Case Report

Toxic Epidermal Necrolysis

Aamer Naseer, Fauzia Aamer, Hamayun Iqbal Khan, Amjad Hussain, Mohammad Ali Khan and Tayyaba Khawer Butt

Abstract: Toxic epidermal necrolysis (TEN) is a clinical syndrome characterized by severe exfoliative skin changes, erosive mucosal involvement, and potentially life-threatening multisystem involvement. We present a 1 year old boy with recurrent rashes and fever, who turned out to be a case of toxic epidermal necrolysis.

Key words: Toxic Epidermal Necrolysis, Nikolsky sign, Keratinocyte

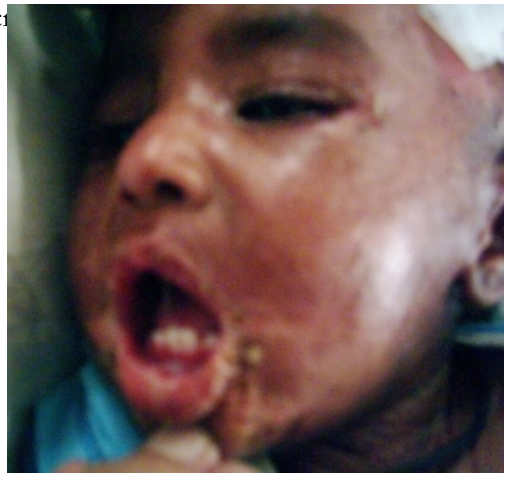
Introduction

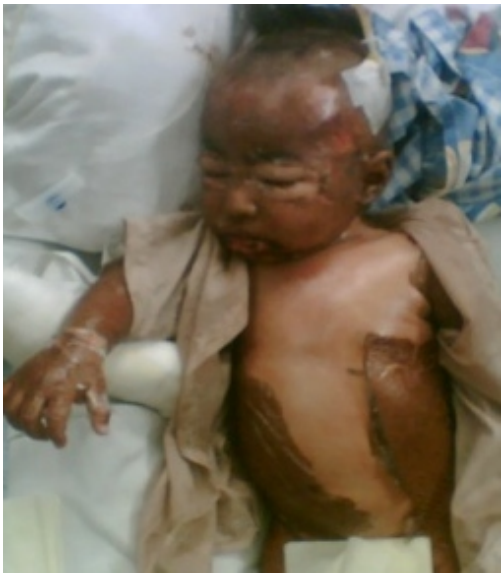
Toxic Epidermal Necrolysis (TEN) is a severe acute exfoliative skin and mucosal disorder[1] that is characterized by full-thickness epidermal necrosis, at least focally and involvement of more than 30% of the cutaneous surface.[2] TEN can be idiopathic but most often is an idiosyncratic, dose-independent, delayed hypersensitivity reaction to a drug. More than 100 drugs have been implicated. Medications most often involved are systemic sulfonamides and other antibiotics, allopurinol, antiepileptics, and non-steroidal anti-inflammatory agents. Commonly the mucous membranes are also involved. Case fatality rate can approach 40%.[3]

Case Report

We report a case of TEN, Shaheer, 10 months of age, resident of Jhang who presented for the first time with the symptoms of high grade fever and macular rashes, initially over the extremities then involving the whole body followed by desquamation. There was erythema of oral cavity and cervical lymph-adenopathy. At that time our differential diagnosis included Mixed Connective Tissue Disorder, Systemic Onset Juvenile Rheumatoid Arthritis and Kawasaki disease.

Disprin was started (80-90mg/kg/day). His symptoms responded but then after 15 days fever, pain in the left hip joint and rash appeared. This time rashes were initially maculopapular involving face, abdomen and limbs. These lesions later coalesced measuring 5-10 cm in size and were associated with itching. These lesions had central dusky purpura, an adjacent edematous pale zone, and a surrounding macular erythema. After 5-7 days flat blisters developed with wrinkled paper appearance and after another 3-5 days Nikolsky sign became demonstrable on back and feet. The area of denuded epidermis was dark red with oozing surface. There was also cr

