Idiopathic obstructive eosinophilic enteritis with raised IgE: response to oral disodium cromoglycate

N. H. GILINSKY
M.B.Ch.B. (U.C.T.), M.R.C.P. (U.K.).

R. E. KOTTLER
M.B.Ch.B., M.Med. (Rad. D.)

Gastrointestinal Clinic and the Departments of Medicine and Radiology, Groote Schuur Hospital, University of Cape Town, Observatory, Cape Town, South Africa

Summary

A 65-year-old man with a 20-year history of recurrent abdominal pain and vomiting was found to have eosinophilic enteritis affecting the muscularis layer of the distal ileum. Tests for malabsorption were negative. The IgE was raised but there was no evidence of an allergic predisposition. The symptoms, eosinophilia, and radiological abnormality responded to oral disodium cromoglycate.

Introduction

Eosinophilic gastroenteritis is an uncommon disease characterized by peripheral eosinophilia and eosinophilic infiltration of the gastrointestinal tract. The bone marrow shows a reactive eosinophilia and the symptoms and signs usually reflect the layer of bowel which is most severely affected. Predominant mucosal disease may be associated with malabsorption, muscle disease with obstructive symptoms and serosal disease with ascites. Laparotomy may be necessary to substantiate a diagnosis or to relieve obstruction. Corticosteroid therapy has been the most specific medication used while elimination diets have proved unsuccessful. This report is of a patient with clinical and histological evidence of eosinophilic enteritis involving the muscularis layer of bowel which responded to oral disodium cromoglycate.

Case report

A 65-year-old male was referred in 1981 for evaluation of recurrent abdominal pain. It had first begun in 1960, was situated in the upper abdomen and associated with vomiting. A barium meal failed to demonstrate peptic ulcer disease. The pain settled eventually after a few months but recurred in 1964. A repeat barium meal was negative and an enzyme-stimulated pancreatic function test, done in view of the episodic nature of the pain with intermittent radiation to the back, was also normal. There were recurrences in 1967 and 1973. On these occasions the pain was situated in the right iliac

fossa, was cramp-like and was accompanied by vomiting and diarrhoea.

In 1974 a barium follow-through demonstrated thickened folds in the terminal ileum. The haemoglobin was 12.5 g/dl and the ESR was 18 mm/hr. There was an absolute eosinophilia of $2.744 \times 10^9/l$. No evidence of parasitic infection could be found. In 1978 upper gastrointestinal endoscopy and a sigmoidoscopy, done after another episode of pain, were normal. Abdominal ultrasound, intravenous pyelogram and an oral cholecystogram done during three further bouts were normal. An admission abdominal radiograph in 1981 demonstrated localized air-fluid levels in the right upper quadrant.

There was no personal or family history of allergy and no drug ingestion of note. The exacerbations were not associated with a pyrexia or skin rash and at no stage were the stools positive for occult blood. Dietary review revealed no specific food intolerance. Examination revealed no stigmata of Crohn's disease, polyarteritis nodosa or lymphoma. The abdomen was slightly distended without free fluid being present. The bowel sounds were active. The Mantoux test was negative.

Investigations

Hb 12.6 g/dl; WBC $9.5 \times 10^9/l$; eosinophil count $3.515 \times 10^9/l$; ESR 57 mm/hr (Westergren). The bone marrow revealed prominent eosinophil precursors but was otherwise normal.

Plasma urea, electrolytes, calcium, phosphate, creatinine, cholesterol and liver transaminases were within normal limits. The total serum protein was 71 g/l and serum albumin 36 g/l. The serum alkaline phosphatase was 150 mmol/l and was of bowel and liver origin.

At endoscopy, the stomach and upper small bowel appeared normal and biopsies from these areas were normal. There were no parasites in the jejunal aspirate. Sigmoidoscopy and a rectal biopsy were normal. The stools did not contain Charcot-Leyden crystals, parasites or pus cells and bacteriology was negative.

A Schilling's test, 72-hr faecal fats, D-xylose excretion, glucose tolerance test, lactose breath test, serum iron, folate, vitamin B₁₂ and a prothrombin index were all normal.

Alpha chains, *Yersinia* antibodies, hepatitis B virus antigen and antibody tests were negative. Protein electrophoresis, IgG, IgA and IgM were normal. The IgE radio-immunoassay (Phadebas, Pharmacia) was 1304 mu./l. (normal <150 mu./l) Intradermal skin tests to 7 inhaled and 25 ingested antigens were negative. Radio-allergosorbent (RAST) tests for specific IgE antibodies to milk, egg white, wheat and fish were negative.

The chest radiograph was normal. A barium follow-through (Fig. 1) revealed an abnormal distal ileum with a thickened wall and consequent narrowed lumen. The folds were swollen without mucosal ulceration.

