Extensive Erythema Multiforme With an Unusual Delineated Presentation: A Case Report

Morgan O'Donoghue, MD; Kate Ross, MD

Erythema multiforme majus (EMM) is a hypersensitivity reaction usually secondary to medications, viruses, or other infections. Its presentation is fairly typical with a symmetrical distribution of vesicles, bullae, or tagetoid lesions on the upper body, arms, legs, palms, feet, and oral mucosa. The authors present a case of EMM with a very unusual clinical presentation evolving over time into a unique, almost dermatomal distribution. Typical therapies were not initially helpful and intravenous immunoglobulin antibody had to be administered.

Erythema multiforme majus (EMM), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) were once believed to be on a spectrum of severe cutaneous adverse reactions. In the past few years, it has been debated that EMM is, in fact, a separate entity from SJS and TEN.[1]

Auquier-Dunant et al[1] reported that EMM occurs most often in young male individuals, with a 10-fold higher rate of recurrence and a milder presentation than are found in patients with SJS or TEN. Herpes has been identified as the principal risk factor, occurring in 70% to 80% of cases of EMM.[1,2] Multiple target lesions are present, affecting less than 10% of the body surface area (BSA). It is often symmetric, with the distribution beginning acrally (dorsal surfaces of hands, feet, elbows, and knees).[2,3] Oral lesions are found in 70% of cases but are not required for diagnosis.[2,3]

Stevens-Johnson syndrome and TEN are now believed to be severity variants of a single entity.[1] Stevens-Johnson syndrome affects less than 10% of the BSA, and TEN is more severe, with more than 30% of the BSA involved. Drugs are the highest etiologic risk factor for both SJS and TEN.[1] A flu-like prodrome is common 7 to 14 days before lesions are visible. The initial rash is in a morbilliform pattern beginning in the face, neck, chin, and central trunk. The spread is rapid and lesions often coalesce. The Nikolsky sign is often present. Mucosal involvement is extensive.[2] Treatment options are limited for these conditions and many are controversial. There are no standard guidelines for treatment of either EMM or SJS. Studies have shown that treatment with corticosteroids may lengthen the duration of these reactions, whereas others show that it may offer some benefit. For patients with EMM, early treatment of herpes simplex virus (HSV) is believed to be the best option.[2] For patients with SJS/TEN, first-line management is to stop any potential offending drugs. Replacement intravenous fluids are often needed.[2]

Dr. O'Donoghue is the medical director of O'Donoghue Dermatology in Sarasota, Florida. Dr. Ross is with the Department of Dermatology, University of South Florida, Tampa.

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Correspondence: Morgan O'Donoghue, MD, 1952 Field Road, Sarasota, Fl 34231 (dermatologyexperts@yahoo.com).

CASE REPORT

A 32-year-old woman presented to the Walgreens Take Care clinic with a 3-day history of "rash" on the dorsal surfaces of her hands and arms. She was diagnosed with hives and given methylprednisolone and dyphenhydramine. On day 7, she presented to the dermatology office with worsening rash, covering about 30% of her BSA, which had spread to her legs and trunk. The distinct demarcation of areas involved compared with noninvolved areas was striking. Although this did not follow neural dermatomes, it did have a dermatomal-like pattern (Figure 1). The patient had complained of a fever and cough approximately 3 days before the onset of her rash. She had no history of HSV infection. The patient had known allergies to sulfa drugs and shellfish. A biopsy of the edge of the lesion showed orthokeratosis of the stratum corneum, with vacuolization of the basal layer, and sparse superficial perivascular lymphoid infiltrate. Mild spongiosis and exocytosis with necrosis of individual keratinocytes in the malpighian stratum was evident. Satellite cell necrosis was also present with papillary dermal edema. Laboratory tests revealed a white blood cell (WBC) count of 14.4×10^9/L (reference range $4.5-11.0\times10^9$/L), a platelet count of 4.71×10^9/L (reference range $150-350\times10^9$/L), and a neutrophil count of 1.3×10^9/L (reference range $1.8-7.8\times10^9$/L). Her HSV-1 and *Mycoplasma pneumoniae* titers were elevated. The hepatitis panel was negative. She denied any oral lesions. Current medications were triamterene and hydrochlorothiazide, cetirizine, and ethinyl estradiol and levonorgestrel. She had been taking ibuprofen for pain in the past week. Laboratory tests showed a high HSV and *M pneumoniae* titer. She was placed on 70 mg of prednisone orally once daily, as well as valacyclovir, ciprofloxacin, and cetirizine.

