during the first 14 days of this treatment. To eliminate the risk of contaminating the fluid the calcium concentration was not measured before instillation. The estimated mean amount of calcium instilled during each cycle was 23.2 mmol and that in each bag after drainage was 7.4 mmol (range 4.1-9.8). The estimated mean amount of calcium absorbed per bag was therefore 15.8 mmol (range 13.4-19.1), roughly 69% of the total in the bag. Fasting serum calcium concentration was measured daily before instillation of the first bag of dialysis fluid. Two attempts to stop the intraperitoneal calcium supplements resulted in symptomatic hypocalcaemia. The supplements were finally stopped on the 150th postoperative day, the oral calcium and 1,25-dihydroxyvitamin D₃ supplements being continued.

Serum magnesium concentration in the months preceding operation averaged 1.54 mmol/l (range 1.21-1.87). Symptoms were not due to hypomagnesaemia as the serum magnesium concentration did not fall below the normal range at any time postoperatively.

Clinical course after subtotal parathyroidectomy. Arrows indicate symptomatic hypocalcaemia.

Comment

Although hypocalcaemia often occurs after parathyroidectomy for secondary hyperparathyroidism, the associated symptoms are seldom as severe or protracted as in our patient. Previous studies have shown that calcium supplementation may be necessary for more than a year after operation,^{4,5} but parenteral treatment is seldom required beyond the first week.^{3,5}

Intraperitoneal administration of calcium has a distinct advantage over intravenous administration in patients receiving continuous ambulatory peritoneal dialysis who have protracted symptomatic hypocalcaemia not controlled by oral supplements as it can be managed by the patient on an outpatient basis with minimal medical supervision. In the immediate postoperative period, however, intravenous infusion is better suited to the unstable situation. The peritoneal route is effective, convenient, and safe in patients receiving continuous ambulatory peritoneal dialysis who require parenteral calcium for more than a few days after operation.

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Rash mediated by immune complexes associated with ranitidine treatment

Ranitidine has established an important place in the treatment of peptic ulceration: rates of healing at six weeks are between 80 and 90%.¹ In its standard dose of 300 mg daily it is well tolerated and has few side effects. We report a vasculitic rash occurring in association with ranitidine.

Case reports

Case 1—A 65 year old man was treated with ranitidine 150 mg twice daily as the sole treatment for duodenal ulcer that had been proved endoscopically. One month after starting treatment he developed a maculopapular rash on his arms, legs, and trunk. The rash was itchy and scaly and made up of discrete papules, some of which had coalesced to form lesions up to 3 cm in diameter. Full blood count, erythrocyte sedimentation rate, biochemical profile, and serum immunoglobulin and complement concentrations were all normal, while tests for circulating immune complexes and autoantibodies yielded negative results. Routine histological examination of a skin biopsy specimen showed nothing remarkable, but immunofluorescence showed deposition of C3 and IgA in the dermal capillaries, which suggested that the condition was mediated by immune complexes. The rash faded two weeks after ranitidine was stopped. After giving his informed consent he was re-exposed to the drug several weeks later. Within one week of challenge a similar rash developed and the findings on immunofluorescence were identical with those seen previously.

Case 2—A 79 year old man with a benign gastric ulcer that had been proved endoscopically was treated with ranitidine 150 mg twice daily. Four weeks after starting treatment he noticed erythematous, itchy, scaly lesions on his arms and legs. No haematological, biochemical, or immunological abnormalities were found. Routine histological examination of a skin biopsy specimen showed perivascular lymphocytic infiltration, and immunofluorescence showed C3 and IgA in the smaller vessels, findings consistent with vasculitis. The rash cleared completely within two weeks of the drug being stopped.

Case 3—A 60 year old man with rheumatoid arthritis and ulceration of the pyloric channel was started on ranitidine 150 mg twice daily. Within two weeks he developed an itchy, scaly, erythematous rash on his trunk, arms, and legs. Histological examination of a biopsy specimen of the skin lesion showed nothing remarkable; immunofluorescence, however, showed fine granular deposition of IgA at the dermal-epidermal junction, a finding consistent with a diagnosis of dermatitis herpetiformis. Duodenal biopsy showed no evidence of enteropathy, and his rash resolved completely on withdrawal of ranitidine.

Comment

All three patients seem to have had a rash mediated by immune complexes and associated with treatment with ranitidine. The rash cleared on withdrawal of the drug, and an identical rash developed in the one patient rechallenged. Immunofluorescence showed deposition of C3 and IgA in the small vessels, which is typical of a vasculitic rash; drugs are a well recognised trigger for such a reaction.² Rashes such as urticaria that are due to a type I allergic reaction have been described in association with treatment with ranitidine³ and have been reported to the Committee on Safety of Medicines, but in extensive studies such lesions were associated with ranitidine only slightly more commonly than with placebo.⁴ Nevertheless, of the 87 adverse reactions probably due to ranitidine that had been reported to the Committee on Safety of Medicines by September 1987 (personal communication), 23 affected the skin, but none seem to have been a vasculitic reaction. With increasing use of ranitidine, particularly as maintenance treatment, awareness of this type of rash is important. We have reported these cases to the Committee on Safety of Medicines and to the manufacturer.

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