Norfloxacin Tinidazole induced Steven Johnsons Syndrome: A Case Report

Anshu Kumar[1], Mrinal Kunj[2], U.S.P. Keshri[3], Vineet Kumar[4]

ABSTRACT

Introduction: Steven Johnsons Syndrome is a rare auto immune disorder which mainly includes skin and mucous membrane. It manifests as blisters on the skin, facial swelling and hyper pigmentation. Majority of the SJS cases are precipitated by drug therapy mainly by antibiotics.

Case report: We report an unusual case of 45 year old Indian muslim female who received Nflox-TZ following which she had 4-5 episodes of diarrhoea and developed diffuse skin reaction which was diagnosed as SJS/TEN overlap. Past history revealed this as 3rd episode of skin reaction after the intake of same drug for the same indication.

Conclusion: Our aim is to create an awareness through this report regarding the use of antibiotics injudiciously. Their benefit-risk profile needs careful evaluation as they can induce T cell-dependent reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Health care professionals must be careful before prescribing drugs that are known to have fatal reactions like SJS.

Keywords: Norfloxacin, Tinidazole, SJS, Cutaneous drug reaction.

INTRODUCTION

STEVENS JOHNSON SYNDROME (SJS): SJS and TEN are characterized by blisters and mucosal/epidermal detachment resulting from full thickness epidermal necrosis in the absence of substantial inflammation. In SJS, detachment of the epidermis is less than 10% of the body surface area;10-30% in SJS/TEN overlap and detachment is >30% in TEN.[1] Incidence of SJS and TEN is 0.05 to 2 persons per million populations per year.[2,3] The mortality for SJS varies from 3% to 10% and for TEN from 20% to 40%[4]. Patients with SJS/TEN initially presents with acute onset of painful skin lesions, fever >39° deg, sore throat and conjunctivitis resulting from mucosal lesions. Intestinal and pulmonary involvement are associated with poor prognosis, as are a greater extent of epidermal detachment and older age. Patient may initially present with SJS, which subsequently evolves into TEN or SJS-TEN overlap.

CASE REPORT

A 45 year muslim lady presented to the Dermatology Out patient department of RIMS, Ranchi on 15th March'17 with complaints of diffuse exfoliation all over the body. The lesions started to appear on 09th March after she took Nflox-TZ (Norfloxacin-400mg+Tinidazole-500mg) for 4-5 episodes of diarrhoea. 1st episode occurred on 1st Nov-Dec '15, 2nd episode on 1st April '16.

To begin with she developed pruritic lesions all over the body following which blackening of the skin occurred and finally the affected zones were covered with fluid filled vesicles. The ulcerative lesions began in the lips and later got spread to other parts of the body.

She had problem in intake of food because her mouth was blistered and eroded. The ulcerative lesions of lips healed later. The skin over the affected area denuded and got excoriated. She underwent cataract surgery in the left eye in March'16 and had blurring of vision post surgically. She is also taking eye drops for above complaints. She is a known epileptic since childhood and had been taking Carbamazepine (ZEN-200) BD for the past 2-3 years but had stopped its intake since 1yr. Further adding to it her frequency of epileptic attacks used to worsen when she slept inadequately. Diseases that present as bullous eruptions in the similar manner like Bullous pemphigoid, Pemphigus vulgaris, Herpes zoster were excluded. Temporal relationship with the other drugs were also excluded mainly Carbamazepine.

She was admitted to the hospital after proper examination and was treated with intravenous fluids, antibiotics (Ceftriaxone), systemic administration of corticosteroids (Prednisolone), mouth washes, eye lubricants and topical preparation of corticosteroid for intraoral application. The condition was diagnosed by dermatologists using Bastuji Garin classification. Valproic acid (Encorate-500) was started as she was suspected to have Juvenile Myoclonic Epilepsy (JME). General examination was normal. Cutaneous examination revealed diffuse exfoliation of the skin over the abdomen, back, buttocks, thighs and arms as shown in Fig 1 and 2. Oral mucosal examination showed presence of healed lesions on the lips. Nail examination was normal. WHO-UMC causality assessment revealed 'Probable category' for Norfloxacin-TZ induced SJS/TEN.

DISCUSSION

Patients who develop SJS have an increased risk for another episode of SJS[5]. Differential diagnosis were Pemphigus vulgaris, stomatitis medicamentosa. The exact pathogenesis

[1]PG Student 2nd Year, [3]Professor, [4]PG Student Final Year, Department Of Pharmacology and Therapeutics , Rajendra Institute of Medical Sciences, Ranchi, Jharkhand, [2]DM Cardiology (1st Year Student), Department of Cardiology, S.C.B Medical College and Hospital, Cuttack, Orissa

Corresponding author: Dr. Anshu Kumar, Department of Pharmacology and Therapeutics, RIMS, Ranchi, Jharkhand, India

How to cite this article: Anshu Kumar, Mrinal Kunj, U.S.P Keshri, Vineet Kumar. Norfloxacin tinidazole induced steven johnsons syndrome: a case report. International Journal of Contemporary Medical Research 2017;4(11):2336-2337.

