Azathioprine-induced shock: An uncommon, unpredictable and potentially fatal adverse effect of azathioprine

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ABSTRACT
A 60 year-old male was initiated on azathioprine 50 mg/day for airborne contact dermatitis. As the patient showed a satisfactory response to this initial therapy, azathioprine dose was escalated to 100 mg/day after two weeks. However, the patient started feeling unwell from that day onwards and developed features of azathioprine-induced shock leading to discontinuation of azathioprine. Within the next 24 hours, there was complete resolution of nausea, malaise, abdominal pain, hypotensive episodes, fever and diarrhea in a pattern similar to that in which they had appeared. Rechallenge with a single dose of azathioprine (50 mg), resulted in the recurrence of nausea, vomiting and the characteristic fever spike four hours later. His blood pressure showed a marginal fall from 130/80 to 100/70 mm Hg. However, a clinically manifest episode of hypotension did not develop. This case is being reported for its rarity and clinical interest.

KEY WORDS: Azathioprine, airborne contact dermatitis, shock

Azathioprine is an imidazolyl derivative of mercaptopurine and has been used extensively for immunosuppression in inflammatory dermatoses. The most common conditions treated with azathioprine are pemphigoid, pemphigus, atopic eczema and airborne contact dermatitis. Bone marrow suppression, hepatic and renal toxicity, gastrointestinal upset, development of opportunistic infections are among the important adverse effects associated with the use of azathioprine. Azathioprine-induced shock is an uncommon, unpredictable and potentially fatal outcome of treatment with azathioprine and has been reported mainly in patients with rheumatism but rarely in dermatology patients. Here, we describe a case of azathioprine-induced shock in a patient with airborne contact dermatitis.

A 60 year-old male was initiated on azathioprine 50 mg/day for airborne contact dermatitis after a thorough laboratory evaluation including hemogram, liver and renal function tests and chest radiography. His blood pressure ranged between 130/80 and 140/100 mm Hg. As the patient had satisfactory response while on azathioprine therapy, the dose was escalated to 100 mg/day after two weeks. The patient started feeling unwell from that day onwards and developed nausea and vomiting. He had no history of drug allergies in the past. In the following two days, he developed vague abdominal pain, high spiking fever with chills usually in mid-mornings, watery diarrhea and two episodes of hypotension (his blood pressure fell from 140/100 mm Hg to 90/60 mm Hg on two separate occasions on two days in the mid-morning) which were detected when he collapsed in the ward.

While he had hypotension, he had a thready pulse rate of 106 beats/min. Minimal tenderness was noted in lower abdomen and the rest of the general and systemic examination was unremarkable. Laboratory investigations showed a total leucocyte count of 9 x 10^9/ml with 0.01 x 10^9/ml eosinophils; liver and renal functions were normal. All relevant investigations for the evaluation of fever were not rewarding, which included repeated blood, urine and stool cultures, chest radiography, abdominal ultrasound and peripheral smears for blood parasites. In view of a suspected allergic reaction, azathioprine was discontinued. Within the next 24 hours, there was complete resolution of nausea, malaise, abdominal pain, hypotensive episodes, fever and diarrhea in a pattern similar to that in which they had appeared.

Rechallenge with a single dose of azathioprine (50 mg) resulted in recurrence of nausea, vomiting and the characteristic fever spike four hours later. His blood pressure showed a marginal fall from 130/80 to 100/70 mm Hg. However, a clinically manifest episode of hypotension did not develop. Azathioprine is being increasingly used in dermatology for the treatment of various inflammatory dermatoses. Adverse effects due to azathioprine can be dose-dependent (nonallergic) or dose-independent (allergic). Azathioprine-induced shock is one such dose-independent adverse effect due to a hypersensitive reaction to the imidazole component of the drug. It has been
mainly reported in patients with rheumatism and autoimmune conditions\(^5\) but only rarely in dermatology patients.\(^6\) Patients usually present in the first month after starting azathioprine with a myriad of symptoms including nausea, vomiting, vague pain in the abdomen, circulatory collapse, fever and acute deterioration in renal functions.\(^5,6\)

Since this presentation can be seen similarly with sepsis, cholecystitis, circulatory failure due to cardiopulmonary causes, azathioprine-related pancreatitis\(^5\) or worsening of renal function in transplant recipients,\(^6\) it becomes mandatory to investigate the patient’s history for these other causes before considering a hypersensitivity reaction to azathioprine to discontinue the drug. Abrupt cessation of the drug brings about dramatic improvement in symptoms. Temporal profile of the development of symptoms and dramatic (improved) response on withdrawal of the drug in the absence of other identifiable causes supported the diagnosis of azathioprine-induced shock in our patient. To the best of our knowledge, this is the first case report of azathioprine-induced shock in a patient of airborne contact dermatitis. This report illustrates the potentially hazardous and treatable complication of this commonly prescribed drug.

References