International Journal of Research in Dermatology
Choudhary N et al. Int J Res Dermatol. 2019 Aug;5(3):649-651
http://www.ijord.com

DOI: http://dx.doi.org/10.18203/issn.2455-4529.IntJResDermatol20193122

Case Report

Toxic epidermal necrolysis treated with filgrastim and dexamethasone

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Received: 05 June 2019
Revised: 02 July 2019
Accepted: 04 July 2019

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ABSTRACT

We report a case of 22 year female with toxic epidermal necrolysis while on carbamazepine. One hospital outside treated her with steroids but she didn't show any improvement and rather worsened. The patient reported to us with fluctuating blood pressure and dyselectrolytemia. Patient also developed neutropenia (3,200/mm^3) and sepsis. Patient was treated with filgrastim and dexamethasone. Filgrastim was added because of neutropenia and earlier case reports suggesting it aid in faster healing. Patient made a complete recovery.

Keywords: Toxic epidermal necrolysis, Filgrastim

INTRODUCTION

Toxic epidermal necrolysis (TEN) is a life threatning serious cutaneous drug reaction. It is characterised by fever and confluent erythema followed by necrolysis. Two or more mucosal sites are affected and epidermal detachment is >30% of total body surface area (BSA)[1]. Flat, atypical target lesions may also be seen (TEN with spots) and sometimes, extensive necrolysis can occur without target lesions (TEN without spots).[1] Antiepileptics like carbamazepine and phenytoin are known to cause severe rash like Stevens Johnson syndrome (SJS) and TEN.[2] Steroids, cylosporine, IVIG and plasmapheresis have been used in the treatment of SJS and TEN. We report a case of TEN with neutropenia treated with filgrastim.

CASE REPORT

22 year old female was prescribed carbamazepine, propranolol, flunarizine, gabapentin and nortriptyline by a psychiatrist for complaint of right sided headache, right hand weakness and tremor. Patient is a known case of hypothyroidism and hypertension and is on medication for the same. Five days later she developed fever and rash over face for which she was prescribed oral prednisolone from a local hospital and carbamazepine was stopped. Eight days later her condition worsened and she presented to our emergency department with fever and erythematous rash over face, trunk and extremities (Figure 1). On examination she was semi-conscious, pulse rate was 130/minute and blood pressure was 160/90 mm of mercury (Hg). Breath sounds were audible; heart sounds (S_1 and S_2) were audible. Skin exfoliation involving face, chest, both upper limbs and lower limbs was noted. Purpuric lesions were present over both arms. Oral and genital mucosa were also involved. Nikolsky's sign was positive. Haemoglobin (Hb) was 11.2 g/dl, total leucocyte count (TLC) 3,200/mm^3, platelet count 410,000/mm^3. Erythrocyte sedimentation rate (ESR) was 45 mm/hr and C-reactive protein (CRP) was 6.5 mg/l. SCORTEN at time of admission was 4. Patient was given injection piperacillin-tazobactum, injection linezolid, injection dexamethasone, I.V. fluids and injection filgrastim. Injection dexamethasone was given at a dose of 4 mg I.V. thrice daily for 5 days. IVIG was

administered 2 gm/kg body weight in 5 divided doses. No significant improvement noted after 48 hours of starting IVIG. Next injection filgrastim was given at a dose of 300 µgm for 5 days. Two days after starting filgrastim TLC was 5400/cmm. SCORTEN after 2 days of admission was 3. No new lesions developed after 3 days. Cutaneous lesions improved and rash subsided completely in two weeks. Patient was discharged after 16 days following full recovery (Figure 2). At time of discharge Hb was 11.3 g/dl, TLC was 12,300/mm^3 and platelet count 430,000/mm^3.

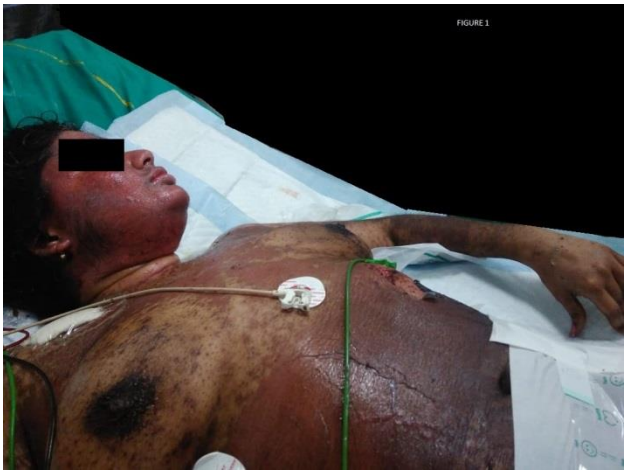

Figure 1: At time of admission.

