CLINICAL MANAGEMENT extra

A Review of the Diagnosis and Management of Erythroderma (Generalized Red Skin)

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PURPOSE:

To provide information about the diagnosis and management of erythroderma.

TARGET AUDIENCE:

This continuing education activity is intended for physicians and nurses with an interest in skin and wound care.

OBJECTIVES:

After participating in this educational activity, the participant should be better able to:

1. Identify erythroderma causes, symptoms, and diagnostic testing.

2. Summarize treatment and management recommendations for erythroderma.

ABSTRACT

Erythroderma is a condition caused by several etiologies that result in red inflamed skin on 90% or more of the body surface. To optimize the diagnosis and management of the erythrodermic patient, healthcare professionals should be familiar with the underlying etiologies and treatment modalities. Patients with erythroderma require immediate attention as they may face a variety of medical complications. Early detection and effective management of these complications significantly reduce mortality and morbidity of this potential dermatologic emergency. This review highlights the underlying common diagnoses, assessment, and management of the patient with erythroderma.

KEYWORDS: erythroderma, erythema, skin scaling and erosions, exfoliative dermatitis

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INTRODUCTION

Erythroderma is defined as a generalized or nearly generalized sustained erythema of the skin, involving more than 90% of the body surface area with a variable degree of scaling. Some cases are also associated with erosions (loss of epidermis with an epidermal base), crusting (serous, sanguineous, or pustular), and the potential for hair and nail changes.[1,2] Exfoliative dermatitis and erythroderma (the preferred term) have been used synonymously in the literature.[3]

The red skin is frequently the morphological presentation of an underlying systemic or cutaneous disease.[4] The diagnoses can be remembered with the mnemonic SCALPID: (Table 1)

- seborrheic dermatitis/sarcoidosis
- contact (allergic or irritant) dermatitis (eg, stasis dermatitis with generalization)
- atopic dermatitis/autoimmune disease (systemic lupus/dermatomyositis/bullous pemphigoid/pemphigus foliaceus/lichen planus/graft-versus-host disease)
- lymphoma/leukemia (including Szary syndrome)
- psoriasis, including Reiter syndrome/pityriasis rubra pilaris (PRP)
- infections (human immunodeficiency virus, dermatophytosis), ichthyoses, infestations (Norwegian scabies)
- drug reactions

The most common disorders are contact dermatitis, atopic dermatitis, and psoriasis (remember the mnemonic CAP), along with drug hypersensitivity reactions.[5] The most common malignancy is cutaneous T-cell lymphoma (CTCL). However, in previously published series, 9% to 47% (average, 25%) of cases do not have an identified cause because of difficulty in diagnosing the underlying condition.[4–6]

Persons with erythroderma may be medically stable with a subacute or chronic course or alternatively have an acute or even life-threatening onset. They can present both in a hospital or an outpatient setting, given the wide spectrum of severity of associated systemic symptoms. The underlying disease can be a condition requiring the involvement of a wound care team. Thus, healthcare professionals need to be aware of the diagnosis and management of this condition.

GENERAL CLINICAL CHARACTERISTICS

Excluding children, the average age at onset varies from 41 to 61 years.[4,5] A male predominance has also been observed with a male-to-female ratio varying between 2:1 and 4:1.[4,5] Erythroderma can present with associated shivering (loss of temperature regulation), malaise, fatigue, and pruritus.[4] The onset of scaling is typically seen 2 to 6 days after the onset of the erythema.[3] The nails can become thick, dry, and brittle.[3] Nail pitting, pretibial, and pedal edema are observed in approximately 50% of cases.[4]

Erythroderma may lead to a series of metabolic and physiological complications, including fluid and electrolyte imbalance, high-output cardiac failure, acute respiratory distress syndrome, and secondary infections.[4] Many factors affect the clinical course and prognosis, including patient's age, underlying etiology, coexisting medical conditions, speed of erythroderma onset, and finally initiation of early therapy.[5] Acute supportive therapy and, when possible, early diagnosis are important to correct the underlying cause and improve morbidity and mortality rates. Mortality rates have been reported ranging from 3.73% to 64%, depending on the patient population studied.[5] More recent advances in diagnosis and treatment, however, have resulted in lower mortality.[7]

