Derma Dilemma

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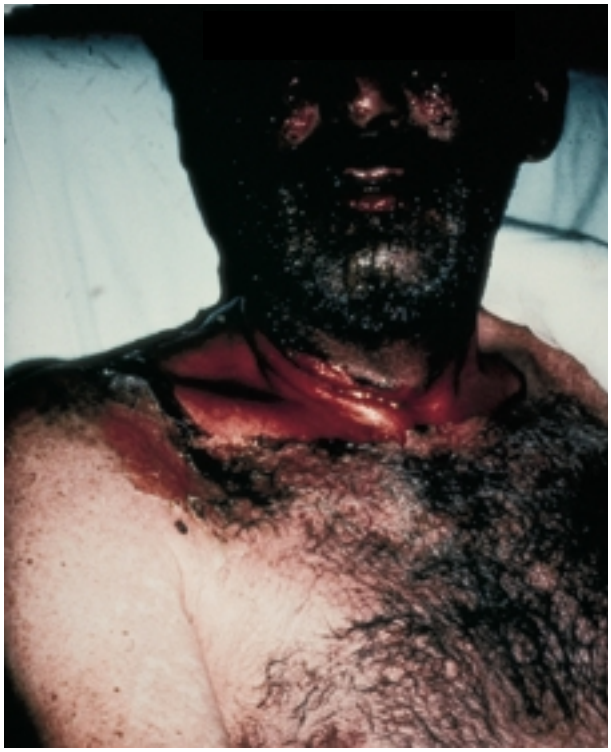

Figure 1. Blotchy erythema involving the trunk and proximal extremities.

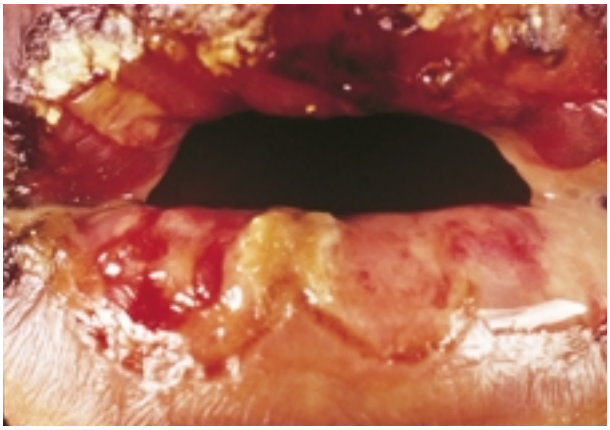

Figure 2. Erosions and crusting of the oral mucosa.

CASE PRESENTATION

A 40-year-old white man presents to the emergency department with complaints of a 1-day history of painful, diffuse, erythematous rash of sudden onset. The patient reports a low-grade fever and sore throat that developed 6 days prior to presentation. In addition, the patient was placed on trimethoprim-sulfamethoxazole 2 weeks prior to presentation for treatment of an acute upper respiratory infection.

Physical examination reveals a blotchy erythema on the trunk and proximal extremities (**Figure 1**); erosions and crusting of the oral mucosa are also evident (**Figure 2**). Flaccid blisters on the trunk demonstrate a positive Nikolsky's sign (ie, lateral extension of a blister with pressure) on the application of lateral pressure.

WHAT IS YOUR DIAGNOSIS?

A) Bacterial exanthem
B) Toxic epidermal necrolysis
C) Pemphigus vulgaris
D) Staphylococcal scalded skin syndrome

WHAT IS THE APPROPRIATE TREATMENT?

A) Methotrexate
B) Hospitalization and intensive treatment in a burn unit
C) Nonsteroidal anti-inflammatory drugs (NSAIDs)
D) Antimalarial agents

ANSWERS

The correct answers are toxic epidermal necrolysis (B) and hospitalization and intensive treatment in a burn unit (B).

DISCUSSION

Toxic epidermal necrolysis (TEN) is a severe, idiosyncratic, exfoliative disease of the skin and mucous membranes. TEN primarily manifests as a dramatic

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Table 1. Treatment Protocols for Toxic Epidermal Necrolysis

Primary emergency care
Withdraw any suspect drug
Avoid skin trauma
Insert a peripheral venous line
Begin administration of macromolecular solution
Direct the patient to a burn unit or an intensive care unit
Symptomatic therapy
Evaluation of severity
Evaluate epidermal lesions: actual detachment plus blisters and areas of positive Nikolsky's sign
Use burn tables
Fluid replacement
Use peripheral veins if possible
Fluid requirements are two-thirds to three-fourths of the requirements recommended for burns of same extent, 4–6 L/day, including 1–2 L macromolecular solutions
Antibacterial policy
Sterile handling of patients
Topical antiseptic solutions (silver nitrate, chlorhexidine)
Nonadherent dressings
Bacterial sampling of altered skin
Systemic antibiotics only if high suspicion of sepsis
Nutritional support
Nasogastric tube, 3000–4000 calories/day
High protein diet
Pulmonary care
Aerosols
Bronchial aspiration
Reduce calorie loss
Raise environmental temperature to 30°–32° C
Use air-fluidized beds and warmed antiseptic solution
Eye lesions
Provide for daily examination by an ophthalmologist
Antiseptic/antibiotic drops every 2 hours
Disrupt synechiae with a blunt instrument
Other supportive therapies
Heparin
Tranquilizers
Analgesics

