Stevens–Johnson syndrome following astemizole therapy

Sir,

Astemizole is a long-acting H1-histamine receptor antagonist of the non-sedating type, which is in widespread use for allergic rhinitis.[1] We report a case of severe Stevens–Johnson syndrome developing after a short course of this drug, bought as the proprietary preparation Pollon-eze, containing astemizole 10 mg.

A 28-year-old man on a walking holiday in England took astemizole 10 mg daily for hayfever. He had used terfenadine on previous occasions with no ill effects. He took no other medications and had no significant past medical history. The onset of fever, headache and mouth ulceration was followed within 24 h by a generalised rash. He was admitted to hospital five days after the last dose of astemizole with fever, widespread blistering skin lesions and mucosal ulceration; a diagnosis of Stevens–Johnson syndrome was made. Despite high-dose systemic steroids, adult respiratory distress syndrome developed, necessitating prolonged mechanical ventilation. He eventually made a full recovery apart from minor corneal scarring. Antibody titres for *Mycoplasma pneumoniae*, Herpes simplex and antistreptolysin O were all negative.

It is often difficult to establish definitively the cause of Stevens–Johnson syndrome; as in this case, the severity of the illness precludes rechallenge with the drug considered responsible.[2] Reports to the Committee on Safety of Medicines on suspected adverse cutaneous reactions to astemizole include cases of photosensitivity and urticaria, but to our knowledge no cases of Stevens–Johnson syndrome have been reported as a complication of anti-histamine use.[3] Recognised drug causes of erythema multiforme and Stevens–Johnson syndrome are listed in the box.

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Drug causes of erythema multiforme and Stevens–Johnson syndrome

sulphonamides	tetracyclines
penicillins	sulphones
barbiturates	codeine
thiazides	ethosuximide
phenytoin	tocainide
phenylbutazone	rifampicin
chlorpropamide	gold salts
salicylates	

Sweet syndrome in chronic myeloid leukaemia

Sir,

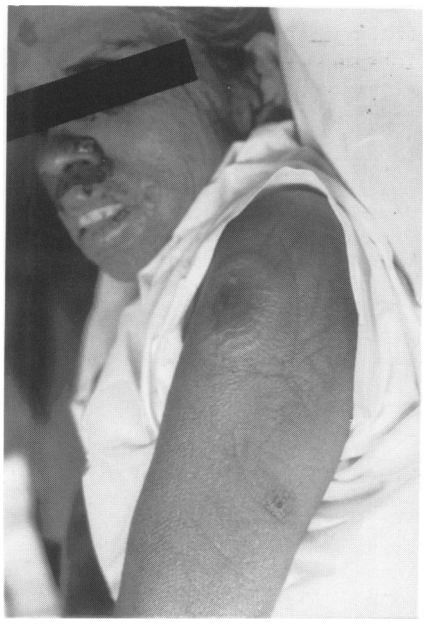
We hereby report a case of Sweet syndrome in a patient with chronic myeloid leukaemia. Sweet syndrome (acute febrile neutrophilic dermatosis)[1] is an acute non-infectious dermatosis characterised by sudden onset of painful, erythaematous nodules or plaques on the upper limbs, head and neck (see box). It may be idiopathic (80–90%) or secondary, usually associated with an occult malignancy, which is of haematologic origin in about 85% of cases.[2]

A 48-year-old woman with chronic myeloid leukaemia who had been receiving Busulfan for four years, presented with fever and skin lesions on left forearm, face and lips (figure). The major lesion was an ulcer 15 × 10 cm^2, margins punctuated with discrete vesiculopustular lesions, with crusting, induration and oedema, encircling the left forearm, extending from the arm to the back of the hand. Other lesions were vesiculopustular, seen over both lips, the angle of mouth, right eyebrow, right ear, scalp, submandibular region, palms and soles. Oropharyngeal and vaginal mucosae were normal.

Blood counts revealed a neutrophilic leucocytosis (12.9 × 10^9/l, 86% neutrophils). Culture from the forearm ulcer grew *Streptococcus pyrogenes*. However, fever did not respond to appropriate antibiotics. While in hospital, the patient developed three fresh erythematous, annular plaques with central depression on the left forearm. Repeat blood counts revealed a worsening leucocytosis (19.1 × 10^9/l, 94% neutrophils).

Histopathological study of the new plaques revealed acanthosis, dermal neutrophilic infiltrates with leucocytoclasia, but no evidence of vasculitis, suggestive of Sweet syndrome.

In view of the infected ulcer and immunocompromised status of the patient, she was administered oral potassium iodide (900 mg/day), instead of corticosteroids, which is the recommended treatment for Sweet syndrome. The patient demonstrated a dramatic response to treatment, with decrease of fever and regression of skin lesions within 48 hours.



Clinical features of Sweet syndrome

- fever, malaise, headache
- arthralgias, myalgias
- asymmetrical arthritis involving both small and large joints
- conjunctivitis
- symptoms of acute pneumonitis and recurrent respiratory symptoms with pulmonary infiltrates
- Dressler's syndrome with pleuro-pericardial effusions
- abrupt onset, tender violaceous or erythaematous plaques/nodules on skin of upper limb, head and neck
- skin ulcerations (rarely involving mucous membranes)
- hepatomegaly, splenomegaly

When associated with malignancies, Sweet syndrome has a more severe clinical manifesttion, characterised by a tendency to ulcerate, and involve mucous membranes and extracutaneous sites. The secondary form has no sex predilection, but the primary form is more common in women. The commonest haematologic malignancy with which it is associated is acute myeloid leukaemia;[3] the association with chronic myeloid leukaemia, although uncommon, does not herald an aggressive transformation of the disease. It may precede, accompany, or follow the malignancy. Oral corticosteroids, potassium iodide, non-steroidal anti-inflammatory agents, dapsone, and colchicine are all used in the treatment of Sweet syndrome.[4]

Pathogenetically, Sweet syndrome is hypothesised to be a neutrophilic hypersensitivity reaction to a non-specific immunological response in malignancy[5], to as yet unrecognised antigens present in the skin. A role for cytokines is also being considered.

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