Case report

Jejunal villous atrophy with morbid obesity: death after jejunoileal bypass

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SUMMARY A 49-year-old woman with morbid obesity was found to have subtotal villous atrophy in an operative jejunal biopsy, taken when a jejunoileal bypass was created. After the operation, the patient developed marked weight loss, vomiting, hepatic failure, and a bizarre mental state with sudden losses of consciousness. Six months after the first operation the bypass was reversed but the patient developed hepatorenal failure and died one week after the second operation. The histological features of several biopsies of jejunum were typical of a gluten sensitive enteropathy. This, previously subclinical, small bowel disease may have contributed to her hepatic failure and death by interfering with jejunoileal adaptation. In the absence of any of the other, rarer, causes of villous atrophy, this woman appears to have had coeliac disease.

The unexpected finding of an abnormal jejunal mucosa, with villous atrophy, is usually due to subclinical coeliac disease, or dermatitis herpetiformis, although immunodeficiency, giardiasis, or gastrinoma^{1 2} are other, rarer, causes. This report concerns a woman who was found to have jejunal villous atrophy at the time of jejunoileal bypass surgery, and in whom the diagnosis is likely to have been coeliac disease.

Case report

A 49-year-old woman weighing 140 kg (22 stone) was referred to the Gastro-Intestinal Unit, Western General Hospital, Edinburgh, in June 1978 for assessment for jejunoileal bypass surgery (Fig. 1). In her early 20s she had weighed 89 kg (14 stone) and had increased to 120 kg after the birth of her only child when aged 28 years. For the two years before referral she had attended an obesity clinic where, despite weekly visits, repeated dietetic advice and treatment with fenfluramine, she had managed to lose only a few kilograms, quickly regained. Besides her obesity and some features of reactive

depression, there was no medical history of note.

During her preoperative assessment the serum folate was found to be reduced at 1.2 ng/l (normal >2 ng/l) and the mean red cell volume increased slightly at 106 fl (normal 76-98 fl) on single occasions only. The haemoglobin was 14.1 g/dl, plasma protein 69 g/l (normal 60-80 g/l) with normal immunoglobulins and plasma albumin 36 g/l (normal 35-57 g/l). Immediately preoperatively, tests of liver function were normal, although within the previous two years the serum aspartate aminotransferase (serum GOT) had been found to be slightly increased with values up to 49 IU/l (normal 9-43 IU/l) and serum alkaline phosphatase similarly increased, with values up to 111 IU/l (normal 20-85 IU/l). Serum calcium was 2.48 mmol/l (normal 2.25-2.50 mmol/l). Other normal investigations included a coagulation screen, oral cholecystogram, barium follow-through examination, and double contrast barium enema.

In November 1978 an end-to-side jejunoileal bypass (Mr C W A Falconer) was created by anastomosing 14 in of jejunum, measured from the duodenal jejunal flexure, to the ileum 4 in proximal to the ileocaecal valve. As part of the routine procedure of the Unit a 3 cm full thickness jejunal biopsy was taken. No villi were identified under the dissecting microscope. Histology confirmed the presence of subtotal villous atrophy (Fig. 2) with

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Fig. 1 Forty-nine year-old patient with morbid obesity and probable coeliac disease (photograph taken three weeks after the first operation).

crypt hyperplasia, abnormal surface enterocytes, increased numbers of intraepithelial lymphocytes, and increased plasma cell infiltrate of the lamina propria.

Early postoperative progress was uneventful. Ten days after the operation, however, she began vomiting after meals. Barium meal and follow-through showed no evidence of obstruction and the vomiting settled with reduction of food intake. At about this time the patient, who, until then, had been co-operative and cheerful, became intermittently emotionally distressed and unco-operative with bouts of weeping and apparent voluntary incontinence. In the absence of other explanations, it was assumed that her disturbed mental state was the consequence of long-standing marital problems, which it had been hoped a successful operation

would alleviate. Although the possibility of a gluten sensitive enteropathy was regarded with some scepticism, a gluten free diet was prescribed but not pursued aggressively, in view of the patient's fraught mental state and reluctance to eat at all. Three weeks after the operation she was discharged home, passing four or less semi-formed stools daily.

