Gold colitis, therapy and confirmation of mucosal recovery by measurement of rectal potential difference

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Summary

A 38-year-old man with rheumatoid arthritis developed colitis after a course of 320 mg sodium aurothiomalate. Recovery comparable with that reported with corticosteroids or chelating agents was achieved by fluid replacement alone. Mucosal recovery was confirmed by measurement of rectal potential difference.

Introduction

Gold-induced enterocolitis is a rare but potentially fatal complication of chrysotherapy. Previous reports have described this reaction in women receiving < 245 mg of elemental gold (equivalent to < 485 mg of sodium aurothiomalate (Roe, Sears and Arnot, 1972; Kaplinsky, Pras and Frankl, 1973; Stein and Urowitz, 1976). Early recognition of this complication is essential as it carries a 50% mortality. Neither antibiotics, steroids nor dimercaprol are of proved value in treatment (Stein and Urowitz, 1976). In this case in a man (which appears to be the first reported), fluid repletion alone led to complete recovery. Return of normal mucosal cell function was confirmed by measurements of rectal potential difference (Edmonds and Pilcher, 1973).

Case report

In 1973, a 38-year-old lorry driver developed seropositive (Rose Waaler titre 1/64) rheumatoid arthritis affecting the metacarpophalangeal (MCP) and metatarsophalangeal joints.

His disease was initially controlled on chloroquine and aloxiprin, but because of increased MCP discomfort and erosive bone damage weekly chrysotherapy was started in July 1979. After a test dose of sodium aurothiomalate 10 mg, he had 2 injections of 20 mg and then the first of a weekly series of 50 mg doses. This was followed by 5 days' diarrhoea. During a 2-week holiday, he had no further gold. On return he was given 20 mg and then restarted 50 mg weekly injections of sodium aurothiomalate to a total dose

of 320 mg. His joint symptoms improved but diarrhoea developed again, increasing during 12 days to 20 green fluid stools/day and associated with malaise and vomiting. Examination showed an apyrexial patient with epigastric tenderness and increased bowel sounds. Rectal examination and sigmoidoscopy revealed green liquid stool, and a loss of mucosal vascular pattern with granularity between 10 and 15 cm. Rectal potential difference was between 0 mV and -4 mV (normal -33 to -45 mV) (Edmonds and Pilcher, 1973) in areas up to 12 cm from the anal verge. Rectal biopsy showed a reduction in the number of goblet cells in the crypts and an increase in non-specific inflammatory cells and eosinophils in the lamina propria. Electrolytes, liver function tests and plasma proteins were normal. Blood and stool cultures were negative on 4 occasions, *Salmonella* 'O' antibody titres were less than 1/20; Hb was 13.8 g/dl, the WBC was raised at $12.3 \times 10^9/l$ with a normal differential. Plasma Clq-binding activity was 6.3% (normal < 15%).

The patient was treated with 6 litres of i.v. fluids including potassium supplementation daily, food was stopped and gold therapy discontinued. His diarrhoea settled during the next 10 days. Two months later sigmoidoscopy showed normal mucosal appearances and the rectal potential difference had also returned to normal. Rheumatoid factor test had become negative. The patient described a marked improvement in his joint symptoms and sense of well-being as a result of chrysotherapy.

Discussion

Enterocolitis has been described after administration of gold, as gold sodium thiosulphate (Anderson and Palmer, 1940), the disodium salt of 4-sulphomethyl-amino-2-auriomercaptophenyl-sulphonic acid (Goldhammer, 1935) and as sodium aurothiomalate, suggesting that elemental gold is responsible for this toxic reaction. Toxicity may occur with low mucosal

gold concentrations which have been reported as being < 0.2 mg/100 g tissue in a fatal case (Anderson and Palmer, 1940). Such cases are associated with oedema, haemorrhage and ulceration throughout the gastrointestinal tract (Roe *et al.*, 1972). Fatal cases have been characterized by a decrease in serum albumin and globulins with a concurrent fall in rheumatoid factor titre. Surviving patients have characteristically maintained their serum proteins but undergone a decrease in IgM rheumatoid factor titre and a concurrent improvement in joint symptoms (Stein and Urowitz, 1976).

Rectal biopsy usually resembles ulcerative colitis with inflammatory cells in the lamina propria and occasional micro-abscesses in the crypts (Kaplinsky *et al.*, 1973). The finding of a moderate number of eosinophils in the lamina propria of this patient whose illness ran a benign course is of interest as it has been shown that patients with less aggressive ulcerative colitis have a greater number of eosinophils in the lamina propria than do those with severe disease (Heatley and James, 1978). It has been suggested that these eosinophils may moderate histamine-induced mucosal damage by elaborating prostaglandin E_1 and E_2 (Beeson, 1977). The finding of one normal Clq-binding activity taken mid-course in the illness is insufficient to rule out the association of immune complex deposition with gold colitis.

There may occasionally be difficulty in distinguishing gold-induced colitis from ulcerative colitis arising in a patient suffering from rheumatoid arthritis. In this patient, the return of rectal potential difference, the maintenance of which depends on the

mucosa's ability to transport sodium ions against a concentration gradient (Edmonds and Marriott, 1968), to normal 2 months after resolution of the colitis was supportive evidence that the colitis was a response to an acute insult rather than the beginning of a chronic inflammatory process.

Acknowledgments

We thank Dr P. W. Blower for permission to describe a patient under his care.

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