CLINICAL VIGNETTE

Redness Everywhere: a Rare Drug-Related Skin Eruption

Divya Sachdev, MD[1], Uzma Khan, MD[2],
Department of Internal Medicine, University of Los Angeles[1,2]

Case Report

A 46-year-old male presented to our hospital with a 2-day history of progressively worsening diffuse pruritic cutaneous eruption, which began on his legs and spread upwards to his trunk and arms. His medical problems included obesity, alcoholic cirrhosis, and hidradenitis suppurativa. The patient was not on any medications until two weeks prior to his presentation when he started hydroxyzine and ciprofloxacin for increasing pruritus related to his hidradenitis suppurativa. He denied any oral or genital lesions, constitutional symptoms, or arthralgias.

Physical examination revealed generalized redness with diffuse multiple blanching erythematous patches and papules coalescing into plaques with overlying desquamation and scaling over his arms, legs and trunk (Figure 1). Palms bilaterally had some erythematous papules but there were no lesions on the soles. There was no mucosal involvement, blistering, or lymphadenopathy. Exam was positive for gynecomastia, testicular atrophy, and 1+ pitting lower extremity edema bilaterally was noted. Laboratory results were significant for leukocytosis with normal differential along with elevation in the liver enzymes, alkaline phosphatase and aspartate aminotransferase, and elevation in inflammatory markers, erythrocyte sedimentation rate and c-reactive protein, and hypoalbuminemia. Infectious serologies, including Rickettsia ricketsii antibodies, Chlamydia antibodies, Epstein-Barr virus antibody, Rapid Plasma Reagin, Hepatitis B PCR, Hepatitis C antibody, and HIV antibody, were negative. Punch biopsy showed "interface dermatitis with superficial perivascular and interstitial lymphocyte predominant inflammatory infiltrate" (Figure 2). There was no eosinophilia or evidence for fungal organisms, vasculitis, or malignancy. In addition, a drug etiology was suggested due to the mixture of reaction patterns present. There was also spongiosis of the epidermis with overlying confluent parakeratosis as well as hyperkeratosis. The clinical findings along with the pathology suggested erythroderma, likely secondary to a drug etiology.

Discussion

Erythroderma is generalized redness of the skin covering at least 90% of the skin surface and often accompanied by overlying scaling[1,2]. It is a rare skin condition with an annual incidence of 1-2 cases per 100,000 people being reported in a study in Netherlands[3]. Despite the low incidence, the mortality has varied from 18 to 64% and this has been reduced due to diagnostic and therapeutic advances[1]. Erythroderma is most prevalent in males aged 40-60 years[4]. Common etiologies include preexisting skin conditions, malignancy, drugs, or idiopathic[1].

The exact pathogenesis of erythroderma is unknown. There appears to be an interaction between cellular adhesion molecules and cytokines causing increased epithelial cell turnover leading to an increased rate of mitosis[1,4]. Although there are no specific laboratory findings implicated in erythroderma, common laboratory findings include leukocytosis with eosinophilia, hypoalbuminemia, mild anemia, elevated sedimentation rate, elevated uric acid, hyperglobulinemia with increased IgE levels[1,4].

The histopathology often is nonspecific, revealing hyperkeratosis, parakeratosis, acanthosis, and perivascular inflammatory infiltrate that may or may not be accompanied by eosinophilia[1,4]. Pruritus, our patient's presenting complaint, is the most common symptom. Erythroderma can manifest as acute, with large scales, or chronic, with small scales[1]. Other clinical findings include nail changes, weight loss, fever, chills, lymphadenopathy, abnormal pigmentation, hepatosplenomegaly, edema, gynecomastia suggesting a high estrogen state although the exact significance remains unclear[1,4,5]. Our patient had the latter two findings, though these maybe be confounded by his underlying liver disease and may have been exacerbated by the erythroderma.

The most common cause of erythroderma is a preexisting skin condition, with psoriasis as the leading cause[1]. Other skin conditions that often result in erythroderma include contact dermatitis, seborrheic dermatitis, atopic dermatitis, staphylococcal scalded syndrome, stasis dermatitis, pityriasis rubra pilaris, pemphigus foliaceus and congenital ichthyosiform erythroderma[1]. We could not identify any literature to demonstrate a link between hidradenitis suppurativa and erythroderma.

Erythroderma can represent a manifestation of underlying malignancy. The most common malignancies presenting as erythroderma are mycosis fungoides and Sezary syndrome[1]. One case report of an elderly male without preexisting liver disease who presented with erythroderma and was found to have hepatocellular carcinoma[6]. Our patient's skin pathology did not reveal any evidence of cutaneous lymphoma. As cirrhosis is a risk factor for developing hepatocellular carcinoma, we pursued malignancy screening with abdominal ultrasound and serum alpha-fetoprotein, which were negative.

Erythroderma may occur as a drug reaction, which is often acute in onset; some of the commonly reported drugs include penicillin, carbamazepine, allopurinol, and chinese herbal medications[5]. Both of the drugs that our patient used, ciprofloxacin and hydroxyzine, were likely drug culprits for our patient's drug-induced erythroderma as our patient was on no other recent medications and his condition improved throughout his hospitalization after withdrawal of these medications. Ciprofloxacin has been associated with adverse cutaneous events; the most common reaction being a drug exanthem (42%) followed by photosensitivity (14.9%) and urticaria (14.0%)[7]. Ciprofloxacin has been shown to induce erythroderma in the setting of anaphylactoid reactions[8]. Our patient did not exhibit a full anaphylactoid reaction, but it is notable that he developed erythroderma after the initiation of ciprofloxacin. Hydroxyzine has been associated with systemic contact dermatitis[9] and hydroxyzine could have caused systemic contact dermatitis in our patient, which in turn, predisposed him to erythroderma. Our literature search did not identify a link between hydroxyzine and erythroderma.

