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ALLOPURINOL INDUCED ADVERSE DRUG REACTIONS: CASE SERIES

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ABSTRACT Allopurinol is widely used drug for patients of hyperuricemia and gout. The few adverse drug reactions related to allopurinol are diarrhea, fever, hepatotoxicity, Steven Johnson Syndrome- Toxic Epidermal Necrolysis (SJS-TEN), congestive heart failure and renal failure. In this article we have described eleven cases to evaluate the causality, cause and management of this syndrome. In this study eleven retrospective cases were selected from the ADR reports. The full details of the cases were collected from Christian Medical College from the period of 2012 to 2016. Causality was established using Naranjo scale and classification was done based on severity and resolution of ADR. It was observed that cases presented with mild to severe reactions of allopurinol, which is the suspected offending agent. Cases were resolved with supportive treatment while five case had a prolong hospitalization and two cases had a life threatening drug reaction. Early detection and management of this severe form of systemic reaction is very important for better will be the prognosis.

KEYWORDS : Allopurinol, Fever, SJS-TEN and Renal failure.

INTRODUCTION

Allopurinol was developed in 1956 for the use as adjuvant in chemotherapy for leukemia. In due course of time it was found that it lowers serum uric acid by inhibiting the conversion of hypoxanthine to xanthine[1]. The alterations in purine metabolism explain how allopurinol is effective in treatment for both idiopathic gout and hyperuricemia[2]. There are various adverse drug reactions related to allopurinol which accounts for 3 to 5 % and range from mild to severe ones like rash, allopurinol hypersensitivity syndrome (AHS), drug fever, diarrhea, hepatotoxicity, SJS-TEN, hemolytic anemia, congestive heart failure and renal failure[3]. The mechanism by which these adverse reactions take place is not well understood[2]. However, for the development of AHS immunologic factors, genetic predisposition and accumulation of drug have been documented[4].

SJS-TEN is a rare adverse drug reaction but life threatening, which is considered as immune mediated reaction to drug. These severe cutaneous adverse reactions (SCAR) are characterized by epidermal necrosis, erosion of mucous membrane and severe constitutional symptoms[5].

The known indications for allopurinol are hyperuricemia associated with chronic gout, acute uric acid nephropathy, enzyme disorders and cancer chemotherapy[5].

In the following case series we present eleven such cases of drug induced adverse drug reactions by allopurinol in our hospital.

Case 1

A 47 years old male patient, weighing 65 kg complaint of fixed drug eruption due to allopurinol indicated for joint pain. Fixed drug eruption was seen within 2 hours of the drug intake. There is no known medical history. The outcome to the adverse drug reaction was unknown. The Adverse drug reaction (ADR) was reported. Naranjo score was applied for the causality assessment and it was reported as a probable ADR of allopurinol.

Case 2

A 55 years old female, weighing 90 kg was admitted in the hospital with chief complaints of burning sensation and redness in both the eyes, ulcers in mouth and history of rash, which started on upper trunk and then became generalized. Patient was diagnosed as a case of SJS-TEN associated with allopurinol. The reaction started after 15 days of allopurinol 100 mg for the indication of joint pain. Complete blood count was normal. The toxicity was graded as grade III. Seriousness of the reaction was life threatening and patient recovered fully. The ADR was reported. Naranjo score was applied for the causality assessment and it was reported as a probable ADR of allopurinol.

Case 3

A 45 years old female patient, weighing 65 kg was admitted in the hospital with Toxic Epidermal Necrolysis (TEN) due to allopurinol. Patient developed symptoms within 2 days after taking allopurinol 100 mg. Reaction was life threatening, the drug was withdrawn and patient recovered fully. The ADR was reported. Naranjo score was applied for the causality assessment and it was reported as a probable ADR of allopurinol.

Case 4

A 35 years old female patient, weighing 65 kg was admitted to the hospital with an adverse drug reaction in the form of Erythema Multiform from Allopurinol. Patient developed this reaction with 100 mg of allopurinol within two days of starting the medication. The sole indication for allopurinol was hyperuricemia. The ADR was reported. Naranjo score was applied for the causality assessment and it was reported as a probable ADR of allopurinol.

