CASE REPORT

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Allopurinol Induced Stevens-Johnson Syndrome

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ABSTRACT

Stevens-Johnson Syndrome (SJS) is an acute, self-limited, rare but life-threatening disease that manifests as severe mucocutaneous blistering and erosions. Here we report a rare case of allopurinol-induced SJS. A 25-year-old male patient with no other comorbidities was admitted to the hospital with complaints of fever, redness of eyes, swelling of lips with discharge and crusting, extensive erosions in the oral mucosa for the last 4 days, following consumption of allopurinol for a duration of 1 month. Investigations were within normal limits. The offending drug was withdrawn and he was treated with corticosteroids, antimicrobials, and other supportive measures. Allopurinol, a Xanthine oxidase inhibitor is mostly used for the treatment of primary and secondary hyperuricemia, Health care professionals must be aware of the spectrum of adverse effects of this drug and must take urgent measures once the diagnosis is suspected especially to save the patient from such severe or fatal reactions like SJS/Toxic epidermal necrolysis (TEN).

INTRODUCTION

Stevens-Johnson Syndrome (SJS) is a very rare inflammatory reaction that can be life-threatening. It is frequently a drug-induced condition. SJS affects the skin, mucous membrane, mucocutaneous junction with systemic involvement. It can affect the skin, oral cavity, and genitals. The patient initially develops flu-like symptoms within the first 1 to 14 days which abruptly progresses to painful erythematous and purpuric macules, papules, or vesicles where the clusters of outbreaks persist for 2 to 4 weeks. The most frequent causative agents are drugs like allopurinol, anticonvulsants, antibiotics, and non-steroidal anti-inflammatory drugs. SJS is an immunologically mediated reaction.

Though SJS occurs rarely, it has a significant impact on the health and quality of life of the patients. Sometimes it can be fatal. Sometimes it resolves with post-inflammatory hypopigmentation or hyperpigmentation. So, this can be a condition with high morbidity and mortality. Here we present a case of SJS induced by allopurinol. The patient was successfully treated using systemic steroids, antibiotics, and other supportive measures. The case is presented to highlight the importance of early identification of the drug reaction, withdrawal of the offending drugs, and proper management to save the life of the patient.
CASE REPORT

A 25-year-old male patient presented with complaints of fever for four days along with redness of eyes and oral mucosa. The mucopurulent discharge was coming from the eyes. Lips were swollen with erosions and crusting. The oral cavity showed multiple erosions with swelling and discharge for four days. The patient had no other co-morbidities. The patient was apparently normal three weeks back when he had a dental extraction and was prescribed ofloxacin, ornidazole, aceclofenac, paracetamol, rabeprazole, and Serratiopeptidase. He took these medicines for 5 days and stopped. He had been taking Allopurinol for raised uric acid level for 1 month. He had complaints of fever 4 days back which was acute in onset, continuous in nature, and was associated with chills and rigors. There were no complaints of associated vomiting, nausea, and loose stools. He had a headache and earache. He also noticed the redness of his eyes and discharge. Extensive crusted lesions and erosions were noticed on the lips along with swelling of lips associated with pain. The next day he developed small linear blisters over the lips with swelling which was acute in onset and fast in progress. Back pain was present. He had no dysuria or redness of urine, no abdominal pain, and no joint pain. He had complaints of heartburn.

On dermatological examination, the patient showed multiple crusted plaques and erosions over both lips. The oral cavity showed extensive erosions. Eyes were congested. No other skin lesions were present.

His blood counts, blood sugar, LFT, BUN, serum electrolytes, urine examination were within normal limits.

He was started on the prophylactic antibiotic Azithromycin. He was also put on tapering doses of IV steroids- Dexamethasone 8 mg IV, later tapering to 6 mg daily, IV fluids, antibiotic ointments, and saline gargle. ENT and Ophthalmology consultation was sought and was advised to use Mucaine gel, Refresh teardrops, respectively. Candid mouth paint was prescribed for oral candidiasis. He was closely monitored for any progression of lesions.

DISCUSSION

Stevens-Johnson Syndrome (SJS) is a potentially fatal (mortality rate of 5-10%) immune-mediated type IV hypersensitivity reaction belonging to the group of severe cutaneous adverse reactions (SCAR). The incidence of SJS is very rare- that is approximated to be 1-6 per million, where the risk was found to be 2-fold higher in the Asian population than in the Caucasian population (Bastuji-Garin, 1993; Chan, 1990).