After 12 days of high-dose corticosteroids, the patient continued to worsen. The vesicles became bullae and coalesced. The patient was still stable but in constant pain, and the WBC count remained elevated. At this point, approximately 70% of her BSA was involved. The distribution of her lesions spared her head, face, upper chest, groin, and buttock regions, with all other areas diffusely involved. The rash continued to be extremely well delineated, following dermatomal planes (Figure 2). On day 19, she returned to the office with new evidence of oral lesions and worsening condition of her skin. The decision was made to begin intravenous immunoglobulin (IVIG) antibody in an outpatient infusion center at a dosage of 2 mg/kg over 4 hours.

One day following IVIG treatment, the patient's lesions were beginning to resolve, and by day 5, most of the denuded skin had peeled away, revealing a healthy layer underneath (Figure 3). The patient was treated with wound care, and the reaction subsided completely within a couple of weeks.

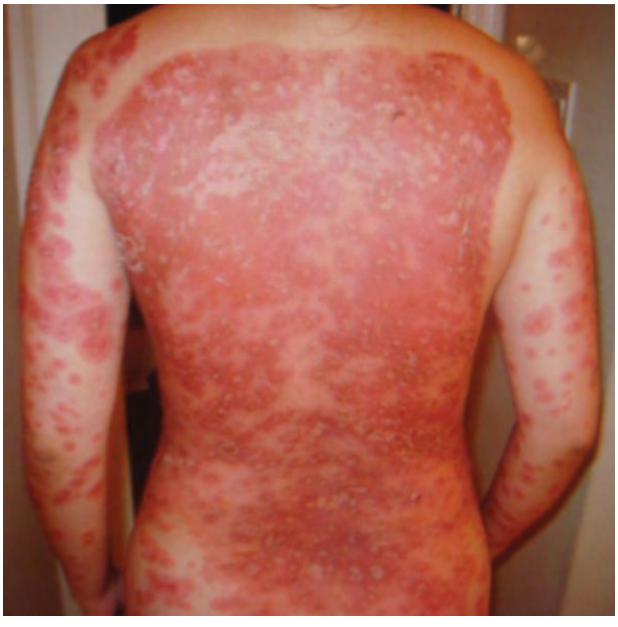

Figure 1. At day 7, dermatomal-like distribution of targetoid vesicles and bullae.

COMMENT

This case is particularly difficult to classify. The rash initially presented on the acral surfaces, which is consistent with EMM; however, the delineated, almost dermatomal appearance that it took as it progressed was unique. Throughout its course, it continued to spare the head, neck, face, and upper chest, which are commonly affected areas with SJS/TEN. The high titers of HSV and *M pneumoniae* also support a diagnosis of EMM. The mucus membrane involvement is seen in both EMM and SJS/TEN. The lack of commonly associated drugs also points to EMM; however, the patient reported a prodromal illness 3 days prior to onset of her rash, which is more often found in SJS or TEN. The extensive involvement of her skin, up to 70% of her BSA, further supports a diagnosis of TEN. The histology showing sparse vascular involvement was more consistent with SJS/TEN; however, the necrotic keratinocytes could support either diagnosis. The high WBC count is more consistent with a diagnosis of SJS/TEN as well.

Although treatment options are still limited and controversial for these reactions, our patient did not seem

