Case Report ISSN (O):2395-2822; ISSN (P):2395-2814

Toxic Epidermal Necrolysis- A Caution before Prescribing Anti-Epileptics.

Thabish Syed[1], Dilip Ahir[1], Yogesh Garg[2], Shruti Behal[1]

[1]Junior Resident, Department of Medicine, NIMS Medical College, Rajasthan, India.

[2]Senior Resident, Department of Medicine, NIMS Medical College, Rajasthan, India.

ABSTRACT

We report a case of Toxic Epidermal Necrolysis (TEN) in a 10 year old male child resulted from inadvertent anti-epileptic usage. Steven-Johnson Syndrome (SJS) /TEN has been seen as a side-effect of many drugs like Cotrimoxazole, Phenytoin, Carbamazepine, Valproic acid, NSAID'S, Allopurinol. Etc., but TEN in a patient who is on valproic acid with addition of lamotrigine is rare which is a point of interest in our case which was successfully treated with Intravenous immunoglobulins.

Keywords: Lamotrigine, Intravenous immunoglobulin, SJS, TEN.

INTRODUCTION

Steven-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are severe life-threatening conditions resulting in epidermal necrosis mucosal erosions, epidermal detachment and severe constitutional symptoms.[1,2] SJS is characterized by widespread small blisters with skin detachment of less than 10% of total body surface area, skin detachment of 10-29% of total body surface area is overlap of SJS and TEN. Widespread detachment of epidermis greater than or equal to 30% is called as TEN.[3]

Drugs (sulfonamides, NSAIDS, Anti-epileptics etc.) are considered to be the major etiology about 75% of SJS/TEN. However infections such as upper respiratory, Mycoplasma pneumonia, flu like illness have also been reported to be the causes.[4,5] The pathophysiology of SJS/TEN remains unknown.

Name & Address of Corresponding Author
Dr Thabish Syed
Junior Resident,
Department of Medicine,
NIMS Medical College,
Rajasthan, India.
Email. syedthabish@gmail.com.

Hence the treatment approach is primarily supportive and symptom targeted.[6] The immediate management of SJS/TEN is withdrawal of all potential medication triggers.[7] This is a disease of poor prognosis, death within 6 weeks on onset of disease, has been seen in 9% of patients with SJS, 29% with SJS/TEN overlap, 48% in TEN. However with increased supportive measures and quality care morbidity and mortality rates has come down.[8]

CASE

A 10 year old male child presented to emergency with blister like lesions and peeling of skin for 2 days. Lesions started first on chest, later on extremities gradually progressed to almost all over the body. Patient also complains of burning sensations in eyes, unable to open eyes and difficulty and pain during swallowing. Patient attendants give history of one episode of low grade fever.

Table 1: Consensus definition of Steven-Johnson syndrome and toxic epidermal necrolysis[4]

Criteria	EM majus	SJS	SJS/TEN overlap	TEN with maculae	TEN with widespread erythema (without spots)
Skin detachment (%)	< 10%	< 10%	10%-30%	>30%	>10%
Typical target lesions	+	-	-	-	-
Atypical target lesions	Raised	Flat	Flat	Flat	-
Maculae	-	+	+	+	-
Distribution	Mainly limbs	Widespread	Widespread	Widespread	Widespread

EM, erythema multiforme; SJS, Stevens-Johnson syndrome; TEN, Toxic epidermal necrolysis.

On examining the patient, his heart rate was 130/minute, BP recorded 110/70 mm of Hg and temperature 100 degree F, with blisters and peeling of skin over 70% of body surface area with conjunctiva redness and oral mucosal shedding [Figure 1]. Coming to past history, patient had history of seizures since childhood. He was on phenytoin for 3 years, later on valproic acid. His last episode of seizure was 20 days back for which he was prescribed lamotrigine in addition to valproic acid.

A skin specialist was consulted immediately who diagnosed the case as TEN based on drug history and clinical presentation. He was kept on symptomatic supportive treatment with fluid management, adequate calorie intake through nasogastric tube, daily skin dressing, topical antibiotics, short course of corticosteroids(dexamethasone 8mg twice daily for 3 days) and Intravenous Immunoglobulin(30g/day for 5 days). Patient improved dramatically over a period of 10 days without any complications.

