderma is a complex pathology and its prognosis depends on the underlying etiology. It is considered a dermatological emergency requiring immediate therapeutic intervention. Diagnosing the etiology and the complications associated with erythroderma is a key element in disease management and results in the reduction of the morbidity and mortality associtated with this pathology. Individualized treatment based on the underlying cause should be combined with the supportive management of erythroderma to achieve an optimal outcome.

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Conflict of interest
NONE DECLARED

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