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IP Indian Journal of Clinical and Experimental Dermatology

Journal homepage: www.ijced.org/

Case Report

Two cases of toxic epidermal necrolysis successfully treated with cyclosporine in covid pandemic

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ARTICLE INFO

Article history:
Received 20-08-2022
Accepted 27-08-2022
Available online 29-09-2022

Keywords:
Cyclosporine
SJS/TEN
Adverse cutaneous drug reaction

ABSTRACT

Toxic epidermal necrolysis (TEN) is a rare, life-threatening drug-induced skin disease with a mortality rate of approximately 30%. The clinical hallmark of TEN is a marked skin detachment caused by extensive keratinocyte cell death associated with mucosal involvement. We have two cases of TEN presented within 3 months and successfully treated with cyclosporine.

1. Introduction

Toxic epidermal necrolysis (TEN) also known as Lyell's syndrome is a rare but potentially lifethreatening condition with widespread epidermal detachment and mucosal erosions.Toxic epidermal necrolysis is more commonly seen in women compared to men and the incidence of TEN increases sharply with age.[1] The incidence rate is 0.5-1.4 million/year and the average mortality is estimated to be 25-35 %.[2] SJS includes cases with mucosal erosions and widespread purpuric macules and epidermal detachment up to 10%, transitional SJS-TEN represents epidermal detachment between 10 to 30% and TEN represents skin detachment of more than 30% of the body surface areas. TEN is a consequence of extensive keratinocyte cell death that results in the separation of significant areas of skin at the dermal-epidermal junction with the production of bullae followed by skin sloughing. As SJS‑TEN is a fatal condition, prompt withdrawal of culprit drug, supportive care, and early institution of immuno modulating drugs are the mainstay of treatment. Though several treatment protocols exist, none has been universally accepted. Several studies have demonstrated variable success with corticosteroids,[3] intravenous immunoglobulin,[4] plasmapheresis,[5] cyclophosphamide,[6] and tumor necrosis factor-α inhibitors.[7]

2. Case Report 1

A 58 year old female came with peeling of skin with vesicle and bullae of size ranging from 0.5 cm to 5 cm in diameter, few erythema multiforme like lesions and erosions involving chest, abdomen, back, bilateral upper and lower limbs including palm and sole.[Fig-1a & 2a] She was a known case of autoimmune hepatitis and was on tab telmisartan for hypertension. Patient had taken tab moxifloxacin 400 mg once a day for 5 days before appearance of lesions. There was 80% body surface are (BSA) involvement with SCORTEN of 4 which is having 58% of mortality. On admission patient had total count of 16.4, albumin of 2.2 and electrolyte imbalance. Patient's creatinine was 2.48 and urea was 85, so the drug of choice, Cyclosporin could not be started. After consultation with nephrologist patient was started on intravenous

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https://doi.org/10.18231/j.ijced.2022.041

Dexamethasone 8 mg BD and IV Immunoglobulins (IVIG) as per 2 g/kg body weight. Patient's body weight was 60 kg so we planned to give total of 120gm of IVIG. Patient was also started with inj Meropenem 100 mg IV three times a day. Dressing of the eroded part was done with gentian violet and soframycin cream along with liquid paraffin gauze on patients bed to avoid spread of eroded area. On 5^{th} day as patient's creatinine improved so we started with cyclosporine 100 mg twice a day .On 6^{th} day clindamycin 600 mg IV three times a day was started. On 8^{th} day patient started developing pancytopenia and patients creatinine started to rise, thus cyclosporin was discontinued. On 9^{th} and 23rd day patient was given 2 and 3 unit of PCV. On 10^{th} day, according to culture and sensitivity report inj Colistin 9 MIU STAT was given and was continued as 3 MIU twice a day was given for 2 days and 2 MIU twice a day was given for 1 day. But patient's creatinine increased to 2.24 mg/dl so Colistin was also discontinued. On 24^{th} day patient's potassioum, bicarbonate and magnesium level decreased so correction was given. The dressing with soframycin was replaced with Megaheal and Neosporin. On 28^{th} day patient improved metabolically and clinically. On 29^{th} day patient clinically improved so steroid was tapered and she was discharged on faropenem and linezolide. Patient was on regular followup. After 50^{th} day patient had normal skin with post inflammatory pigmentation. [Fig 1b & 2b]