It has been postulated that some various factors or agents may precipitate Stevens-Johnson Syndrome. The factors contemplating SJS vary from various drugs to diverse biological agents like bacteria, viruses, fungi, mycoplasma, many malignancies, deep radiation therapy, collagen vascular diseases; of which the most frequently reported are the drug-induced (Martínez-Cabriales and Martínez-Cabriales, 2015; Beveridge et al., 1964). The pro-drome of SJS includes mucocutaneous tenderness, a red or purple skin rash. Later develop erosion of the mucous membranes, hemorrhagic erosions, blisters on the skin and mucous membrane of the mouth, nose, eyes, and genitals, and fever. Unexplained skin pain, denuded skin which develops as a result of the severe detachment of epidermis from the dermis layer of the skin are the hallmarks of the disease. SJS involves the skin detachment or detachable skin lesion in less than 10% of the total body surface area (Figure 1).

(HLA)-B12, HLA-B*5801, HLA-B*1502 are associated with a greater risk of SJS (Roujeau, 1987; Thiers, 2006). A large scale study to compare the risk for developing SJS or TEN in the short term, as well as long term use of drugs, documented the highest risk for trimethoprim-sulfamethoxazole, other sulfonamide antibiotics; chloromazepine, cephalosporins, quinolones, and aminopenicillins in the first group whereas the longer used drugs for months or years showed the greatest risk for carbamazepine, oxicam nonsteroidal anti-inflammatory drugs, phenytoin, allopurinol, phenobarbital, and valproic acid within the initial two months of drug use (Roujeau, 1996).

The pathogenesis of SJS is thought to be an idiosyncratic reaction by the suspected drug, mostly be a
type 3 immune complex reaction as well as a type 4 cell-mediated hypersensitivity reaction. The damage to the keratinocytes possibly resulted due to the immune response generated by the CD8 positive T cell area, or it may be due to the metabolites of the drugs that behave as substitutes for the haptens that links with the keratocytes or with the surface proteins. The promulgated keratinocyte death is mainly mediated by the granulysin and is found to be higher in the sera of SJS/TEN than in other drug-related dermatologic reactions or healthy individuals (Guitart, 1995).

SJS mostly occurs within the 4 to 40 days of administration of the drug. The initial presentation of SJS includes fever and influenza-like symptoms. In approximately 90% of the patients, the signs found to appear in the mucous membrane of the eyes, nose, mouth, and genitalia in the following 1 to 3 days. The earlier generalized macules with purpuric centers later progress to disseminating blisters with epidermal necrosis, though not involving the hair. In the subsequent 3-5 days, epidermal separation advances causing denuded regions that are extremely painful, bleeding, that cause loss of proteins and fluids, evaporative heat loss followed by hypothermia and infections (Roujeau et al., 1990).

A suspected case of SJS should be immediately hospitalized as the condition is considered to be life-threatening. The treatment approach should be targeted in managing the symptoms, preventing the spread of the lesions as well as in preventing complications. The patient was on allopurinol which caused the reaction and the drug was immediately stopped. He was managed with the cessation of therapy, IV steroids, and other supportive measures. Though there are studies not favouring the use of steroids in SJS, these are used in the management. The use of steroids in SJS is mainly objected to because of the high rate of bacterial infections and sepsis as well as slow progression in the re-epithelialization.

CONCLUSIONS

SJS is a severe, mostly drug-induced hypersensitivity reaction requiring immediate medical management which otherwise can be fatal. Drugs including allopurinol, phenytoin, carbamazepine, oxicam non-steroidal anti-inflammatory drugs, a certain antibiotic are associated with the risk of developing SJS. Therefore, it is advisable that the physicians, as well as other health care professionals, must be thoroughly aware of this side effect of the drugs. The need for checking HLA-B*5801 before allopurinol administration is recommended. Treatment should be initiated immediately once the diagnosis is made. A multidisciplinary approach is highly advocated. The importance of a detailed medical history of the patient is highlighted as identification of the offending drug and cessation of therapy are essential and life-saving.

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Conflict of Interest

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