WORKUP/INVESTIGATION

History

A detailed history is crucial for diagnosing the underlying etiology. Patients must be asked about preexisting medical conditions, allergies, and skin diseases (atopic or other dermatitis, psoriasis, etc).[5] A complete medication history is very important, and this must include details about all prescription, over-the-counter, naturopathic, and herbal medications.[5]

The timing of symptoms is also very important. Generally speaking, the onset of symptoms is sudden and faster for drug-induced erythroderma, while primary skin disease may have a slower course.[5] Pruritus is observed in up to 90% of patients with erythroderma, and it is most severe in patients with atopic dermatitis or Szary syndrome.[8]

Physical Examination

Physical examination is critical to detect the potential complications and to assess the underlying etiology. A complete physical

examination should be conducted on all patients for this systemic condition. The general examination should include documentation of the total area of skin involved and if there are any islands of sparing (well-demarcated areas of spared skin). The patient should be palpated for any organomegaly (liver-spleen) or lymphadenopathy. In addition, the lungs and heart should be auscultated for signs of congestive heart failure (high output with increased fluid to the dilated skin capillaries)[5,8,9] or infection (eg, pneumonia where an area of consolidation may be associated with decreased breath sounds or wheezing with bronchitis or asthma).

Features of the skin examination that may help diagnostically include the following:

- blisters and crusting—think of secondary infection, autoimmune blistering disorders (bullous pemphigoid, pemphigus foliaceus)[4]
- scale[8] is often most prominent with psoriasis; fine scales with atopic dermatitis/dermatophyte infection, bran-like scales with seborrheic dermatitis, and posterythema desquamation are common with drug reactions[8] or bacterial infections
- islands of sparing with PRP—along with a yellow tinge to the skin and hyperkeratosis of the palms and soles.

Clinical clues include nail changes, such as onycholysis (distal separation of the nail plate from the nail bed with a white discoloration), which are most common with psoriasis but can be seen with any acute erythrodermic process and can result in the shedding of the nails that will regrow with recovery unless a scarring process (eg, lichen planus) is involved. Lymphadenopathy (neck, axillae, and groin) should be documented suggesting either a reactive lymphadenopathy or lymphoma.[5] Hepatomegaly occurs in approximately one-third of patients and is more commonly seen in drug-induced erythroderma.[5] Splenomegaly may be associated with lymphoma, but it has rarely been reported in cases of erythroderma.[5] Persons with long-standing erythroderma may also present with cachexia (loss of weight, fatigue, weakness), diffuse alopecia, palmoplantar keratoderma (thickened palms and soles), nail dystrophy, and ectropion (lower eyelid turns outward).[8]

Biopsy: Skin and Lymph Nodes

The skin should be examined carefully for one or more characteristic sites for biopsy often on the extremities or trunk. If there is more than one clinical morphology (eg, red and scaly skin vs thicker plaques vs blisters), it is often important to perform a biopsy on each different skin change for the best chance of a correct diagnosis. A 4-mm punch biopsy should be performed from the representative sites for histology, with immunofluorescence biopsy checking for immunoglobulins at the dermal-epidermal junction in the case of possible autoimmune disease.[10]

If lymphadenopathy is detected and considered potentially abnormal and not reactive, referral should be made to a lymphoma, internal medicine, or surgical specialist. The complete workup may include computed tomography scan, positron emission tomography scan, magnetic resonance imaging, and lymph node biopsy. This referral is important for patients with suspected lymphoma or leukemic infiltrates, including an acute erythrodermic form of CTCL (Szary syndrome).

The skin biopsy is a helpful diagnostic tool to identify the underlying etiology. However, diagnostic cutaneous features may be masked by the nonspecific changes of erythroderma, and the biopsy may need to be repeated when the nonspecific clinical signs improve.[11] Some of the nonspecific pathology findings present with erythroderma include the following[3]:

- hyperorthokeratosis (thickened keratin layer without retained nuclei)
- acanthosis (thickened epidermis)
- chronic perivascular inflammatory infiltrate with or without eosinophilia.

