

ADVERSE DRUG REACTIONS, INCLUDING SJS, TEN

## AZATHIOPRINE HYPERSENSITIVITY SYNDROME PRESENTING AS ERYTHEMA NODOSUM WITH HEPATOTOXICITY

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Background: Azathioprine(AZA) is an immunosuppressant widely used in off-label prescription of dermatologic diseases. AZA hypersensitivity syndrome is a rare and potentially fatal adverse drug reaction, which is important to be early recognized.

Observation: A 37-year-old female presented to the emergency department due to fever and rash. Two months ago, she presented as refractory generalized erythematous plaques suspicious of chronic urticaria. AZA(50mg/day) was introduced to control symptoms. Two weeks later, she suffered from vomiting and diarrhea. Spiking fever with chills subsequently occurred with skin eruptions. On physical examination, several tender and indurated subcutaneous nodules were noted on both legs. Laboratory surveillance revealed white blood cell 6.8 × 103/µL and increasing C-reactive protein 8.7mg/dL. Elevated aspartate transaminase(123 U/L), alanine transaminase(184 U/L) and total-bilirubin(2.3 mg/dL) implied the mixed hepatitis. Serology for viral hepatitis, CMV, EBV, antibody of autoimmune hepatitis were negative. Chest X-ray and QuantiFERON-TB test reported unremarkable results. Microscopically, skin biopsy revealed a septal panniculitis with mixed infiltrates of lymphocytes, neutrophils, eosinophils, and presence of Miescher's granuloma, suggestive of erythema nodosum(EN). Blood and tissue cultures did not yield microorganisms. Hypersensitivity reaction to AZA with hepatotoxicity was suspected, and AZA was discontinued. The symptoms of fever and skin eruption gradually resolved within one week. On 2-week follow up, the laboratory data showed declined liver enzymes without sequelae.

Key message: EN is an extremely rare in cutaneous presentation of AZA hypersensitivity syndrome which only seven reported cases are in existence. The incidence of AZA-induced hepatotoxicity was 2.1%, and most cases manifests as mixed hepatitis. The reactions mostly occur within the four weeks of drug initiation. After withdrawal of AZA, the cutaneous lesions usually resolve within one week. Differential diagnosis of EN-like lesions should consist of infectious and autoinflammatory disorders. Clear communication with other physicians and accurate medical records are essential in clinical practice.





