

## Ibuprofen Induced Stevens Johnson Syndrome -A Case Report

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### Abstract

The Stevens-Johnson syndrome (SJS) is a rare immune-complex-mediated hypersensitivity disorder which affects 7 cases per million persons per year. This article describes a case study of a 22 year old male patient who was admitted to the Sheth Vadilal Sarabhai General Hospital, Ahmedabad, with chief complaints of congestion of eyes with mucosal involvement included erythema, edema, sloughing, blistering, ulceration for last three days prior to admission. He had multiple purpuric macular lesions on face, neck, upper limb and lower limb. Past history of medication revealed intake of non steroidal anti-inflammatory drug (Ibuprofen) and Vicks VapoRub ointment for sneezing, cough and overall body pain for last five days prior to admission to the hospital. Based on signs and symptoms, with causality assessment analysis diagnosis of drug induced Stevens Johnson syndrome was confirmed. In the scarcity of evidence of effective treatment, patient was managed with symptomatic therapy. As Stevens-Johnson syndrome is a potentially fatal multiorgan disease with a strong etiologic link to some medications, one must have a high index of suspicion to be able to diagnose and treat patients with SJS in time and must therefore consider Stevens-Johnson syndrome as a potential complication of treatment.

**Key words:** Ibuprofen, Non-steroidal anti-inflammatory drug, Stevens Johnson Syndrome, Erythema

### INTRODUCTION

Stevens Johnson Syndrome (SJS) is a hypersensitivity reaction characterized by skin rashes with hyper pigmentation and cutaneous target lesions involving blistering/erosions over face, trunk & limbs.<sup>1</sup> The incidence of SJS ranges from 7 to 49 cases per million persons per year with higher incidence in male compare to female. SJS presents in three different forms which reflect the same condition: a mild form, called erythema multiforme (EM) (where <10% Total Body Surface Area is affected), the main form (between 10 and 30%), and the severe form, called toxic epidermal necrolysis (TEN). Stevens-Johnson syndrome (SJS) is a serious systemic disorder with the potential for severe morbidity and even death. SJS has the mortality rate is approximately 1-5%. However, when more than 30% Body Surface Area sloughing is present, the mortality rate is between 25% and 35%.<sup>2,3</sup>

Various etiologic factors have been implicated as a cause of SJS, including infection, vaccination, drugs, systemic diseases, physical agents, and food. Stevens-Johnson etiology is mainly a reaction to medication with more than 80% of cases of SJS/TEN related to drug only.

Among the drugs used for longer periods, the increased risk is confined largely to the first two months. The commonly implicated drugs in this category include carbamazepine, phenobarbital, phenytoin, valproic acid etc. Such kinds of reactions are independent on dose of drug and are idiosyncratic.<sup>4,5</sup> Ibuprofen is widely used non steroidal anti-inflammatory drug for pain relief and fever.<sup>6</sup> A literature search revealed very few previously reported cases of mucocutaneous drug reactions secondary to non-steroidal anti-inflammatory therapy.<sup>7</sup> We report a case of ibuprofen induced Stevens Johnson Syndrome.

### CASE REPORT

A 22 year old male patient from rural area of Gujarat was admitted in emergency department of the Sheth Vadilal Sarabhai General Hospital, Ahmedabad (India) with chief complaint of congestion of eyes since 3 days with involvement of tongue and oral mucosa and skin lesions since two days. (See Figure 1) Mucosal involvement included erythema, edema, sloughing, blistering, ulceration, and necrosis. He had history of sneezing, cough and generalized body pain for the last three days prior taking any medication. He took the medication pain killer ibuprofen and Vick VapoRub ointment for the treatment of the same for last four days. On the 3<sup>rd</sup> day of

the administration of ibuprofen, reaction in the eye appeared with congestion followed by redness in the eye on the 5th day.

On physical examination, it was observed that patients had multiple purpuric macular lesions on face, neck, upper limb and lower limb.(See Figure 2) Trunk showed multiple, purpuric, macular lesions with few vesiculobullous lesions on base of purpuric macules. Purpuric lesions were confluent covering majority of trunk and few types of erosion present. Few erythema multiforme (EM) form lesions were also present. In conjunctiva, congestion was present. Patients had erosion over lips with crusting with single well-defined erosion over dorsum of tongue with few vesicle with no genital involvement.