Complete Hemogram	
Hb	11.8g/dl
TLC count	6300cells/cumm
RBC count	4.26mill/cumm
PLT Count	1.76lakh/cumm
LFT (Liver Function Test)	
Total bilirubin	.6mg/dl
Direct bilirubin	.3mg/dl
Indirect bilirubin	.3mg/dl
Total protein	5.2g/dl
Albumin	3.5g/dl
Globulin	1.7g/dl
SGOT	68U/L
SGPT	71U/L
ALP	155U/L
RFT (Renal Function Test)	
Serum urea	43mg/dl
Serum creatinine	1.3mg/dl
Investigations	

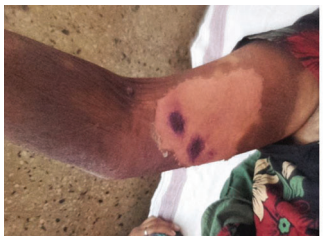
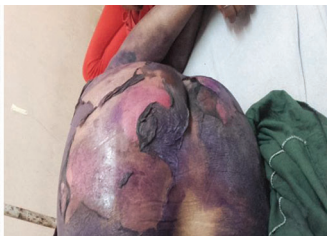

Figure-1: Denuded skin over the arm; **Figure-2:** Excoriation over back and buttocks

of SJS and TEN remains to be elucidated but apoptotic mechanisms, including involvement of cytotoxic T cells, tumor necrosis factor (TNF)-α, and Fas (CD95), Fas ligand (FasL) interaction are considered to be relevant to these diseases. Drugs are most commonly implicated for SJS, TEN and SJS-TEN overlap and other possible causes are infections, immunizations, environment chemicals and radiation therapy.

WHO-UMC causality assessment revealed 'Probable/Likely category' for Norfloxacin-TZ induced SJS/TEN in this case report based on the criteria to comply with probable category. According to Naranjo's assessment points were estimated and 'Probable' category was allotted.

Diagnosis mainly relies on clinical signs and histopathology of skin lesions. Cases with widespread purpuric macules and epidermal detachment below 10% are called SJS. Cases with SJS/TEN involvement 10-30% called as SJS/TEN overlap and cases with epidermal detachment >30% called as TEN. Similar case was reported by Jolanta Maciejewska et al. Another study on drug induced SJS,TEN and SJS/TEN overlap in a Tertiary care hospital of North east India was done by Ratan J. Lihite et al. Similar case was reported by Kubo-Shimasaki et al in June 1992 in the article 'Norfloxacin induced Infectious mononucleosis (IM) like syndrome with 'Stevens Johnson Syndrome'. Therapy for SJS includes corticosteroids (Prednisolone**),** Benzydyamine hydrochloride . 15% oral rinse for oral ulcers. Gentian violet for lip lesions. Clotrimazole cream for vaginal lesions and.3% Ofloxacin eye drops for eye lesions. Liquid and soft diet is advised to the patient.

CONCLUSION

Patients who have had SJS in the past should wear a medical bracelet to indicate the drug hypersensitivity. As far as this patient is concerned skin reaction developed the same day after introduction of the suspected drug. She was discharged on after 12 days of hospitalization after recovery.

ACKNOWLEDGEMENT

The authors would like to thank the Pharmacovigilance Programme of India (PvPI) running under Indian Pharmacopoeia Commission(IPC),Ministry of health and family welfare for providing technical logistical support to this centre for ADR reporting.

REFERENCES

1. Bastuji-Garin S, Rzany B, Stern RS, Shear NH, Naldi L, Roujeau JC. Clinical classification of cases of toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme. Arch Dermatol. 1993;129:92–6.
2. Li LF, Ma C. Epidemiological study of severe cutaneous adverse drug reactions in a city district in China. Clin Exp Dermatol. 2006;31:642–7.
3. Borchers AT, Lee JL, Naguwa SM, Cheema GS, Gershwin ME. Stevens-Johnson syndrome and toxic epidermal necrolysis. Autoimmun Rev. 2008;7:598–605.
4. Mokenhaupt M, Schopf E. Epidemiology of drug-induced severe skin reactions. Semin Cutan Med Surg. 1996;15:236-243.
5. Y. Finkelstein, G. S. Soon, P. Acuna et al. Recurrence and outcomes of Stevens-Johnson syndrome and toxic epidermal necrolysis in children. Pediatrics 2011;128:723–728.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 07-11-2017; **Accepted:** 10-12-2017; **Published:** 17-12-2017