Case reports

Chronic non-specific ulcerative duodenojejunoileitis: report of four cases

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SUMMARY Four patients with chronic non-specific ulcerative duodenojejunoileitis (CNSUDJI) are reported. The clinical picture included abdominal pain, fever, and a malabsorption syndrome. Main radiological findings were diffuse narrowing of the jejunal loops with total effacement of the mucosal folds. Multiple peroral biopsies of the small intestine showed various degrees of mucosal abnormalities from total villous atrophy to normal villi, but ulcerations were diagnosed only by operative full thickness biopsies or resection of the small bowel. The ulcerative process was associated with well-documented coeliac disease in two patients: in one of them it occurred as a fatal complication involving also the colon, three years after the start of a gluten free diet, while the disease was in full clinical and histological remission. In the other case, coeliac disease was revealed by obstructive symptoms due to stenosing ulcerations; five months after surgical resection of the stenosis, institution of a gluten free diet induced a dramatic improvement. In the two other patients ulcerations were not associated with coeliac disease: one of them had a patchy villous atrophy and resisted a gluten free diet and total parenteral nutrition; she was improved by and dependent upon steroids but finally died. The last patient had normal villous height; ulcerations were located exclusively along the mesenteric border of the small bowel; he had a low-grade protracted evolution resisting any form of therapy and developed a peripheral neuropathy of unknown aetiology. On the basis of our cases and of a review of the literature the discussion focuses on the difficulty in diagnosing CNSUDJI, its relationship with coeliac disease, and its management and prognosis.

Chronic non-specific ulcerative duodenojejunoileitis (CNSUDJI) is an entity characterised by the association of chronic ulcers of the small bowel with a malabsorption syndrome. Though initially described about 30 years ago (Nyman, 1949) this syndrome remains of unknown aetiology, uncertain nosology, and difficult diagnosis and treatment. We report here four patients with this disease who were seen in our department during the past five years.

Case reports

CASE 1

V.J., a 65 year old woman, was referred to Hospital Saint-Lazare in May 1973 for evaluation of ab-

dominal colic without diarrhoea, vomiting, 15 kg weight loss, and fever (38°-39°C) of six months' duration. Her past medical history was unremarkable, except for a low grade asthma (three to four short attacks per year) treated by oral betamethasone (0.5 mg at each attack). On physical examination, she appeared emaciated (weight 45 kg; height 156 cm), and chronically ill. Results of laboratory tests were haemoglobin 11.5 g/dl, WBC 5700/ μ l with a normal differential, ESR 22 mm/h. Absorption tests are reported in the Table. Serum immunoglobulin levels were IgG 9.2 g/l (N = 11.7 $\pm$ 2.7 mean $\pm$ SD), IgA 2.85 g/l (N = 2.2 $\pm$ 0.8), and IgM 1.5 g/l (N = 1.2 $\pm$ 0.5). HLA type was A2, A3 and BW5. A barium radiograph of the small intestine (Fig. 1) revealed total effacement of the mucosal pattern, scarce and coarsened folds with intervalvular spaces of varying width (up to 1 cm), and spiculated margins in the jejunum; jejunal loops were diffusely narrowed but no ulcerations or stenosis were seen; the ileum

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Table Evolution of main parameters related to intestinal absorption in four cases of chronic non-specific ulcerative duodenojejunoileitis

	Normal values	Case 1			Case 2			Case 3				Case 4	
		May 73	Jan. 75	Aug. 76	Dec. 76	May 77	Sept. 77	Oct. 75	Apr. 76	Dec. 76	July 77	Nov. 74	Apr. 77
Weight (kg)	—	45	51	48	41	39	59	46	44	51	44	33	36
Stool weight (g/24 h)*	100 -200	50	80	80	450	500	110	800	500	187	250	450	300
Serum proteins (g/l)	65 - 75	35	62	61	60	48	57	42	55	56	47	54	50
Serum albumin (g/l)	35 - 45	12	34	30	34	24	28.5	14	24	27	24	28	22.5
Serum calcium (mmol/l)	2.25-2.5	1.75	2.3	2.1	1.6	2	2.2	1.8	2.05	2.2	2	2.05	2.0
Serum iron (μmol/l)	14.3- 26.8	6.2	ND	2.7	ND	7.1	11.7	7.1	16.1	14.7	6.2	17.9	8.9
Serum folate (μg/l)†	5 - 15	2.3	3	2.6	ND	3.5	ND	4.4	4.3	ND	ND	9.6	ND
D-xylose test (mg/l)‡	> 250	168	308	300	107	16	136	148	84	330	128	210	320
FATT (μg/l)§	> 40	10	70	ND	ND	ND	ND	12	16	ND	ND	12	ND
Schilling test (%)q	> 8	9.2	17	ND	ND	0.8	4.6	9.3	6.9	19	ND	1.0	0.6
Faecal fat (g/24 h)*	< 6	2.1	2	2.6	9.5	26	6.5	35.5	33.3	15.7	ND	12.2	36
Faecal nitrogen (g/24 h)*	< 2	0.3	0.5	0.9	ND	2.8	1.0	3.3	5.4	2.1	ND	2.1	2.6
⁵¹ Cr albumin test (ml/24 h)	< 45	187	ND	142	ND	ND	ND	ND	ND	144	ND	ND	ND

*Mean of three-day stool collection.

