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Case reports

Association of coeliac disease and inflammatory bowel disease

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SUMMARY The association of coeliac disease and inflammatory bowel disease is rare, as only three individual cases have been reported. Four additional cases of the association are described. A review of the prevalence figures for the two disorders suggests that this is more than a chance association.

The association of coeliac disease and inflammatory bowel disease is rare, as only three individual cases have been reported. The first report concerned a patient with established coeliac disease who eventually developed Crohn's disease,[1] the second was a patient with Crohn's disease and severe growth retardation who was later found to have coeliac disease,[2] and the third was a patient with ulcerative colitis and coeliac disease associated with selective immunoglobulin A deficiency.[3] Salem and his colleages[4] described a patient with ulcerative colitis and a flat jejunal biopsy and similar changes in a second patient.[5] Other authors have accepted that both these patients have coeliac disease and inflammatory bowel disease and thus might constitute two additional examples of the association.[6]

This paper describes four patients who had coexistent coeliac disease and inflammatory bowel disease. Three patients had ulcerative colitis and the other Crohn's disease. The prevalence rates of the two disorders have been examined to assess the significance of the association.

Case reports (Table)

CASE 1

J S, who was born on 13 December 1944, presented in August 1975 with a six month history of diarrhoea, discomfort in the left iliac fossa, and intermittent rectal bleeding. He had not travelled abroad. Physical examination was normal. Investigations showed haemoglobin 12 g/dl, serum albumin 41 g/l, serum seromucoids 0·98 g/l (normal $<1{\cdot}50$ g/l). Sigmoidoscopy revealed perianal skin tags, and an abnormal rectal mucosa with contact bleeding. Infiltration of the lamina propria by polymorphonuclear cells, plasma cells, and eosinophils was noted on rectal biopsy. There were similar changes in the rectal biopsy obtained three months later but, in addition, non-caseating granulomata were identified in the submucosa. Radiological examination of the large intestine demonstrated an asymmetrical loss of the haustral pattern and an abnormal mucosa in the sigmoid colon compatible with Crohn's disease.

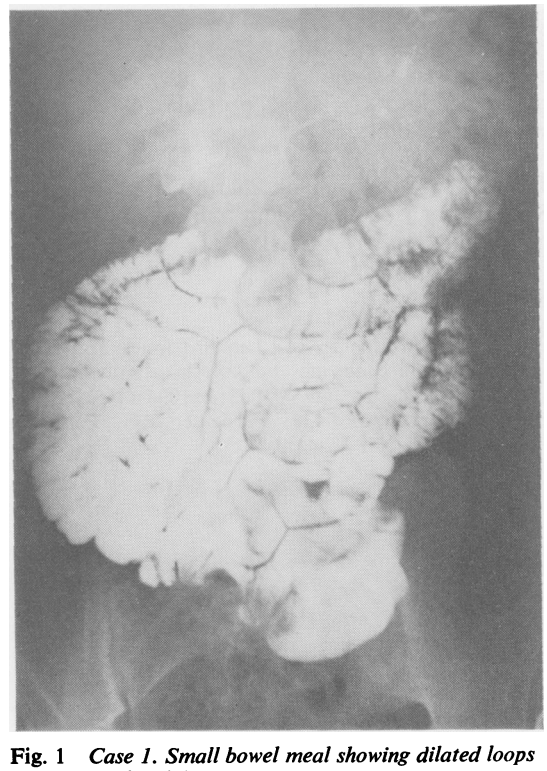

Fig. 1 *Case 1. Small bowel meal showing dilated loops suggestive of malabsorption.*

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Table *Summary of clinical data*

