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Case Report

ALLOPURINOL-INDUCED STEVENS–JOHNSON SYNDROME AND TOXIC EPIDERMAL NECROLYSIS: A CASE REPORT

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ABSTRACT

Allopurinol is used for the treatment of gout and related conditions; it is associated with various adverse drug reactions (ADRs) such as Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). A 50-year-old female was presented to the emergency ward with chief complaints of reddish pinpoint lesions over the back, chest, abdomen, and lower limb-upper limb for the past 6 days. She was diagnosed with SJS. On medication interview, it was revealed that she was on allopurinol therapy, which she took 5 days back as a self-medication. The World Health Organization - Uppsala Monitoring Centre (WHO) scale was used to access the causality assessment, ADR was found to be probable. The drug was withdrawn from the therapeutic regimen of the patient. The patient was discharged after 25 days from the hospital. Allopurinol has the strongest association with SJS with TEN. There should be a screening of HLA-B 5801 antigens before commencing the allopurinol therapy to the patients.

Keywords: Allopurinol, Stevens–Johnson Syndrome, Toxic epidermal necrolysis, Corticosteroid therapy, Mucocutaneous adverse drug reactions.

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INTRODUCTION

Whenever a drug therapy is initiated, risk is taken beside the therapeutic effects and that risk may result in adverse drug reactions (ADRs). ADRs are a sixth leading cause of death worldwide [1]. Risk of ADR with marketed pharmaceutical formulation is assessed through voluntary reporting of ADR by various health-care professionals who further decides the marketing of that particular pharmaceutical formulation [2]. The most serious ADRs are the mucocutaneous ADRs through their rate of occurrence is relatively low but are potentially fatal and endanger patient's life [3]. Most common culprits of mucocutaneous ADR are antiepileptic drugs, antimicrobial drugs, sulfa drugs, nonsteroidal anti-inflammatory drugs (NSAIDs), and antirheumatic drugs [4]. Stevens–Johnson syndrome (SJS) and toxic epidermal necrosis (TEN) are categorized under cutaneous ADRs. SJS and TEN are rare, responsible for around 1 or 2/100,000 cases annually and are potentially fatal due to which they are considered as a medical emergency. In the year 1922, SJS was described for the 1st time in two young boys [5]. As per the criteria laid by international group of dermatologist, SJS is an acute mucocutaneous adverse reaction, characterized by erosion or bullae with erythematous base. Reaction covering ≥20% of body surface area with three distinct involvement of anatomical areas, peeling of area of skin larger than 3 cm, frequent involvement of mucous membrane with character of appearance of tenderness within 48 h of onset of rash, drug-induced basal necrosis TEN, and specimen compatible with SJS [6]. This definition excludes staphylococcal skin syndrome and appearance of the lesion that has been exposed to sunlight. Both SJS and TEN relatively affect 1 or 2/1000,000 people every year [7]. Habitually patients diagnosed with SJS-TEN complain of burning rash with symmetric origin on the face and upper part of the torso. The rash starts to begin as macules and on progression, it develops into papules, vesicles bullae, and urticarial plaques. Later on, signs of mucosal involvement include erythema, edema, sloughing, blistering, ulceration, and necrosis [8].

CASE REPORT

A 50-year-old female presented to the emergency department with reddish pinpoint lesions over the back, chest, abdomen, and lower limb-upper limb for the past 6 days was slowly progressing and had a complaint of gradually increasing oral ulceration for the past 5 days. History dates back to 5 to 6 days back, she took allopurinol for joint pain as a self-medication after 2 days of administration of allopurinol, she developed erythematous maculopapular rashes all over the body which started over upper limbs and gradually involved chest, abdomen, back, and lower limb gradually, she developed ulceration over mouth and followed by blistering of the lips. She also developed redness of eye along with photophobia and mucopurulent discharge from both eyes. Nikolsky's sign appeared to be positive. The patient had a history of epistaxis and burning micturition; the patient case of hypothyroidism previously and was on irregular medication for the past 3 months. On examination, the patient was semiconscious and her blood pressure was 140/90 mmHg, respiratory rate was 18 per min, pulse rate was 78 beats per minute, and oral temperature was 97.8°F on day admission, but after 3 days, she turned febrile with high-grade fever, her oral temperature was 103°F which was relieved by administration of paracetamol. All the laboratories investigations were almost normal, her hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, and hematocrit were low-indicating megaloblastic anemia, urine examination was also normal, IgE and IgM antibodies were negative, random blood sugar was 165 mg/dL, RFT were quite normal, and total serum protein and albumin were normal. Her liver enzymes were elevated, serum glutamic oxaloacetic transaminase was found to be 75 IU/L, SGPT was 84 IU/L, and 25% of body surface was affected. Differential diagnosis like herpes simplex virus autoimmune disorders of skin like pemphigus vulgaris, fix drug eruptions, erythema multiforme were ruled out. The final diagnosis of SJS was made. The causality of ADR and allopurinol was accessed using the WHO causality scale and ADR was found to be probable. Details of the drug therapy administered to the patient are shown in Table 1.