Multiple biopsies can enhance the accuracy of histopathologic diagnoses and that features of underlying disease are usually retained.[3] The approach to erythrodermic patients is based on general treatment measures of the signs and symptoms, as well as correcting the underlying cause.

Laboratory Investigations

Blood work should include a complete blood count, where a low hemoglobin may indicate an anemia of chronic disease, increased loss of blood from the skin, or malabsorption of the gut. A high white blood cell count could indicate infection, or abnormal cells can indicate a leukemic condition. Eosinophilia may be associated with many drug reactions, allergic contact dermatitis, or bullous pemphigoid. The loss of fluids and electrolytes needs to be monitored with serum blood urea nitrogen, sodium, potassium, and chloride along with an albumin level that will be decreased with malabsorption and malnutrition that often accompanies erythroderma.

Skin swabs of the nostrils or areas of secondary impetiginization (pustular crusts) of the skin may be important to administer appropriate topical or systemic antimicrobial agents. Blood cultures may be required if septicemia is suspected. In Norwegian scabies, the mites can be identified from direct examination of the skin with the dermatoscope (finger webs, axilla, penis, toe webs) or from skin scrapings (burrows in the finger webs) examined microscopically or with the dermatoscope. Similarly, fungal organisms can be identified with potassium hydroxide mounts microscopically, and the skin scrapings can also be cultured in the laboratory on Sabouraud media.

Human immunodeficiency virus testing is important with a high index of suspicion or in high-risk populations. Clues to immunodeficiency disorders include weight loss, lymphadenopathy, and low hemoglobin and white blood cell counts, but similar changes can be found in other types of erythroderma. A chest radiograph can identify infections, inflammatory disorders such as sarcoidosis with hilar lymphadenopathy, and congestive heart failure.

Severe drug reactions (systemic hypersensitivity syndromes) that involve the skin may also result in liver and kidney function changes with baseline testing required. Patients with possible collagen diseases should have a screening test panel for associated autoantibodies including antinuclear factor, extractable nuclear antigen, rheumatoid factor, anti-DNA antibodies, and compliment levels (usually C4 and C3). In addition, indirect pemphigus and pemphigoid antibodies can be detected from serum samples, along with skin biopsies of the edge of the lesions for direct immunofluorescence examination.

MANAGEMENT

General Treatment of Erythroderma

Erythroderma is a dermatologic emergency and will necessitate hospital admission for severe cases. The loss of thermoregulation will prevent shivering and temperature hemostasis requiring warming blankets. The vasodilation of the skin can also result in high-output cardiac failure states, and this needs to be corrected and monitored with temperature readings and other vital signs (blood pressure, pulse). Hydration to maintain a normal volume status must be monitored on an ongoing basis.[7] Any electrolyte abnormalities must be corrected, and efforts made to keep patients afebrile.[7]

General skin care measures include using oatmeal baths or wet compresses of no more than a quarter of the body at a time with lukewarm compresses. Clinicians should be careful not to expose large areas of the skin to cooling from the ambient environment with the loss of thermal regulation. Bland emollients or petrolatum or a low-potency topical steroid (eg, 1% hydrocortisone) may increase patient comfort.[7] Erythrodermic skin has lost its normal barrier function to prevent bacterial infections, and this needs to be addressed through skin swabs, blood cultures, and appropriate systemic antimicrobial treatment if there is secondary infection or sepsis.[4] Sedating antihistamines can be used to relieve pruritus and to control anxiety.[4] If the peripheral edema is not relieved with leg elevation or tubular bandages, cautious administration of systemic diuretics may be required.[4]

Determining the underlying etiology of erythroderma is crucial, and any external aggravating factors must be eliminated.[7] Specifically, any potential drugs inducing erythroderma must be stopped.[7] Otherwise, once the underlying etiology is determined, disease-specific management can be initiated.