	Coeliac disease							*Inflammatory bowel disease*			
Case no. and sex	*Age at onset of symptoms (yr)*	*Age at diagnosis (yr)*	*Presentation*	*Maximum faecal fat (mmol/24h)*	*Small bowel radiology*	*Jejunal biopsy*		*Nature*	*Age at onset of symptoms (yr)*	*Age at diagnosis (yr)*	*Presentation*
						Before GFD	*After GFD*				
1 M	32	32	Diarrhoea Weight loss	Not done	Dilated jejunal loops	Flat	Normal villous pattern	Crohn's disease	31	31	Diarrhoea Rectal bleeding Pain LIF
2 M	33	33	Severe diarrhoea	36	Dilated loops Coarse mucosal pattern	Flat	Normal villous pattern	Ulcerative colitis	40	41	Diarrhoea Rectal bleeding
3 M	17	17	Steatorrhoea Weight loss	26	Dilated jejunal loops Coarse mucosal pattern	Flat	Normal villous pattern	Ulcerative colitis	18	18	Diarrhoea Rectal bleeding
4 F	31	53*	Steatorrhoea	70	Dilated SI loops Coarse mucosal pattern	Flat	Not done	Ulcerative colitis	35	35	Diarrhoea Rectal bleeding

	Laboratory tests				
Case no.	*Hb (g/dl)*	*Serum albumin (g/l)*	*Serum seromucoids (g/l)*	*Large bowel radiology*	*Histological findings*
1	12·0	41	0·98	Aphthoid ulcers in descending and sigmoid colon	Rectal granulomas
2	10·6	33	2·10	Symmetrical changes in left colon	Active proctitis
3	8·8	29	3·44	Symmetrical changes in left colon	Active proctitis
4	5·5	31	—	Symmetrical changes in left colon	Total colitis Ca. colon*

*Necropsy.

He was treated with sulphasalazine and predsol enemata with marked improvement in his symptoms.

He was referred to this unit in October 1976 with recurrent diarrhoea, abdominal discomfort, and weight loss. Physical examination was normal. Investigations showed haemoglobin 11·9 g/dl, serum iron 23 μmol/l (normal range 8–28 μmol/l), TIBC 66 μmol/l (normal range 45–72 μmol/l), serum folate 3·0 μg/l (normal range 7–16 μg/l), serum B12 480 ng/l (normal range 200–800 ng/l). Serum albumin 41 g/l, serum seromucoid 2·20 g/l. Radiological examination of the small intestine showed dilated loops and a slow transit time suggestive of malabsorption (Fig. 1). Jejunal biopsy showed a flat mucosa (Fig. 2a). His symptoms persisted despite adhering to a strict gluten free diet.

Further radiological examination of the large intestine in January 1977 showed multiple aphthoid ulcers in the descending and sigmoid colon with rectal sparing (Fig. 3). Sigmoidoscopic examination revealed perianal skin tags and an abnormal

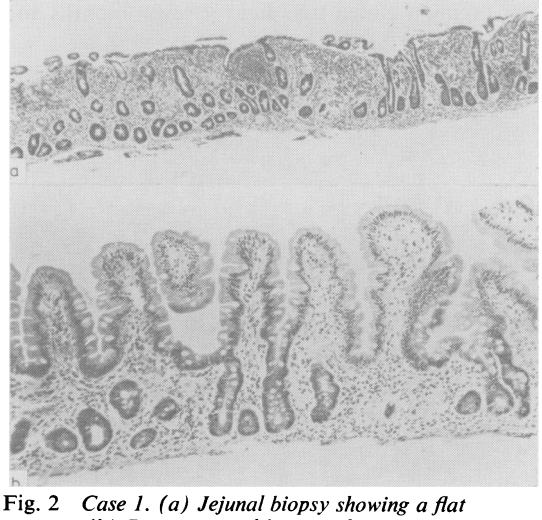

Fig. 2 *Case 1. (a) Jejunal biopsy showing a flat mucosa. (b) Repeat jejunal biopsy after seven months on a gluten free diet showing a normal villous pattern.*