Table 2: At-risk medications and recommendations for identifying casual medications in Stevens-Johnson syndrome and toxic epidermal necrolysis.

Drugs with a high risk to induce SJS/TEN[9,10]. Their use should be carefully determined and they should be suspected promptly.
Allopurinol
Carbamazeine
Co-trimoxazole (And other anti-infective sulfonamides and sulfasalazine)
Lamotrigine
Nevirapine
NSAIDs (Oxicamtype; i.e., meloxicam)
Phenobarbital
Pheytoin

Drugs with a moderate (Significant but substantially lower) risk for SJS/TEN[11-13]
Cephalosporines
Macrolides
Quinolones
Tetracyclines
NSAIDs (Acetic acid type; i.e., diclofenac)

Drugs with no increased risk for SJS/TEN[11-15]
Beta-blockers
ACE – inhibitors
Calcium channel blockers
Thiazide diuretics (with sulfonamide structure)
Sulfonylurea anti-diabetics (with sulfonamide structure)
Insulin
NSAIDs (propionic acid type; i.e., ibuprofen)

DISCUSSION

Toxic epidermal necrolysis (TEN) is also known as Lyell's syndrome is a rare but potentially life threatening condition with widespread epidermal detachment and mucosal erosions [Table 1].[16]

The incidence of SJS is 1-6 cases/million person years and TEN is 0.4-1.2cases/million person years.[14] In previous case reports and studies, more than 100 drugs have been implicated as causes of SJS/TEN.[9] Among which sulfonamides, allopurinol, carbamazepine, phenytoin, NSAIDS, Valproic acid are major culprits.

Index day was designated as the date of onset of symptoms or signs that progressed within 3 days to definite erosions or blisters of the skin or mucous membranes.[3] Generally a drug doesn't induce a reaction when no longer present in a body. Hence a window period of 7 days from the date of exposure to index day is being considered. However it varies with half life of drugs for example it is 14 days for NSAIDS to 3 weeks for Phenobarbital.[3] Most common drug that leads to this disease is sulfonamides (cotrimoxazole). Antiepileptics like valproic acid and carbamazepine are also considered. Combination of lamotrigine to valproic acid has been recently reported as a cause of TEN[15], but very rare hence it has become point of interest in our case [Table 2].

Diagnosis is mainly done by history and clinical presentation. After withdrawal of offending drugs, other treatment protocols include supportive care with fluid and electrolyte management, adequate calorie intake, empiric treatment for infections, sedation and pain management.[11] Skin directed biological dressing[11], eye care[6], glucocorticoids,

immune-suppressants like cyclosporine[6] are also advised. Role of intravenous immunoglobulins,[12,13] plasmapharesis is also suggested in recent trials.

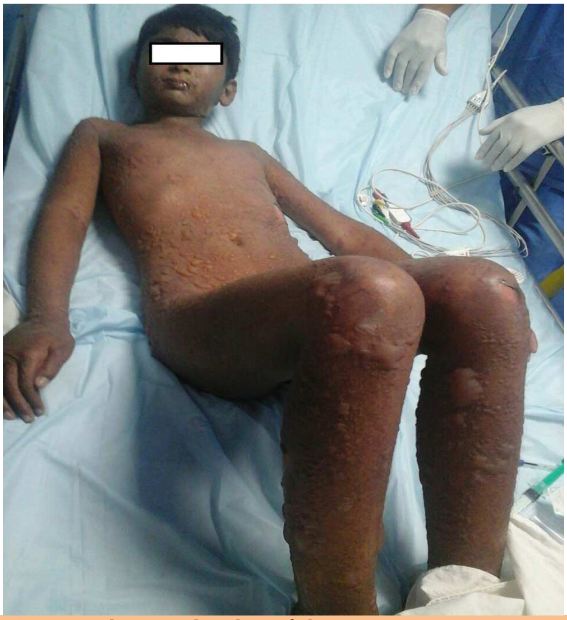

Figure 1: Blisters and peeling of skin.

CONCLUSION

SJS/TEN are serious life threatening cutaneous reactions with poor prognosis. As most common cause is drug related care should be taken before prescribing sulfonamides and anti-epileptics. Addition of lamotrigine to valproic acid resulted in TEN in a young child who survived after passing through series of life threatening events. Symptomatic supportive is the main treatment strategy. I.V immunoglobulins has also been considered to improve outcome of this disease.