DIFFERENTIAL DIAGNOSIS OF THE UNDERLYING CAUSE

Psoriasis

Erythrodermic psoriasis indicates unstable disease. There are several patterns, most commonly including a diffuse erythema from bacterial sepsis, drug reactions to systemic/topical therapy, or UV light burns (Table 2).[5] The typical features of psoriatic plaques are lost with generalization of the erythema (Figure 1); however, nail changes such as oil-drop changes (darker yellow circles on a pink nail bed visible through the nail plate) and onycholysis or nail pits (loss of immature keratin on the nail surface) may still be present because of slower turnover rate.[8] Oftentimes, the face is spared. Pustular psoriasis can present with lakes of pustules or an annular pustular pattern as psoriatic plaques evolve into an erythrodermic pattern. The subcorneal pustules (superficial collections of pus centered within the epidermis and not in hair follicles) may be accompanied with acute inflammatory arthritis.[8]

Psoriasis is the most common underlying cutaneous disease known to cause erythroderma, responsible for approximately 23% of cases.[5] Khaled et al[1] determined that in 21 of 27 cases of psoriasis, associated erythroderma developed after psoriasis had been present for 10 years or more (mean duration, 13 years; median duration, 6.75 years). They also observed that all patients with psoriatic erythroderma in their study group had a relapse.[1] Similarly, Boyd and Menter[12] reported an average of 14 years between the onset of psoriasis and the first erythrodermic episode for 48 of 50 patients.

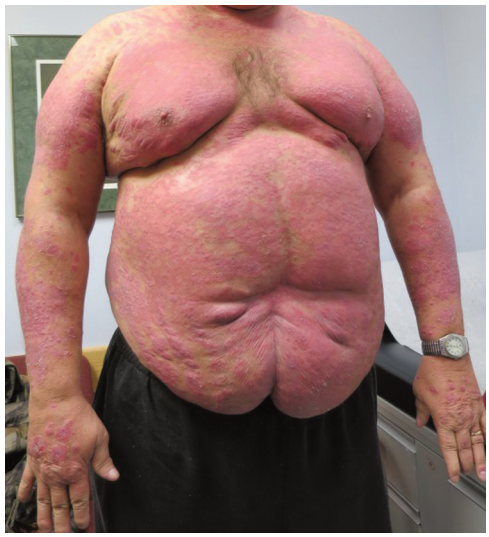
Treatment of Psoriatic Erythroderma[13,14]

Systemic treatment of psoriasis includes methotrexate, acitretin, cyclosporine, and anti–tumor necrosis factor biologics.[15,16] Methotrexate is contraindicated with active hepatitis B or C, active hepatic disease, and alcohol consumption. The dose is usually 0.2 to 0.4 mg/kg administered weekly (or sooner with very acute episodes) either orally or subcutaneously. An average dose would

Table 1.
ERYTHRODERMA AS A PRESENTATION OF AN UNDERLYING DISEASE

Dermatitis: Atopic dermatitis, seborrheic dermatitis, allergic contact dermatitis, irritant contact dermatitis, stasis dermatitis
Papulosquamous disorders: Psoriasis, pityriasis rubra pilaris, Reiter syndrome, lichen planus
Connective tissue diseases: Systemic lupus erythematosus, dermatomyositis
Malignancy related: Leukemia, lymphoma (including Szary syndrome), graft-versus-host disease
Bullous diseases: Bullous pemphigoid, pemphigus foliaceus
Infection related: HIV, dermatophytoses, Norwegian scabies
Drug reactions

Figure 1.
A 50-YEAR-OLD MAN WITH ERYTHRODERMIC PSORIASIS AND PSORIATIC ARTHRITIS



The patient's skin was aggravated by an abscess/nonhealing wound post abdominal surgery.

be between 15 and 40 mg/wk with monitoring of liver function. To protect the gut, folic acid is often administered 5 mg/d but may be omitted on the day(s) of methotrexate administration.

