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Case Report

Allopurinol causing generalized exfoliative dermatitis: a case report

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ABSTRACT

Erythroderma is a scaly, erythematous dermatitis of the skin, which occurs in drug allergy, malignancy and underlying skin disorders. The diagnosis is challenging because the extent of skin involvement does not always correlate with the extent of internal organ involvement. Therefore, early recognition of symptoms is vital to minimize morbidity and mortality. Case report: A 52 years old man had asymptomatic hyperuricemia and prescribed allopurinol 300mg, daily. One month later, the rashes started to appear on his trunk and then progressed to the face and upper limbs. Then it continued to spread to the lower extremities. Management involves prompt cessation of the culprit drug, administration of corticosteroids and supportive treatment. It is Concluded that Allopurinol is commonly used in clinical practice for the treatment of symptomatic hyperuricemia and gout. It has been associated with erythroderma especially when used indiscriminately.

Keywords: Allopurinol, Adverse drug reactions, Erythroderma, Generalized exfoliative dermatitis

INTRODUCTION

The elevated uric acid level (hyperuricemia) occur in 5% of the general population and most of them are asymptomatic.[1] Since 1963, allopurinol has been introduced and widely using to reduce the uric acid level.[2] In vivo, allopurinol converts into oxypurinol which serves as xanthine analog and combine with xanthine oxydase enzyme, which intern prevents the formation of uric acid in the body.[3] Although, allopurinol is generally well tolerated, life-threatening toxic effects have been reported from different regions.[1,2,4,5] Erythroderma alternatively termed as generalized exfoliative dermatitis is one of the adverse reactions triggered by allopurinol.

Erythroderma is a scaly, erythematous dermatitis that involves at least 90% of the surface of the skin. It is a rare disease, and its occurrence might be closely linked to:

1. Drug use such as allopurinol, carbamazepine, phenytoin

2. Malignancy such as cutaneous T-cell lymphomas or
3. Other underlying skin disorders such as contact dermatitis, seborrheic dermatitis, psoriasis.[6,7]

Even so, in some circumstances, it might be difficult to establish its underlying cause and challenging for the clinicians.

CASE REPORT

A 52 years old man had asymptomatic hyperuricemia and prescribed allopurinol 300mg, daily. One month later, the rashes started to appear on his trunk and then progressed to the face and upper limbs. Then it continued to spread to the lower extremities. Three weeks after the appearance of rashes, the skin started to scale on trunk and limbs; since then, the patient complained of chills and fever. The patient denied of known drug allergy previously.

He was admitted to a private hospital in Myanmar and was assessed by the dermatologist. The patient's symptoms and signs at the arrival of the dermatology ward were as following:

- Generalized rashes for three weeks
- Malaise and fatigue for one week
- Focal patches of scaling of skin on trunk and extremities for 2 days
- Fever with chills for 2 days

On examination at the dermatology ward, the pulse rate was 102 beats/ minutes, blood pressure was 120/ 75 mmHg, temperature 39ºC, respiratory rate 19 breaths/ minutes. He had periorbital oedema, erythematous rashes and focal patches of scaling on his trunk and extremities. All the other systemic examinations were normal.

Past history

He is a known case of Type II Diabetes Mellitus and treated with metformin 500mg, twice a day for 4 years.

Personal history

He is a non-smoker and non- alcoholic. No known drug allergy and food allergy.

Family history

He is married, has a son and living with his family.

Laboratory investigations were done on the day of admission. Haemoglobin was 13.2gm/dL, total WBC count of 10.5 $x10^9$/L and platelet count of 285$x10^9$/L. The serum uric acid level was raised as 663umol/L. The liver function and renal function test were within the normal range. Random blood sugar (RBS) was 4.6mmol/L. Hepatitis B Ag, Hepatitis C antibody and HIV screening tests were non-reactive. The details of the patient's laboratory investigation results were shown in Table 1.

Management involved prompt cessation of Allopurinol, Corticosteroids administered and IV fluids (normal saline) given to the patient. The fluid intake output and body temperature were monitored in hospital. The patient's general condition was improved and fever was subsided after two days. The skin lesions, rashes and scaling were improved and he was discharged from the hospital on day 7 after admission.

Table 1: Patient's laboratory investigation results.