The patient's condition was improved and was discharged after 25 days from the hospital. The patient was advised not to administer allopurinol in the future. Prediction of course of a disease was done with score TEN scale to predict the percentage of mortality rate with the risk factor associated with SJS-TEN. Score TEN is well described in Tables 2 and 3 [9].

Table 1: Drug therapy administered to the patient

Inj. pheniramine 22.75 mg was given IV twice a day	An oral paste containing Triamcinolone acetonide was applied 6th hourly a day
Inj. hydrocortisone 100 mg IV was given 3 times a day	Inj. ranitidine was given 25 mg IV once a day
Mouthwash hexidine was given in diluted form 3 times a day	Mucaine gel suspension (aluminum hydroxide) 2 tsp before oral intake
GV (GV dye) paint 1% was applied over erosions	Tab. cyclosporine 100 mg twice a day
Tab. fluconazole 100 mg was given once a day	The whole body was cleaned daily with $KMnO_4$ daily
Paraffin oil was applied over the body after cleaning	Eye drops of tobramycin 0.3% were applied every 2nd h in both eyes
Eye ointment of carboxyl methyl cellulose 0.5% was applied 3 times daily to both eyes	Ointment Neosporin H was applied 4 times a day over lips
Tab. paracetamol 650 mg was given as SOS	Tab. calcium 500 mg was given 1 time in a day
Tab. linezolid 600 mg was given 2 times a day	Inj. tramadol 50 mg was given twice a day
Calamine lotion was applied during night time over the whole body	Intravenous dextrose and normal saline were administered

GV: Gentian violet

Table 2: The score TEN scale used for calculations of the risk factor

Risk factors	0	1
Age	<40 years	>40 years
Associated malignancy	No	Yes
Heart rate (beats/min)	<120	>120
Serum BUN (mg/dL)	<28	>28
Compromised BSA	<10%	>10%
Serum bicarbonate mEq/L	>20	<20
Serum glucose	<252	>252

Table 3: Mortality rate with number of risk factor calculated by score TEN scale

Number of risk factors	Mortality rate (%)
0–1	3.2
2	12.1
3	35.3
4	58.3
5 or more	>90

DISCUSSION

Long back in the year 1922, SJS was described for the 1st time as rare, unspecified epidermal eruptions characterized by pyrexia, swelling of buccal mucosa, and austere conjunctivitis by American pediatricians Albert Mason Stevens and Frank Chambliss Johnson in two young boys of age 7 and 8 years. Both these cases were misdiagnosed by primary physician as hemorrhagic measles [10]. The incidence of SJS is relatively very low. Multiple etiologies are involved in the pathophysiology of this syndrome. Various drugs such as NSAIDs, sulfonamides, and antiepileptic, including allopurinol, several infectious agents, and idiopathic reasons are responsible for the cause of SJS [11]. Their strong evidence of the association between HLA-B 5801 and occurrence of SJS-TEN allopurinol induced [12]. The mortality rates are higher in younger and older age. There are various studies, suggesting that patients suffering from HIV are at higher risk of developing SJS and TEN. The terminology of SJS and TEN is assigned as if the 10% of the body surface is covered than the subject is having SJS similarly if 10–30% of body surface area than SJS and TEN overlaps and >30% is said to be TEN [13].

An approach to treatment is based on the symptoms and is supportive begins with cessation of the culprit drug responsible for its etiology [14]. Treatment was initiated with the management of airways, fluid electrolyte management, and wound care. For skin, lesions, or skin loss, patients are treated as burn patients with extra care and are shifted to burn care units. Paradesi *et al.* found that patients who were on etanercept therapy were more promising with the median healing time of 8.5 days [15]. There are studies, which are not favoring the use of corticosteroids, but still, these are used in the management of SJS TEN.

CONCLUSION

Allopurinol has the strongest association with SJS-TEN. Early diagnosis of SJS-TEN and initiation of therapy with the systemic corticosteroid and supportive medication proved to be useful in the management of the patients. An early approach is to withdraw the drug and initiation of supportive measures [16-21]. Better how there should be a screening of HLA-B 5801 before commencing the therapy of allopurinol to the patients.

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ETHICAL DECLARATION

Authors informed consent was taken from the patient before data collection stating that no identity of the patient will be disclosed.

AUTHORS' CONTRIBUTIONS

Manik Chhabra did acquisition of data, analysis of case report, and drafting of case report and Ankit Gaur did critical revision of manuscript.

CONFLICTS OF INTEREST

Authors declare that they have no conflicts of interest.

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