Allopurinol Induced Stevens – Johnson Syndrome: A Rare Case Report

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ABSTRACT

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Adverse drug reactions occur in about 3-5% of all hospital admissions and are associated with increased morbidity and mortality. Drug induced allergic reactions are categorised as IgE mediated and non IgE-mediated hypersensitivity reactions. These reactions vary from mild rashes to severe life threatening reactions like Stevens Johnson syndrome (SJS). SJS is a rare but potentially fatal adverse drug reaction. It can be associated with infection or combination of infection and adverse drug reactions. A case of 50 year old male normotensive, non diabetic, non alcoholic suffering from gouty arthritis is reported here. Diagnosis of SJS was made on history and clinical examination and the patient was successfully treated with parenteral antibiotics, antihistamines, corticosteroids and IV fluids.

Keywords: Stevens-Johnson Syndrome (SJS), Allopurinol, Adverse Drug Reaction

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INTRODUCTION

Adverse cutaneous drug reactions occur in about 3-5% of hospitalized patients with approximately 1 in 1000 hospital patients suffering from life threatening drug reactions.[1] Most commonly observed drug reactions are cutaneous drug reactions in 65-85% of cases.[2] SJS is induced by various drugs like trimethoprim-sulfamethaxazole, cephalosporines, quinolones sulphonamides, antibiotics, carbamazepine, phenytoin, valproic acid, phenobarbital, non steroidal anti-inflammatory drugs (NSAIDs), allopurinol etc.[3,4]

Allopurinol, a uric acid lowering drug, can cause life threatening severe adverse reactions in the form of hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidural necrolysis.[5] SJS is diagnosed clinically by fever (100.4°F), skin tenderness, mucositis and blistering.[6]

CASE REPORT

A 50 years old man, non diabetic, non hypertensive, non alcoholic presented with joint symptoms in the form of pain and tenderness mainly of the lower limbs especially left great toe. He was diagnosed as a case of gouty arthritis on clinical examination and laboratory profile. He was put on tablet allopurinol 300 mg daily. After 2 weeks, he complained of itchy diffuse skin lesions with burning sensation involving face, chest, abdomen, eyes, upper and lower extremities. He also complained of nausea, headache, burning micturition and constipation. After 2 days, there was involvement in mucosal areas in the form of erythema of the conjunctiva, nasal mucosa, buccal mucsa in the form of eye discharge, lid swelling, dysphagia, angular stromatitis and crusted lips. The skin lesions were erythematous macules and papules of varying size with dark brown centres bilaterally. Nikolsky's sign was positive. Systemic examination was unremarkable. Laboratory investigations revealed total leucocyte count 12300/mm^3, DLC P=77, L=23, E=0, B=0, ESR 25 mm at the end of first hour. C-reactive protein 6 IU/L, serum sodium 135 meq/L, serum potassium 5.6 meq/L, FBS 110 mg/dl, RA factor –ve, HIV non reactive and X-ray chest normal. Based on history of allopurinol exposure, clinical examination and laboratory investigations, a diagnosis of SJS was made. Allopurinol was withdrawn immediately and the patient was put on parenteral antibiotics, corticosteroids, IV fluids, nutritional support, oral and ocular care. The skin lesions

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started to slough leaving extensive desquamation after 10 days. The patient was discharged in a satisfactory condition and now is on regular follow up.

DISCUSSION

Stevens Johnson syndrome (SJS) is a severe mucocutaneous reactions characterised by extensive necrosis and epidermal sloughing. It is common in HIV infected individuals.[7] The incidence of allopurinol induced SJS has increased due to its increase use and dosage.[8] Other cases of SJS include infections.[9] The pathogenesis of SJS is poorly understood. But the hypothesis is that drug induced hypersensitivity reaction causes keratinocyte cell death, occurring as a result of role played by CD8 + cytotoxic T cells, fatty acid synthetase (FAS) and fatty acid synthetase ligand (FASL). This ultimately results in epidermal sloughing and detachment.[10] Apoptosis also plays a role in keratinocyte cell death.[11] The onset of symptoms following initial drug administration varies from few hours to 3 weeks but symptoms reappear after rechallenge within 48 hours or less in an acquired immune response.[12] Once the diagnosis is made, the offending drug must be stopped immediately in order to reduce mortality. Higher antibiotics are used in SJS patients in view of dreadful complications of sepsis and lung involvement. Successful therapeutic management includes parent eral administration of antibiotics, cyclosporins, corticoids, N acetylcysteine, plasmophresis thalidomide, anti-TNF alpha, pentoxyfylline, IO IV Immunoglobulins although none of the pharmacological agent has conclusively been shown to be beneficial as treatment modality.[13]