3. Case Report 2

A 28 years old female came to trauma center with multiple flaccid bullae and few erosion present over face, chest, abdomen, back, buttocks, groins, bilateral upper limb including palm and lower limb. [Fig 3a & 4a] Few vesicles with crusting present over bilateral upper and lower eyelid. Multiple erosion with crusting present over lips. Pseudonikolsky sign was positive. Patient had taken inj Tetracycline and tab paracetamol for fever for 3 days following which the lesion appeared. There was peeling of skin involving 90% of body surface area with SCORTEN of 3 having 35% mortality. On admission the patient had total count of 2.1, albumin of 3.0 mg/dl and electrolyte imbalance. Patient's creatinine was 1.31 and urea was 91. Patient's blood sugar level was 170 mg/dl and bicarbonate level was 21.6. So we started the patient on inj Dexamethasone 2 cc IV twice a day which we gradually tapered over days. We also started inj Meropenem 100 mg IV three times a day to control the secondary bacterial infection. Dressing of the eroded part was started with gentian violet and soframycin cream. We also applied Liquid paraffin gauze on patients bed to avoid spread of eroded area. Patient improved skin wise but was having difficulty in breathing so she was given ventilatory support which gradually weaned off with T piece and ultimately patient was stable on room air. Inj G-CSF 300 mcg SC once a day and tab Linezolid 600 mg twice a day started on 3^{rd} day of admission. Patient developed hypokalemia for which correction was given. Patient was started on inj Teicoplanin 200 mg IV twice a day and continued for 13 days and Inj Caspofungin 50 mg IV once a day for 11 days. Tracheostomy was performed as patient had abolished cough reflex on 10^{th} day of admission. So drug of choice Syrup Cyclosporine was started at dose of 30 mg twice a day which was gradually increased upto 80 mg twice a day and gradually tapered. Due to low albumin patient was given 6 doses of inj Albumin. Patient had remarkable regeneration of skin over subsequent few days and she was discharged home in a stable condition after 1 month.[Fig 3b &4b]