Over the subsequent 12 weeks, the patient required frequent admissions to hospital. She ate little and her weight fell rapidly from 137 kg in November 1978 to 98 kg in April 1979. When in hospital she continued to vomit intermittently and be incontinent of faeces. Her mental state fluctuated with long periods of unexplained weeping and refusal to co-operate with staff interspersed between periods of apparently rational conversation and behaviour.

She also developed sudden episodes of disturbed consciousness, their duration varying from several minutes to 24 hours, and there being spontaneous recovery without injury or incontinence. During these episodes her conscious level ranged from drowsiness to being unconscious and unresponsive to painful stimuli. Initially there was no evidence of hepatic encephalopathy and the possibility of these episodes being hysterical or drug-induced was considered. With time, they became more frequent and by March 1979 her electroencephalogram, which had at first shown only minor abnormalities, had developed a repetitive slow wave pattern typical of hepatic encephalopathy.

Laboratory investigations during this period confirmed an increasing disturbance of hepatic function with serum bilirubin between 37–77 $\mu\text{mol/l}$ (normal 3–14 $\mu\text{mol/l}$) and slight increases in serum aspartate aminotransferase (range 52–69 IU/l) and in serum alkaline phosphatase (range 88–124 IU/l). The serum albumin fell steadily from a post-operative level of 36 g/l to 20 g/l 10 weeks after operation before rising slightly to 26 g/l. Serum globulins showed a steady rise from a postoperative level of 18 g/l to 33 g/l 12 weeks after operation. The prothrombin time ratio after administration of vitamin K was 1.7. Peroral jejunal biopsies were performed and subtotal villous atrophy again demonstrated. Reticulin antibody was present in serum. HLA tissue type for A and B antigens was A1 B8.

By April 1979, although tests of liver function had ceased to deteriorate, the patient's disturbed mental state with continuing episodes of unconsciousness confined her to hospital and made reversal of the bypass seemingly unavoidable. On 20 April 1979 the bypass was taken down and biopsies taken from the liver, jejunum, and ileum. In the immediate post-operative hours, satisfactory blood pressure and

Fig. 2 Jejunal biopsy taken at first operation (H and E $\times 50$).

pulse rate were maintained but the patient became oliguric, passing <30 ml urine per hour. Despite vigorous resuscitative measures over the ensuing days there was a steady rise in blood urea and bilirubin and the patient died one week after the second operation.

Necropsy was not performed. The operative liver biopsy showed extreme fatty change affecting the majority of hepatocytes with slight expansion of the portal tracts by an inflammatory infiltrate (Fig. 3). Two jejunal biopsies taken at operation showed similar subtotal villous atrophy with crypt hyperplasia, abnormal surface enterocytes, increased intraepithelial lymphocytes, and chronic inflammatory infiltrate of the lamina propria (Fig. 4). Operative ileal biopsies, taken from the ileum proximal and distal to the jejunoileal anastomosis, showed partial villous atrophy. The operative biopsies were also examined using a microdissection technique³ and assays of disaccharidases performed.⁴ Results summarised in the Table confirmed the villous atrophy, crypt hyperplasia and disaccharidase deficiency in the jejunum incontinuity, with less severe pathological changes in the biopsies from the bypassed jejunal loop.

Discussion

The histopathological appearances of the first, operative, biopsy from this patient were well outside

the bounds of normal variation, or of artefact associated with poor orientation. The finding was so unexpected that it might reasonably have been ascribed to a laboratory error – for example, in specimen identification. However, the original findings were confirmed by peroral biopsies, and biopsies taken at the second operation. The cause of the extensive jejunal pathology was not unequivocally established. Of the many recognised diseases which are accompanied by villous atrophy in the adult, most can readily be dismissed, with only protein calorie malnutrition or gluten sensitive enteropathy requiring serious consideration. In children with protein calorie malnutrition, villous atrophy has been reported.^{5,6} The pathology returns to normal after appropriate feeding, and crypt hyperplasia is not typically found in this condition. Although this patient gradually became hypoalbuminaemic in the weeks after jejunoileal bypass, there was no evidence of protein calorie malnutrition before her surgery.

