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Case Report

Allopurinol Induced Dress Syndrome--- A Case Report

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ABSTRACT

Allopurinol is a drug used primarily to treat hyperuricemia and its complications including chronic gout. It causes DRESS (Drug Rash with Eosinophilia and Systemic Symptoms) syndrome as a hypersensitivity reaction as a rare side effect of it. We report a case of 62 year old female presented with complaints of fever, jaundice, dyspnea, and generalized rash after 3 months of allopurinol treatment for hyperuricemia. She was diagnosed as a case of DRESS syndrome. Allopurinol treatment was stopped and steroid treatment was started. Patient was discharged after 4 weeks in a satisfactory condition.

Key Words: Allopurinol; DRESS; Hyperuricemia

INTRODUCTION

Allopurinol, an analog of hypoxanthine, has been widely used in clinical practice for more than 30 years for the treatment of hyperuricemia and gout. Two percent of patients develop a mild exanthema while on this drug, which usually resolves after withdrawal of the drug. Allopurinol can rarely cause DRESS syndrome in 2-6 weeks after allopurinol therapy. [1,2] DRESS syndrome is a multisystem condition associated with certain drugs in predisposed individuals characterised by fever, rash, internal organ involvement and eosinophilia. [3] We report a case of 62 years old female who developed DRESS syndrome as a rare side effect of allopurinol treatment.

CASE REPORT

A 62 year old female diagnosed case of gouty arthritis on allopurinol 100 mg OD, presented with chief complaints of intermittent fever from one month. It was associated with breathlessness along with wheezing from 15 days. She was also having decreased urinary output for 7 days. Physical examination detected fever (38.5°C), jaundice, diffuse erythema and maculo-papular rash all over the body. Analysis of blood revealed the following: Hemoglobin, 7.1 g/dl; WBC, 18900/mm^3; platelet, 2,26,000/mm^3; eosinophil, 7300/mm^3; SGPT 317 IU/L, SGOT- 257 IU/L; alkaline phosphatase (ALP), 873 IU/L; blood urea, 76 mg/dl; serum creatinine, 3.1 mg/dl; uric acid, 4 mg/ dl; International Normalized Ratio (INR), 1.4; total bilirubin, 16.9 mg/dl; direct bilirubin, 8 mg/dl; and IgE, 574 IU/ ml. Urine showed proteinuria (24 hrs urinary albumin 1.2 gm) with abnormal sediment. Urine complete analysis detected no abnormality. Blood and urine culture did not reveal growth of any organism. HIV, anti HCV and HBsAg were negative. ANA was positive (1:80), anti dsDNA and p-ANCA were negative. C3 and C4 level were normal. Abdominal ultrasonography showed a normal liver size, grade-2 hepatosteatosis and sludge in the

lumen of the gallbladder. Endoscopic Retrograde Cholangiopancreatography (ERCP) was performed to rule out mechanical icterus and was found normal. The case was diagnosed as DRESS syndrome. Allopurinol was stopped and steroid treatment initiated. On tapering prednisolone (day 7) she developed swelling of upper lip and complained of breathlessness and discomfort in the throat, respiratory rate of 36/min, bilateral coarse crepitations upto middle zones. She responded to oxygen, injectable hydrocortisone. Skin biopsy revealed superficial perivascular lymphocytic infiltration with focal basal cell vascularisation and mild focal spongiosisand parakeratosis suggestive of interface dermatitis .A diagnosis of DRESS syndrome secondary to allopurinol was established. Prednisolone was continued for 2 weeks and tapered over 1 week. Her eosinophil count dropped over a period of 14 days to 21. Serum creatinine came to 2.7 mg/dl. Her rash and discolouration of toes cleared in 3 weeks. She was discharged after 4 weeks in satisfactory condition. Now she is on continuous follow up with no complaints.

DISCUSSION

Differential diagnosis for skin rash, eosinophilia and hepatorenal involvement include acute infections (e.g. Hepatitis viruses, Ebstein Barr Virus, Cytomegalovirus, HIV Virus), collagen vascular disorder, drug reactions, lymphoma and hypereosinophilic syndrome. [4]

DRESS syndrome is a severe adverse drug-induced reaction. It is a syndrome, caused by exposure to certain medications, which may cause rash, fever, inflammation of internal organs, lymphadenopathy, and characteristic hematologic abnormalities such as eosinophilia, thrombocytopenia, and atypical lymphocytosis. The incidence of DRESS syndrome in patients treated with allopurinol is about 0.4%. [5] It causes multiorgan failure as a result of conditions such as nephritis, hepatitis, and encephalitis. Liver involvement and eosinophilia generally begin 2-6 weeks after administration of first dose of allopurinol, occurring generally after the skin reactions. Peripheral eosinophilia is a common finding in DRESS. It is not related to dose or serum concentration of drug. Re-exposure to the offending agent may cause development of symptoms within one day. [6]

The most common drugs known to cause DRESS syndrome are lamotrigene, phenobarbital and phenytoin, long acting sulphonamides sulphamethoxazole, sulphadiazine, sulphasalzine, allopurinol, nevirapine, abacavir, dapsone, minocycline and even vancomycin. [7,8] The pathogenesis of DRESS syndrome is not fully understood. The pathophysiology of it is assumed to be multifactorial. Immunological factors, genetic factors, and human herpes virus-type 6 are also implicated. A possible mechanism may be oxipurinol which is a major metabolite of allopurinol. It can cause hypersensitivity hypersensitivity, and immune complex mediated vasculitis. The DRESS syndrome sometimes can be associated with life-threatening multi-organ failure. The syndrome has a mortality rate of 10%. [7]

There is no standard treatment of DRESS syndrome. If recognised early and culprit drug (S) discontinued, the syndrome resolves over next few weeks. Rash disappears with mild desquamation. High-dose corticosteroids can be useful and predict better outcome in the disease. Early cessation of the drug implicated in the development of DRESS syndrome will result in a better outcome. [9] Symptoms in some patients may flare up 3-4 weeks especially after rapid withdrawal of a corticosteroid.

CONCLUSION

The DRESS syndrome is a severe adverse drug reaction and can cause multi organ failure and a high mortality rates. It needs initiation of an early treatment. Drug history is very important if patient presents

with clinical symptoms like DRESS syndrome. And drug should be discontinued early and treatment should be started early. Judicious use of allopurinol may decrease the incidence and morbidity caused by this syndrome.

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