Acknowledgement

All praises and thanks to Allah and peace be upon his Messenger Muhammed, whom I follow. I am deeply indebted to my parents, teachers and friends who supported me in doing this work.

REFERENCES

1. Lyell A. Toxic epidermal necrolysis (the scalded skin syndrome): a repraisal. Br J Dermatol 1979;100:69-86.
2. Roujeau JC, Stern RS. Severe cutaneous adverse reactions to drugs. N Engl J med 1994;331:1272-85
3. Rojeau JC. Medication use and the risk of Stevens-Johnson syndrome or Toxic Epidermal Necrolysis. N Engl J med 1995;333(24):1600-7.
4. Bastuji-Garin S, Rzany B, Stern RS, Shear NH, Naldi L, Roujeau JC. Clinical classification of cases of toxic epidermal necrolysis, Stevens-Johnsonsyndrome, and erythema multiforme. Arch Dermatol.1993;129(1):92-6.
5. Grosber M, Carsin H, Leclerc F. Epidermal Necrolysis in associations with mycoplasma pneumonia Infection [Abstract 121]. J Invest Dermatol. 2006;126(S3):S3-S116.
6. Mockenhaupt M. Severe drug induced drug reactions: clinical pattern, diagnostics and therapy [in English, German]. J Dtsch Dermatol Ges. 2009;7(2):142-60.
7. Garcia-Doval I, LeCleach L, Bocquet H, Otero XL, Roujeau JC. Toxic eepidermal necrolysis and Stevens-Johnsons syndrome: Does easy withdrawal of causative drugs decrease the risk of death? Arch Dermatol. 2000;136(3):323-7.
8. Mockenhaupt M. Severe cutaneous adversereactions. In: Burgdorf WHC, Plewig G, Wolff HH, Landthaler M, eds. Braun-Falco's Dermatology. 3rd ed. Heidelberg, Germany: Springer Medizin Verlag; 2009:473-84.
9. Guillaume J-C, Roujeau J-C, Revuz J, Penso D, Touraine R. The culprit drugs in 87 cases of toxic epidermal necrolysis (Lyell's syndrome). Arch Dermatol.,1987;123:37-42.
10. Mockenhaupt M, Viboud C, Dunant A, et al. Stevens Johnson syndrome and toxic epidermal necrolysis: assessment of medication risks with emphasis on recently marketed drugs. The EUroSCAR-study. J invest Dermatol. 2008;128(1):35-44.
11. Ghislain PD,Roujeau JC. Treatment of severe drug reactions: Stevens-Johnson syndrome, toxic epidermal necrolysis and hypersensitivity syndrome. Dermatol Online J. 2002;8(1):5.
12. Faye O, Rojeau JC. Treatment of epidermal necrolysis with high dose intravenous immunoglobulin (IV Ig): clinical experience to date. Drugs. 2005;65(15):2085-90.
13. Schneck J, Fagot JP, Sekula P, Sassolas B, Roujeau JC, Mockenhaupt M. Effects of treatments on the mortality of Stevens-Johnson syndrome and toxic epidermal necrolysis: A retrospective study on patients included in the prospective EuroSCAR Study. J Am Acad Dermatol. 2008;58(1):33-40.
14. Schof E, Stuhmer A, Rzany B, Victor N, Zentgraf R, Kapp JF. Toxic epidermal necrolysis and Stevens-Johnsons syndrome: an epidemiologic study from West Germany. Arch Dermatol 1991;127:839-42.
15. Kocak S. Stevens –Johnson syndrome due to concomitant use of lamotrigine and valproic acid. Am J Clin Dermatol. 2007;8(2):107-11.
16. Saha K. Toxic epidermal necrolysis: Current concepts in pathogenesis and treatment. Indian J Dermatol Venerol Leprol. 2000;66:10-7.

How to cite this article: Syed T, Ahir D, Garg Y, Behal S. Toxic Epidermal Necrolysis- A Caution before Prescribing Anti-Epileptics. Ann. Int. Med. Den. Res. 2015;1(3):350-52.

Source of Support: Nil, **Conflict of Interest:** None declared