ADVERSE DRUG REACTIONS, INCLUDING SJS, TEN

AZATHIOPRINE HYPERSENSITIVITY SYNDROME IN AN ASIAN WOMAN

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Background: Azathioprine (AZA), the nitroimidazole of 6-mercaptopurine (6-MP), was first used in 1961 as an immunosuppressant for kidney transplantation. Since then it has become an effective corticosteroid-sparing agent in a variety of autoimmune inflammatory diseases. Dose-dependent toxic side effects (myelosuppression, gastrointestinal side effects, hepatotoxicity) have been well recognized. Less well-characterized is AZA hypersensitivity syndrome. Life threatening high fever and myopathy may occur if such a hypersensitivity reaction remains unrecognized in patients with autoimmune diseases.

Observation: A 42-year old Chinese woman was admitted to our hospital with high fever, chills, nodular erythema and myopathy. Further examinations showed intracranial hypertension and hepatotoxicity. In the past, the patient took azathioprine for 7 days because she suffered from demyelinating disease. The temperature decreased in 2 days and erythema disappeared after discontinuation of all medicines she took before. However, 3 days later, the high fever and erythema present again. she developed arthralgia, malaise, and cutaneous lesions. The skin lesions again erupted on the forearms and distal legs with an appearance similar to that of the initial lesions (Figure C). After a detailed inquiry, the patient told us that after clinical improvement of the skin rash, a 50 mg dose of AZA was restarted by herself because she worried about the onset of demyelinating disease. Otherwise no change was made.
Therefore, azathioprine was discontinued again. The next day, high fever and nodular erythema abated again. DNA sequence showed mutation in methylenetetrahydrofolate reductase (MTHFR), inosine triphosphatase (ITPA) and thiopurine S-methyltransferase (TPMT) genes.
The patient was diagnosed as azathioprine hypersensitivity syndrome and discontinued azathioprine then recovered.

Key message: Prompt recognition, evaluation, and treatment are needed to prevent complications. Skin findings may be an important early clue to the diagnosis of AZA hypersensitivity and aid in prompt recognition and treatment of this potentially life-threatening adverse drug effect.