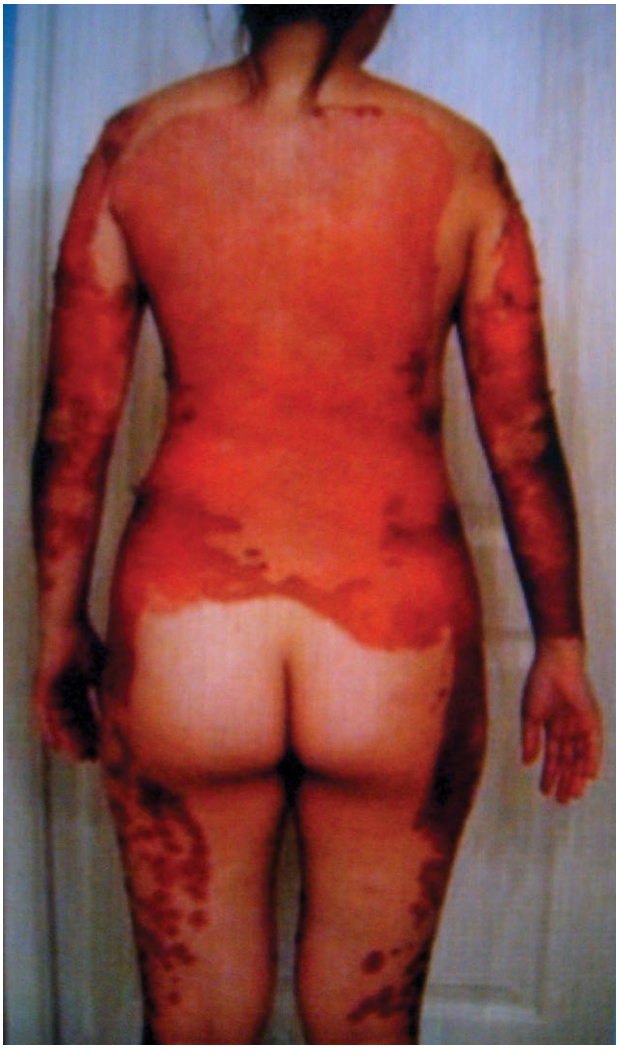

Figure 2. At day 12, evolution of rash onto extremities in a symmetrical dermatomal pattern with marked sparing of some areas.

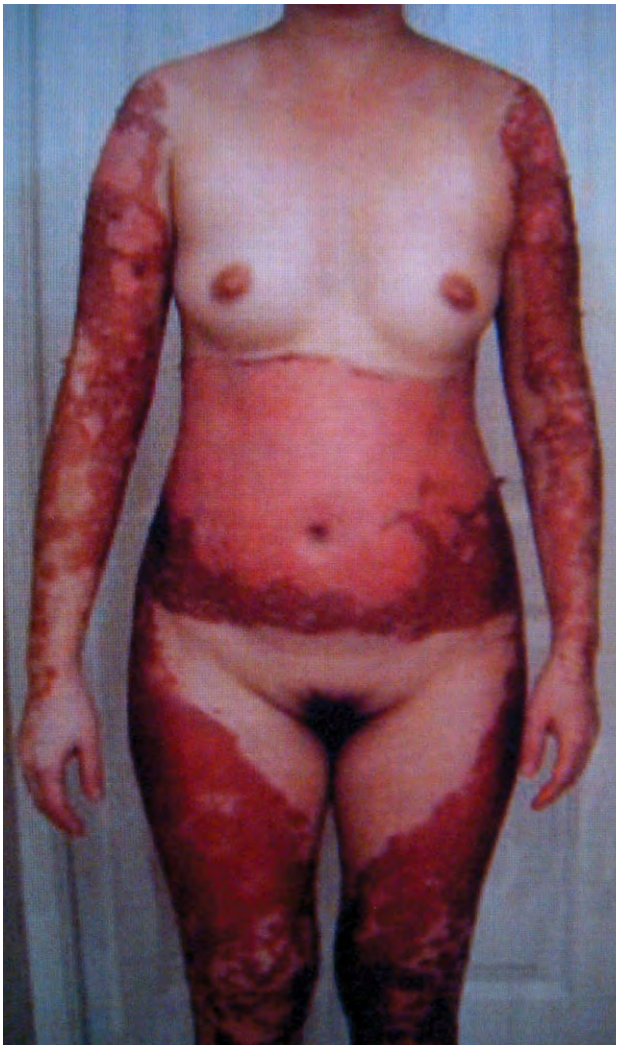

Figure 3. At day 24, several days after treatment with intravenous immunoglobulin, slow resolution of new bullae and exfoliation revealing pink healthy skin.

to benefit from corticosteroid treatment. Intravenous immunoglobulin treatment, although started late in the course of the reaction, seemed to offer immediate relief to the patient and turned the corner of the disease progression toward the recovery phase. While we await further research into treatment success for these severe cutaneous adverse reactions, it is difficult to know if the patient would have simply recovered on day 19 without IVIG, or if it was truly of benefit to her. Treatment options aside, this case is an interesting example of what we believe to be EMM in a very unique and conflicting presentation.

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