Subsequent course

A repeat eosinophil count after a course of anthelmintic therapy was $3.696 \times 10^9/l$. A full thickness ileal biopsy was done to substantiate a diagnosis of eosinophilic enteritis. At laparotomy there was no ascites or lymphadenopathy. The large bowel appeared normal but the distal ileum was markedly thickened and rigid. The mucosa, visualized via a small sigmoidoscope passed through an enterotomy, appeared normal. Full thickness ileal biopsy revealed a normal villous pattern and cell population. However, the muscularis mucosa contained a dense infiltrate of eosinophils and the muscle fibres were splayed by a mild interstitial oedema (Fig. 2). A skeletal muscle biopsy revealed no evidence of arteritis and the only abnormality in a needle liver biopsy was occasional eosinophils in the portal tracts.

FIG. 1. Widespread distal ileal abnormality consisting of thickened walls (arrowed), swollen folds and narrowed lumen.

FIG. 2. Ileal biopsy showing infiltration of the muscularis by a dense infiltrate of eosinophils. The fibres are splayed with a mild interstitial oedema (HE, $\times 400$).

FIG. 3. Three months after starting treatment, appearances are virtually normal.

Oral disodium cromoglycate was prescribed, but as the patient would only consent to a maximum of fifteen 20 mg capsules (the only locally available strength) per 24 hr, he received a total of 300 mg in divided doses per day. After 14 days of medication the eosinophil count was $0.378 \times 10^9/l$ and IgE was 540 mu./l. Two months later the eosinophil count was $0.325 \times 10^9/l$ and IgE was 240 mu./l. His weight had increased from 69 kg to 75 kg and he was asymptomatic. The serum albumin had increased to 42 g/l and the alkaline phosphatase had decreased to 110 mmol/l. A repeat small bowel barium study at 3 months was virtually normal (Fig. 3).

Discussion

Eosinophilic gastroenteritis, an uncommon disorder, probably occurs more often than is generally realized. Although a proportion of patients are atopic individuals and have evidence of a food allergy (Klein *et al.*, 1970; Ureles *et al.*, 1961) there are a number where no secondary cause such as parasites, drugs or associated vasculitis can be found. There have been reports of an association with eosinophilic infiltrations of other organs (Gregg and Utz, 1974; Rodriquez *et al.*, 1973) but these cases may be part of the hypereosinophilic syndrome which can involve multiple organs other than the gastrointestinal tract (Chusid *et al.*, 1975).

There is conflicting evidence on the role of food allergy. One text includes abnormal symptoms or signs following ingestion of specific foods as a criterion for diagnosis (Greenberger and Gryboski, 1978), while another concludes that hypersensitivity to food is not required in order to establish a diagnosis (Caldwell *et al.*, 1978).

Food allergy appears to be an unlikely mechanism in this patient in view of the negative history, normal mucosa, distal involvement of the gut, negative skin tests and negative RAST. It is difficult to attribute involvement of the deeper layers to contact with allergen in the absence of mucosal involvement.

Oral sodium cromoglycate has been used in the treatment of inflammatory bowel disease (Henderson and Hishon, 1978; Mani *et al.*, 1976), food allergy (Vaz, Tan and Gerrard, 1978) and, more recently, in gold-induced eosinophilic enterocolitis (Martin *et al.*, 1981). However, in the latter case improvement occurred with the withdrawal of the offending agent. In the only other report of response to sodium cromoglycate in eosinophilic enteritis (Heatley, Harris and Atkinson, 1980), the patient developed polyarteritis nodosa and this may have been the disease from the outset. In both cases the patients had the mucosal form of the disorder which was secondary to another cause.

The response to the sodium cromoglycate in this

patient was impressive in that there was a dramatic early fall in the long-standing eosinophilia. The patient gained weight, became asymptomatic and a repeat barium study was virtually normal. It is possible that the disodium cromoglycate was either absorbed through the gut wall to act on the abnormal muscularis section of bowel or, alternatively, acted on the mucosal surface preventing the release of mediators which act at the level of the muscularis mucosa.

This case also illustrates the difficulty encountered in diagnosing and monitoring patients whose sole involvement is limited to the muscularis layer. In this setting conventional endoscopic biopsies and a wide range of tests for malabsorption can be completely normal. Peripheral eosinophilia can be the only clue for diagnosis and therefore a simple differential white cell count is mandatory in all patients with 'obscure' abdominal complaints.

Caldwell *et al.* (1978) failed to demonstrate any evidence for an IgE-mediated mechanism in the obstructive form of eosinophilic gastroenteritis. However, this case demonstrates that such mechanisms may indeed be operative in those with predominantly muscle layer involvement, and that disodium cromoglycate is of value in the IgE-dependent group. This would be useful where the alternative therapy, corticosteroids, is inadvisable.

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