Despite the patient's obesity, subclinical coeliac disease appears to be the most likely explanation of the jejunal pathology. Folate deficiency and increased red cell volume are in keeping with such a diagnosis, and detection of coeliac disease in patients with similar minimal abnormalities is increasingly common.^{7,8} The finding of serum reticulatin antibody also supports a diagnosis of coeliac disease.⁹ Although morbid obesity in a

Fig. 3 Section from liver biopsy taken at second operation (H and E $\times 125$).

Fig. 4 Jejunal biopsy taken at second operation from jejunum discontinuity (H and E $\times 125$).

Table Peroral and operative jejunal biopsies – disaccharide activities and measurements of mucosal architecture

Date	Site of biopsy	Lactase (u/g)	Sucrase (u/g)	Trehalase (u/g)	Villus length (μ m)	Crypt length (μ m)	Mitoses/ micro- dissected crypt
January 1979 (peroral)	Proximal jejunum in continuity	0.20	0.0	0.0			
March 1979 (peroral)	Proximal jejunum in continuity	0.10	0.28	0.0			
April 1979 (operative)	Proximal jejunum in continuity	0.0	1.29	0.54	<100	574	16.4
	Distal ileum in continuity	0.0	1.47	0.09	406	242	15.5
	Jejunum of bypassed loop*	0.31	2.46	0.51	<100	393	16.8
					135	192	9.0
Normal range	Proximal jejunum	1.9–7.0	2.5–9.3	0.8–3.4	500–1100	150–300	1–12

* Mucosal measurements performed in two biopsies; disaccharidases in one.

coeliac is, indeed, remarkable, the presence of lesser degrees of obesity in treated coeliacs has previously been noted.¹⁰ Furthermore, the histopathological features in this patient – crypt hyperplasia, abnormal surface enterocytes, and increased intraepithelial lymphocyte infiltration – are more characteristic of a gluten sensitive enteropathy such as coeliac disease than of other causes.⁶

Although the jejunum incontinuity showed a poor histological response to prescribed gluten free diet, this may have been due to incomplete gluten restriction and the relatively short duration of diet.¹¹ The mucosa of the bypassed jejunum was, of course, protected from any dietary gluten and it is interesting that, at the second operation, the pathological changes in the bypassed jejunal mucosa were less severe than in the jejunum incontinuity.

Whatever the cause, the presence of villous atrophy throughout the jejunum incontinuity is likely to have contributed to the patient's postoperative decline. After jejunal bypass surgery, adaptation of the small intestine occurs over a period of months and is manifest by hypertrophy of ileal villi.^{12 13} Failure of small bowel adaptation must exacerbate any malabsorption and malnutrition, and hence contribute to the development of severe hepatic steatosis and hepatic failure.¹⁴ Continued vomiting, and rapid weight loss, as were found in this patient, are well-recognised features of this often fatal syndrome.¹³

The decision as to when to reverse jejunoileal bypass remains a difficult one. In retrospect, this patient might have survived if the bypass had been reversed within a few weeks of its creation, before hepatic failure had developed. At that time her bizarre mental state appeared to be psychogenic and typical signs of hepatic failure were not present. Even so, operations to reverse bypasses are reported to have a high mortality.¹⁵ Moreover, transient hepatic failure after jejunoileal bypass develops in many patients, usually reaching its nadir

after two to four months before spontaneously improving, possibly as a result of small bowel adaptation.¹³ With hindsight a period of parenteral nutrition might have benefited this woman, although the problems presented by her obesity and hepatic failure would have been considerable.

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