Proctosigmoiditis and coeliac disease

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SUMMARY Of 80 children with proved coeliac disease, 2 presented with an associated disease of the distal portion of the large intestine. In one child the family history and the extension, localisation, and characteristics of intestinal lesions made us suspect ulcerative colitis; in the other we made a diagnosis of milk-induced colitis.

In nine years we have diagnosed 80 cases of proved coeliac disease using ESPGAN diagnostic criteria (Meeuwisse, 1970). We report 2 patients in whom active coeliac disease was associated with proctosigmoiditis.

The association of coeliac disease with other gastrointestinal disorders such as cystic fibrosis (Goodchild *et al.*, 1973) and duodenal ulcers has been reported (Bayless *et al.*, 1974); Bayless *et al.* (1977) described one case and reviewed many more in which proved or presumed coeliac disease was complicated by multiple ulcerations of the small intestine, but to our knowledge this association has not been described in children.

Case reports

Case 1. A 5-month-old girl was admitted to hospital in January 1974 because of failure to thrive, anorexia, intermittent diarrhoea, and occasional vomiting. She had been born by caesarean delivery after a slightly prolonged (42 weeks) normal pregnancy. At birth she weighed 4 kg and her condition was satisfactory. A sister had died of asphyxia immediately after birth; her mother suffered from ulcerative colitis; her father had irritable colon syndrome. She was fed with a humanised milk formula from birth to age 3.5 months, when a formula of fresh cows' milk conventionally diluted and with added sucrose and ground biscuits was introduced. Up to age 4.5 months she passed infrequent formed stools; then her bowel movements became irregular with bouts of loose, watery, mucous stools. On admission she looked moderately wasted, with dependent oedema; her weight was below the 3rd centile and the abdomen was distended and rather tense; craniotabes and

Trousseau's and Chvostek's signs could be demonstrated.

Hb, red and white blood cell (WBC) counts, and serum iron were normal. Serum proteins: total 5.65 g/100 ml (56 g/l), albumin 4.9 g/100 ml (49 g/l), globulin 1.56 g/100 ml (15 g/l) A/G ratio 2.63. Serum calcium 3.0 mEq/l (1.5 mmol/l) (normal range 4.4-5.3), alkaline phosphatase 177 mU/ml (normal range 34-162). Urine normal. Sweat chloride normal (32 mEq/l). Stool examination showed abnormal quantities of digested fats; average faecal fat excretion was 3.61 g per day, reducing substances (Kerry test) were absent, tryptic activity was normal. Stool cultures showed a prominent growth of *Aerobacter aerogenes*. Stool specimens gave positive tests for blood.

One-hour blood D-xylose, performed about 20 days after gluten withdrawal was 27 mg/100 ml. Jejunal biopsy showed total villous atrophy. X-rays showed diffuse demineralisation of bones, atony, and dilatation of small bowel loops with barium column segmentation and clumping. A barium enema examination after evacuation with air contrast showed irregular mucosal thickening in the transverse and sigmoid colon, suggestive of an active inflammatory process.

Sigmoidoscopic examination to 20 cm disclosed an oedematous hyperaemic friable mucosa and at 7 cm a small irregular ulcer surrounded by pseudopolyps. From the margin of this lesion a punch biopsy was obtained which on histological examination showed oedematous thickening of the lamina propria with a chronic nonspecific inflammatory infiltrate of plasma cells and some eosinophils.

She was put on a gluten-free diet and was treated for 4 months with sulphasalazine 25 mg/kg per day given in 3 divided doses. She progressed satisfactorily for a year on a gluten-free and acidified milk-containing diet.

One year later all signs and symptoms of colitis had disappeared; they were not present on a third readmission after 7 months of gluten challenge, notwithstanding the total atrophic changes in jejunal mucosa, and they have not reappeared.

Case 2. A girl aged 29 months was admitted to hospital in December 1973 because of failure to thrive and anorexia. The disturbance had started when she was 7 months, with anorexia, stunted growth, irregular bowel movements with dark loose greasy, frothy, bulky, foul stools, alternated with formed mucous stools. Five months before admission she suffered an acute nonspecific gastroenteritis and began losing weight. She was born at 37 weeks' gestation weighing 2.9 kg. She was fed for the first 3 months with a humanised cows' milk formula, then with fresh cows' milk conventionally diluted and with added cereals. Her father and maternal grandmother suffered from irritable colon syndrome.