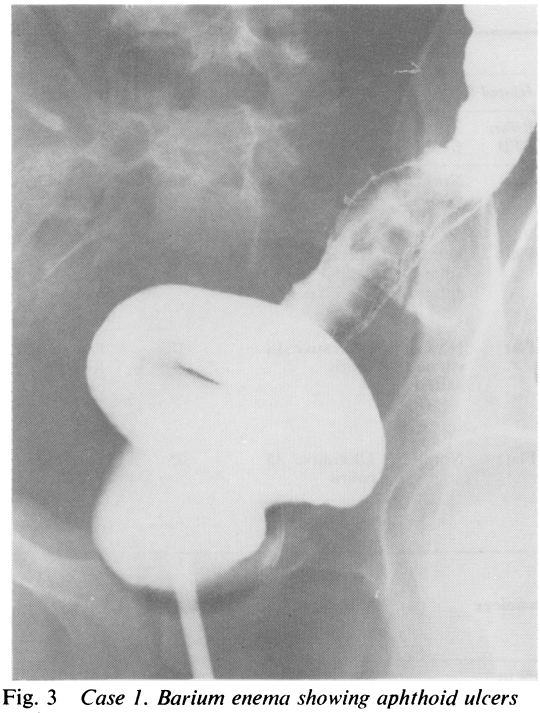

Fig. 3 *Case 1. Barium enema showing aphthoid ulcers in the descending colon.*

granular rectal mucosa with contact bleeding. Rectal biopsy showed an active proctitis (Fig. 4). He was treated by local corticosteroids with symptomatic relief. He had exacerbations of his colitic symptoms in June 1977 and June 1978 treated by systemic corticosteroids. A second jejunal biopsy after taking a gluten free diet for seven months and systemic corticosteroids for one week (ACTH 20 units intramuscularly daily) was normal apart from minimal plasma cell infiltration of the lamina propria (Fig. 2b). He is now in good health, though he is still receiving local and systemic corticosteroids with potassium supplements. He adheres strictly to a gluten free diet.

CASE 2

RP, who was born on 28 September 1931, presented in March 1962 with a five year history of intermittent epigastric pain relieved by food and alkalis, recent vomiting, and weight loss. A chronic duodenal ulcer was demonstrated by barium meal examination. He was treated initially by antacids but because of persistent symptoms he subsequently required selective vagotomy and later a Bilroth II gastrectomy. He returned in June 1964 with a four week history of severe diarrhoea. Physical examination was normal. Investigations showed haemoglobin 13·0 g/dl, serum folate 1·6 μg/l, serum B12 145 ng/l, faecal fat excretion 36 mmol/24 hours (normal range <18 mmol/24 hours). Radiological examination of the small intestine was suggestive of malabsorption (Fig. 5). Jejunal biopsy revealed a flat mucosa (Fig. 6a). He did not adhere strictly to a gluten free diet and steatorrhoea was demonstrated on several occasions. A repeat jejunal biopsy in March 1968 was still flat. He was eventually persuaded to take a strict gluten free diet with good symptomatic improvement and another jejunal biopsy in 1977 was virtually normal (Fig. 6b).

He was admitted in May 1972 with a six month history of diarrhoea and rectal bleeding. Physical examination was normal. Investigations showed haemoglobin 10·6 g/dl, serum iron 6 μmol/l, serum

