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Case Report

Plasmapheresis: an effective treatment in patients of toxic epidermal necrolysis: case report of two patients

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Abstract Toxic epidermal necrolysis (TEN) is an acute, life-threatening cutaneous drug reaction that predominantly involves the skin and mucous membranes. It is a rare disorder and treated as a medical emergency, due to its fatal outcome. The principles of management include immediate removal of culprit drug(s), supportive management and specific drug therapies or procedures, of which plasmapheresis is one treatment modality. We report two patients of TEN, being successfully treated with plasmapheresis, proving it to be a life saving treatment modality.

Key words
Toxic epidermal necrolysis (TEN), plasmapheresis, SCORTEN Score.

Introduction

Toxic epidermal necrolysis (TEN) is the most severe form of drug-induced exfoliating mucocutaneous disorder. It was first described in 1956 by Alan Lyell. Its incidence is 0.4-1.2 per million worldwide. It has high female to male ratio of 1.5:1.[1] In a study carried out in Lahore, Pakistan Gardezi *et al*.[2] found that co-trimoxazole was the leading cause followed by dipyrone and mefenamic acid. Mortality rates are as high as 27.3% for TEN patients. It results in widespread keratinocyte apoptosis that results in separation of significant areas of skin at dermal-epidermal junction presenting as bullae formation, detached epidermal sheets and mucosal erosions.[1] TEN is a T cell-mediated immune reaction. The proposed pathophysiological mechanism includes keratinocyte apoptosis receptor fas (CD95) or cytotoxic release of perforin and granzyme B causing cell lysis. SCORTEN score is used to assess severity of illness and predict mortality **(Table 1).** Prompt identification and removal of any offending drug is the mainstay of treatment. Acute management is mainly supportive, consisting of wound care with special emphasis on care of eyes, oral, gastrointestinal and respiratory mucosae. Also fluid and electrolyte management, nutrition and pain relief are important. Systemic therapies for TEN still remain controversial.[3] These include IV corticosteroids, IV immunoglobulins, plasmapheresis and immunosuppressant drugs e.g. cyclosporine (3-4 mg/kg/day), cyclophosphamide (100-300 mg/day) and N-acetylcysteine.[1]

Table 1 SCORTEN prognosis score

*Parameter**	
Age > 40 years	
Presence of a malignancy	
Epidermal detachment > 30%	
Heart rate > 120/min	
Bicarbonate < 20 mmol/l	
Urea > 10 mmol/l	
Glycaemia > 14 mmol/l	
Scroten of death	*Probability*
0-1	3
2	12
3	35
4	58
≥5	90

1 point awarded for each parameter; scorten derived by totalling scores

* Worst recorded value in the 24 h after admission

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Case Report 1

A 45-year-old male patient presented on 7th day of his illness in the medical emergency of Jinnah Hospital, Lahore. He took oral allopurinol for 10 days for asymptomatic hyperuricemia. His presenting complaint was grittiness, watering, redness and burning in both eyes for six days for which he took treatment from local ophthalmologist. This was followed by oral erosions and difficulty in swallowing. Then he developed generalized maculopapular rash, starting from neck and spreading to involve trunk and limbs. On presentation he had bullae formation with sheets of epidermal detachment and erosions involving 50% of body surface area **(Figure 1a,b, c)**. Nikolsky's sign was positive. He was afebrile and vitally stable. All his labs were normal. SCORTEN score calculated was 3. He was shifted to high dependency unit of Dermatology Unit I, Jinnah Hospital Lahore. He was started with supportive management including general wound care, care of mucosae, fluid and electrolyte balance and nutritional support. Despite all this his condition did not improve and deteriorated even further. So on 6th day of his admission plasmapheresis was planned in collaboration with ICU department. ICU staff passed double lumen catheter in the right external jugular vein under ultrasound guidance. Three sessions of plasmapheresis were done on alternate days. Haemaccel infusion was used as replacement fluid. After first session marked improvement was noticed as ongoing bullae formation stopped, epidermal sheets began to dry up and erosions started to heal **(Figure 2a, b)**. After three sessions double lumen catheter was taken out. His condition improved and he was discharged after 5 days.

Case Report 2

A 45-year-old female presented in the medical emergency of Jinnah Hospital, Lahore on her 9th day of illness. She was referred as a case of severe drug reaction from a local hospital. She was taking intramuscular NSAIDs for generalized muscular aches and pains. She came with generalized maculopapular rash with bullae formation and sheets of epidermal detachment involving 40% of body surface area. **(Figure 3a)** Three of her mucosae were involved including eyes, oral and genital mucosae. Nikolsky's sign was positive. SCORTEN score calculated was 2. She was afebrile and vitally stable. Her labs showed neutropenia 1800/cm, however, other labs were normal. She was shifted to high dependency Unit of Dermatology Unit I, Jinnah Hospital, Lahore where supportive management was started. As her condition did not improve, her plasmapheresis sessions were started on 3rd day of admission and similarly three sessions were done on alternate days with infusion Haemaccel as a replacement fluid. Marked improvement was noticed **(Figure 3b)**. She was discharged 4 days later.