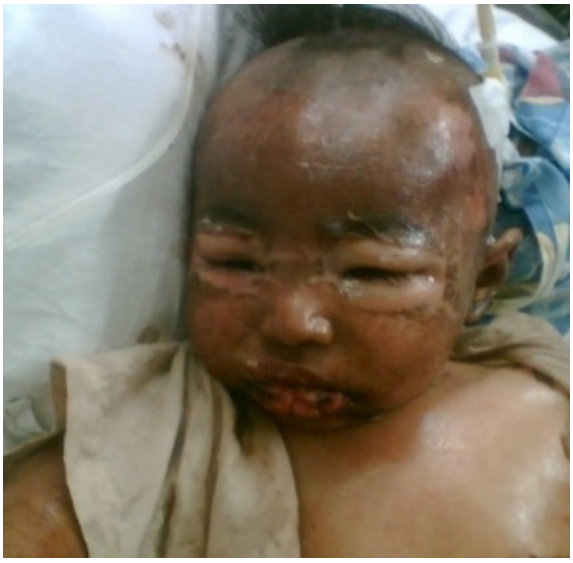


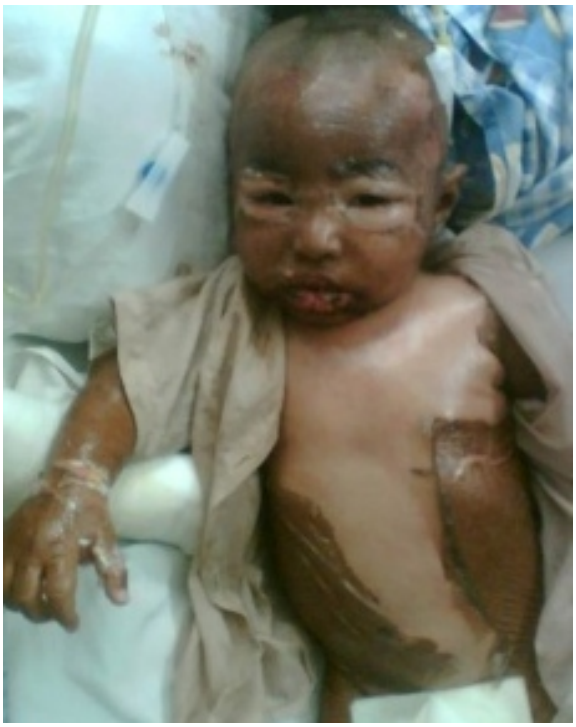


of lips and erythema of conjunctiva. The patient also had vomiting and dark coloured stools which were loose in consistency.

Past history was not significant. He was a well fed child and vaccination was up to date.

On physical examination, Shaheer was conscious but irritable with urticarial maculopapular rashes





at the back, feet and around the eyes. There was crusting of lips and conjunctival erythema. Epidermal detachment involved more than 30% of the whole body. Systemic examination showed hepatomegaly and lymphadenopathy. Investigations showed, albumin 2.9g/dl, SGPT was 51U/l. Blood count was normal initially but later showed a rise in WBC (21,350/mm^3) and a fall in platelets count (40000/mm^3). Echocardiography was normal. The patient was given broad spectrum antibiotics including meropenum and vancomycin. He was also given intravenous immunoglobulin (IVIG). The child's condition deteriorated continuously despite full supportive care and he died after remaining admitted for 3 months. Cause of death was septicemia.

Literature Review

TEN is a severe acute exfoliative skin and mucosal disorder[1] that is characterized by (a) widespread blister formation and confluent erythema associated with skin tenderness, (b) absence of target lesion, (c) sudden onset and generalization within 24-48 hours and (d) histological finding of full thickness skin necrosis. The incidence of TEN has been reported to be 0.5 per million per year.[4] Numerous epidemiologic studies have shown that females have higher incidence of TEN than males. While some patients rapidly progress to lose very large areas of the epidermis in a matter of days, the process suddenly ceases in others and re-epithelialization begins a few days later. Re-epithelialization is usually complete within 3 weeks, but pressure and mucosal areas may remain eroded and crusted for 2 weeks or longer. Survivors of SJS/TEN may experience numerous long-term sequelae; the most disabling are those of the eye. [5] Other complications of TEN may include cutaneous, mucosal, pulmonary and hematological manifest-ations. TEN is often drug induced, but the pathophysiologic mechanism is unknown. Apoptosis of keratinocytes has been proposed secondary to a cell-mediated cytotoxic reaction. [6,7,8]