On examination she looked ill and wasted and was well below the 3rd centile for height and weight. She showed a diffusely increased pigmentation of skin, pale lips and nail-beds, prominent frontal bossing, funnel-shaped thorax with beading of the ribs; the teeth showed defects of the enamel and

extensive caries. The abdomen was prominent and distended but soft; the liver was firm and moderately enlarged, its smooth inferior edge reaching 4 cm below the costal margin; the spleen was palpated at the costal margin.

Hb 11.7 g/100 ml (11.7 g/dl) with moderately hypochromic film, Hb electrophoresis normal, WBC normal. ESR 11 mm in 1 hour. Total serum proteins 5.85 g/100 ml (58 g/l), albumin 4.45 g/100 ml, globulin 1.40 g/100 ml (14 g/l). Serum immunoglobulins: increased IgG and IgA, normal IgM. Serum calcium 4.2 mEq/l (2.1 mmol/l) normal phosphorus, lowered serum iron 20 µg/100 ml (3.6 µmol/l). Sweat test 38 mEq/l chloride. Stool examination: moderately lowered tryptic activity, copious fats and starches, identifiable meat fibres. Tests for occult blood in stools markedly positive. Faecal fat excretion 4.5 g a day. One-hour blood D-xylose: 5 mg/100 ml; 5-hour urinary xylose excretion: 11%.

A peroral jejunal biopsy showed total villous atrophy (Fig. 1). X-rays showed marked demineralisation of bones, distended small bowel loops, with barium column clumping and flocculation; appendix proximally filled; normal colonic haustration.

A barium enema showed an essentially normal

Fig. 1 Duodenal mucosa (Case 2) showing flattened villi covered with cuboidal surface epithelium heavily infiltrated with lymphocytes; in the markedly thickened lamina propria, plasma cells are particularly prominent. (H. and E. $\times$ 310).

colon. Rectosigmoidoscopic examination to 15 cm showed a hyperaemic, friable bleeding mucosa, pseudopolyps at 7 cm, at 5 cm a small bleeding ulcer with irregular, slightly elevated margins. A mucosal biopsy showed marked oedema of the lamina propria with diffuse chronic inflammatory infiltrate, the glands and superficial epithelium were well preserved (Fig. 2). She was treated with a gluten- and cows' milk-free diet and daily enemas of 6-methyl-prednisolone acetate, guaiazulene and gefarnate for a month. She was seen again after one year of poor dietary compliance. The signs of colitis had disappeared, the test for occult blood in stools were repeatedly negative, and the jejunal mucosal biopsy showed subatrophic changes. Two years later cows' milk was introduced and it did not cause relapse of colitis.

Discussion

In both these cases of proved coeliac disease, involvement of the colon was suspected mainly because occult blood was present in the stools. In Case 1, the rapid downhill course, and the onset of diarrhoea a fortnight after the introduction of gluten pointed to the presence of an associated disorder. X-ray examination showed involvement of the transverse and sigmoid colon, sigmoidoscopic examination demonstrated a small irregular ulcer to 7 cm, which on histological examination showed oedema, and chronic inflammatory reaction of the lamina propria.

In Case 2 x-ray examination was negative, while sigmoidoscopic and histological examinations

showed lesions similar to those of Case 1. In Case 1 several features suggested an initial episode of ulcerative colitis, the severity of symptoms, the extension and localisation of lesions on x-rays and the family history favoured this hypothesis. The ensuing favourable course and the absence of relapses for 2 years may seem scarcely compatible with the diagnosis, but in the remitting type of ulcerative colitis, after the initial stage, a permanent remission may occur (Roy *et al.*, 1975). The connection between coeliac disease and lesions of the colon is obscure. In adult coeliac disease Bayless *et al.* (1974, 1977) have described the development of multiple small bowel ulcers which they regarded as a complication of coeliac disease of uncertain cause. Falchuk and Falchuk (1975) reported a case of coeliac disease, IgA deficiency, and ulcerative colitis in an adult; in this patient treatment with corticosteroids and a gluten-free diet produced a remission of the malabsorption syndrome but the colitis failed to respond to the treatment.

In Case 2 we think that milk-protein-induced proctosigmoiditis should be considered: the disappearance of symptoms after the simultaneous withdrawal of milk and gluten from diet seems to support the diagnosis as milk-protein intolerance is a likely complication of coeliac disease (Kuitunen *et al.*, 1975). In these cases clinical course and laboratory studies make specific infection seem unlikely. In both patients the challenge with gluten induced total atrophic changes in the jejunal mucosa but did not elicit symptoms of involvement of the colon.

Fig. 2 Rectal mucosa (Case 2) showing lamina propria markedly thickened and densely infiltrated with mononuclear cells. (H. and E. $\times 125$).

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