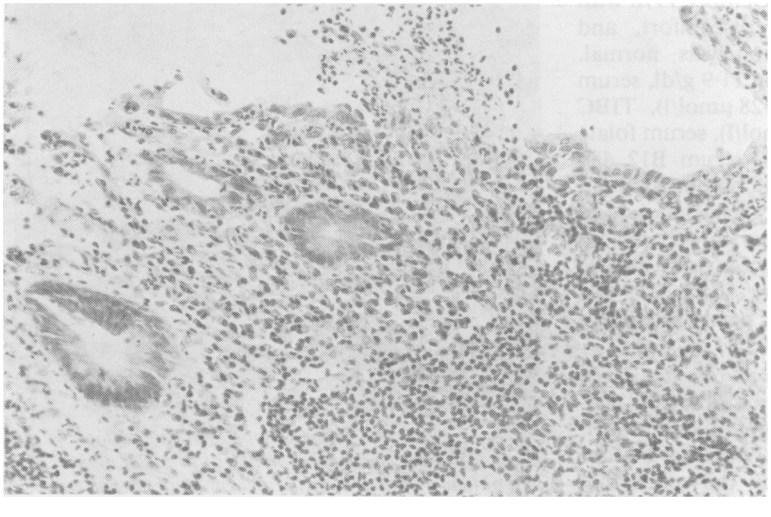

Fig. 4 *Case 1. Rectal biopsy showing an active proctitis.*

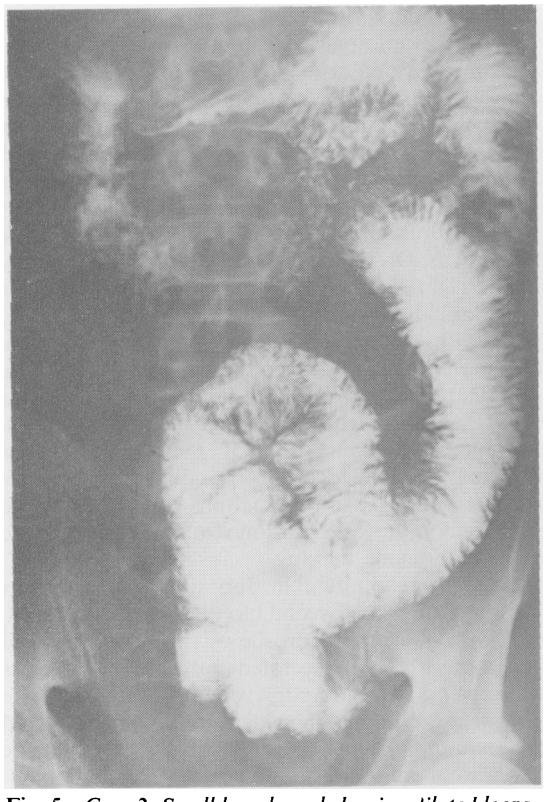

Fig. 5 *Case 2. Small bowel meal showing dilated loops suggestive of malabsorption.*

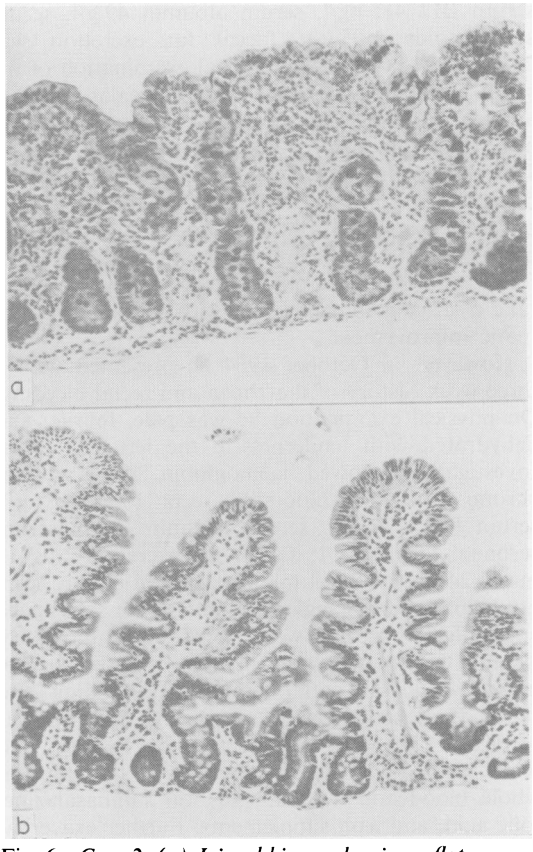

Fig. 6 *Case 2. (a) Jejunal biopsy showing a flat mucosa. (b) Repeat jejunal biopsy while taking a gluten free diet showing a normal villous pattern.*

folate 3 μg/l, serum B12 130 ng/l, serum albumin 33 g/l, serum seromucoids 2·10 g/l. Radiological examination of the large intestine demonstrated an abnormal mucosal pattern in the descending and sigmoid colon with rectal involvement (Fig. 7). Sigmoidoscopic examination and rectal biopsy confirmed an active proctitis. He was transfused with three units of blood and treated with sulphasalazine and iron supplements. Steroid enemata were later added to this regime. Another radiological examination of the large intestine in 1976 confirmed an abnormal mucosal pattern in the left side of the colon. Apart from psyschological problems he is now in good health and adheres strictly to a gluten free diet.