Acitretin is a retinoid (vitamin A derivative) that can help the skin, but it will cause dry eyes, mouth, and distal extremities. It is best administered with meals, and serum lipids need to be monitored as they can elevate in approximately 25% of patients. The retinoids are teratogens and must not be given to any females of childbearing potential without being celibate or practicing 2 forms of contraception (such as birth control pill and condom). Because of the relatively short half-life, 13-*cis*-retinoic acid would be the preferred drug for any female of childbearing age, as it is cleared from the body 21 days after the last dose. Cyclosporine is a very quick-acting drug that may be associated with increases in blood pressure and renal toxicity. There are also numerous drug-drug interactions with cyclosporine. The anti-TNF biologics, etanercept, adalimumab, and infliximab, have been associated with clearing of long-term erythrodermic psoriasis and psoriatic arthritis in case reports when combined with methotrexate. Newer biologic agents such as ustekinumab may also prove to give similar results.

Systemic steroids should not be used in patients suspected to have underlying psoriasis,[4] as their withdrawal can result in a pustular flare that may be life threatening. These agents may be necessary in specific instances (more commonly used in some parts of Europe) or, for example, as the only safe agent for pustular psoriasis of pregnancy. Steroids need to be withdrawn gradually, often with co-coverage using other systemic therapies.

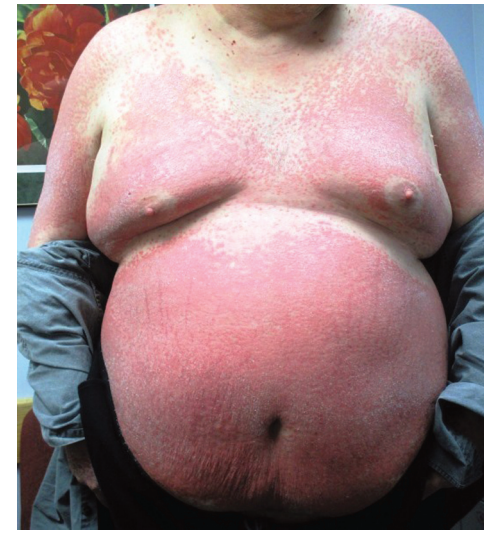
Pityriasis Rubra Pilaris

Pityriasis rubra pilaris is a group of disorders with the acquired condition most likely to become erythrodermic. The name *pityriasis* refers to the predominant scale, *rubra* to the distinctive orange red color, and *pilaris* to the follicular papules around the hair follicles (Figure 2). Clinically, the disorder is distinct with islands of sparing and thick yellow scale on the palms and soles that extend toward the wrists and ankles.[4] Pityriasis rubra pilaris typically begins with a seborrheic dermatitis–like eruption of the scalp or face and spreads at a variable rate over most of the body. It is more common in males over the age of 50 years. It is often mistaken for psoriasis, and skin biopsy can frequently be nonspecific. Therefore, it is important that the clinician recognize the distinctive clinical presentation. Pityriasis rubra pilaris may resolve over many years, but long-term minor residual sequelae are not uncommon.

Treatment of PRP

The treatment of PRP often requires stronger fluorinated steroids on the palms and soles with a moderate-strength topical steroid on the trunk and extremities and a mild topical steroid cream for the face and skinfolds. First-line oral therapy is with systemic retinoids

Figure 2.
A 65-YEAR-OLD MAN WITH SUDDEN-ONSET ERYTHRODERMA OVER 3 TO 4 MONTHS



A biopsy revealed pityriasis rubra pilaris, which clinically has characteristic ''islands of sparing.''

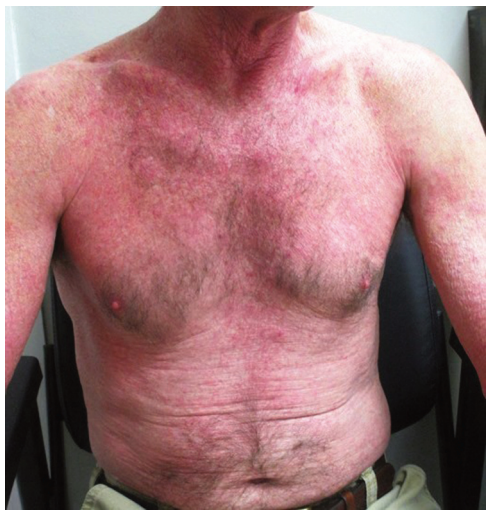
(acitretin), whereas other first-line and alternative agents are cyclosporine, methotrexate, and azathioprine.[17]

