CASE REPORT

Toxic Epidermal Necrolysis of Unknown Aetiology: A Case Report

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Abstract:

A young female was admitted with sudden development of painful erythema, macular rash, blisters on the face, trunk and extremities, conjunctiva, and oral and genital mucous membrane for three days. Along with the skin lesions, she also had fever, generalized body ache and decreased appetite. The case was diagnosed as toxic epidermal necrolysis (TEN) after clinical and histopathological evaluation. Though most of the cases are associated with drugs, this patient did not have any such history. That is why this case is reported here for future references.

Introduction:

Toxic epidermal necrolysis (TEN) is a mucocutaneous reaction characterized by skin tenderness and erythema of skin and mucosa, followed by extensive cutaneous and mucosal epidermal necrosis and sloughing. It is potentially a life threatening condition due to multisystem involvement[1]. In 80% cases TEN is associated with medication and in rest of the cases it is idiopathic[2]. It is a variant of Stevens-Johnsons Syndrome (SJS). When epidermal detachment is more than 30%, the condition is said to be TEN[3].

Cytotoxic immune reaction causes the destruction of keratinocytes expressing foreign antigens. In drug induced cases the drug itself or its metabolites acts as haptens and renders keratinocytes antigenic by binding to their surfaces[4]. The pathophysiology of idiopathic TEN is not well understood.

The rash is initially erythematous and morbilliform. Necrotic epidermis first appears as macular areas with crinkled surface that enlarge and coalesce. Then raised flaccid blisters appear that spread on lateral pressure on erythematous areas (Nikolsky sign)[5]. With trauma there is epidermal detachment and sheet like loss of epidermis that yields exposed, oozing and red dermis resembling a second-degree burn[6]. Regrowth of epidermis begins within days and gets completed by three weeks except for the pressure areas[1]. Lesions normally start appearing on the face and extremities first and then get generalized. Scalp, palms and soles are less affected or spared[2].

About 90% patients have painful oral and genital mucous membrane lesions and 85% patients have conjunctival hyperaemia, pseudomembrane, synechiae, keratitis and corneal erosions[7]. Eye lashes and nails may be shed. There may be associated lower respiratory and gastrointestinal epithelial erosion and acute renal failure[2].

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On histopathological examination, there is vacuolization/necrosis of basal keratinocytes throughout the epidermis in the early stage, and full thickness epidermal necrosis and detachment with formation of subepidermal split above basement membrane in the late stage[1]. Fluid and electrolyte imbalance, prerenal azotaemia, sepsis, hypermetabolic state and difuse interstitial pneumonitis are the common complications of TEN[8]. Mortality rate is about 30% and mainly in elderly patients[9]. In case of drug induced TEN, reexposure to the same drug causes more severe episode of illness than the initial one[1].

Case report:

A 33 year old lady was admitted in the Holy Family Red Crescent Medical College Hospital with painful and itchy skin lesions for three days and fever, loss of appetite and dysuria for two days. The disease was of sudden onset and there was no history of ingestion of any drug prior to the illness. On examination, there were multiple erythematous maculopapular lesions and blisters at various parts of the body specially on the trunk, back, face, neck and extremities. There was sheet like epidermal loss at different sites and the dermis was red and oozing. The lesions were extremely tender to touch and Nikolsky sigh was positive. More than 50% of the epidermis was affected. Oral mucosa was oedematous, and had erythema and blisters. Ruptured blisters formed extensive hemorrhagic erosions with grayish white pseudomembranes.

The patient had fever (102^0 F) and conjunctival hyperaemia but there was no associated respiratory or gastrointestinal infection. Laboratory examination showed neutrophilic leucocytosis. Liver and renal function tests were normal. The patient had mild hyponatraemia.

Histopathology of the lesion revealed necrosis of basal keratinocytes, full thickness epidermal detachment and supra basal bullae containing acantholytic and inflammatory cells. History, clinical examination and laboratory investigations all prompted to the diagnosis of TEN.

The patient was managed with adequate amount of intravenous fluid, both systemic (cephalosporin) and local antibiotic (2% mupirocin) and dexamethasone. Her eyes were treated with chlorampheicol, dexclor and tears eye drop. Paracetamol and antihistamine were also given. During the whole course of treatment autoclave sheets were used to prevent secondary infection.

The response of the patient was dramatic. Pyrexia subsided on the third day. There was no new lesion. Erythema and blisters started to disappear from the fourth day. Healthy epidermis started regrowing from the fourth day and completely regressed by the second week. By the end of the third week, almost 90% of the epidermal regrowth was completed.

Discussion :

Toxic epidermal necrolysis is an acute dermatological emergency. Water and electrolyte imbalance, over whelming sepsis and multi-system involvement make this disease a life threatening one. That is why prompt diagnosis and proper treatment is a must[9].

