Erythrodema after clodronate treatment

Drs J PARS, P LESTANG, F LOZET, 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 safety, 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 hypercalcaemia which led to the diagnosis of stage IlA amimostimelya. A single infusion of 300 mg of clodronate was given, and a course of vincristine, melphalan, cyclophosphamide, and prednisolone every four weeks. A haematological examination of the skin showed epidermal changes, with a dermal lymphohistiocytic and eosinophilic infiltration strongly suggestive of toxiderma.

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 drug had been administered.

The cutaneous side effects of bisphosphonates are uncommon. They have been reported with pamidronate1 and tiludronate,2 but only rarely during 10 years' prescription of etidronate. No cutaneous reactions to clodronate have been reported to the French National Centre for Pharmaco vigilance or the drug company.

Agranulocytosis associated with cephalosporin

Drs C H Htn and L C CHAN (Department of Pathology, University of Hong Kong, Queen Mary Hospital) write: A healthy 15 year old boy was given cefuroxime (Zinacef) 750 mg intravenously every eight hours for four days associated with a maximum dose which developed after orthopaedic surgery. As neither fever nor pneumonia improved cefuroxime was discontinued after 17 days and cefazolin substituted as a dose of 1 g intravenously twice a day. Twenty four hours later the patient had no fever and a full blood count showed haemoglobin 132 g/l, white cell count 6.30 x 10⁹/l with neutrophils 3.75 x 10⁹/l, and platelet count 379 x 10⁹/l. Coagulation and renal and liver function were normal.

On the seventh day of cefazolin administration fever recurred, and isolated leucopenia (white cell count 1.90 x 10⁹/l) associated with agranulocytosis (white cell differential +10% neutrophils, 1-25 lymphocytes, 0-61 monocytes, 0-04 eosinophils) was noted. Cefazolin was stopped and a bone marrow aspirate the next day showed a normocellular marrow with strikingly reduced myelopoiesis. Bacterial cultures and viral screen were negative. In view of the agranulocytosis, subcutaneous injection of granulocyte macrophage colony stimulating factor 1 phial daily was started. Both total white cell (4 x 10⁹/l) and neutrophil count (2-2 x 10⁹/l) recovered within 24 hours. Altogether two doses of granulocyte macrophage colony stimulating factor 1 phial daily were given, and the white cell counts remained sustained since then.

Transient leucopenia is recognised after cephalosporin administration and is more likely to occur after high doses and prolonged therapy.3 In our case we could not determine whether the agranulocytosis was due to cefazolin or cefuroxime (or both). The prompt recovery may have been due to the cessation of cephalosporin treatment rather than the granulocyte macrophage colony stimulating factor treatment. We suggest that patients should have regular full blood count while receiving cephalosporins.


Cyclosporin induced colitis

Drs J R C BOWEN and S SAMI (BMJ Rinteln, BFPO 29, Germany) write: A 40 year old woman presented with a two year history of weight loss, lethargy, and pruritus. Biochemistry tests showed raised alkaline phosphatase concentrations and a high titre of antinonochondrial antibody. Liver biopsy confirmed a clinical diagnosis of primary biliary cirrhosis. Cholestyramine was started for her pruritus, to which cyclosporin was added. Serum concentrations of cyclosporin at a dose of 150 mg daily were 92-900 nmol/l (124 nmol/l).

Five months later she complained of abdominal pain with increased bowel frequency, loose motions, and mucus per rectum. Investigations showed peripheral blood eosinophilia, 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." 4 Cyclosporin was stopped, and all gastrointestinal symptoms resolved within one week. Colonoscopy shortly afterwards showed improved macroscopic and histological appearances.

With the patient's permission she was rechallenged with cyclosporin. This resulted in a recrudesence 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 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 a patient 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 concentrations in the therapeutic range.


Transcutaneous overdrive of terbutaline

Drs G J INGRAMS (Kidderminster General Hospital, Kidderminster DY10 2QH) and F B MORGAN (Aylmer Lodge Surgery, Kidderminster) write: A 15 year old mildly asthmatic boy was admitted with tachycardia (rate 130 beats/min), a lushest systolic murmur at his left sternal edge, and tremor. Feeling slight tightness of his chest after playing football, he had inhaled two puffs (500 µg) of terbutaline. He then discovered that the aerosol pipe on to which itching tinea cruris in his groin produced cooling relief and administered at least eight puffs. Ten minutes later he developed fast, regular palpitations and an uncomfortable feeling in his chest and therefore inhaled a further two puffs.

Investigations showed hypo-kalaemia (2-7 mmol/l), hyponatraemia (14-8 mmol/l), normal arterial blood gas values, and sinus tachycardia. A subsequent echocardiogram showed normal ventricular size and function, and symptoms were consistent with terbutaline overdose and settled over 24 hours without specific treatment. The total inhaled dose (1 mg) was insufficient to produce toxic symptoms, as indicated by a normal electrocardiogram in vitro. Over-dose of β2 agonists is associated with hypokalaemia,5 which can cause sudden death.6 Transcutaneous absorption should be considered, particularly when numbing topical children with facial eczema and those with facial dermatitis.

5 Bedy DJ, Barton K, Stanford C. Irritant contact facial dermatitis due to nebulizer therapy. Forag Med 1988;64:360-7.