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CASE REPORT

A case of toxic epidermal necrolysis in a young infant successfully treated with intravenous immunoglobulin

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ABSTRACT

Toxic epidermal necrolysis (TEN) is a severe adverse cutaneous drug reaction characterized by widespread keratinocyte death. Clinically, TEN is characterized by rapidly progressing erythematous, purpuric rash to widespread blistering and denudation of skin and severe mucositis, with fatal complications like sepsis and multiorgan failure. TEN is considered to be rare in infants and usually has a fatal outcome due to sepsis. As yet, only few reports have been documented in the literature. We hereby report a case of TEN in a young infant successfully treated with intravenous immunoglobulin (IVIG).

Key words: Drug rash, intravenous immunoglobulin, toxic epidermal necrolysis

INTRODUCTION

Toxic epidermal necrolysis (TEN) is a severe adverse cutaneous drug reaction characterized by widespread keratinocyte death.[1] Clinically, TEN is characterized by rapidly progressing erythematous, purpuric rash to widespread blistering and denudation of skin and severe mucositis, with fatal complications like sepsis and multiorgan failure. Drugs are the commonest cause of TEN, and the commonly implicated drugs include antiepileptics, sulfonamide antibiotics, penicillins, allopurinol, and oxicam nonsteroidal anti-inflammatory drugs (NSAIDs).[2] The pathophysiology of TEN is incompletely understood; massive keratinocyte apoptosis seems to be due to Fas-mediated mechanisms, and cytotoxic T-cell and natural killer cell damage by perforin/granzyme B/granulysin and tumor necrosis factor-alpha.[3] TEN is considered to be rare in infants and usually has a fatal outcome due to sepsis. Until now, only few reports have been documented in the literature.[4-9] Treatment with intravenous immunoglobulin (IVIG) has been unsuccessful in an infant who reported with TEN.[9] We hereby report a case of TEN in a young infant successfully treated with IVIG.

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CASE REPORT

A 5-month-old female baby born prematurely at 32 weeks of gestation was treated with inj. ceftriaxone intravenous (IV) for fever since 2 days. One day later, she developed rapidly progressing reddish rash which started on face, chest, arms, and later to trunk and lower limbs. As the rash worsened, the child developed oral and lip ulcers, redness of eyes, and was poorly feeding. The parents brought the child to pediatric OPD after 2 days of onset of rash. On examination, the baby was irritable and febrile. Vital parameters were suggestive of tachycardia and tachypnea. She had an extensive, generalized, purpuric rash predominantly seen on face, chest, thighs, buttocks, and perineal region. There were blisters leading to separation of sheets of skin and erosions with positive Nikolsky's sign at sites where the rash was confluent [Figure 1]. Skin lesions involved more than 30% of total body surface area (TBSA). She had hemorrhagic erosions of the lips, with ulcers in the oral cavity and vulva and congested eyes. At birth, weight of the baby was 2.5 kg (preterm). Postnatally, the newborn was hospitalized for respiratory distress and treated with IV cefotaxime for 5 days without any adverse effects.

Investigations showed that there was leukopenia (1500 cells/mm^3), and hemoglobin was 10.8 g/dl and

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the platelet count was 1.15 lakh/mm^3. Urinalysis and serum chemistry were normal. Urine and blood cultures were negative, and chest radiograph was within normal limits. Bacteriologic cultures of specimens collected from cutaneous lesions were negative. A diagnosis of TEN was made and the baby was treated in an intensive care unit. She received IVIG therapy for 5 days with a daily dose of 0.4 g/kg. Additional supportive treatment was given with IV hydration and IV vancomycin and amikacin. Topically mupirocin cream was applied on erosions with skin debridement, as necessary. The child progressively improved [Figure 2] and the skin gradually re-epithelialized, leukocyte counts became normal, and she was discharged home after 2 weeks. At 3 weeks of follow-up, she had only post-inflammatory hypopigmentation [Figure 3].

DISCUSSION

TEN is a severe adverse cutaneous drug reaction clinically characterized by sudden onset of fever, systemic toxicity, a rapidly progressing erythematous, and purpuric rash, which usually starts on face and chest and progresses downward to trunk and extremities, with positive Nikolsky's sign leading on to widespread blisters with separation of sheets of epidermis and erosions. Mucosa is denuded producing oral ulcers, red crusted lips, dysphagia, diarrhea, genital and urinary tract ulcers, and severe purulent conjunctivitis. Epidermal detachment is more than 30% BSA in TEN. Histologically, there is widespread keratinocyte necrosis with separation at the dermo-epidermal junction and a mild mononuclear infiltrate in the dermis.

30% of TEN patients die due to fatal complications like sepsis, metabolic abnormalities, multiorgan failure, gastrointestinal hemorrhage, and pulmonary embolism.[2] Mortality rates in children are much lower than in adults, but in contrast, outcome is usually fatal in neonates and young infants probably due to increased incidence of sepsis.[4-9]

There are more than 200 medications reported to cause TEN, but the drugs most often implicated are antibiotics such as sulfonamides; beta-lactam antibiotics; anticonvulsants such as phenytoin,