Toxic epidermal necrolysis is generally preceded by a day to several-day prodrome of high fever, cough, sore throat, and malaise[2]. As the disease progresses, mucosal membrane involvement becomes evident. The most frequently affected mucosal membrane is the oropharynx followed by the eyes and genitalia[9].

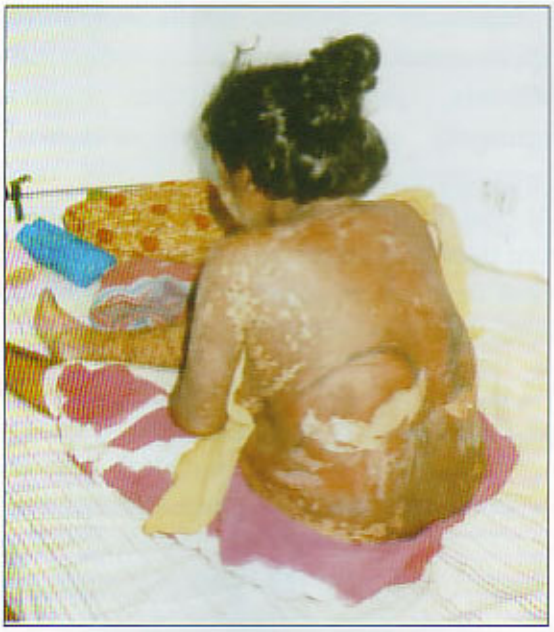

Figure : 1

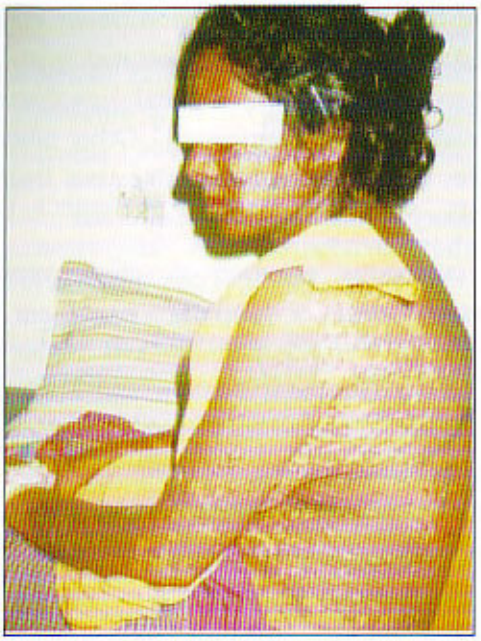

Figure : 2

Figures 1 and 2: Blisters and sheet like loss of epidermis at various parts (picture taken on the fifth day of admission)

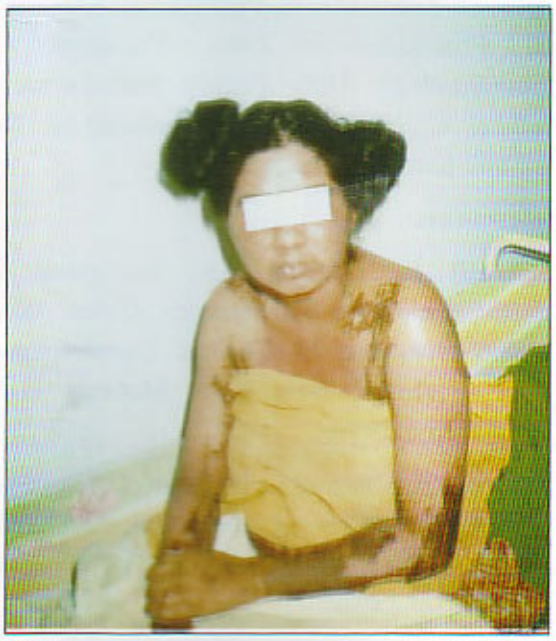

Figure : 3

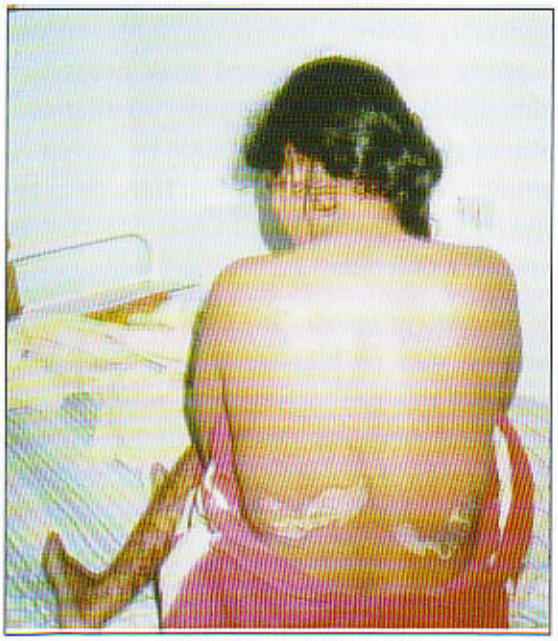

Figure : 4

Figures 3 and 4: Epidermal regrowth on the third week of treatment

Oral cavity involvement typically presents as sore or burning sensations. Food intake may be limited because of pain associated with the oropharyngeal lesions. Genital involvement may result in painful urination[9]. Other mucosal surfaces such as oesophagus, intestinal tract, or respiratory epithelium may be affected[9].