Dermatitis

Patients with underlying atopic dermatitis may present with erythroderma (Figure 3) with accompanying lichenification. They also may have thickened skin with indiscrete margins and increased skin surface markings, as well as prurigo nodularis (thick itchy lumps most common on the arms and legs).[8] Atopic dermatitis, contact allergic or irritant dermatitis, seborrheic dermatitis, and autosensitization dermatitis (eg, stasis dermatitis with secondary contact allergy) can lead to autosensitization or generalization of the reaction. Lymphocytes sensitized in the skin (with the help of Langerhans cells) migrate to the regional lymph nodes where they sensitize other lymphocytes and then distribute themselves to distant skin sites where they will elicit an allergic response that may lead to erythroderma.[18] Generalized contact allergic dermatitis may occur at any age with erythroderma developing more commonly in patients with moderate to severe atopic dermatitis.[8] The causes of eczematous erythroderma include intrinsic factors (dysfunction of T cells), and liver or kidney disease. Common extrinsic factors resulting in erythroderma can be traced to inappropriate topical (heat rubs, certain herbal remedies) or systemic treatment of eczema and environmental changes.[19]

Khaled et al[1] studied 82 cases of acquired erythroderma, where the mean age was 55.13 years, and there was no usual sex predilection. They found eczema was the underlying etiology in 9 patients, and 3 of these patients had preexisting contact dermatitis to cement.[1]

Figure 3.
A 45-YEAR-OLD MAN WITH MULTIPLE SKIN CONDITIONS



This patient has atopic dermatitis and hyper-IgE syndrome (~55,000 U/mL) with erythroderma due to active atopic disease and *Staphylococcus aureus* on the skin surface.

Table 2.
POTENTIAL AGGRAVATING FACTORS OR TRIGGERS FOR ERYTHRODERMA

Ultraviolet light	Phototherapy burns
	Phototoxic drugs: coal tar, tetracyclines, sulfonamides, nalidixic acid
	Underlying collagen vascular disease
Systemic illnesses	Abnormal T cells (Szary syndrome)
	Liver disease
	Kidney disease
Withdrawal of systemic medications	Oral corticosteroids
	Methotrexate
	Biologic agents
Infection	*Staphylococcus aureus*
	Streptococcus
	HIV
Topical agents	Benzocaine
	Tincture of benzoin
	Balsam of Peru
	Lanolin

Eight of the nine patients presented with pruritus.[1] Agents responsible for the allergic contact dermatitis leading to erythroderma included topical benzocaine, tincture of benzoin, balsam under a cast, and lanolin in a leg ulcer patient.

Treatment of Dermatitis-Related Erythroderma Related to Contact Allergies

Topical steroids are effective treatment for localized eczema; however, oral steroids may be necessary for acute contact dermatitis with erythroderma. In general, a dose of 0.5 mg/kg needs to be administered each morning, and the systemic steroids need to be tapered slowly, similar to an episode of acute poison ivy or poison oak with generalization over the entire body. For a person weighing approximately 150 lb, 35 mg of prednisone would be started, and then the oral steroid reduced by 5 mg or 1 tablet every 5 days (35 days and 105 pills each 5 mg of prednisone). Blood pressure should be monitored, and baseline documentation should include laboratory studies for diabetes (blood glucose, HbA1c) and a chest radiograph.[15,19] After completion of an oral course of therapy, patch tests should be performed if the responsible allergen has not been identified. Antihistamines may be useful as they can relieve itch during relapses.[15,19] In the treatment of severe atopic dermatitis, cyclosporine, methotrexate, azathioprine, mycophenolate mofetil, and interferon have been used with success.[20]

Persons with severe atopic dermatitis may have hyper–immunoglobulin E (IgE) syndrome[21] with high levels of IgE in the peripheral blood. These individuals often carry *Staphylococcus aureus* on their skin and nares. The staphylococcus acts as a superantigen, further increasing IgE levels. Treatment with anti-inflammatory antibiotics to control the staphylococcus[22] on the skin (eg, doxycycline, cotrimoxazole) may be necessary in addition to the use of topical emollients, topical steroids, topical immune response modifiers, and the systemic agents previously mentioned for severe atopic eczema.