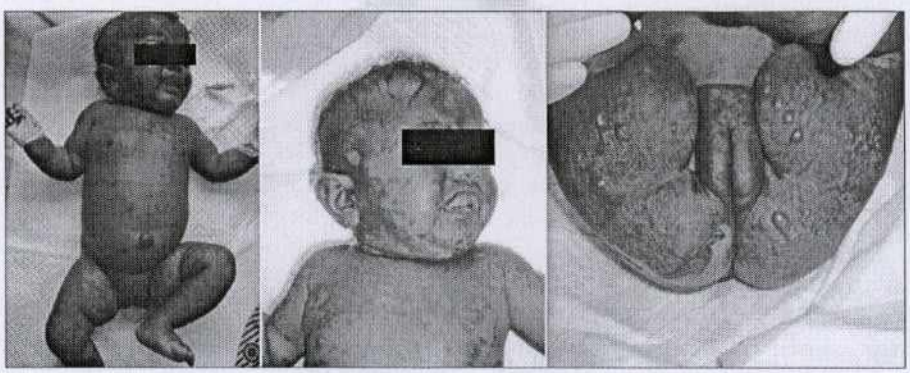

Figure 1: Purpuric macules, bullae, and erosions on the skin and oral mucosa

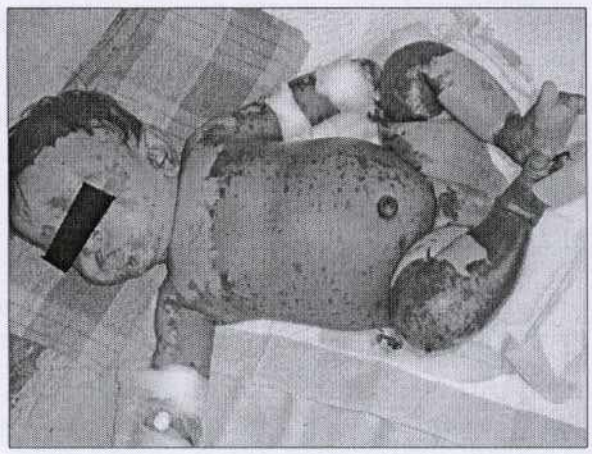

Figure 2: Recovery after 8 days showing new skin

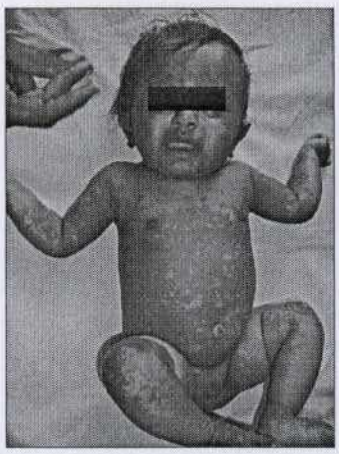

Figure 3: Post-inflammatory hypopigmentation after 3 weeks

phenobarbital, and carbamazapine; nevirapine; abacavir; NSAIDs, particularly the oxicams; allopurinol; lamotrigine; tetracyclines; and quinolones. TEN has also rarely been caused by vaccination and *Mycoplasma pneumoniae* infections.[2]

The pathogenesis of TEN is not completely understood, but several mechanisms have been implicated. These include various immunologic mechanisms leading to keratinocyte apoptosis, such as Fas–Fas ligand interaction, cytotoxic T-cell and natural killer cell damage by perforin/granzyme B/granulysin and tumor necrosis factor-alpha, in addition to genetic predisposition.[3]

Differential diagnosis to be considered especially in neonates and infants is staphylococcal scalded skin syndrome (SSSS). SSSS is a generalized erythematous and blistering disorder caused by toxin-producing strains of *Staphylococcus aureus*, it usually follows a local or systemic *S. aureus* infection, initially presenting with fever, erythema, and painful skin; subsequently, blistering occurs predominantly in the areas of friction and around body orifices. Mucosa is not involved in SSSS, whereas mucositis is prominent in TEN. Histologically, there is subcorneal blister without necrosis or inflammation in SSSS.[2] In our case, we made the diagnosis on clinical grounds.

The offending drug should be immediately stopped and therapy is primarily aimed at supportive care with complementary adjuvant therapies like systemic corticosteroids, IVIG, immunosuppressives such as cyclosporine, cyclophosphamide, and thalidomide, and plasmapheresis.[2] Although many adjuvant therapies have been proposed, none is widely accepted and proven to be effective.[10]

Recently, IVIG therapy has gained much importance as it acts by blocking Fas–Fas ligand-mediated apoptosis of keratinocytes, and other proposed mechanisms include elimination of circulating immune complexes, modulation of cytokine milieu, functional blockade of antibody Fc receptors, and regulation of cellular immune responses.[11]

Treatment with IVIG has been effective in children with TEN as reviewed by Koh and Tay,[3] but in neonates and infants, none of the adjuvant therapies are successful and most of the cases reported so far had a fatal outcome.[4-9] Fernandez *et al*.[9] reported a neonate with TEN treated with IVIG, but therapy was not successful as the neonate died due to septicemia. In our case, the infant was irrationally treated with ceftriaxone for fever without sepsis prior to the onset of rash. Due to extensive skin involvement and poor prognostic factor of leukopenia, IVIG was the first option to treat TEN. To our knowledge, our case is the youngest patient who survived TEN treated with IVIG. The causative drug was ceftriaxone; the baby had received inj. cefotaxime after birth for respiratory distress, but did not develop any skin lesions following the injection. Probably due to prior sensitization and cross-reactivity, the patient may have developed TEN after inj. ceftriaxone was administered. In spite of having leukopenia, our case recovered well due to timely initiation of treatment with IVIG and supportive measures.

What's known: TEN is usually fatal in infants and successful treatment with IVIG has not been reported yet.

What's new: Our case is the youngest patient who survived TEN treated with IVIG.

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