The cutaneous eruption develops rapidly, evolving from a papular exanthem or widespread erythematous and purpuric macules to confluent blisters and epidermal detachment[10]. The lesions predominate on the trunk and face, sparing the scalp. Pain is often the predominating symptom[10].

Ideally, patients of TEN should be treated in specialized burn unit as burn patients are treated. At first, potentially offending medication (if any) must be discontinued[11]. Fluid and electrolyte status of the patient need to be assessed and corrected[11]. Areas of skin erosion should be covered with non-adherent protective dressings such as petroleum gauze. Respiratory distress may result from mucosal sloughing and oedema, and may necessitate endotracheal intubation and ventilation[12]. Antibiotic prophylaxis should be given to prevent sepsis. Systemic steroids and intravenous immunoglobulin may demonstrate favourable outcome[12].

The overall prognosis of TEN is poor, with mortality rate as high as 40%[13]. Numerous complications can arise as a result of the widespread cutaneous and mucosal membrane inflammation and necrosis. In skin, epithelial loss predisposes to septicaemia caused by *Pseudomonas aeruginosa, S. aureus,* gram-negative species, and *Candida albicans*)[11]. Ulceration of various mucosal membranes results in pain, scarring, and stricture formation. Affected surfaces include oral, ocular, and urogenital mucosa[5]. Inflammation of respiratory epithelium results in bronchial hypersecretion, hypoxaemia, interstitial infiltrates, pulmonary oedema, bacterial pneumonia, and bronchiolitis obliterans[13]. Gastrointestinal hemorrhage results from intestinal inflammation[13]. Hypovolemia results from poor oral intake and/or septic shock that result in renal hypoperfusion, acute tubular necrosis, and renal insufficiency[7].

Although most of the cases of TEN, as mentioned earlier, are associated with drug ingestion, there may be instances like this particular case, where no positive drug history would be revealed. So, clinicians must consider idiopathic TEN while managing any such patient even if there is no correlating history of taking any of the enlisted drugs prior to the onset of the disease.

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References:

1. Wolff K, Johnson AR, Suurmond D (Editors). In: Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology, Fifth edition. New York: McGraw Hill, 2005. pp- 144-6.
2. Odom R.B (editor). Andrews' Diseases of the Skin: Clinical Dermatology, Ninth edition, New York: Saunders Publications, 2000. pp-136-9.
3. Ayangco L, Rogers RS. Oral manifestations of erythema multiforme. Dermatol Clin 2003; 21: 195-205.

4. Bachot N, Roujeau JC. Differential diagnosis of severe cutaneous drug eruptions. Am J Clin Dermatol 2003; 4: 561-72.

5. Magina S, Lisboa C, Leal V, et al. Dermatological and ophthalmological sequels in toxic epidermal necrolysis. Dermatology 2003; 207: 33-6.

6. Neff P, Meuli-Simmen C, Kempf W, et al. Lyell syndrome revisited: analysis of 18 cases of severe bullous skin disease in a burns unit. Br J Plast Surg 2005; 58: 73-80.

7. Prendiville J. Stevens-Johnson syndrome and toxic epidermal necrolysis. Adv Dermatol 2002; 18: 151-73.

8. Roujeau JC, Guillaume JC, Fabre JP, et al. Toxic epidermal necrolysis (Lyell syndrome). Incidence and drug etiology in France, 1981-1985. Arch Dermatol 1990; 126: 37-42

9. Becker DS. Toxic epidermal necrolysis. Lancet 1998; 351:1417-20.

10. Smoot EC. Treatment issues in the care of patients with toxic epidermal necrolysis. Burns 1999; 25: 439-42.

11. Criton S, Sofia B. Toxic epidermal necrolysis: A retrospective study. Int J Dermatol 1997; 36: 923-5.

12. Zaki I, Emerson R, Clark CM. Toxic epidermal necrolysis associated with severe hypocalcaemia, and treated with cyclosporin. Br J Dermatol 1995; 133: 337-8.

13. Rasmussen JE, Michael GS. Erythema multiforme, Stevens-Johnson syndrome and toxic epidermal necrolysis. Dermatol Nurs 1995; 7: 37-43.