

**INDUCED STEVENS-JOHNSON SYNDROME IN A HUMAN IMMUNODEFICIENCY VIRUS PATIENT:
A CASE REPORT****AMBED MISHRA¹, RAM MANIDEEP¹, RAMESH ADEPU^{1*}, MOTHI SN², SWAMY VHT²**¹Department of Clinical Pharmacy, JSS College of Pharmacy, Mysuru - 570 015, Karnataka, India. ²Department of Infectious Diseases, Asha Kirana Hospital, Center for HIV Care, Hebbal, Mysuru - 570 016, Karnataka, India. Email: adepu63@gmail.com*Received: 14 April 2016, Revised and Accepted: 19 May 2016***ABSTRACT**

Stevens-Johnson syndrome (SJS) is an acute life-threatening condition. In 95% of case reports, drugs were found to be an important cause for the development of SJS. About 100 drugs have been identified to causes of SJS. Very few reports were published on diclofenac-induced SJS. The incidence rate of SJS is approximately 1-2/1000 individuals with human immunodeficiency virus. In this case report, we present a 58-year-old female developed SJS after taking of diclofenac tablets.

Keywords: Stevens-Johnson syndrome, Diclofenac, Human immunodeficiency virus patients.**INTRODUCTION**

Stevens-Johnson syndrome (SJS) is a rare but very serious disorder of skin and mucous membranes. It is usually a reaction due to a medication or due to an infection. Often, in SJS, patient experiences flu-like symptoms, followed by a painful red or purplish rash that spreads and blisters. This is later followed by the top layer of the affected skin to die and shed. It is considered as an acute life-threatening condition and a medical emergency and requires hospitalization. Eliminating the underlying cause, controlling the symptoms, and minimizing complications were the aim of the treatment. In SJS recovery takes weeks to months, depending on the severity of the patient's condition [1].

In 95% of the SJS cases, drugs are an identified as the important cause [2]. Infections or a combination of infections and drugs have also been reported as the etiology of the syndrome [3]. As per case reports and studies, more than 100 drugs have been identified as causes of SJS [4,5]. In human immunodeficiency virus (HIV) cases, the incidence rate of SJS was reckoned as 1-2/1000 HIV cases [6]. Although non-steroidal anti-inflammatory drugs (NSAIDs) are a rare cause of SJS in adults, these risks may not be ignored. The risk is much higher in older patients, women and immunocompromised patients [7].

CASE REPORT

A 58-year-old female patient came to our hospital with complaints of multiple rashes on skin all over the body, burning sensation in the oral cavity, and lips. She is a known case of HIV acquired immune deficiency syndrome and on antiretroviral therapy since 3 years. On physical examination, lesions were observed on her lips, floor of the mouth, and the surface of the tongue. In addition, she had reddish lesions all over her all limbs as well as on the upper body. All of these manifestations supported the diagnosis of SJS (Fig. 1). History taking, clinical examination, serological test, and bacteriological culture tests were also conducted to rule out infectious causes of SJS.

The patient history suggests that she has used diclofenac tablets 50 mg for the last 2 weeks to treat her severe body pains took the medication as over-the-counter. It was her self-medication. Diclofenac tablets were discontinued and started with IV dexamethasone, oral levocetirizine, oral doxycycline, chloramphenicol eye drop, and betadine mouthwash along with salbutamol nebulization for her breathlessness in the hospital. During the treatment period, the patient's lesions were

monitored closely after she got admitted to the hospital. After 5 days, lesions were started to disappear and after 2 weeks, she was healed with cutaneous and mucosal ulcers. The patient was recovered successfully and got discharged.

DISCUSSION

In 1922, Stevens and Johnson described 2 male patients of 7 and 8 years old, who developed extraordinary generalized eruption with fever and inflamed buccal mucosa [2,8]. Numerous studies have shown that adverse drug reaction related hospital admissions are up to 10% of the total number of hospital admissions [9].

SJS is frequently associated with drug use. More than 100 drugs have been associated with the development of SJS that is reported as a single case report or retrospective studies. Three most classes of drugs responsible for SJS are antimicrobials, NSAIDs, and anti-epileptic drugs. Causing SJS in descending order of frequency are cephalosporins, quinolones, aminopenicillins, tetracyclines, macrolides, imidazole antifungals, and anticonvulsants (phenobarbital, phenytoin, valproic acid, carbamazepine, and lamotrigine), and then NSAIDs (especially piroxicam), allopurinol, and others are known to cause SJS. Among NSAIDs, paracetamol was found the most common cause of skin reaction in Indian studies [2,10]. Furthermore, valproic acid, NSAIDs, and acetaminophen were significantly associated with SJS in children [11]. SJS is a severe adverse drug reaction characterized by widespread lesions affecting the eyes, mouth, larynx, pharynx, esophagus, skin, and genitals. It almost involves oral mucosa [7,12].

For overlapping SJS (when 15-30% body surface area involvement exists), oxicam class of NSAIDs such as piroxicam, meloxicam, tenoxicam, and sulfonamide are most commonly implicated to cause SJS in the United States and other western nations. In contrast, allopurinol has been reported as the most common offending agent in the Southeast Asian nation [13].

