Acta Dermatovenerol Croat 2007;15(2):103-107 REVIEW

Exfoliative Erythroderma

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Received: Janurary 8, 2007.
Accepted: February 20, 2007.

SUMMARY Exfoliative erythroderma refers to the skin that is diffusely red and inflamed with varying degrees and types of scaling. There are many causes of erythroderma, but the most common are exacerbations of an underlying skin disease, drug reactions and underlying malignancies. Erythroderma is a rare, potentially serious skin condition. Protein loss in the form of desquamation and exudation is significant, resulting in hypoproteinemia. Usually more than one skin biopsy should be done. Biopsy analysis is important to rule out cutaneous T-cell lymphoma. Patients should be carefully evaluated for underlying disease. Erythroderma can represent a serious medical threat to the patient, and may require hospitalization. Various forms of exfoliative erythroderma are presented, considering the etiopathogenesis, physical findings, differential diagnosis and treatment.

KEY WORDS: exfoliative erythroderma, exfoliative dermatitis, Sézary syndrome, cutaneous T-cell lymphoma

INTRODUCTION

Erythroderma refers to the skin that is diffusely red and inflamed with varying degrees and types of scaling (1). There are many causes of erythroderma, but the most common are exacerbations of an underlying skin disease, drug reactions and malignancies, primarily mycosis fungoides (MF). Usually more than 90% of the skin is involved, but residual islands of normal skin may be of great importance in clinical diagnosis. For example, pityriasis rubra pilaris (PRP) and MF are characterized by such spared areas. The scales may vary greatly, coming off in sheets in acute drug induced erythroderma, but being smaller or finer in psoriasis or PRP. Pruritus is common and often unbearable (1).

Erythroderma can be classified into primary and secondary types. In primary erythroderma, skin changes arise on the previously normal skin, usually as part of malignant lymphoma or of drug reactions. In secondary erythroderma, an underlying skin disease is spreading and it involves the entire skin (e.g., psoriasis, allergic contact dermatitis, PRP or lichen ruber planus) (2).

EPIDEMIOLOGY

Erythroderma is a rare, yet easily recognized, potentially serious skin condition. Its reported incidence varies widely, from 1 to 71 *per* 100,000 dermatologic outpatients (3-5). Studies in large patient series focused on male to female ratio,

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mean age and underlying diseases (3-11). Men are more commonly affected (male to female ratio of approximately 2:1 to 4:1) and the mean age is between 40 and 60 years (12). Among 746 patients, the most common underlying causes of erythroderma were dermatitis (24%), psoriasis (20%), drug reactions (19%) and cutaneous T-cell lymphoma (CTCL) accounting for 8% of cases (12).

In 25%-39% of patients, the cause of erythroderma remains unknown (idiopathic) and some of these patients eventually develop CTCL (13). This group consists primarily of elderly men with a chronic course of relapsing pruritic erythroderma in association with dermatopathic lymphadenopathy and extensive palmoplantar keratoderma (13).

PATHOGENESIS

Erythroderma has profound effects on the entire body. The widespread inflammatory response, increased blood flow and marked desquamation all take their toll. Vasodilatation and increased blood flow lead to chills and impaired temperature control. Hypothermia is a possible complication. Increased evaporation is possible by increased blood flow and damaged epidermal barriers, leading to dehydration and fluid problems. Protein loss in the form of desquamation and exudation is significant, resulting in hypoproteinemia. The daily loss of scales increases from 500-1000 mg to 20-30 g (1,14). Typically, there is hypoalbuminemia with a relative increase in immunoglobulins, especially γ-globulins. Both hair and nails are influenced by the increased demands, telogen effluvium and transverse nail bands are expected. Cardiovascular, renal and hepatic complications are common (1). Generalized lymphadenopathy is found very often (15).

SPECIFIC FINDINGS OF THE UNDERLYING DISEASE

Psorasis

Psoriatic erythroderma (Fig. 1) is preceded by typical psoriatic plaques. Its onset is most often the result of a sudden withdrawal of potent topical or oral corticosteroids, methotrexate, phototoxicity or systemic infection. Nail changes such as oil drops changes, onycholysis, or nail pits, may still be visible and provide valuable clues to the diagnosis of psoriatic erythroderma. According to Tomasini *et al.*, in a group of patients with a discharge diagnosis of psoriatic erythroderma, the histopathologic changes were specific for psoriasis in 40 (88%) cases (16).