Discussion

Keeping in view the high mortality rates in patients of TEN, we opted plasmapheresis as a treatment modality of choice, among various systemic drug therapies available. The efficacy of plasmapheresis for treatment of TEN has been documented in various studies and its use as a first-line management has been increasingly debated over past few years.[4-12] The method is safe and achieves rapid recovery, relief from pain and aids in cessation of cell lysis.

Yamada *et al.*[4] described the efficacy of plasmapheresis for the treatment of toxic epidermal necrolysis in a study carried out in Japan. 47 patients underwent treatment and the rate of effectiveness was recorded as 80.9%. Mean number of sessions done was 3.1.

Narita *et al.*[5] also documented plasmapheresis as a much more effective option for treatment of severe and recalcitrant cases of TEN than any other treatment options such as pulse corticosteroids and IV immunoglobulins. They

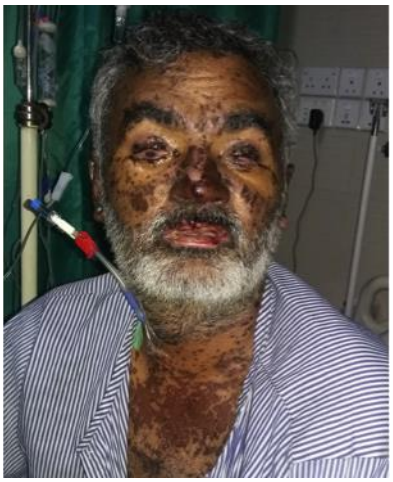

Figure 1 a) Erosions over the face and anterior chest.

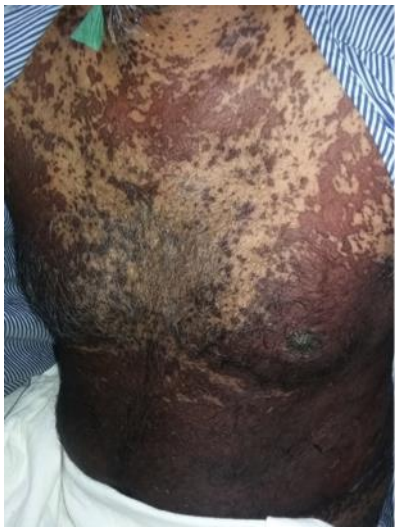

Figure 1 b) Erosions and bullae formation over trunk.

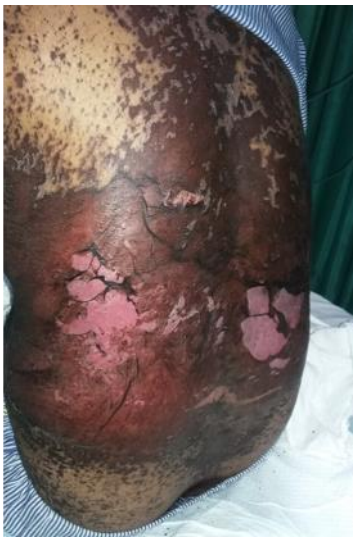

Figure 1 c) Epidermal detachment over back

(**Figure 1a, b, c** showing clinical features of patient before plasmapheresis)

Figure 2 a) Healing of erosions after plasmapheresis.

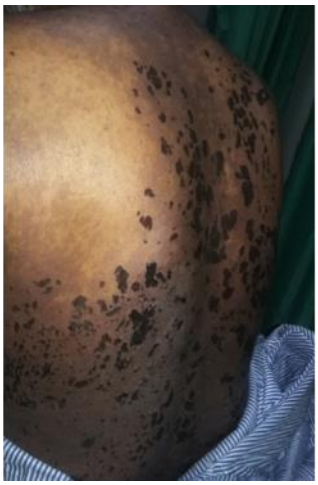

Figure 2b showing improvement after plasmapheresis).

Figure 3 a) showing clinical features of patient before plasmapheresis

Figure 3 b) showing improvement after plasmapheresis

also elaborated the mechanism of action of plasmapheresis. In plasmapheresis, the whole blood of patient is withdrawn, plasma separated from the cellular constituents is discarded and the cellular constituents are reinfused back into the patient, together with

albumin or pooled plasma. It removes pathogenic, non-dialyzable factors such as proinflammatory cytokines from plasma of TEN patients. They also provided the evidence to support their proposed mechanism of action of plasmapheresis by investigating the correlation between disease intensity and serum cytokine levels before and after treatment with plasmapheresis.[5]

Mahale *et al*.[6] also proposed that the theoretical mechanism of action involves the actual removal of the toxin or drug metabolite that was potentially responsible for the direct killing reaction of the epidermal keratinocytes. There has been a hypothesis that the mechanism involves the removal of cytokines which are involved in the destruction of the keratinocytes. However, the exact mechanism is still cintroversial.[8]

Studies in Poland and Czech republic also emphasized that the treatment of TEN with plasmapheresis should be considered in patients refractory to corticosteroid and IV immunoglobulins.[7,8]

The alternate day sessions of plasmapheresis are considered preferable to the everyday regimen.[12]

To our knowledge no published case reports on plasmapheresis in patients of TEN in Pakistan are available. Also the unavailability of drugs/procedures, cost-effectives and proper ICU setup are also the main hurdles in opting effective treatment option.

Plasmapheresis is an efficacious method, halting the ongoing disease process, providing rapid relief from agony and disease. It could be listed in the first-line therapy in the treatment of TEN.

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