Adapted with permission from Dover JS, Arndt KA, LeBoit PE, et al: *Pocket Guide to Cutaneous Medicine and Surgery*. Philadelphia: WB Saunders, 1996:255.

detachment of the epidermis from the dermis, which can affect 20% to 100% of the total body surface area.[1]

The pathogenesis of TEN involves a drug-induced or graft-versus-host–induced necrosis of the basal cell layer of the epidermis, with the production of a subepidermal separation rather than the more superficial split seen in patients with staphylococcal scalded skin syndrome.

The incidence of TEN is rare. In a nationwide survey of dermatologists and health care facilities performed in France, the incidence was approximately one case per million per year.[1] TEN most commonly occurs as a reaction to drugs.

Clinical Presentation and Course

As noted previously, the primary clinical manifestation of TEN is dramatic detachment of the epidermis from the dermis, and 20% to 100% of the total body surface area can be affected. Extensive blistering of the skin develops and large sheets of skin peel away leaving denuded dermis, similar to a burn wound. Severe erosive mucositis of the eyes, mouth, and genitalia is almost universal. Mucous membranes are involved in 85% to 95% of patients; the most common sites involved include the oropharynx, eyes, genitalia, and anus.[2,3] Reepithelialization of the damaged skin occurs in 2 to 3 weeks with no resultant scarring.[4] Histologically, TEN demonstrates extensive necrosis of keratinocytes with epidermal detachment. The mortality rate in patients with TEN can be as high as 25% to 75%.

Etiology

The etiology of TEN is unknown. Some researchers believe that TEN may be an extreme form of erythema multiforme (ie, Stevens-Johnson syndrome), but other researchers contend that TEN is an entirely separate disease.[1] The onset of TEN has been primarily associated with drug triggers, especially penicillins, sulfonamides and other antibiotics, anticonvulsants, phenylbutazone and other NSAIDs, barbiturates, and allopurinol. Infections, as seen in erythema multiforme, are not thought to be a major cause of TEN. Direct evidence of an immune mechanism is still lacking.[1] More than 50% of TEN cases are idiopathic, with no known inciting factors.

Diagnosis

A diagnosis of TEN should be considered when a patient presents with generalized or focal erythema with tenderness, bullae, a positive Nikolsky's sign, and large areas of exfoliation (more than 30% of the cutaneous surface). History of ingestion of a drug known to incite TEN is additional evidence for diagnosis. Skin

biopsy can help establish the diagnosis of TEN in indeterminate cases.

Differential Diagnosis

Before the peak stage of TEN is reached, the impending disorder may be difficult to distinguish from other morbilliform drug eruptions. Differentiation from Stevens-Johnson syndrome is quantitative based on the extent and severity of the patient's clinical presentation. Stevens-Johnson syndrome is a severe form of erythema multiforme with involvement of at least two mucosal surfaces; this syndrome is also associated with systemic toxicity. The most common medications associated with TEN and Stevens-Johnson syndrome include antibacterial sulfonamides, aromatic anticonvulsants, aminopenicillins, NSAIDs, and allopurinol. Other entities included in the differential diagnosis for TEN are staphylococcal scalded skin syndrome, burns from scalding or caustic agents, and primary blistering diseases such as pemphigus vulgaris or bullous and mucosal pemphigoid.

Treatment

There is no specific therapy for patients with TEN, although several treatment protocols are suggested (**Table 1**). TEN should be treated as a deep second-degree burn, and patients with severe cases are best managed in a burn unit. A careful drug history is critical, and any possible inciting drugs should be discontinued. Careful attention should be paid to fluid and electrolyte balances, and the patient's airway should be monitored closely and protected with intubation if necessary. Prophylactic antibiotic treatment should be started and adjusted based on culture findings. Ophthalmologic consultation should be obtained because of the risk of conjunctival and corneal scarring.

Corticosteroid therapy. The usefulness of corticosteroid treatment of TEN remains controversial. Several uncontrolled studies have suggested that steroid treatment of TEN was associated with an increased morbidity and mortality.[5–7] A recent study compared the characteristics of 13 patients with TEN, who were also undergoing long-term steroid therapy for other underlying diseases, with 166 other patients with TEN.[8] This investigation concluded that long-term steroid therapy may delay the onset of TEN, but therapy does not halt progression of TEN. Despite this data, many clinicians treat TEN early in its progression with high doses of intravenous steroids for several days in an attempt to abort the process.

SUMMARY

TEN is a serious and possibly life-threatening condition. Early detection and treatment are critical. A careful history is especially important to identify and quickly discontinue possible inciting medications. Treatment of TEN is primarily supportive and directed toward prevention of such complications as infection and blindness. **HP**

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