Investigations	Results	Reference range
Full blood count		
RBC count	5.3 $x10^{12}$/L	4.5-5.9
Haemoglobin	13.2gm/dL	13.5-17.5
Haematocrit (PCV)	42%	41-53
WBC count	10.5 $x10^9$/L	4.3-10.5
Platelets	285 $x10^9$/L	150-450
WBC differential count		
Neutrophil	52.2%	40-75
Lymphocyte	36.3%	20-45
Eosinophil	2.8%	0-6.0
Monocyte	8.4%	1-11
Basophil	0.3%	0-2
Renal Function Test		
Uric acid	663umol/L	202-434
Urea	3.3mmol/L	2.0-6.8
Creatinine	70umol/L	51-124
Lipid profile		
Total cholesterol	5.1mmol/L	<5.2
Triglycerides	1.27mmol/L	<1.71
HDL cholesterol	1.22mmol/L	>1.42
LDL cholesterol	3.4mmol/L	<2.6
Chol/HDL cholesterol	4.2mmol/L	Up to 4.0
Liver Function Test		
Total protein	74g/L	63-83
Albumin	48g/L	35-50
Globulin	25g/L	25-40
A/G ratio	1.9	1.0-2.0
Total bilirubin	21.3umol/L	2.0-28.0
SGOT/AST	36U/L	7-44
ASPT/ALT	47U/L	7-48
Alkaline phosphatase	101U/L	40-128
Gamma-GT	42U/L	7-55

DISCUSSION

In this 52-year-old man, the erythema started to appear and progressed to scaling after taking the allopurinol. The previous case reports had been indicated that patients with erythroderma presented with erythematous papular lesions with constant scaling.[8] The other reason why the patient might have diagnosed with general exfoliative

dermatitis was that this skin disease has a considerably low prevalence among the young population and is common among the people above the age of 50.[6,9,10] The previous research on prevalence of this disease among the different gender also narrowed down the findings that men were at a higher risk of developing the disease than women.[9,10]

In patients suffering from exfoliative dermatitis, there is increased rate of mitosis and cells in the germinative layer.[6] The cells of the erythroderma patients usually have a shortened transit time through their epidermis. Consequently, there is an incomplete keratinization of the exfoliated scales. These scales contain materials that are often retained in the dermis such as the nucleic acid, amino acids, and the proteins that might contribute to the negative balance of nitrogen. The amount of scales lost among the patients with erythroderma varies by its severity and the underlying condition. The shortened duration of transit might also contribute to the impaired function of the skin as a barrier from incomplete keratinization.[6]

The other widely known pathophysiology process of all forms of erythroderma is the increased flow of blood to the skin, which when combined with the function of the impaired skin barrier results in significant loss of fluid through transpiration.[6] Reflex tachycardia and dehydration are common. Parallel pathophysiology has also unveiled that increased flow of blood to the cutaneous surface might also lead to loss of heat, which may further cause cachexia and compensatory hypermetabolism.[6] Because of this metabolic derangement and skin manifestation, this patient suffered from fever and chills through the illness. Eosinophilia is common finding in the patients with adverse drug reactions; however, a retrospective study of 60 patients with DRESS in Taiwan found out that 48% of them did not have eosinophilia.[11] In this patient, mild anemia was identified; however, eosinophil count was within the normal range.

The correlation of the disease's etiology and its clinical presentation is usually weak since the drug reactions or changes to specific dermatosis are occasionally masked by exfoliative dermatitis changes that are non-specific.[12] Therefore, a conclusive correlation of a clinical histology might necessary to take series of biopsies. Even so, the significance of histopathology examination to ascertain the etiology of erythroderma remains to be clear.[12,13]

Based on the past empirical pieces of research and diagnoses, the common drug that has contributed for the occurrence of erythroderma is allopurinol.[1] Besides, other drugs have also been suggested to be the known causes of similar condition such as carbamazepine, phenytoin, penicillin, vancomycin, etc.[13,14]

Since allopurinol has a desirable uric acid-lowering capacity, it is the commonest drug prescribed to treat the hyperuricemia. A review on allopurinol hypersensitivity syndrome had revealed that most of the patients who suffered from adverse reaction of that drug were prescribed to treat the asymptomatic hyperuricemia.[15] The physicians and clinical researchers who came up with one of the most dominant series of allopurinol's drug reactions suggested that this drug should not be given in uncomplicated gout, asymptomatic hyperuricemia, and acute attacks of gout as well as renal impairment associated with hyperuricemia.[6,16] According to that suggestions, allopurinol was discontinued in this 52-year-old man who had a history of asymptomatic hyperuricemia and developed erythroderma after taking that drug. The studies conducted on allopurinol indicated that its adverse effects are severe and can have a potential of high fatality among the affected patients.

CONCLUSION

Concisely, allopurinol is a complex drug responsible for lowering the effect of the uric acid in the blood in a time-honored manner. Nevertheless, considering its adverse effects, mortality, and morbidity, it should only be administered when truly indicated.

Its prescription should be done after excluding a systematic clinical diagnosis with critical consideration of the patients' history of skin diseases and other cutaneous disorders. It is also crucial to note that asymptomatic hyperuricemia does not guarantee the administration of this medication.

Finally, it is important to note that when prescribing allopurinol for the patients, special precautions have to be taken for those who suffer from renal impairment and those having the history of gout.

It is also crucial for the health care providers to have awareness of the allergic symptoms that the patients may have when administered with allopurinol such as rashes, scaling and fever.

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