CASE 3

RT, born on 29 April 1946, presented in June 1963 with a three month history of diarrhoea, epigastric discomfort, and weight loss. There was no history of rectal bleeding and he had not travelled abroad. Physical examination was normal. Investigations showed haemoglobin 14·9 g/dl, serum folate 5·2 μg/l,

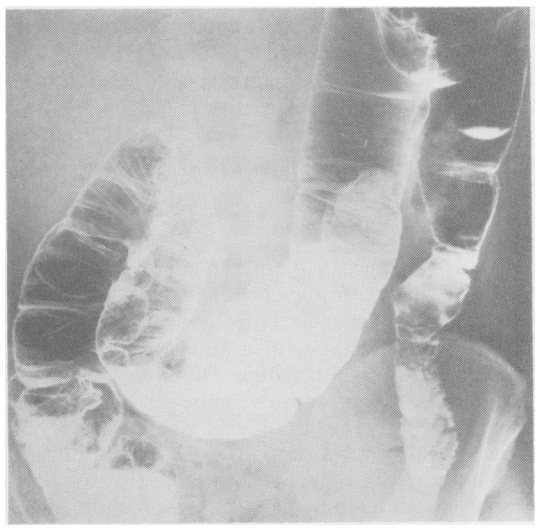

Fig. 7 *Case 2. Barium enema showing abnormal mucosal pattern in the descending colon.*

serum B12 485 ng/l, serum albumin 49 g/l, serum seromucoids 1·05 g/l; faecal fat excretion was 26 mmol/24 hours. Radiological examination of the small intestine was suggestive of malabsorption, and jejunal biopsy showed a flat mucosa. He did not adhere to a gluten free diet and was readmitted in June 1964 with fatigue, abdominal pain, and diarrhoea. Apart from aphthous ulcers of the soft palate, physical examination was normal. Investigations: blood count, biochemical profile, serum iron, folate, and B12 were normal. He was persuaded to take a strict gluten free diet with marked symptomatic improvement.

However, in October 1964 he presented with a three week history of diarrhoea and rectal bleeding. On physical examination he was pale, febrile, and dehydrated with tenderness in the left iliac fossa. Investigations showed haemoglobin 8·8 g/dl, hypochromic, microcytic blood film, serum folate 3·6 μg/l, serum B12 405 ng/l, serum albumin 29 g/l, serum seromucoids 3·44 g/l; faecal fat excretion was 12 mmol/24 hours. Stool microscopy and culture were not helpful. Serum agglutination tests for salmonella and shigella species were negative. Radiological examination of the large intestine showed an abnormal mucosal pattern in the descending and sigmoid colon and rectum. An active proctitis was confirmed by sigmoidoscopic examination and rectal biopsy. He was transfused with five units of whole blood and treated with oral sulphasalazine, folic acid, and iron supplements. Further exacerbations of his ulcerative colitis required inpatient treatment in March 1966 and May 1969. Sigmoidoscopic examination and rectal biopsies on both occasions confirmed an active proctitis. A second jejunal biopsy in 1966 showed improvement and a third specimen obtained in 1968 was virtually normal. He is now in good health and adheres strictly to a gluten free diet. Recent sigmoidoscopic and radiological examination showed mucosal changes in the rectum, sigmoid, and descending colon.

