Azathioprine induced drug fever and elevated procalcitonin in a patient with autoimmune hepatitis

Michelle Zur DO, Meghana Singh MBBS, and Vanessa Pauig MD
University of Connecticut Health Center and St. Francis Medical Center

**INTRODUCTION**

- Drug-induced fever is an elevated temperature 7-10 days after starting a drug, with resolution after discontinuation.
- Diagnosis of drug fever is usually a diagnosis of exclusion.
- Underdiagnosis can lead to expensive workup, extended hospital stays, and unnecessary antibiotic treatments.
- Azathioprine is an immunomodulatory drug often used in inflammatory conditions like inflammatory bowel disease, rheumatoid arthritis, or sarcoidosis.

**CASE REPORT**

- 45 year-old woman with a history of Sjögren’s syndrome, hypothyroidism, and autoimmune hepatitis presented with self-reported fever of 102˚F.
- In the ED, temperature was 102.2˚F and procalcitonin was elevated to 7.70 and peaked at 27.17.
- Associated symptoms included nausea, but no vomiting, diarrhea, blurry vision, sinus pressure, ear pain, shortness of breath, cough, abdominal pain, or rash.
- Three weeks prior to presentation patient was diagnosed with autoimmune hepatitis.
- Eleven days prior to presentation patient was started on azathioprine 100mg daily.
- An extensive infective work up including labs, chest x-ray, CT of the chest, abdomen and pelvis, and urine analysis were negative for source of infection.
- All home medications were stopped including Plaquenil and azathioprine, however her prednisone 7.5mg daily was continued.
- The following day, her procalcitonin trended down and she was afebrile the rest of admission.
- She was sent home restarted on Plaquenil, but not on azathioprine.
- Shortly after discharge, patient was placed back on azathioprine at half the dose of 50mg.
- The next day patient presented back to the ED with recurrence of fever to 100.9˚F.

**DISCUSSION**

- Drug fever is a rare side effect of azathioprine and is reported to happen <1%.
- Whereas, procalcitonin elevations are only reported in a few case reports.
- With the increased use of azathioprine in a wide spread of inflammatory condition, the true incidence of drug fever and procalcitonin may be underestimated.
- In this case, the rapid resolution of fever and procalcitonin elevation in this patient after discontinuing azathioprine highly suggests that it was the causative source.
- Drug fever and procalcitonin elevations are likely to lead to expensive workups and prolong hospital stays.
- Thus, azathioprine adverse reactions should be considered as a differential when providers encounter similar patients.

**SIGNIFICANCE**

- Drug reactions can manifest with varied symptoms in different organ systems and can lead to expensive workup by clinicians unaware of recent medication changes.
- Fever is a rare side effect of azathioprine and procalcitonin elevation is a yet more rare effect.
- There have been several reports of azathioprine induced fever in the above conditions, but few in autoimmune hepatitis.
- There have been even fewer reports of azathioprine induced elevation in procalcitonin.

**TAKEN HOME POINTS**

- Fever and procalcitonin elevations are rare side effects of azathioprine.
- Practitioners should have drug reaction as a differential when they encounter patients on azathioprine without reported symptoms of infections.
- High suspicion should be maintained to help avoid expensive testing, extended hospital stay, and unnecessary antibiotic treatments.