Drug-Induced Erythroderma

Patients with drug reactions may also present with facial edema, and they may become purpuric in dependent areas.[8] There are a number of medications implicated with erythroderma (Table 3).[5,8] Allopathic and naturopathic medications have also been suggested to cause erythroderma.[5] The introduction of recent new oral or other systemic medication may be directly related to the increased incidence of erythroderma.[3] Additional manifestations that may be observed include fever and peripheral eosinophilia, along with facial swelling, hepatitis, myocarditis, and allergic interstitial nephritis.[2] This constellation of findings is referred to as DRESS (drug reaction with eosinophilia and systemic symptoms).[2] Most of the clinical features of erythroderma are nonspecific (Figure 2). The presentation of erythroderma in individuals without a preexisting skin disease is more common with drug-induced erythroderma or malignancy. Compared with other causes, the onset of erythroderma secondary to medication is typically more sudden and rapidly progressing, and the resolution is often quicker.[4]

Treatment of Erythroderma Secondary to Drugs

Drugs suspected to be causative agents should be discontinued. Oral steroids and pulse intravenous solumedrol therapy are effective in early stages.[19] Patients with the DRESS syndrome will often require careful monitoring of the cardiac, liver, and kidney status with slow tapering of systemic steroids.

Table 3.
MEDICATIONS ASSOCIATED WITH ERYTHRODERMA

Antimicrobials: β-Lactam antibiotics (aztreonam, cephalosporins, penicillins,) dapsone, gentamicin, indinavir, isoniazid, minocycline, trimethoprim, vancomycin
Antihypertensives/antiarrhythmics: Amiodarone, calcium-channel blockers, thiazides
Antiepileptics: Carbamazepine, phenytoin, lamotrigine, phenothiazines
Gastrointestinal drugs: Cimetidine, omeprazole
Miscellaneous: Codeine phosphate, isosorbide dinitrate, quinidine, St John's wort

Grant-Kels et al.[5]

Table 4.
PEDIATRIC CAUSES OF ERYTHRODERMA

Dermatitis: Atopic dermatitis, seborrheic dermatitis, nutritional dermatitis
Immunodeficiencies: Omenn syndrome, Wiskott-Aldrich syndrome
Infections: Staphylococcal scalded skin, congenital cutaneous candidiasis
Inherited ichthyosis: Epidermolytic ichthyosis, congenital ichthyosiform erythroderma, Netherton syndrome
Metabolic diseases: Holocarboxylase synthetase deficiency, biotinidase deficiency, essential fatty acid deficiency
Papulosquamous disorders: Psoriasis, pityriasis rubra pilaris
Drug reactions

Sterry and Steinhoff.[8]

