Erythrodema after clodronate treatment

Dr S PARS, P LESTANG, F LLOTE, and Prof A DRYLL (Hôpital Lariboisière, 75010 Paris, France) write: The bisphosphonates, including clodronate, are powerful inhibitors of bone resorption. Until now clinical studies of clodronate have shown good tolerability and, with no reports of any cutaneous side effects. We report here erythrodema with lesions of the mucous membranes after oral and intravenous clodronate administration.

A 70 year old man was admitted in June 1991 for vertebral pain and hypercalcemia which led to the diagnosis of stage II A amputinemia. A single infusion of 300 mg of clodronate was given, and a course of vincristine, melphalan, cyclophos- phamide, and prednisolone was also added with no mucous membrane lesions or punctate keratitis. On 10 June, clodronate (400 mg daily) was prescribed for a tachycardia. After the end of clodronate, no side effects were reported by the patient. He was admitted in Hospital, Kidderminster (letter).

Agranulocytosis associated with cefazolin

Dr C H Hsu and L C CHAN (Department of Pathology, University of Hong Kong, Queen Mary Hospital) write: A healthy 15 year old boy was given cefuroxine (Zinced) 750 mg intravenously every eight hours for eight days. He was treated with 1 g of clodronate which was stopped, and the patient was discharged from hospital. On 10 July his white blood cell count was normal, without eosinophilia; he had no infection; viral serology gave negative results. A histological examination of the skin showed epidermal changes, with a dermal lymphohistocytic and eosinophilic infiltration strongly suggestive of toxidermia.

Within a few days the eruption gradually regressed without residual pigmentation. Other drugs were continued without reappearance of the rash.

The delay in the appearance of the rash after the first administration of clodronate, the relapse following its reintroduction, and the regression after the end of clodronate treatment all support clodronate as the cause of the erythrodema, as do the pathological features and the fact that no other drugs were taken. The cutaneous side effects of bisphosphonates are uncommon. They have been reported with pamidronate1 and iodoxonate, but only rarely during 10 years' prescription of etidronate. No cutaneous reactions to clodronate have been reported to the French National Centre for Pharmacovigilance or the drug company.


Cyclosporin induced colitis

Dr J R C BOWEN and S SAIH (BMH Rinteln, BFPO 29, Germany) write: A 40 year old woman presented with a three year history of weight loss, lethargy, and pruritus. Biochemistry tests showed raised alkaline phos- phatase concentrations and a high titre of antinuclear antinuclear antibody. Liver biopsy confirmed a clinical diagnosis of primary biliary cirrhosis. Cholestatic syndrome was started for her pruritus, to which cyclosporin was added. Serum concentrations of cyclosporin on a dose of 150 mg daily were 92-90 ng/ml (124 ng/ml).

Five months later she complained of abdominal pain with increased bowel frequency, loose motions, and mucus per rectum. Investigations showed peripheral blood eosino- philia, but stool microscopy and culture gave negative results, as did upper gastrointestinal endoscopy and a histological examination of the lower duodenum. Colonoscopy, however, showed widespread colitis, confirmed histologically as a "non- specific" colitis.

Cyclosporin was stopped, and all gastrointestinal symptoms resolved within one week. Colonoscopy shortly afterwards showed improved macroscopic and histological appear-ances.

With the patient's permission she was rechallenged with cyclosporin. This resulted in a recrudescence of her symptoms within four days. Repeat colonoscopy showed a patchy colitis, which was worse than on her previous examination. Histologically the inflammation was comparable in specimens from the second examination, but this might have been due to the necessarily brief rechallenge.

Colitis associated with cyclosporin A has been reported on two previous occasions.1,2 In the first of these, however, drug concentrations were in the toxic range exceeding 640 nmol/l (800 ng/ml), and in the second case typical ulcerative colitis started while she was receiving cyclosporin and continued despite its withdrawal. To our knowledge this is the first reported case of a reversible cyclosporin induced colitis occurring in a patient with cyclosporin concentra- tions in the therapeutic range.


Transcutaneous overdose of terbutaline

Dr G J INGRAMS (Kidderminster General Hospital, Kidderminster D59, UK) and F B MORGAN (Aylmer Lodge Surgery, Kidder- minister) write: A 15 year old mildly asthmatic boy was admitted with tachycardia (rate 130 beats/min), a systolic murmur which left his sternal edge, and tremor. Feeling slight tightness of his chest after playing football, he had inhaled two puffs (500 g) of terbutaline. He then disappeared, leaving the aerosol on to a patch of itching tinea cruris in his groin produced cooling relief and administered at least eight puffs. Ten minutes later he developed respiratory failure, fast, irregular pulse rates and an uncomfortable feeling in his chest and therefore inhaled a further two puffs. Investigations showed hypo- kalaeemia (2.7 mmol/l), hypergly- caemia (14.8 mmol/l), normal arterial blood gas values, and sinus tachycardia. A subsequent echocardio- gram showed normal valves, and symptoms were consistent with terbutaline overdose and settled over 24 hours without specific treatment. The total inhaled dose (1 mg) was sufficient to produce a typical picture, but the total dose sprayed on to the skin (2 mg) was four times greater than the maximum dose for subcutaneous injection (500 g).

Although transcutaneous absorp- tion has not been documented for β2 agonists, the absorption of ter- butaline is increased across damaged tracheal epithelium in vitro.2 Over- dose of β2 agonists is associated with hypokalaeemia, which can cause sudden death.3 Transcutaneous absorption should be considered, particularly when nebulising atopic children with facial eczema and those with facial dermatitis.4


5 Bedy DJ, Barton, K, Stanford C. Irritant contact facial dermatitis due to nebulizer therapy. Toxicon 1989;24:1035-9.