In this case, diclofenac sodium was found to be as cause for SJS based the patient's recent medication consumption history. The causality assessment of diclofenac-induced SJS, in this case, was done. The scores on WHO probability scale and Naranjos suggest that the event was possible. To resolve the SJS symptoms, patient will be recommended with topical silver nitrate 0.5% or chlorhexidine 0.05% along with oral antibiotics to treat skin lesions and to prevent secondary infections [7]. In this patient, oral doxycycline, betadine mouthwash and



Fig. 1: (a-d) Lesions in patient's face and both upper and lower limbs after few days of treatment

chloramphenicol eye drops were used to treat the lesions. Levocetirizine was given to prevent histamine reactions. This patient was recovered without any further complications and the patient got discharged.

With the use of diclofenac, complications such as thromboembolism and disseminated intravascular coagulation and damage to the vital organs such as kidney function deterioration could occur [14]. However, in this case, no such complications were developed.

Diclofenac-related skin rash especially severe reactions like SJS is very rare [16]. In literature review in PubMed and Google Scholar, three papers were found that directly discussed about diclofenac and SJS or skin rash cases [14-17]. Shetty *et al.* reported a 45-year-old female patient who developed SJS treated with diclofenac after dental operation and its usage as analgesic drug has developed SJS [14]. Lin *et al.* reported that a case of 78-year-old man who got admitted to the hospital after taking diclofenac with the symptoms of SJS and the causality assessment corroborated the confirmation of diclofenac-induced SJS [17]. Wiwanitkit presented a case with diclofenac-induced skin rashes in a 52-year-old female patient [16]. Babamahmoodi *et al.* also reported a case of 65-year-old female patient who developed diclofenac-induced SJS [11]. All these reports corroborate the diclofenac-induced SJS. As it is apparent, diclofenac-induced skin reactions are commonly found in elderly people, and in this case, the patient is a 58-year-old female patient. Thus, the diclofenac-induced SJS in our case is confirmed based on the causality assessment scores and also the clinical manifestations and also ruling other pathogenic causes.

The event was attributing to diclofenac. As the patient has consuming only diclofenac before developing SJS.

REFERENCES

1. Mayo Clinic. USA: Stevens-Johnson Syndrome; 2014. Available from: <http://www.mayoclinic.org/diseases-conditions/stevens-johnson-syndrome/basics/definition/con-20029623>. [Last cited on 2016 Feb 07].
2. Barvaliya M, Sanmukhani J, Patel T, Paliwal N, Shah H, Tripathi C. Drug-induced Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and SJS-TEN overlap: A multicentric retrospective study. *J Postgrad Med* 2011;57(2):115-9.
3. Yetiv JZ, Bianchine JR, Owen JA Jr. Etiologic factors of the Stevens-Johnson syndrome. *South Med J* 1980;73(5):599-602.
4. Schöpf E, Stühmer A, Rzany B, Victor N, Zentgraf R, Kapp JF. Toxic epidermal necrolysis and Stevens-Johnson syndrome: An epidemiologic study from West Germany. *Arch Dermatol* 1991;127(6):839-42.
5. Roujeau JC, Stern RS. Severe adverse cutaneous reactions to drugs. *N Engl J Med* 1994;331(19):1272-85.
6. Medline Plus. Bethesda, (MD): US. National Library of Medicine; c2009. *Am J Clinical Dermatology*; 2012 Feb 01. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/22145749>. [Last cited on 2016 Feb 01].
7. Ward KE, Archambault R, Mersfelder TL. Severe adverse skin reactions to nonsteroidal antiinflammatory drugs: A review of the literature. *Am J Health Syst Pharm* 2010;67(3):206-13.
8. Steven AM, Johnson FC. A new eruptive fever associated with stomatitis and ophthalmia: Report of two cases in children. *Arch Pediatr Adolesc Med* 1922;24:520-5.
9. Hallas J, Harvald B, Gram LF, Grodum E, Brøsen K, Haghfelt T, *et al.* Drug related hospital admissions: The role of definitions and intensity of data collection, and the possibility of prevention. *J Intern Med* 1990;228(2):83-90.
10. Sharma VK, Sethuraman G, Minz A. Stevens Johnson syndrome, toxic epidermal necrolysis and SJS-TEN overlap: A retrospective study of causative drugs and clinical outcome. *Indian J Dermatol Venereol Leprol* 2008;74(3):238-40.
11. Babamahmoodi F, Eslami G, Babamahmoodi A. Diclofenac-induced Stevens-Johnson syndrome: A case report. *Iran J Pharmacol Ther Tehran Iran*, 11 December; 2012. Available from: <http://www.ijpt.iuims.ac.ir/index.php/ijpt/article/view/1048>. [Last cited on 2016 Feb 23].
12. Wolf R, Orion E, Marcos B, Matz H. Life-threatening acute adverse cutaneous drug reactions. *Clin Dermatol* 2005;23(2):171-81.
13. Fernando SL, Broadfoot AJ. Prevention of severe cutaneous adverse drug reactions: The emerging value of pharmacogenetic screening. *CMAJ* 2010;182(5):476-80.
14. Shetty SR, Chatra L, Shenai P, Rao PK. Stevens-Johnson syndrome: A case report. *J Oral Sci* 2010;52(2):343-6.
15. Neuman M, Nicar M. Apoptosis in ibuprofen-induced Stevens-Johnson syndrome. *Transl Res* 2007;149(5):254-9.
16. Wiwanitkit V. Diclofenac-related skin rash, a case report. *Thail J Pharmacol* 2002;24:169-72.
17. Lin TK, Hsu MM, Lee JY. Clinical resemblance of widespread bullous fixed drug eruption to Stevens-Johnson syndrome or toxic epidermal necrolysis: Report of two cases. *J Formos Med Assoc* 2002;101(8):572-6.