Case reports

Coeliac disease presenting with intestinal pseudo-obstruction

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SUMMARY A 22 year old woman presenting with recurrent intestinal pseudo-obstruction is reported. Jejunal biopsy showed subtotal villous atrophy which improved markedly during a period of total parenteral nutrition and with steroid treatment. It did not relapse on a gluten free diet. The reasons why this patient represents a case of coeliac disease with secondary pseudo-obstruction, rather than primary intestinal pseudo-obstruction with secondary bacterial overgrowth, is discussed.

Intestinal pseudo-obstruction is a syndrome in which the symptoms and signs of intestinal obstruction occur without an obvious mechanical cause.¹ This rare condition may occur in patients with collagen, neurological, and endocrine diseases or may be iatrogenic.² In some cases no aetiological factor is apparent – primary idiopathic intestinal pseudo-obstruction.²

Coeliac disease has been suggested as a cause of intestinal pseudo-obstruction.^{3,4} Ineffective intestinal propulsion of any aetiology, however, may result in bacterial overgrowth³⁻⁹ with attendant intestinal mucosal damage^{6,9} and subtotal villous atrophy in extreme cases.⁷ It has been suggested² that those cases described as secondary to coeliac disease, may in reality, have been cases of primary pseudo-obstruction complicated by bacterial overgrowth.

We report here a patient who presented with intestinal pseudo-obstruction and in whom the diagnosis of coeliac disease is not in reasonable doubt.

Case history

A 22 year old female secretary presented in June 1981 with increasingly frequent attacks of watery

diarrhoea, abdominal bloating, and nausea. The most recent attack had been continuous for six weeks and was associated with 5 kg weight loss. Her mother recalled that symptoms began at the time of weaning, abated during childhood, and recurred in 1979 when they were precipitated by milk products. The patient had lost no time from school and had developed normally with menarche at the age of 12. Examination revealed a thin, normally developed woman, height 1.63 m, and weight 50 kg. She was afebrile, clinically euthyroid, and without finger clubbing or skin rash. The abdomen was mildly distended with an increase in bowel sounds but no visible peristalsis. Systemic examination was otherwise normal, as was sigmoidoscopy. Full blood count, urea and electrolytes, and liver function tests were normal (Na^+ 136 mmol/l, K^+ 3.9 mmol/l, Ca^{2+} 2.1 mmol/l, serum albumin 35 g/l). Abdominal radiograph suggested distal small bowel obstruction. Laparotomy showed a mobile caecum with a thick congenital fibrous band running across the terminal ileum to the caecum, and a redundant sigmoid colon. Although the band was not obviously obstructing, it was divided and the caecum plus 10 cm of ileum resected. Ileal histology showed a patch of lymphoid hyperplasia in an otherwise normal mucosa.

Postoperatively, the patient was asymptomatic for three months but then returned with continuous diarrhoea, 10 kg weight loss and abdominal cramping pains, initially intermittent, but later

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continuous, and accompanied by vomiting. Examination showed a pale, apyrexial, hypotensive (BP 90/60), dehydrated, ill patient, with generalised muscle wasting, deep vein thrombosis in the left calf, bilateral pitting oedema of the ankles, and widespread superficial bruises. Her abdomen was distended with obstructive bowel sounds. Rectal examination showed steatorrheic stool.

Relevant investigations were: Hb 10.9 g/dl, serum folate 0.5 $\mu\text{g/l}$ ($n=3-16$), red cell folate 109 $\mu\text{g/l}$ ($n=200-600$), prothrombin time 28 seconds, serum sodium 131 mmol/l, potassium 3.1 mmol/l, albumin 20 g/l, corrected calcium 2.33 mmol/l. Serum cortisols were normal and three day faecal fat output was 154 mmol despite a restricted fat input. Plain abdominal radiograph showed recurrent intestinal obstruction.

The patient was heparinised and total parenteral feeding instituted. One month later her weight had increased by 3 kg, haemoglobin was 13.5 g/dl, and serum albumin 29 g/l. Despite the biochemical and clinical improvement, intestinal obstruction recurred whenever oral feeding was attempted. Consideration of systemic diseases reportedly associated with intestinal pseudo-obstruction showed no clinical evidence of primary muscle, nerve, or collagen vascular disease. Serum thyroxine was 93 nmol/l; repeated blood glucose estimations were normal. Antinuclear factor, antimitochondrial antibody and autoantibodies to double stranded DNA were not detected, but antireticulin antibodies were very strongly positive. Serum immunoglobulins were normal. HLA tissue type was A10, 29; B12, 17. Intestinal fluid was not cultured, but metronidazole 200 mg tds was given to treat a possible bacterial overgrowth of the small intestine, and ampicillin and cloxacillin for an infection in her central venous cannula.