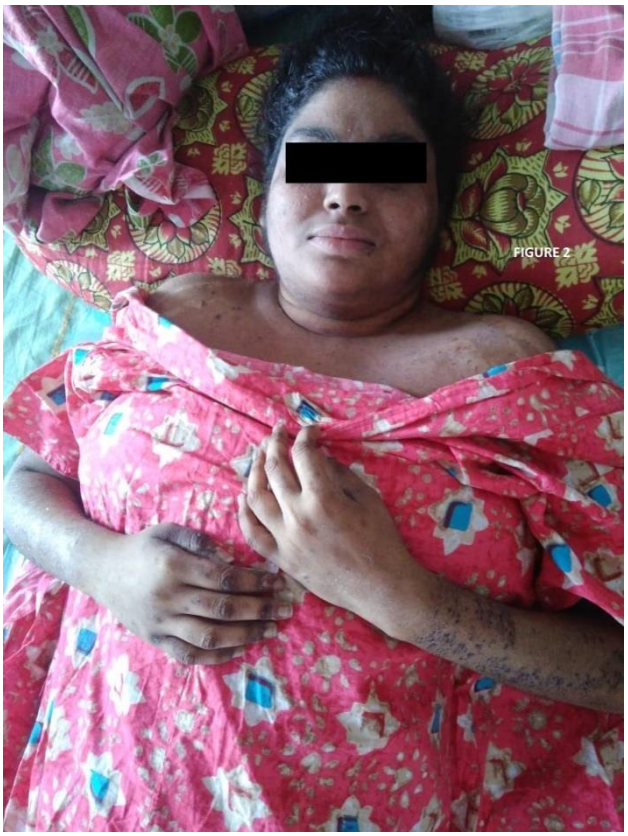

Figure 2: After treatment.

DISCUSSION

TEN is a severe cutaneous adverse drug reaction that is mostly caused by drugs such as antiepileptics, allopurinol, co-trimoxazole (sulfonamides), anti-retroviral drugs, anti-tubercular drugs and fluoroquinolones.[2-4] In our case carbamazepine was probably the possible cause. SCORTEN is used as a prognostic factor to predict patient outcome in SJS and TEN.[5] Several treatment modalities have been used for treatment of SJS and TEN with variable results. These include corticosteroids, cyclosporine, IVIG, plasma-pheresis, cyclophosphamide and thalidomide.[6-11] Apoptosis is believed to be the primary mechanism responsible for keratinocyte death in SJS/TEN. Fas-Fas ligand and cytotoxic T-cell, play a vital role in the pathogenesis of SJS/TEN. Filgrastim is a recombinant human Granulocyte-colony stimulating factor (G-CSF) and has been found to be useful in chemotherapy induced neutropenia.[12] Filgrastim has also been used to treat nuetropenia in SJS.[13] Neutropenia is associated with poor prognosis in TEN. Administration of filgrastim (recombinant human G-CSF) not only helps in countering sepsis but is also supposed to have immunomodulatotry action and causes rapid re-epithelialization in TEN by increased bioregeneration of damaged tissue.[14] Immunosupressive effects are increased as G-CSF induces activation and mobilization of CD4+ CD25+ regulatory T cells (Tregs).[15] G-CSF cause increased production of IL-10, TGF-β along with decreased production of IL-2, TNFα and interferon-γ.[15] Genetically modified granulocyte-macrophage colony stimulating factor 'knock-out' mice (GM-CSF KO) have delayed re-epithelialization compared to wild type, suggesting a role of G-CSF in rapid re-epithelialization.[16]

Our patient was treated with dexamethasone and filgrastim. Her TLC returned to normal after 2 days of starting filgrastim. Epidermal detachment was interrupted 3 days after the start of treatment and complete skin re-epithelialization occurred in 2 weeks. Patient was successfully treated with dexamethasome, IVIG and filgrastim and was discharged on full recovery.

CONCLUSION

We therefore recommend that irrespective of TLC we can try G-CSF (filgrastim) in SJS-TEN. It promotes rapid epithelialization and facilitates early recovery.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Choudhary N, Sharma N, Sinha S, Das S. Toxic epidermal necrolysis treated with filgrastim and dexamethasone. Int J Res Dermatol 2019;5:649-51.