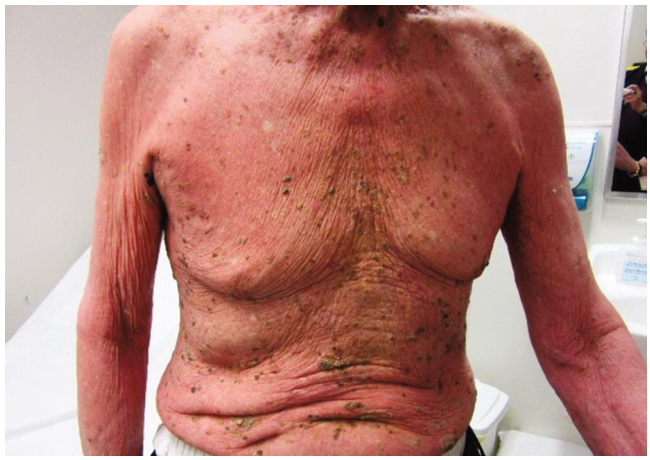
Cutaneous T-Cell Lymphoma

Cutaneous T-cell lymphoma is the most common malignancy associated with erythroderma.[2] It has been reported to be responsible for up to 25% of cases of erythroderma in some series.[2] Patients with CTCL may also have, but are not limited to, mycosis fungoides and Szary syndrome. In advanced stages of mycosis fungoides, there are lymph node swelling and fixed dermal erythema with intense pruritus that can extend across the entire body surface.[15] Cutaneous T-cell lymphoma may present with a deep purple-red hue, alopecia, and painful, fissured keratoderma.[8] Szary syndrome is defined by erythroderma, circulating malignant T lymphocytes, and generalized lymphadenopathy.[8] Other clinical features of Szary syndrome include a leonine facies along with a characteristic of CTCL that may include a diffuse alopecia and painful palmar and plantar keratoderma.[8] There are 3 characteristics of CTCL that distinguish this disorder from other non-Hodgkin lymphomas: skin honing helper T4 cells, potential leukemic infiltrate with remarkable sparing of the bone marrow, and infiltration of the T-cell zones of the lymph nodes and spleen.[23]

Erythroderma is labeled as idiopathic in 9% to 47% of cases.[4] Longitudinal monitoring of patients with idiopathic erythroderma and another biopsy may reveal undiagnosed CTCL.[2] This group is composed mainly of older adult men with a chronic and relapsing course of pruritic erythroderma.[8] In Figure 4, a 95-year-old man with extensive benign pigmented seborrheic keratosis on his back had a underlying, stable erythroderma for 50 years. This condition has not caused the patient to become ill. The biopsy was diagnostic of CTCL, and other than occasional topical steroid application for mild itch, he required no therapy.

Figure 4.

A 95-YEAR-OLD MAN WITH 50-YEAR HISTORY OF GENERALIZED SKIN ERUPTION



The patient's biopsy diagnosed cutaneous T-cell lymphoma. He has done well with occasional topical steroids (betamethasone 1% valerate). There is no lymphadenopathy/organomegaly.

Treatment of CTCL Erythroderma

Patients with mild disease may simply require UV light or potent topical steroids. The disease needs to be staged with the extent of skin involvement along with lymph nodes and bone marrow. Patients with more severe disease (extensive cutaneous involvement, lymph node or bone marrow infiltration) require systemic treatment. There are systemic agents specifically Food and Drug Administration approved for CTCL including denileukin diftitox (combination of interleukin 2 and diphtheria toxin) administered intravenously, bexarotene (an oral retinoid), and 2 oral histone deacetylase inhibitors: vorinostat and romidepsin. In addition, some patients may benefit from electron beam therapy, but this has not been shown to increase survival. However, some patients with erythrodermic CTCL may need more traditional chemotherapeutic agents.

PEDIATRIC CAUSES OF ERYTHRODERMA

The most common cause of erythroderma in children is drug eruptions followed by psoriasis (Table 4).[8] In neonates and infants, erythroderma is frequently related to genodermatoses (especially the various forms of ichthyosis), atopic dermatitis, severe psoriasis or seborrheic dermatitis, primary immune deficiencies, and metabolic diseases.[18] Leclerc-Mercier et al[18] studied 72 patients 1 year or younger admitted for exfoliative erythroderma and found that the most frequent diagnosis was immunodeficiency, followed by ichthyosis, Netherton syndrome (a form of autosomal recessive ichthyosis), atopic dermatitis, and psoriasis.[18]

Sehgal and Srivastava[24] conducted a study that identified the causes of erythroderma: 27% drug induced, 29% genodermatoses, 18% staphylococcal scalded skin, 12% atopic dermatitis, and 5% seborrheic dermatitis.

CONCLUSIONS

Patients with erythroderma may be an urgent medical condition requiring immediate attention.[4] Every effort should be made to determine the underlying etiology and document complications. Treatment should be directed at both the complications and the underlying cause. Early diagnosis is paramount as it allows early treatment and prevention of erythroderma-associated morbidity and mortality. Early medical treatment and newer dermatologic therapies have significantly improved the prognosis of patients with erythroderma.[4]

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