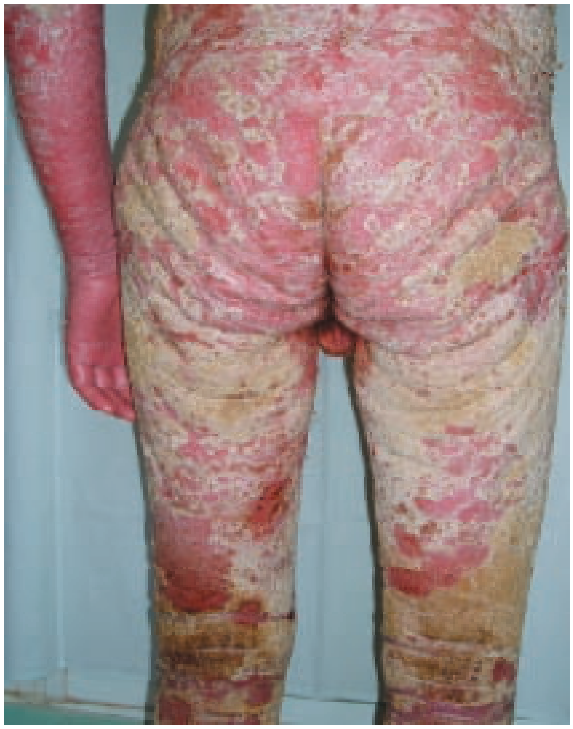

Figure 1. Psoriatic erythroderma.

Atopic dermatitis

Atopic erythroderma (Fig. 2) is most frequently found in patients with a history of moderate to severe atopic dermatitis. The pruritus is intense. Increased serum IgE and eosinophilia may be accompanied with other signs and symptoms of atopy. A constant histologic finding in atopic erythroderma is mild to moderate spongiosis, which is sometimes located in the follicular infundibulum. Almost always, acanthosis and parakeratosis are additional histologic features (12).

Drug reactions

The list of drugs that cause exfoliative dermatitis is large and continuously growing. Histologically, changes vary considerably. More than 60 drugs have been implicated in the causation of erythroderma. Among the most commonly implicated are pyrazolone derivatives, carbamazepine, hydantion derivatives, cimetidine, lithium salts, and gold and gold salts (1).

Netherton's syndrome

Netherton's syndrome manifests as an erythroderma in neonates. It is associated with trichor-

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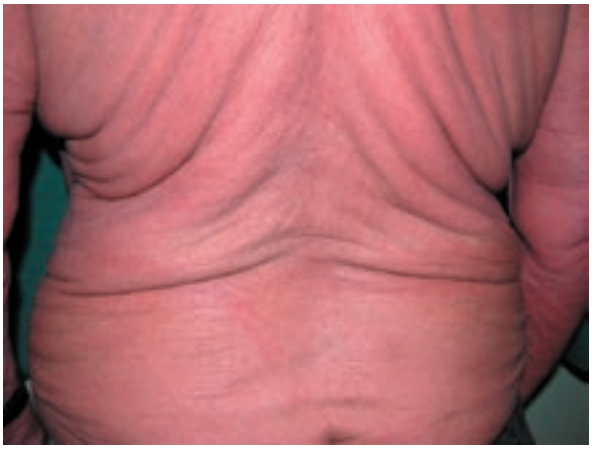

Figure 2. Atopic erythroderma

rexis invaginata ("bamboo hair"), atopic dermatitis and an immune defect that can result in life threatening infections (17).

Cutaneous T-cell lymphoma

Erythroderma due to CTCL is subdivided into Sézary syndrome and erythrodermic mycosis fungoides. Sézary syndrome (Fig. 3) is defined by the triad of symptoms: erythroderma, circulating malignant T lymphocytes, and generalized lymphadenopathy. Additional clinical features include painful and fissured keratoderma, diffuse alopecia and leonine facies. The skin may be strongly infiltrated and severe pruritus is common. The manifestations of erythrodermic mycosis fungoides are clinically identical to Sézary syndrome, but leukemic Sézary cells are absent. The histologic picture of typical erythrodermic CTCL consists of a band-like infiltrate in the papillary dermis containing small to medium sized mononuclear cells with hyperchromatic, cerebriform nuclei as well as a variable number of inflammatory cells (18).

Paraneoplastic erythroderma

Erythroderma can also be a paraneoplastic marker for a wide range of hematologic malignancies, and rarely even for other solid tumors. In such cases, the onset is more rapid and there is no history of precursor lesions. Histologic examination of the lymph nodes or other tissue is crucial because the skin changes are rarely caused by infiltrating tumor cells (12).

