Azathioprine-induced acute febrile neutrophilic dermatosis (Sweet's syndrome)

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DESCRIPTION

A 75-year-old man with a medical history significant for Crohn's disease was admitted with suspected sepsis. The physical examination revealed fever and a maculopapular rash involving upper and lower extremities (figure 1).

Over the next 2 days, the rash became pustular and painful (figure 2). It progressed to involve the trunk, palms and soles of the feet. Owing to concerns over a drug-related rash, the patient's medications were reassessed, and it was determined that azathioprine had been initiated 2 weeks prior to hospitalisation. Based on the above-mentioned temporal relationship, azathioprine-induced reaction was suspected. A skin biopsy was performed, and the results were consistent with acute febrile neutrophilic dermatosis: Sweet's syndrome (figure 3). Azathioprine was discontinued and no steroids were given with prompt subsequent resolution.

Sweet's syndrome is defined as the constellation of fever, neutrophilia and painful erythematous cutaneous plaques consisting of mature neutrophils, diffusely infiltrating the upper dermis.¹ The syndrome can be idiopathic, malignancy-associated or drug-induced. The latter form is most commonly caused by granulocyte colony-stimulating factor agents, but has been associated with other medications.

Azathioprine-induced Sweet's syndrome and azathioprine hypersensitivity reaction, a more severe and systemic reaction often involving neutrophilic dermatosis, are rare adverse effects.²⁻³ The exact pathogenesis of these reactions is unknown. Both are dose-independent and typically occur in the first 4 weeks of therapy. Most cases resolve within 2–3 days after medication discontinuation and may not require corticosteroids. Rechallenge with azathioprine is not recommended.²

Figure 2 Rash on the right hand on day 5 of hospitalisation.

Learning points

- ▶ A febrile rash in the absence of infection within the first 4 weeks of azathioprine therapy should alert the clinician to the possibility of azathioprine hypersensitivity reaction or azathioprine-induced Sweet's syndrome.
- ▶ Drug-induced Sweet's syndrome diagnostic criteria are abrupt onset of painful erythematous plaques, dense neutrophilic infiltrate without evidence of vasculitis on histopathology, fever, temporal relationship between drug ingestion and clinical presentation and temporal resolution of lesions after drug withdrawal.
- ▶ Once the above azathioprine reactions are diagnosed, rechallenge with azathioprine is not recommended and other purine analogues such as mercaptopurine should be avoided.

Figure 1 Rash on the left and right hands on day 1 of hospitalisation.

Figure 3 Skin biopsy showing mature neutrophils diffusely infiltrating the upper dermis.

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