Recurrent Toxic Epidermal Necrolysis (TEN) with different drugs

Mahesh Mathur[1], Neha Thakur[1], Sunil Jaiswal[1], Srijana Maharjan[1], Supriya Paudel[1], and Anjali Shrestha[1]

[1]College of Medical Sciences Teaching Hospital

July 19, 2023

Title of the paper

RECURRENT TOXIC EPIDERMAL NECROLYSIS (TEN) WITH DIFFERENT DRUGS

Introduction

Toxic Epidermal Necrolysis (TEN) is a life-threatening mucocutaneous disorder characterized by diffuse erythema, necrosis, and flaccid bulla involving Body Surface Area (BSA) > 30% and resulting in desquamation. The incidence of TEN is 1-2/1000000 annually. Majority of the cases of TEN are drug-induced.[1]Recurrent episodes are rare in adults, however, reported more frequently in the pediatric population.[2] We hereby present a case of recurrent TEN in an elderly patient with different agents.

Case Presentation

A 60-year-old female, a known case of Hypertension and Chronic Kidney Disease presented to Emergency Department with generalized ill-defined confluent dusky erythematous tender patches and flaccid bullae on the trunk and extremities with peeling of skin over the mammary region for 3 days (fig 1D-F). She had erosions on lips, hard palate, and mucopurulent discharge from the eyes. Skin lesions developed after 16 hours of intake of the last dose of Furosemide as advised by the treating physician for facial puffiness and pedal edema.

Nikolsky's sign was positive. Body Surface Area involved was approximately 40% and she was hemodynamically stable. Blood investigations revealed raised Serum BUN (106.6 mg/dl), raised creatinine (4.6 mg/dl), and hypokalemia (2.9 meq/l). Arterial Blood Gas analysis showed decreased pH (7.24) and bicarbonate levels (12meq/l).

Diagnosis of TEN with Acute on Chronic Kidney Disease and Metabolic Acidosis was made with baseline SCORTEN 5. She was admitted to ICU and was administered intravenous fluids, antibiotics, and parenteral hydrocortisone along with mucocutaneous care. SCORTEN was 5 on the 3rd day of admission. Initial reepithelialization of skin lesion was observed after 7 days (fig 2A-C) and was completed by Day 15 (fig. 2D-F).

The patient had a similar episode of skin lesions 3 years back following intake of Nimesulide for myalgia and developed extensive mucocutaneous lesions as compared to the second episode (fig. 1A-C). She was admitted to our hospital during the previous episode and was managed successfully.

Discussion

TEN is a dermatological emergency mediated predominantly by CD8+ T lymphocytes and is associated with an average mortality of 25%.[2,3] Patients carrying susceptible specific haplotypes, cross-reactivity between the drugs with very similar stereochemical structures, and drug metabolites generated by the Cytochrome P450 enzyme complex may influence the recurrence of SJS and/or TEN.[2]

Our patient had 2 episodes of TEN following intake of Furosemide at present and Nimesulide 3 years back. Literature search revealed a similar chemical structure in Nimesulide and Furosemide as both the drug molecule contains the sulfonamide functional group (R-S(=O) $_2$-NR $_2$) which might have triggered the second episode in our patient.[4,5] In our patient, the skin lesions in the second episode of TEN appeared earlier as compared to the usual duration reported in the literature. The cause of the short latency period may be attributed to the sensitization of the patient to the sulfonamide group of drugs in the first episode. Our patient lacked constitutional symptoms and mucocutaneous involvement was less severe as compared to the first episode which might be due to the early presentation of the patient to our center along with early therapeutic intervention.

Conclusion

Conventionally, Nimesulide and Furosemide are two different groups of drugs but an intense literature search revealed that both drugs have a common sulfonamide functional group which triggered the subsequent episode of TEN. Thus, it is important to note that any patient who has had a previous hypersensitivity reaction to a drug is at high risk for recurrence with another drug having a similar chemical structure, and treating physicians should always consider cross-reactivity between the chosen drugs in order to prevent the subsequent life-threatening clinical episodes.

References

1. Harr T, French, LE. Toxic epidermal necrolysis and Stevens-Johnson syndrome. Orphanet J Rare Dis.2010;**5** (39):1-11.
2. Drateln CR, Gomez-Hernandez N, Martinez NR, Torres-Lozano C. Recurrent Toxic Epidermal Necrolysis Syndrome: A Report of Two Cases. Drug Saf Case Rep.2016;3(9):1-4.
3. Kinoshita Y, Saeki H. A Review of the Pathogenesis of Toxic Epidermal Necrolysis. J Nippon Med Sch. 2016;83(6):216-222.
4. National Center for Biotechnology Information. PubChem Compound Summary for CID 4495, Nimesulide[Internet].US:NLM;[cited 2023 July 11]. Available from:https://pubchem.ncbi.nih.gov/compound/Nimesulide
5. National Center for Biotechnology Information. PubChem Compound Summary for CID 3440, Furosemide[Internet].US:NLM;[cited 2023 July 10]. Available from:https://pubchem.ncbi.nih.gov/compound/Furosemide

Figure legends

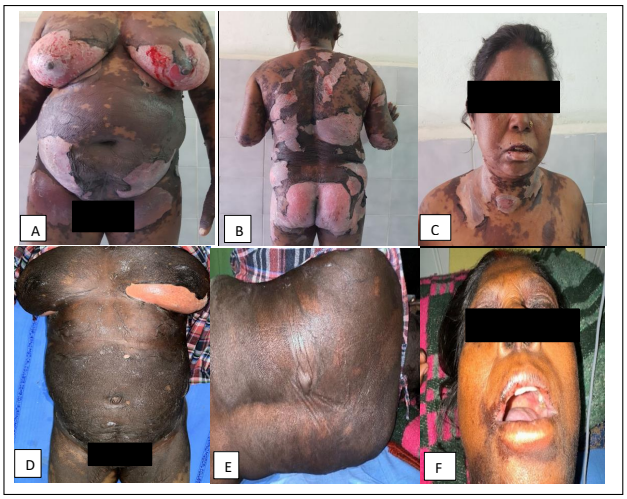

Fig 1A-C shows mucocutaneous involvement in the first episode of TEN 3 years back which was more severe as compared to the second (recent) episode as shown in Fig 1D-F.

Fig 2A-C shows initial reepithelialization over the denuded areas on the 7th day, complete on the 15th day of admission as shown in Fig 2D-F along with the complete resolution of the oral lesion.