Alveolitis associated with sulphamethoxypyridazine

C L STEINFORT, J WIGGINS, E A SHEFFIELD, E E KEAL

From the Brompton Hospital, London

ABSTRACT A woman developed alveolitis which appeared to be caused by sulphamethoxypyridazine and which resolved after withdrawal of the drug and six months' treatment with prednisolone.

We report a case of alveolitis associated with the use of sulphamethoxypyridazine, a long acting sulphonamide, that responded to drug withdrawal and treatment with corticosteroids.

Case report

A 59 year old woman, an ex-smoker, was referred with a six month history of progressive breathlessness and cough. The patient had started sulphamethoxypyridazine, 1 gram a day, 12 months previously for relief of painful mouth ulcers due to cicatricial pemphigoid. On examination she had tachypnoea and reduced chest expansion, but no added sounds. Abnormal results of investigations included an erythrocyte sedimentation rate of 25 mm in the first hour (normal 7-12 mm), widespread reticulonodular shadowing on the chest radiograph (figure), and mild restriction of lung volumes (FEV_1 1.90 litres, forced vital capacity (FVC) 2.16 l (73% predicted), and FEV_1/FVC 88%, with reduced carbon monoxide transfer factor (TLCO, 40% predicted). Serum electrolytes, urea, liver function, full blood count (eosinophil count 0.1/nl) and serum angiotensin converting enzyme were normal. Tests for antinuclear factor, autoantibodies, and avian precipitins gave negative results. The bronchoalveolar lavage fluid differential cell count showed 4% neutrophils, 5% lymphocytes, and 91% macrophages. A transbronchial lung biopsy specimen showed interstitial oedema and lymphoid infiltration with type 2 pneumatocyte hyperplasia but no features to suggest granulomatous lung disease.

A diagnosis of alveolitis associated with sulphamethoxypyridazine was made. The drug was stopped and prednisolone 30 mg/day started. The dose of prednisolone was then slowly reduced and stopped after six months. The patient's FVC increased to 90% predicted and TLCO to 65% predicted. The chest radiograph improved progressively and the patient remains well one year after withdrawal of the steroid.

Discussion

A causal association between sulphamethoxypyridazine and

the development of alveolitis is suggested by the temporal relation between administration of sulphamethoxypyridazine and the development of breathlessness, by the lack of typical histopathological features of any other disease, and finally by the improvement seen after drug withdrawal and corticosteroid treatment, which continued after the latter was discontinued. It was felt unjustifiable to rechallenge the patient with the drug because of the potential gravity of the lung disease.

Most of the previously reported cases of sulphonamide induced lung disease have occurred in patients treated with sulphasalazine for ulcerative colitis,¹⁻⁷ and immunological studies have confirmed that the alveolitis is caused by the sulphonamide component of this drug.⁵ Reactions to other sulphonamides, such as co-trimoxazole and sulphadimethoxine, have also been reported.^{6,8} The lung infiltrates were associated with peripheral eosinophilia in less than half of the reported cases and an underlying vasculitis has been implicated.⁶ Most of reported cases of sulphonamide associated alveolitis have occurred during prolonged drug administration, as in our case; the alveolitis generally responds to drug withdrawal and the addition of corticosteroid treatment, though one case was rapidly fatal despite a brief course

Chest radiograph taken at presentation showing widespread ill defined reticulonodular shadowing.

Address for correspondence: Dr John Wiggins, Brompton Hospital, London SW3 6HP.

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of high dose prednisolone.⁴ Clinicians treating patients with long term sulphonamide treatment should be aware of this unusual side effect.

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