CASE 4

DE, born 7 June 1914, presented in 1946 with a microcytic hypochromic anaemia which was treated with iron supplements. Three years later she was admitted to hospital with a four week history of diarrhoea and rectal bleeding. On close questioning she admitted to intermittent episodes of diarrhoea for four years. The stool was pale, watery, and offensive. She had a smooth tongue but physical examination was otherwise normal. Investigations showed haemoglobin 5·5 g/dl, microcytic hypochromic blood film, serum albumin 31 g/l, serum seromucoids 2·1 g/l; faecal fat excretion was 31 mmol/24 hours. Stool microscopy and culture was negative. Radiological examination of the small intestine revealed distended loops in the distal ileum and a barium enema examination showed features of ulcerative colitis. She was treated with bed rest, blood transfusion, and iron supplements with symptomatic improvement. She was readmitted in 1951 with severe diarrhoea having six to 10 watery bowel actions per day. The stool contained blood and mucus. On physical examination she was tender in the right iliac fossa with erythema nodosum in both legs. Investigations showed haemoblogin 5·3 g/dl, with an iron deficiency picture. Faecal fat excretion was 53–70 mmol/24 hours. Radiological examination showed dilated loops throughout the small intestine with abnormal mucosal pattern. Radiological examination of the large intestine revealed a left-sided ulcerative colitis. She was readmitted on three other occasions between 1952 and 1955 and on the last occasion remission was induced by oral cortisone therapy.

She was readmitted in July 1967 with a short history of diarrhoea, rectal bleeding, and weight loss. On physical examination she was thin with marked hepatomegaly. An ulcerated polypoid rectal mass was seen on sigmoidoscopy which histologically was an adenocarcinoma. She deteriorated rapidly and died two months later. Necropsy confirmed that she had a total colitis with an ulcerated polypoid carcinoma 9 cm in diameter in the upper rectum. Metastases were found in both the adjacent lymph nodes and liver. Dissecting microscopy and histological examination of the whole length of the small intestine revealed a flat mucosa over 75 cm of the proximal jejunum with convolutions in the distal jejunum and ileum and digitate villi in the terminal ileum.

Discussion

Coeliac disease was diagnosed on the basis of a flat jejunal mucosa. Our reasons for adopting a less restrictive definition of the disorder than others have been fully discussed elsewhere.[7] In addition, three of the four cases showed a morphological response to a gluten free diet.

The prevalence of inflammatory bowel disease varies between 96–190 per 100 000 cases.[8] Thus in a population of 420 patients with coelic disease the expected number of patients with inflammatory bowel disease would range from 0·4–0·8 cases. The observed prevalence in this series was four cases, which is five to 10 times the expected prevalence.

The prevalence of coeliac disease is uncertain; we have used the estimated prevalence of 1 in 1800 in the general population in Great Britain.[9] This study was not entirely satisfactory, for it was

calculated from the mean annual number of cases diagnosed in the Royal Hospital for Sick Children, Glasgow, in the years 1948 to 1960 before intestinal biopsy was commonly undertaken and related to indirect estimates of the population served by the hospital. Using this prevalence figure the expected number of patients with coeliac disease among our 1240 patients with inflammatory bowel disease would thus be 0·69 cases. The observed prevalence in this series was four cases, which is nearly six times the expected prevalence, but this figure must be interpreted with caution.

Taken together, these figures suggest that the two disorders may coexist more commonly than would be expected by chance.

It must also be emphasised that these patients have been subject to extensive investigation in a unit with particular interest in both disorders. The principal object of describing this association is to encourage the identification of additional examples.

We have recently drawn attention to the frequency of immunological disorders associated with coeliac disease[10] confirming the hypothesis put forward by Scott and Losowsky[6] based on their review of the literature. Such an immunological disorder in coeliac disease could predispose the individual to inflammatory bowel disease because of the transfer of antigenic material across the damaged small intestinal mucosa.

Alternatively, if the hypothesis that inflammatory bowel disease is of viral aetiology proves to be correct then the presence of coeliac disease—and thus an altered immune response—might render the individual more susceptible to infection.

As both disorders usually present with gastrointestinal symptoms the possibility that they coexist can readily be overlooked. Such an association should be considered in the patient who is not showing the expected response to treatment or where there are unusual clinical features.

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