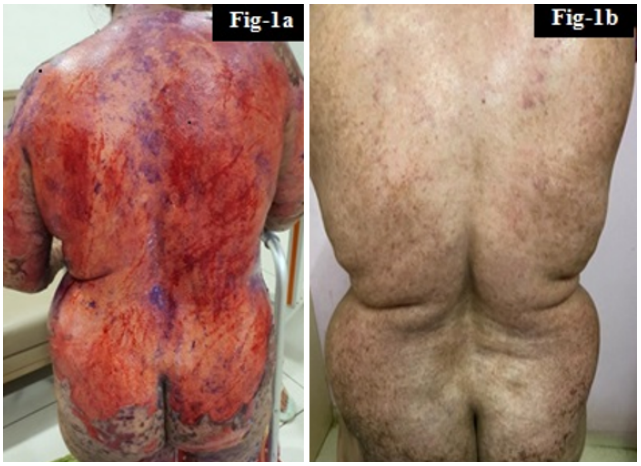

Fig. 1: Multiple erosions over back and buttocks

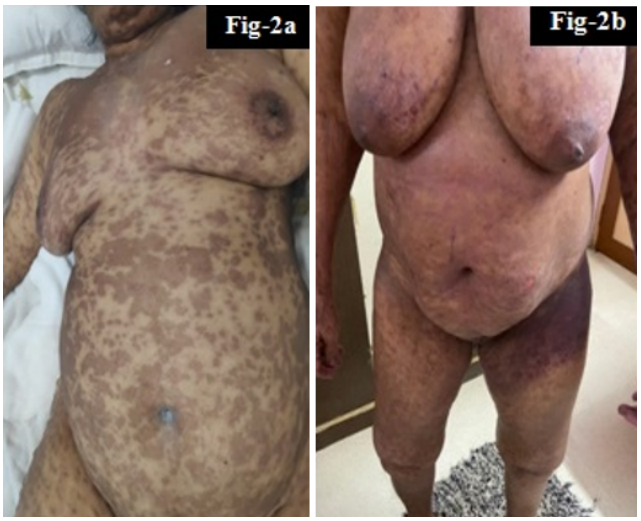

Fig. 2: Multipe vesicle and bullae of size ranging from 0.5 cm to 5 cm in diameter, few erythema multiforme like lesions involving chest, abdomen.

Fig. 3: &2b: Normal skin with post inflammatory hyperpigmentation

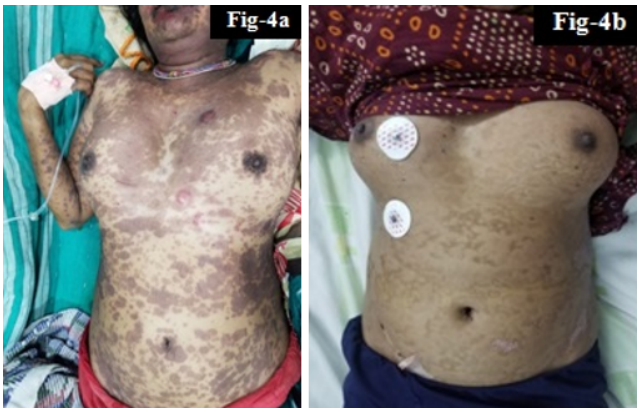

Fig. 4: & 4a: Multiple flaccid bullae and few erosion of diameter 1-2 cm present over face, chest, abdomen.

4. Discussion

Stevens Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are life-threatening dermatological emergencies characterised by skin peeling, hemorrhagic crusting of lips, and erosions of oral and genital mucosa, which are caused by medications. The main symptoms of TEN are usually preceded by non-specific symptoms such as fever, stinging eyes, and discomfort upon swallowing by several hours up to several days. Characteristically, cutaneous lesions first appear in the presternal region as well as the face, palms, and soles of the feet. Mucosal involvement occurs in more than 90% of patients, predominantly affecting the mouth, genitalia, and/or ocular region. TEN is an acute emergency and is potentially life threatening if not treated promptly. The mortality of these patients range from 3% to 90% depending on SCORTEN evaluation.

Cyclosporine has been found to be effective in the treatment of TEN.[8] Cyclosporine acts by calcineurin inhibition which decreases the production of various inflammatory cytokines. It also has antiapoptotic action and inhibit TNF-α production. The present understanding of mechanism of SJS/TEN involves activation of cytotoxic T-cells by a culprit drug with the consequent release of granulysin and activation of caspase cascade resulting in keratinocyte apoptosis.[9] Many case reports, case series, open trials, and retrospective studies have documented the efficacy of cyclosporine in SJS/TEN.[10] Generally, a dose of 3-5 mg/kg body weight, as oral capsule or solution, in two divided doses for 10-14 days has been used.

IVIG has also been wildly used for treatment of SJS/TEN.IVIG likely produces its therapeutic effects via a combination of many pathways, including interfering with the effect or function of T cells, B cells, and monocytes, which involves blocking the interaction of Fas with its natural ligand, FasL.

5. Conclusion

Here by we report a two cases of toxic epidermolysis necrosis successfully treated with cyclosporine and IVIG. The most important therapeutic measure so far remains the rapid identification and withdrawal of the causative drug in addition to supportive care.

6. Conflicts of Interest

None.

7. Source of Funding

None.

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Cite this article: Vora R, Pillai D, Patel J, Hirma S. Two cases of toxic epidermal necrolysis successfully treated with cyclosporine in covid pandemic. *IP Indian J Clin Exp Dermatol* 2022;8(3):198-201.