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Azathioprine-induced Sweet syndrome in ANCA-associated vasculitis

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A 38-year-old man with a history of myeloperoxidase antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis presented after 4 days of fever >38°C, red eye, arthralgias and skin lesions.

The patient's vasculitis was initially treated with a 7-month course of intravenous cyclophosphamide and oral corticosteroids, reaching complete remission. The patient had been transferred, 2 weeks before, to oral azathioprine (200 mg/day) as maintenance therapy.

The physical examination found fever, conjunctivitis and painful erythematous edematous papules, with occasional pustules, involving the neck, upper back and extremities (Figure 1). In the lower legs, there were also erythematous, tender deep nodules (Figure 2). Laboratory findings revealed 12.2×10^9/L leukocytes with 85% neutrophils, elevation of both erythrocyte sedimentation rate and C-reactive protein, acute kidney injury, haematoproteinuria and leukocyturia. Infectious disease was ruled out. A skin biopsy, from an erythematous papule, showed a dense neutrophilic infiltrate in the upper dermis, junctional oedema and focal karyorrhexis. There was no vasculitis in the biopsy specimen and testing for ANCAs was negative.

The diagnosis of Sweet syndrome was established, and the temporal relationship between azathioprine administration and clinical presentation raised the suspicion for drug-induced Sweet syndrome.

Azathioprine was withdrawn and high-dose prednisolone was initiated with a rapid and dramatic response of both cutaneous and extracutaneous manifestations. The diagnosis of azathioprine-induced Sweet syndrome was confirmed. Methotrexate was selected as maintenance therapy.

Azathioprine treats a variety of autoimmune conditions, and, in nephrology, its main indication is maintenance therapy of ANCA-associated vasculitis. Sweet syndrome is one of the several recognized clinical patterns of azathioprine hypersensitivity syndrome.

Sweet syndrome is characterized by fever, constitutional symptoms, peripheral neutrophilia and abrupt onset of erythematous papules, plaques or nodules [1]. Sweet syndrome presents in three clinical settings: classical, malignancy-associated and drug-induced. The criteria for drug-induced Sweet syndrome include: (i) abrupt onset of painful erythematous plaques or nodules, (ii) histopathological evidence of a dense neutrophilic infiltrate without evidence of leukocytoclastic vasculitis, (iii) fever >38°C, (iv) temporal relationship between drug ingestion and clinical presentation and (v) temporal resolution of lesions after drug withdrawal or treatment with systemic corticosteroids [2].

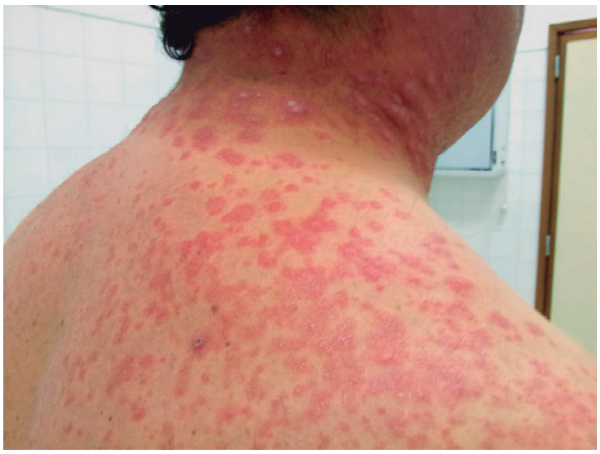

Fig. 1. Erythematous papules, involving the neck and upper back, typical of Sweet syndrome, with occasional pustules.

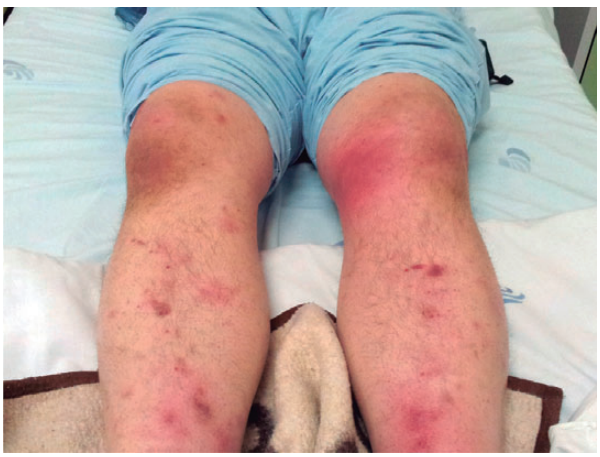

Fig. 2. Erythematous deep nodules in the lower legs (mimic erythema nodosum) typical of the subcutaneous presentation of Sweet syndrome.

The first case of azathioprine-induced Sweet syndrome was reported in 2003 [3] and since then only 18 [4] cases have been described.

We emphasize the importance of considering azathioprine-induced Sweet syndrome, within weeks of azathioprine initiation, in the differential diagnosis of infection and disease flare in patients with ANCA-associated vasculitis. Subsequent azathioprine avoidance is crucial as rechallenge can lead to anaphylaxis [5].

Conflict of interest statement. None declared.

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