Non-coeliac flat jejunal mucosa

MARK BATT

Case history

A housewife aged 42 years, was admitted to hospital after suffering diarrhoea and weight loss over a period of six months. The symptoms were of relatively sudden onset but were not associated with recent travel, dietary changes, or treatment with antibiotics. It was her first such illness and at times she would have her bowels open up to 12 times each day passing pale stools which contained no obvious blood nor mucus. She had lost 9 kg weight and had vomited intermittently for 10 days before admission. Six months previously she had had epigastric symptoms and a subsequent barium meal showed a gastric ulcer and hiatal herniation. The digestive symptoms settled on treatment with cimetidine. On admission the patient looked unwell, was dehydrated but afebrile. Examination was normal except for signs of dehydration and a tachycardia. Sigmoidoscopy revealed pale liquid stool with no evidence of colitis. The histology of a rectal biopsy appeared normal. Routine blood tests showed haemoglobin 12 g/100 ml with normal indices, leucocytosis of $15.4 \times 10^9/l$ with a predominant granulocytosis, hypokalaemia 2.3 mmol/l; hypomagnesaemia 0.5 mmol/l, and hypoalbuminaemia 28 g/l. The following tests were normal: ESR; autoantibodies; serum folate, and B₁₂; renal and liver function tests (excepting hypoproteinaemia); and 5-hydroxyindole acetic acid excretion. There was a mild acute phase response. Detailed microbiological tests revealed no intestinal pathogens. Subsequent investigations provided a normal abdominal plain film, barium follow through (although some loops of small intestine appeared mildly distended), barium enema, indium labelled leucocyte scan, and abdominal ultrasound. Further small bowel investigation revealed a raised faecal fat at 77 mmol/24 hours (normal up to 18 mmol/24 h) and abnormally increased intestinal permeability (Cr-EDTA 2.0%; normal <0.7% against mannitol absorption 6.8%; normal >7.0%).

Endoscopic examination showed a normal gastric mucosa and a featureless duodenal mucosa from which biopsies were taken. Histological examination showed an irregular surface epithelium with subtotal villous atrophy, crypt hyperplasia, a moderate chronic inflammatory cell infiltrate in the lamina propria and a moderate number of epithelial lymphocytes (Fig. 1a). The appearances were consistent with

coeliac disease. The patient was discharged home on a gluten free diet and her condition improved.

The diarrhoea did not resolve completely, however, and three months later the patient was readmitted with further weight loss and diarrhoea. The histology of a biopsy of jejunal mucosa showed changes similar to the previous biopsies of duodenum. Colonoscopy revealed a macroscopically normal bowel although histology of the mucosa was consistent with a non-specific colitis. In an attempt to improve the patient's general condition total parenteral nutrition was instigated but stool volumes continued to average about 1 l per day. In planning

Fig. 1 (a) *Appearances of duodenal mucosa when patient was taking mefenamic acid (750–1500 mg/day).* (b) *Appearances of duodenal mucosa after recovery.*

Fig. 2 Body weight of patient and stool volumes before and during the two weeks after stopping treatment with mefenamic acid.

investigation for the causes of a secretory diarrhoea the patient was questioned closely regarding her dietary intake. She replied that nothing had passed her lips for seven days apart from her headache pills which she had brought into hospital. It was then disclosed that she had been taking mefenamic acid (250–500 mg tds most days) for non-specific headaches for a period of approximately one year. The analgesic was discontinued and the patient reverted to her normal eating habits. The diarrhoea resolved over a period of two weeks (Fig. 2). Four months later the intestinal permeability had returned to normal (Cr-EDTA 0.44% with a mannitol absorption of 12.5%) and further duodenal biopsies were taken. These showed normal morphology (Fig. 1b). Subsequently the patient has remained well. Her bowel habit is normal and she has regained her lost weight.

Discussion

Previous reports on the nature of the diarrhoea caused by mefenamic acid have provided a variety of possibilities. It has been postulated that steatorrhoea may be the result of a disturbance of the intraluminal phase of fat absorption and not of mucosal damage.¹ In contrast, two other patients with a similar clinical picture biopsies of the jejunal mucosa showed

abnormal villi, an inflammatory cell infiltrate, and hyperplastic crypts.² Other workers have reported colitis associated with infiltration of the mucosa of the proximal small intestine with inflammatory cells.³ Exacerbations of previously diagnosed ulcerative colitis have also been observed.⁴

Mefenamic acid is absorbed by the small intestine. A steady state for plasma concentration is reached within two to three days. There appears to be a small enterohepatic circulation (less than 5%) and after stopping the drug concentrations in the blood fall rapidly as conjugates and metabolites are cleared into the urine.

As with other non-steroidal anti-inflammatory drugs (NSAIDs) mefenamic acid alters intestinal permeability to disaccharide molecules and to Cr-EDTA. This may be caused by inhibition of prostaglandin synthetase. Prostaglandins are protective to the gastric mucosa and may have a similar role in the small intestine. Bjarnason and Peters have shown that NSAIDs frequently damage the small intestine⁵ but in this group of drugs mefenamic acid appears to be unique in its ability to cause flattening of the villi in the jejunum and marked steatorrhoea in sensitive subjects.

I would like to thank Drs G Neale and D G D Wight for permission to report this case.

Addenbrooke's Hospital,
Cambridge

References

- 1 Marks JS, Gleeson MH. Steatorrhoea complicating therapy with mefenamic acid. *Br Med J* 1975; iv: 442.
- 2 Chadwick RG, Hossenbous A, Collin-Jones DG. Steatorrhoea complicating therapy with mefenamic acid. *Br Med J* 1976; i: 397.
- 3 Hall RI, Petty AH, Cobden I, Lendrum R. Enteritis and colitis associated with mefenamic acid. *Br Med J* 1983; **287**: 1182.
- 4 Phillips MS, Fehilly B, Steward S, Dronfield MW. Enteritis and colitis associated with mefenamic acid. *Br Med J* 1983; **287**: 1626.
- 5 Bjarnason I, Peters TJ. Intestinal permeability, non-steroidal anti-inflammatory drug enteropathy and inflammatory bowel disease: an overview. *Festschrift. Gut* 1989; 11.