A second laparotomy was undertaken in view of the possibility that the redundant sigmoid colon was producing an intermittent volvulus, and to obtain a full thickness jejunal biopsy. There was no obvious obstructing lesion but a partial sigmoid colectomy was performed and a feeding jejunostomy fashioned. Histology of the jejunum showed subtotal villous atrophy, crypt hyperplasia, and infiltration with inflammatory cells (Fig. 1). The nerves and muscle coats appeared normal on both light and electron microscopy. Symptoms of intestinal obstruction recurred when feeding *via* the jejunostomy was started, and parenteral nutrition was reinstituted on the seventh postoperative day together with neostigmine (on day 14) in an attempt to stimulate peristalsis. From the 13th postoperative day, large volumes of gastric juice, pH 2.0, were aspirated, to a maximum of 8 litres per day. Cultures

Fig. 1 Jejunal biopsy obtained at laparotomy (H & E $\times 140$, orig. mag.). There is villous atrophy, crypt hyperplasia, and mucosal inflammatory cell infiltrate.

of the aspirate and from the jejunostomy tube were negative. Serum gastrin at 35 ng/l was normal. Withdrawal of neostigmine after three days and intravenous infusions of cimetidine and zinc had no effect. A gastrografin meal (Fig. 2) showed diminished propulsion from stomach to duodenum, with duodenal dilatation. Contrast introduced *via* the jejunostomy had not passed into the colon at 24 hours. Throughout the period of parenteral feeding and after the second laparotomy, blood urea and electrolytes, serum calcium, magnesium, and zinc remained within normal limits. There was no apparent metabolic cause for a postoperative ileus.

Continuing clinical deterioration forced the introduction of prednisolone 60 mg/d intravenously on the 23rd postoperative day and resulted in a dramatic fall in gastric aspirate without improvement in the ileus. Intravenous metoclopramide and indomethacin suppositories were started on the 34th postoperative day and thereafter she was able to tolerate oral fluids. A repeat gastrografin meal showed rapid transit of contrast to the duodenum

Fig. 2 *Supine abdominal radiograph taken 24 hours after instillation of gastrografin via the nasogastric tube and jejunostomy. Stomach has not completely emptied, small bowel is dilated and no contrast has reached colon.*

and despite small bowel dilatation there was active peristalsis with contrast appearing in the colon by three hours. After a period of an elemental diet she was weaned on to a gluten free diet and parenteral feeding discontinued. Repeat plain abdominal radiograph showed resolution of distension; although a few fluid levels were visible in the right iliac fossa, these were considered to be within normal limits.

Repeat jejunal biopsy six weeks after the first biopsy and 10 weeks after her last known ingestion

of gluten showed dramatic histological improvement (Fig. 3). Disaccharidase enzymes showed low normal concentrations of lactase, 15.4 U/g protein (n=10–190) and trehalase, 12.2 (10–100); and subnormal levels of sucrase and isomaltase: Maltase 48.2 (130–450), sucrase 0 (60–170), isomaltase 4.3 (40–130). She was discharged on a gluten free diet, prednisolone 15 mg/d, and metoclopramide 10 mg tds. Steroids and metoclopramide were discontinued after two and eight weeks respectively, with no recurrence of symptoms.

Fig. 3 Jejunal biopsy six weeks postoperatively (H & E $\times 140$, orig. mag.). There is marked improvement in villous pattern, although occasional branched forms occur, and a chronic inflammatory cell infiltrate of the lamina propria remains.

During 12 months' outpatient review the patient has remained in perfect health apart from the occurrence of diarrhoea on two occasions after inadvertent ingestion of gluten. Faecal fat excretion has returned to normal at 44 mmol/3 days. Jejunal biopsy in March 1982 showed further improvement histologically and an increase in all disaccharidase levels: lactase 58.6, trehalase 29.7, maltase 79.7, sucrase 9.5, and isomaltase 9.4 U/g protein. Further jejunal biopsy has been precluded by the patient becoming pregnant.