Complications of erythroderma include infections, sepsis, high-output cardiac failure, dehydration, electrolyte imbalances, and temperature dysregulation[1]. A case report demonstrated how severe erythroderma can cause acute decompensation of chronic alcoholic liver disease through the release of nitric oxide which can worsen the hyperdynamic circulation in liver dysfunction[10]. This case illustrates the importance of recognizing and treating eryth-roderma in our patient given his concomitant diagnosis of alcoholic cirrhosis.

It is important to differentiate between various potentially fatal dermatologic conditions that can present with erythroderma. Toxic shock syndrome can involve erythroderma with accompanying desquamation along with hypotension and multi-system end-organ involvement, such as renal and liver failure[2]. Anaphylactic reaction can also present as erythroderma with multi-organ involve-ment, often with respiratory distress, gastrointestinal symptoms, and edema. Additionally, widespread desquamation along with erythroderma and mucosal involvement is seen in Steven-Johnson syndrome and toxic epidermal necrolysis, both frequently caused by drugs[2]. DRESS syndrome also can present with erythroderma with fever, lymphadenopathy, transaminitis, and leukocytosis. It is important to learn about as well as recognize erythroderma, which can be a dermatological emergency and also can be present in many fatal dermatologic conditions.

Treatment of erythroderma depends on the underlying cause. In all cases, it is important to provide adequate hydration, nutrition and electrolyte repletion as these patient's have a compromised skin barrier. Withdrawal of offending medication is the mainstay for treatment of drug-induced eryth-roderma. Topical steroids, such as triamcinolone, are often used along with oral corticosteroids for severe cases if drug etiology is suspected[1,4]. Oral antihistamines can also be used to treat pruritus[1,4]. Superimposed bacterial infections can be treated with antibiotics and dependent edema can be treated with diuretics[4].

During our patient's hospitalization, he was supportively managed with intravenous hydration, diphenhydramine for pruritus, and morphine for pain. Ciprofloxacin and hydroxyzine were discontinued on admission. Triamcinolone ointment 0.1% was applied twice daily to the patient's whole body, and his erythema and lesions significantly improved. His edema was managed with furosemide. His laboratory findings improved with treatment. The patient was discharged on furosemide, spironolactone, triamcinolone ointment, and oxycodone as needed for pain. He was cautioned to avoid ciprofloxacin and hydroxyzine in the future.

Conclusion

Erythroderma is a rare skin eruption that can be fatal if not recognized or treated appropriately. Common etiologies include pre-existing skin conditions, malignancy, drugs, or idiopathic. This case highlights the importance of recognizing erythroderma as it is often a feature of dermatological emergencies and other fatal dermatological conditions, including anaphylactic reactions and toxic shock syndrome. Withdrawal of offending medication is the mainstay for treatment of drug-induced erythroderma. Topical steroids are often used and oral corticosteroids may be necessary in severe cases if drug etiology is suspected. It is imperative that physicians be aware of medication-related cutaneous eruptions as there is a mortality risk if not treated appropriately.

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FIGURE LEGEND

FIGURE 1: A generalized redness with diffuse multiple blanching erythematous patches and papules coalescing into plaques with overlying desquamation on the patient's trunk.

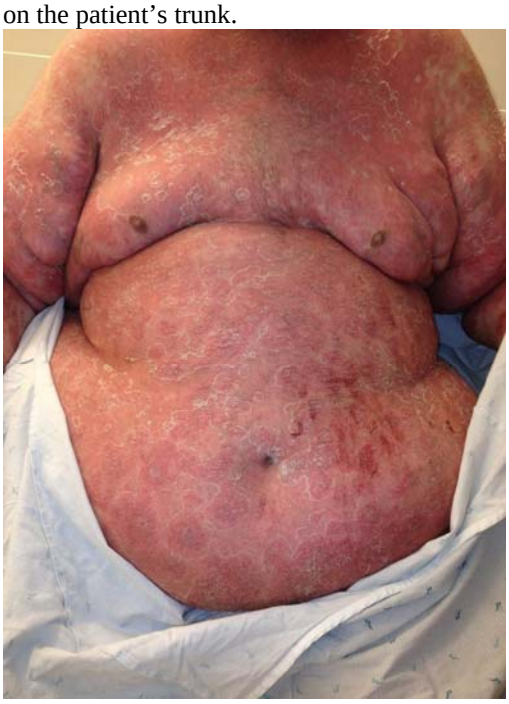
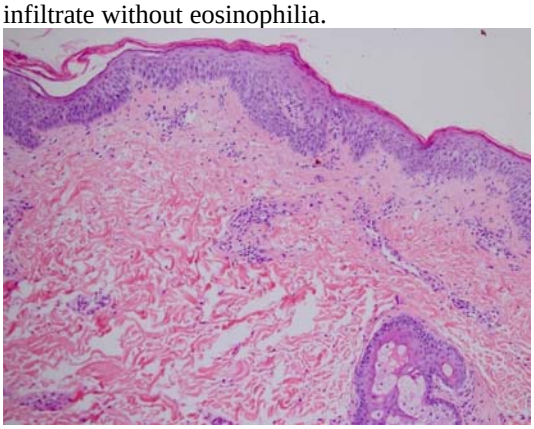


FIGURE 2: This is a skin biopsy sample from the patient's cutaneous eruption showing an interface dermatitis with superficial perivascular and interstitial lymphocyte predominant inflammatory infiltrate without eosinophilia.



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