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Mefenamic acid-induced bullous pemphigoid

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Summary: A 52 year old man developed bullous pemphigoid, Coombs' positive haemolytic anaemia and diarrhoea related to the use of mefenamic acid. Clinical manifestation of the bullous pemphigoid, haemolytic anaemia and diarrhoea resolved following discontinuation of the mefenamic acid. Mefenamic acid should be added to the list of agents that are known to induce bullous pemphigoid.

Introduction

Drug-induced cutaneous reactions are both common and varied. Drug-induced bullous pemphigoid eruptions are rare but have been reported with the use of frusemide (Fellner & Katz, 1976; Castel *et al.*, 1981), psoralens (Thomsen & Schmidt, 1976) and ibuprofen (Pompeova, 1981).

Renal impairment (Robertson *et al.*, 1980) and gastrointestinal manifestations (Hall *et al.*, 1983) have been reported frequently with the use of mefenamic acid (Ponstan). To our knowledge mefenamic acid has not been associated with the development of drug-induced bullous pemphigoid. We report such a case.

Case study

In September 1983 a 52 year old man presented to the local dental hospital. Presenting symptoms were of recurrent chronic oral ulceration with watery diarrhoea, bowels opening up to six times daily. Initial investigations were unhelpful. Punch biopsy of the ulcerated tongue revealed only non-specific inflammatory changes.

By November 1983 he had deteriorated and was referred to the gastrointestinal unit for further investigation. In addition to his tongue and mouth ulceration, he had developed a non-pruritic blistering eruption with firm tense bullae up to 5 cm in diameter affecting predominantly limbs and to a lesser extent trunk. Other features included watery diarrhoea with bowels opening up to 10 times daily, weight loss of 15 kg over the preceding 6 months, conjunctivitis and general malaise. Careful questioning revealed that his symptoms had started following the prescription of mefenamic acid 500 mg t.i.d. for severe osteoarthritis of his hip 9 months before admission. Further investigations showed: haemoglobin 11 g/dl with normal film, erythrocyte sedimentation rate 82 mm in the first hour, serum albumin 32 g/dl. The following investigations were normal: chest X-ray, cold agglutinins, cryoglobulins, cryofibrinogen, syphilis serology, sigmoidoscopy and biopsy, gastroscopy and jejunal biopsy, large and small bowel enemas, pancreatic function tests, circulating immune complexes, antinuclear factor, antimitochondrial antibody, antismooth muscle antibody, DNA binding tests. The Coombs' test was positive and antiparietal cell antibodies were present. Aspirate of fluid from the blisters grew *Staphylococcal aureus*. Skin biopsy demonstrated a subepidermal vesicle with the immunofluorescent finding of a marked deposit of IgG and C_3 in the basement membrane, findings consistent with the diagnosis of bullous pemphigoid. The mefenamic acid was stopped and one week later, without treatment, all the skin lesions were resolving. The diarrhoea ceased and the mouth ulceration improved. Within 4 months his weight increased 7 kg and his Coombs' test had become negative. Haemoglobin, erythrocyte sedimentation rate and serum albumin had returned to normal and his mouth had completely healed without scarring. The patient refused rechallenge with mefenamic acid. A repeat skin biopsy 6 months later demonstrated persistent IgG and C_3 in the basement membrane.

Discussion

Our patient exhibited two recognized side effects of mefenamic acid: Coombs' positive anaemia (Committee on Safety of Medicines, 1977), and diarrhoea, in addition to one not previously reported, bullous pemphigoid. The anaemia, diarrhoea and the clinical

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manifestations of bullous pemphigoid rapidly resolved and have remained quiescent over the past 12 months.

The finding of a subepidermal vesicle as well as marked IgG and C_3 deposition on the basement membrane supports our diagnosis of bullous pemphigoid. Our findings are different from the cicatricial pemphigoid reported with the use of clonidine (Van Joost *et al.*, 1980) and nadolol (Stage *et al.*, 1984) but similar to the bullous pemphigoid noted with ibuprofen and frusemide, where the lesions healed without scarring. Our lesions were therefore consistent with the diagnosis of bullous pemphigoid. It could, however, be suggested that the introduction of mefenamic acid activated subclinical bullous pemphigoid. The reversal of other recognised drug-induced effects of mefenamic acid, particularly that of the antibody-mediated Coombs' positive anaemia, would support a drug-induced effect. We feel that this drug may have induced bullous pemphigoid in our patient and that mefenamic acid should be added to the list of drugs already associated with the development of this complaint.

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