Discussion

The possibility that this patient has the syndrome of primary intestinal pseudo-obstruction with secondary bacterial overgrowth causing villous atrophy is unlikely. The abnormalities on light and electron microscopy that have been described in the muscle coats or nerve plexuses in some patients with

intestinal pseudo-obstruction^{4 9 10} were not present in this case, and treatment with metronidazole and broad spectrum antibiotics made no impact on the clinical course, as might have been expected if bacterial overgrowth were significant. Furthermore, the fact that she has been well and symptom free for over 12 months is strong evidence against primary pseudo-obstruction. There was no evidence radiologically or at laparotomy of ulcerative jejunitis and there was no biochemical abnormality that might have caused an ileus.

We believe that this patient has coeliac disease complicated by secondary intestinal pseudo-obstruction. The classical time course of symptoms with onset at weaning, symptomatic improvement with age and relapse in early adult life, together with the subtotal villous atrophy at jejunal biopsy and clinical and histological remission when gluten ingestion ceased, fulfil accepted diagnostic criteria.^{11 12} We did not feel justified in subjecting a patient who had been so severely ill to a formal gluten challenge early in her remission, although she has inadvertently challenged herself on two occasions with the production of diarrhoea. More recently, gluten challenge has been precluded by her pregnancy. The high titre of antireticulin antibodies, however, is further support for the diagnosis^{13 14} and although she did not have the typical HLA typing of A1, B8 associated with coeliac disease, this combination is absent in 25% of proven cases.¹⁵ It is unusual for sucrase and isomaltase activities to recover more slowly than lactase on gluten withdrawal¹⁶ but we have observed this phenomenon in a previous patient (unpublished data). These levels do not indicate congenital sucrase-isomaltase deficiency, as in that condition the enzymes are absent and would not be expected to recover as in this patient. That this severe case of coeliac disease responded histologically so quickly to gluten withdrawal is probably related to the long period of parenteral feeding and elemental diet which guaranteed total exclusion of gluten, unlike the majority of patients who may continue to ingest small amounts of gluten inadvertently.

To our knowledge, the only previous reports of pseudo-obstruction complicating coeliac disease are those of Ingelfinger³ in 1943, who described a patient with non-tropical sprue with abdominal distension and vomiting whose symptoms persisted despite three operations, and Naish, Capper, and Brown⁴ in 1960, who in a description of three patients with pseudo-obstruction stated that one had the histological appearances of adult coeliac disease on biopsy but gave no further details. In neither case was the possibility of idiopathic pseudo-obstruction with bacterial overgrowth excluded, but our case

confirms that coeliac disease may indeed lead to pseudo-obstruction.

The two previous reports contain no information on the effect of gluten withdrawal on bowel motility. It is recognised that the clinical response to gluten withdrawal is dependent upon the length of histologically involved intestine and may precede by many months reversion of the proximal intestinal lesion to normal.¹⁷ Yet in our patient, pseudo-obstruction persisted for more than eight weeks after gluten withdrawal by which time the histological appearances of the proximal jejunum had markedly improved. Only after the introduction of metoclopramide and indomethacin did motility return. Indomethacin has been used successfully in a previous patient with primary intestinal pseudo-obstruction who had raised prostaglandin E concentrations,¹⁸ but we have no information about the prostaglandin concentrations of our patient. Metoclopramide has also been used,¹⁹ but with no success. It may be that in our patient the drugs served as initiators of function in a bowel returning to normal because of gluten withdrawal.

The cause of the gastric hypersecretory state in the immediate postoperative period remains obscure. Coeliac disease produces a hypersecretory state in the small bowel²⁰ but here the secretion was of gastric origin. Small intestinal resections in animals give rise to hypergastrinaemia^{21 22} and gastric hypersecretion may occur after jejunoileal bypass.²³ Gastrin levels, however, were normal in this patient and no small intestine was resected at this laparotomy. The hypersecretion may have been augmented by the neostigmine, but preceded its introduction and did not abate on its withdrawal.

This case offers the strongest argument to date that coeliac disease may cause intestinal pseudo-obstruction. It should be considered especially in children and young adults, in order that unnecessary laparotomy, as occurred here, may be avoided. This case shows how refractory the motility disorder can be and illustrates the need to persist with a gluten free diet, together with supportive parenteral nutrition as needed. Treatment with metoclopramide and indomethacin may accelerate recovery. Any further case should perhaps be studied with respect to neurohormonal function.

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