The first step in medical treatment is withdrawal of causative drugs. Retrospective studies have indicated that early withdrawal decreases the mortality rate. The use of corticosteroids in the management of the SJS/TEN spectrum is one of the most controversial areas in dermatology. Administration early in the course of disease has been advocated, but multiple retrospective studies demonstrate no benefit or higher rates of morbidity and mortality related to sepsis.[9] Because multiple studies have demonstrated a higher morbidity and mortality in patients receiving corticosteroids, most authorities do not recommend their use.

A number of studies support the use of IVIG in the treatment of TEN. It is suggested that antibodies present in the pooled human IVIG block the process of apoptosis, which is the causative factor of TEN.[10]

Since 2000, a number of case reports and 8 non-controlled clinical studies containing 9 or more patients have analyzed the efficacy of IVIG in TEN. Some studies have not demonstrated a therapeutic benefit, while others have shown decreased mortality.

Six of the 8 studies suggested a benefit of IVIG at doses greater than 2 g/kg.

Cyclosporin (CSA) has also shown to be effective in the management of TEN. It is suggested that CSA when given orally in a dose of 3mg/kg/day 12 hourly, shortens the time from the onset of skin signs to complete epithelialization. It is also associated with less mortality. CSA may prove to be a life saving therapy, but randomanized controlled trials are needed to make definitive recommendations.[11]

Department of Paediatric Medicine
SIMS/Services Hospital, Lahore
theesculapio@hotmail.com
www.sims.edu.pk/esculapio.html

References

1. Stella M, Clemente A, Bollero D, Risso D, Dalmasso P. Toxic epidermal necrolysis (TEN) and Stevens Johnson syndrome (SJS): experience with high-dose intravenous immunoglobulins and topical conservative approach. A retrospective analysis. Burns 2007 Apr 30.
2. French LE. Toxic epidermal necrolysis and Stevens Johnson syndrome: our current understanding Allergol Int 2006 Mar; 55 (1):9-16.
3. Pereira FA, Mudgil AV, Rosmarin DM. Toxic epidermal necrolysis. J Am Acad Dermatol 2007 Feb; 56(2):181-200.
4. Chan HL, Stern RS, Arndt KA, et al. The incidence of erythema multiforme, Stevens Johnson syndrome and toxic epidermal necrolysis. A population-based study with particular reference to reactions caused by drugs among outpatients. Arch Dermatol 1990 Jan; 126(1): 43-7.
5. Yip LW, Thong BY, Lim J, Tan AW, Wong HB, Handa S et al. Ocular manifestations and complications of Stevens Johnson syndrome and toxic epidermal necrolysis: an Asian series. Allergy 2007 May; 62(5):527-31.
6. Inachi S, Mizutani H, Shimizu M. Epidermal apoptotic cell death in erythema multiforme and Stevens Johnson syndrome. Contribution of perforin-positive cell infiltration. Arch Dermatol 1997 Jul; 133(7): 845-9.
7. Roujeau JC, Gelard K, Bensussan A. Epidermal necrolysis: mechanisms of keratinocyte apoptosis Med Sci (Paris) 2006 Feb ; 22(2):188-91
8. Viard I, Wehrli P, Bullani R, et al: Inhibition of toxic epidermal necrolysis by blockade of CD95 with human intravenous immuno-globulin. Science 1998 Oct 16; 282 (5388): 490-3.
9. Halebian PH, Corder VJ, Madden MR, et al. Improved burn center survival of patients with toxic epidermal necrolysis managed without corticosteroids. Ann Surg 1986 Nov; 204(5): 503-12.
10. Tan AW, Thong BY, Yip LW, et al. High-dose intravenous immunoglobulins in the treatment of toxic epidermal necrolysis: an Asian series. J Dermatol 2005 Jan ; 32(1):1-6.
11. Arevalo JM, Lorente JA, Gonzalez-Herrada C, Jimenez-Reyes J. Treatment of toxic epidermal necrolysis with cyclosporin. J Trauma 2000 Mar; 48(3): 473-8.