Pityriasis rubra pilaris

Erythrodermic PRP can be observed in children and adults. Usually the lesions have a salmon or orange-red color. The presence of perifollicular keratotic plugs on the knees, elbows and dorsal side of the hands, as well as *nappes claires* (islands of uninvolved skin) within the erythroderma, is highly suggestive of PRP. The characteristic histologic finding in PRP is orthokeratosis foci alternating with parakeratosis in both vertical and horizontal directions (12).

Omenn's syndrome

Omenn's syndrome represents an autosomal recessive form of severe combined immunodeficiency and is characterized by leukocytosis with prominent eosinophilia and increased T/B cell ratio, hypogammaglobulinemia and elevated IgE levels. Cutaneous findings include exfoliative erythroderma with diffuse alopecia (19,20).

DIAGNOSTIC APPROACH

Clinical recognition of the erythroderma is easy, but the diagnosis of the underlying cause may be very difficult. The issue is deciding which triggered or caused the problem, primary or secondary erythroderma. The existence of previous skin disease and how it was treated are crucial. The age of the patient also play a role. One must search carefully for subtle signs of an underlying disease. Many patients have lymphadenopathy which, while usually reactive or dermatopathic, may reflect an un-

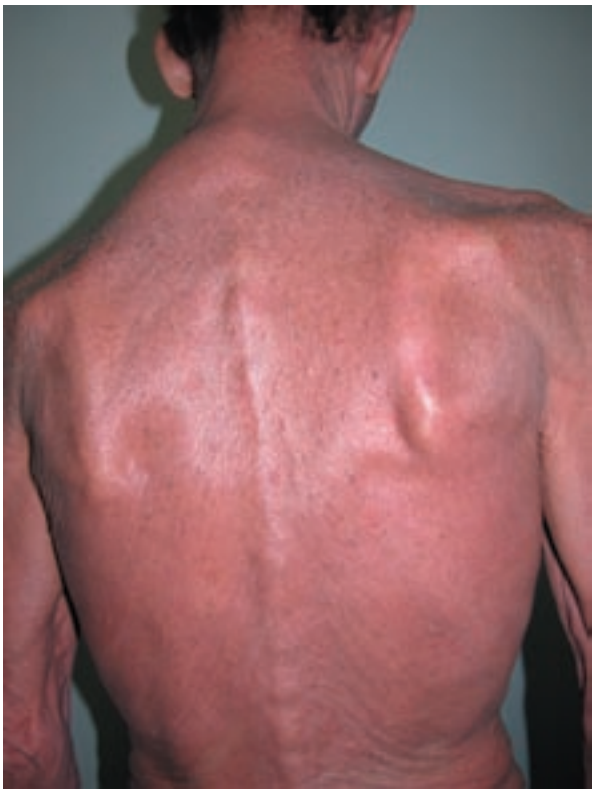

Figure 3. Sézary syndrome

derlying lymphoma. If the diagnosis is unclear, a lymph node biopsy should be considered.

Usually more than one skin biopsy should be done. Multiple biopsies are usually but not invariably helpful because they may not show any distinctive histologic features. The biopsy is important to rule out CTCL. The patients should be carefully evaluated for underlying disease. Lymph node biopsy is advisable if lymphoma is suspected. Useful approaches include chest x-ray, computerized tomography of the abdomen, pelvis and thorax, routine blood evaluation, iron and folic acid levels, immunoelectrophoresis, and bone marrow examination (1).

TREATMENT

Erythroderma can pose a serious medical threat to the patient and may require hospitalization. The patients are more comfortable if they are in warm, humid environment. The initial management consists of nutritional assessment, correction of fluid and electrolyte imbalances, prevention of hypothermia, and treatment of secondary infections. Sedating oral antihistamines may ease the often severe pruritus. Systemic corticosteroids may be necessary in idiopathic erythroderma and drug reactions. Topical therapy includes open wet dressings and bland emollients or low-potency corticosteroid ointments. High-potency topical corticosteroids should be avoided due to increased transcutaneous absorption (21).

PROGNOSIS

Drug induced cases have the best prognosis, as they have rapid improvement (4,10). Secondary erythroderma to underlying skin diseases tends to improve over a few weeks, and as many as two-thirds of patients enter remission (22). Exfoliative dermatitis secondary to CTCL and internal malignancies tends to be more persistent (23).

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