Skin rash, eosinophilia, and renal impairment in a patient recently started on allopurinol

Ashraf Jmeian¹, Amer Hawatmeh¹, Razan Shamoon², Fayez Shamoon¹, Michael Guma¹

¹Saint Michael’s Medical Center, Newark, ²Saint Joseph Regional Medical Center, Paterson, New Jersey, USA

Abstract

Allopurinol is a hypoxanthine analog which inhibits xanthine oxidase, it is a widely used medication for the treatment of hyperuricemia and gout. Allopurinol-induced drug-induced rash with eosinophilia and systemic symptoms syndrome is an infrequent, life-threatening adverse reaction of allopurinol therapy that is remarkable for the higher mortality rate with the use of allopurinol than with the use of another agent. We present a case of a 62-year-old male with a history of chronic kidney disease stage 3, hypertension and gout who developed skin rash, eosinophilia, and renal impairment 2 weeks after he was started on allopurinol therapy for gout. Allopurinol was stopped, and the patient was started on steroids. This case emphasizes that although allopurinol is commonly used the drug for the treatment of gout. However, it can be associated with serious life-threatening complications. Therefore, care should be taken when prescribing allopurinol, and it should be prescribed only for the appropriate indications.

Keywords: Allopurinol, drug-induced rash with eosinophilia and systemic symptoms syndrome, gout, skin rash

Introduction

Allopurinol is a hypoxanthine analog which inhibits xanthine oxidase, it is a widely used medication for the treatment of hyperuricemia and gout. Approximately 2% of patients treated with allopurinol develop skin rash, and some may experience severe drug hypersensitivity reaction.

Case Report

A 62-year-old African American male with past medical history of chronic kidney disease stage 3, hepatitis C virus, hypertension, and gout. He presented to the Emergency Department with a complaint of skin rash which was limited to the extensor surfaces of the upper and lower extremities, he first noticed the rash 5 days before presentation. Two weeks before presentation the patient was started on allopurinol therapy for gout. He was taking a total dose of 1200 mg instead of 300 mg daily as he misunderstood his doctor’s instruction. The patient’s medications included aspirin, allopurinol, and metoprolol. Physical examination was remarkable for low grade, skin examination showed diffuse pruritic erythematous maculopapular papular with bullae limited to the extremities extensor surfaces [Figures 1 and 2]. Swelling and tenderness of the extremities was also noted. The rest of the physical examination including heart, lungs and abdomen was unremarkable. Labs showed worsening of preexisting renal failure, hemoglobin level of 9.5 g/dL, white blood cell count 11.7 × 10³/µL (4.5 × 10³ – 1.1 × 10⁴/µL), 13.6% eosinophils (0–7.5%), aspartate aminotransferase 190 IU/L (15–41 IU/L) and alanine aminotransferase 167 IU/L (17–63 IU/L). Rheumatoid factor, antinuclear antibodies, and serum cryoglobulins were within normal limits. Skin biopsy showed nonspecific mild-to-moderate acute inflammation with scattered eosinophils.

Diagnosis

Our patient had skin rash, eosinophilia, and renal impairment.
Based on the history, laboratory values, and recent use of high doses of allopurinol; allopurinol-induced drug-induced rash with eosinophilia and systemic symptoms (DRESS) syndrome was diagnosed.

Discussion

Allopurinol is a hypoxanthine analog which inhibits xanthine oxidase, it is a widely used medication for the treatment of hyperuricemia and gout. However, it can be associated with serious life-threatening complications. Approximately 2% of patients treated with allopurinol develop skin rash, and some may experience severe drug hypersensitivity reaction. Allopurinol-induced DRESS syndrome (A-DRESS syndrome) is an infrequent, life-threatening adverse reaction of allopurinol therapy. DRESS syndrome is remarkable for the higher mortality rate with the use of allopurinol than with the use of other agents (25% vs. 10%). It typically presents after 1–8 weeks after initiating the offending drug and characterized by skin eruption, hematologic abnormalities (eosinophilia, atypical lymphocytosis), lymphadenopathy, and internal organ involvement (liver, kidney, lung). Although the pathophysiologic mechanism leading to the development of A-DRESS syndrome is unknown, it probably involves an immunologic mechanism following accumulation of allopurinol and its metabolite oxypurinol in patients with poor renal function. Multiple studies have shown that advanced age, underlying renal impairment, higher doses, and concomitant use of thiazide diuretics are potential risk factors for developing allopurinol-induced DRESS syndrome.

Differential diagnosis includes

Churg–Strauss syndrome (CSS), idiopathic hypereosinophilic syndrome, Stevens–Johnson syndrome and toxic epidermal necrolysis, DRESS syndrome due to another medication. CSS was excluded as the patient had no history of asthma, allergic rhinitis, or sinus abnormalities and P-ANCA was negative. The idiopathic hypereosinophilic syndrome was ruled out as it is a diagnosis of exclusion, typically affects men aged 20–50 years, and requires persistence of eosinophilia for at least 6 months. DRESS syndrome due to another medication was also excluded because of all the medications taken by the patient, the only potential trigger documented in literature was allopurinol.

Management

Stop the offending drug, start corticosteroids and supportive management

The mainstay of therapy in DRESS syndrome involves the immediate cessation of the offending drug. The use of systemic corticosteroids for the treatment of DRESS syndrome with organ involvement has not been evaluated in randomized trials. However, there is a general consensus among experts on the use of systemic corticosteroids for the treatment of DRESS syndrome with organ involvement. In our patient, allopurinol was discontinued and high dose steroids were administered along with other supportive measures. During hospitalization, the patient's rash improved and became hyperpigmented and desquamated with clear, fluid-filled vesicles also noticed in some areas. The kidney function continued to worsen, and hemodialysis was started. He was later discharged and continued intermittent hemodialysis for end-stage renal failure.
**Conclusion**

Allopurinol is a commonly used drug for the treatment of gout. However, it can be associated with serious life-threatening complications. Therefore, care should be taken when prescribing allopurinol, and it should be prescribed only for the appropriate indications.

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**Conflicts of interest**

There are no conflicts of interest.

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