Laboratory investigations revealed patients elevated level of white blood cells showed etiology of infectious disease after the administration in the hospital. Patients had elevated level of Serum glutamate pyruvic acid transferase and Serum oxaloacetate transferase which showed hepatotoxicity and further with ultrasonography, intrahepatic cholestasis was confirmed. There were no drug which can cause the hepatic

impairment except ibuprofen. Renal function test was normal. Other test for diabetes, malaria, HIV infections, hepatitis infections were normal. In the absence of etiology of infections, other concomitant medications and timing of occurrence of the Stevens Johnson Syndrome, it can be inferred that it is a case of drug induced SJS with hepatic impairment.

During the hospital administration, patient was managed symptomatically for pain control, skin, mouth blistering and ulceration. After the withdrawal of ibuprofen following which the lesions gradually resolved. Patient's symptoms began to improve after initiation of intravenous dexamethasone and hydroxyzine in conjunction with fluid replacement as supportive therapy. Corticosteroid dose was gradually tapered after the 4th day of treatment. Ceftriaxone and metronidazole was given to cover infections and also topical cream of fusidic acid to cover gram positive infections. For congestion of eyes, tobramycin eye drops with lubricant were administered. Xylocaine for symptomatic improvement in mouth ulcer with vitamin B were administered. Patient gradually recovered and discharged on the 9<sup>th</sup> day of admission with a specific

**Fig.1: Congestion with conjunctivitis of eyes on the 3<sup>rd</sup> day of admission**





**Fig.2: Multiple purpuric macular lesions on face, neck, upper limb and lower limb in the patient**



warning card for sensitivity to drug and with a list of cross reactive medicine to avoid such incidence in future. Discharge medication included the Discharge medications include hydroxyzine, fucidic acid cream, ciprofloxacin eye drop and acetaminophen.

#### **DISCUSSION**

Patients' safety is paramount importance while treating the patients. Physicians writing prescriptions for their patients must warn them about possible side effects. Stevens Johnson syndrome is potentially fatal condition of skin & mucus membrane but can also affect other vital organs. Stevens-Johnson syndrome (SJS) associated with the use of nonsteroidal antiinflammatory drugs (Ibuprofen) is described here. Sternlieb et al reported the first case report on Stevens Johnson syndrome with hepatitis secondary to Ibuprofen in the USA in 1978.<sup>8</sup> In 1984, Stern et reported case series of 135 cutaneous reactions secondary to use of non steroidal anti-inflammatory agents to NSAIDs in USA. The study showed high incidence of fixed drug eruption secondary to ibuprofen first time.<sup>9</sup>

A study with adverse reactions of SJS due to NSAIDS revealed that of the available NSAIDs, oxycam

derivatives appeared to have the greatest association with SJS and TEN in USA. The relative risks reported with other NSAIDs are much lower. The risk of SJS or TEN caused by NSAIDs is extremely low (less than 2 per 1 million users per week for oxycam derivatives, less than 1 per 1 million users per week for other NSAIDs, and 6 cases per 1 million person-years for celecoxib).<sup>7</sup> Mahboob et al had reported 19 cases of ibuprofen induced drug eruption cases in Pakistan.<sup>11</sup> By our knowledge from literature search, this is the forth case report of adverse reaction of Stevens Johnson Syndrome due to ibuprofen in India.<sup>12</sup>

SJS/TEN is a rare and unpredictable reaction to medication. However, the mechanism has still not been understood and is complex, evidence has shown various pathological mechanism like drug specific CD8+ cytotoxic lymphocytes, natural killer cell activation, cytokines including perforin/granzyme, Fas-L and Tumour Necrosis Factor (TNF) alpha.<sup>13</sup> Cytokines play a role in the immunopathological and molecular mechanisms of drug-induced hypersensitivity reactions (HSR). A study of ibuprofen-induced SJS showed that in the patient with SJS, high lymphocyte level, and high

cytokine secretion in the patient's sera with the high level of tumor necrosis factor alpha (TNF-alpha) as high as in patients found to have TEN.<sup>14</sup>

Finally, the presented case reinforce that Stevens-Johnson syndrome is a potentially fatal multiorgan disease with a strong etiologic link to some medications. One must have a high index of suspicion to be able to diagnose and treat patients with SJS in time and must therefore consider Stevens-Johnson syndrome as a potential complication of treatment, especially when use of medication is questionable. Affected patients and their first-degree relatives should be instructed to avoid any identified drugs or chemicals that may be responsible. This is critical for the subsequent survival of these patients. Intensive treatment must also be done together with specialist physicians, where available. Treatment with steroid agents may be helpful, but this option remains controversial.

#### CONSENT

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review from the journal's Editor-in-Chief.

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