Case 5

A 69 years old male patient weighing 65 kg was admitted in hospital with adverse drug reaction as exanthamatous rash all over the body due to allopurinol. The reaction developed after 16 days of starting of allopurinol 100 mg oral. The indication for starting allopurinol was gout. Patient recovered fully and was discharged. The ADR was reported. Naranjo score was applied for the causality assessment and it was reported as a probable ADR of allopurinol.

Case 6

A 44 years old male, weighing 75 kg was admitted as adverse drug reaction to allopurinol with exanthamatous rash all over the body, redness and watering from both eyes with fever, chills and headache. The Adverse drug reaction was to be of Steven Johnson syndrome (SJS). Patient had an event after taking allopurinol 100 mg for 19 days. Patient had a prolonged hospitalization and recovered after 11 days since the reaction started. Patient recovered fully and was discharged. ADR was

reported. Naranjo score was applied for the causality assessment and it was reported as a probable ADR of allopurinol.

Case 7

A 64 years old female patient weighing 110 kg was admitted as an adverse drug reaction to allopurinol. The adverse drug reaction was reported as a case of DRESS syndrome. Patient received allopurinol 100 mg for joint pain and developed the reaction after 13 days of starting the medication. Patient had a prolonged hospital stay and recovered fully. The ADR was reported. Naranjo score was applied for the causality assessment and it was reported as a probable ADR of allopurinol.

Case 8

A 53 years old female patient weighing 80kgs was admitted as adverse drug event to allopurinol as Toxic Epidermal Necrolysis (TEN). Patient developed the reaction after 14 days of starting the medication. She had a prolonged hospital stay and recovered fully. The ADR was reported. Naranjo score was applied for the causality assessment and it was reported as a probable ADR of allopurinol.

Case 9

A 34 years old female patient developed skin rash, oral ulcers, conjunctivitis, mucositis and skin lesions after starting on allopurinol for gout. There were target lesions on trunk and erosions over face, arms and genital lesions. The reaction was reported as a case of Steven Johnson Syndrome (SJS). The reaction started after 12 days of starting on allopurinol. Patient is a known case of bronchial asthma. Patient had a prolonged stay and recovered fully. The ADR was reported. Naranjo score was applied for the causality assessment and it was reported as a probable ADR of allopurinol.

Case 10

A 20 years old male patient, weighing 52 kg known case of Acute Myeloid Leukemia on chemotherapy developed exanthamatous rash all over the body as an adverse drug reaction. Patient was on I.V. piperacillin and tazobactam, I.V. vancomycin, and Tab allopurinol. The reaction developed after 14 days of therapy. The patient was prescribed I.V. Colistin and patient was recovered fully. The ADR was reported. Naranjo score was applied for the causality assessment and it was reported as unlikely ADR.

Case 11

A 60 years old female patient, weighing 69 kg was admitted in the hospital with skin lesions over chest and face associated with itching. Skin lesions were describes as erythematous plaques, an adverse drug reaction to allopurinol. Patient developed the reaction within 2 days of starting the medication for hyperuricemia. Patient is a known case of hypertension for 20 years and is taking Tab. Telmisartan 40 mg OD, and Tab. Atorvastatin 10 mg OD. Patient recovered fully from the event. The ADR was reported. Naranjo score was applied for the causality assessment and it was reported as a probable ADR of allopurinol.

Summary

Allopurinol is a uric acid lowering drug and should be prescribed only when there is a need for indication considering its side effects, morbidity and mortality[1]. The eleven adverse drug reactions reported to allopurinol were one fixed drug eruption, five SJS-TEN, one erythema multiforme, two exanthamatous rash, one DRESS syndrome and one erythematous rash. In severity of cutaneous reactions to allopurinol it was reported that it was the major cause of morbidity and mortality, but mostly during the first 2 weeks following reaction onset. There was no mortality reported. In all the cases reported, allopurinol was the offending drug except for one where the causality was unlikely. Cases were resolved with supportive treatment while five case had a prolong hospitalization and two cases had a life threatening drug reaction. Precaution should be taken while prescribing allopurinol as its allergy can present as late as 1 - 2 months after initiating therapy[1].

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Conflict Of Interest

There is no conflict of interest.

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