CONCLUSION

SJS is a rare, serious systemic reaction. Early identification and withdrawl of the offending drug improves the prognosis of SJS, especially after exposure to drug. Efficient pharmacovigilence is the need of hour so that occurrence of adverse drug reactions can be reduced and prevented. For this, proper history must be taken before prescribing drugs like antibiotics, anticonvulsants, NSAIDs, pyrazoles and anti-rheumatic drugs. Reporting of such events is encouraged.

END NOTE

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REFERENCES

1. Fiszenson-Albala F, Auzerie V, Mahe E, Farinotti R, Durand-Stocco C, Crickx B, et al. A 6-month prospective survey of cutaneous drug reactions in a hospital setting. Br J Dermatol. 2003 Nov;149(5):1018–22.
2. Wolkenstein P, Revuz J. Drug-induced severe skin reactions. Incidence, management and prevention. Drug Saf. 1995 Jul;13(1):56–68.
3. Auquier-Dunant A, Mockenhaupt M, Naldi L, Correla O et al. Severe cutaneous adverse reactions. Correlations between clinical patterns and causes of erythema multiforme major, Stevens-Johnson syndrome and toxic epidermal necrolysis: results of an international prospective study. Arch Dermatol 2002; 138(8): 1019-24.
4. Tomy Martin LH. Severe cutaneous adverse drug reactions: a review on epidemiology, etiology, clinical manifestations and pathogenesis: Chinese Med J 2012; 17(125): 3171-4.
5. Halevy S, Ghislain P-D, Mockenhaupt M, Fagot J-P, Bouwes Bavinck JN, Sidoroff A, et al. Allopurinol is the most common cause of Stevens-Johnson syndrome and toxic epidermal necrolysis in Europe and Israel. J Am Acad Dermatol. 2008 Jan;58(1):25–32.
6. Bircher AJ. Symptoms and danger signs in acute drug hypersensitivity. Toxicology. 2005 Apr 15;209(2):201–7
7. Mittmann N, Knowles SR, Koo M, Shear NH, Rachlis A, Rourke SB. Incidence of toxic epidermal necrolysis and Stevens-Johnson Syndrome in an HIV cohort: an observational, retrospective case series study. Am J Clin Dermatol. 2012 Feb 1;13(1):49–54.
8. Fam AG, Dunne SM, Iazzetta J, Paton TW. Efficacy and safety of desensitization to allopurinol following cutaneous reactions. Arthritis Rheum. 2001 Jan;44(1):231–8
9. Wetter DA, Camilleri MJ. Clinical, Etiologic, and Histopathologic Features of Stevens-Johnson Syndrome During an 8-Year Period at Mayo Clinic. Mayo Clin Proc. 2010 Feb;85(2):131–8
10. Miyauchi H, Hosokawa H, Akaeda T, Iba H, Asada Y. T-cell sub-

sets in drug-induced toxic epidermal necrolysis. Possible pathogenic mechanism induced by CD8-positive T cells. Arch Dermatol. 1991 Jun;127(6):851–5.

11. Paul C, Wolkenstein P, Adle H, Wechsler J, Garchon HJ, Revuz J, et al. Apoptosis as a mechanism of keratinocyte death in toxic epidermal necrolysis. Br J Dermatol. 1996 Apr;134(4):710–4.
12. Revuz J, Penso D, Roujeau JC, Guillaume JC, Payne CR, Wechsler J, et al. Toxic epidermal necrolysis. Clinical findings and prognosis factors in 87 patients. Arch Dermatol. 1987 Sep;123(9):1160–5
13. Schneck J, Fagot J-P, Sekula P, Sassolas B, Roujeau JC, Mockenhaupt M. Effects of treatments on the mortality of Stevens-Johnson syndrome and toxic epidermal necrolysis: A retrospective study on patients included in the prospective EuroSCAR Study. J Am Acad Dermatol. 2008 Jan;58(1):33–40.