†Assay by *Lactobacillus casei*.

‡Blood xylose level 120 minutes after ingestion of 25 g xylose.

§Folic acid tolerance test (presaturation by 10 mg calcium folate intramuscularly; oral load of 40 μg per kg body weight of folic acid; blood sampling at 60 and 90 minutes; assay by *Streptococcus faecalis*).

qPercentage of QI excreted in 24 hour-urines; radioactive vitamin B 12 was given with intrinsic factor.

ND = not done.

Fig. 1 Case 1. Radiograph of upper gastrointestinal tract. The 10 minute film shows diffusely narrowed jejunum with effacement of the normal mucosal pattern.

was normal. Three peroral biopsies were taken from ileum to duodenum and showed on histological examination total villous atrophy with a cuboidal lining epithelium, elongated crypts with an increased number of mitosis, and numerous plasma cells in the lamina propria (Fig. 2). On immunofluorescence there was an increased number of IgM plasma cells, whereas IgA and IgG cell populations seemed

normal. The patient was treated by total parenteral nutrition (TPN) during three months, followed by a gluten-free diet to which she adhered carefully. Complete clinical, biological (Table), and histological (Fig. 3) remission was documented in January 1975. Yet radiographs of the small bowel remained unchanged. In June 1976, she took 0.5 mg oral betamethasone during four days (without potassium supplements) for an attack of asthma. In August 1976, while she was still adhering carefully to her gluten free diet, abdominal pain, asthenia, and fever recurred. On examination, she looked tired and the tip of the spleen was palpable. Results of laboratory tests were haemoglobin 14.5 g/dl, WBC 11 800/μl with a normal differential, ESR 32 mm/h. Absorption tests are shown in the Table. Serum immunoelectrophoresis, IgG, IgA, IgM, and total complement levels were normal; no cryoglobulinemia was detected. Oesogastroduodenoscopy was normal. Radiographs of the small intestine were still unchanged. Three specimens of intestinal mucosa (proximal, mid, and distal jejunum) were found to be normal. A lymphoma was suspected and a laparotomy was undertaken: a 90 cm segment of mid-jejunum showed thickening of the bowel wall; the rest of the small bowel and of other abdominal organs was unremarkable. A 3 cm-long mid-jejunal resection, a full thickness ileal biopsy, mesenteric nodes excision, liver biopsy, and splenectomy were performed. Multiple and extensive ulcerations lying on the middle part of the submucosa without undermining of the remaining mucosa were found at histo-

Fig. 2 *Case 1. Peroral jejunal biopsy specimen before treatment. The mucosa shows total villous atrophy, desquamated lining epithelium, and dense cellular infiltrate of the lamina propria. Haematoxylin-eosin-saffron, $\times 120$.*

Fig. 3 *Case 1. Peroral jejunal biopsy specimen taken after 20 months on a gluten free diet. Normal mucosa. Haematoxylin-eosin-saffron, $\times 225$.*

logical examination of the jejunal specimen (Fig. 4). The bed of the ulcers showed a slight sclerosis with numerous capillaries and non-specific inflammatory cells; in the scarce areas of intervening non-ulcerated areas, there was a total villous atrophy; a few aspects of antral metaplasia and numerous crypt abscesses were seen. The muscular and serosal layers were normal. Search for siderophages was negative. Histological study of ileal and hepatic biopsies and of the spleen showed no significant abnormalities and mesenteric nodes were the site of non-specific stimulation. Her postoperative course was complicated by a septic subclavian thrombophlebitis and the patient died in November 1976. At post-mortem examination an extensive ulceration identical to that previously described was found in the mid-jejunum;

autolysis precluded appreciation of villus height. Numerous similar ulcerations and erosions were scattered throughout the rectum and the colon with an aspect of colitis cystica superficialis in the intervening mucosa (Fig. 5). No other abnormalities were found.

CASE 2

Y.J., a 47 year old woman, complained of intermittent diarrhoea since May 1976; in December 1976 she was admitted to another hospital because of abdominal colic and 9 kg weight loss. Physical examination was normal. Routine laboratory tests were normal. Results of absorption tests are given in the Table. Upper gastrointestinal series showed disappearance of proximal jejunal folds and multiple

Fig. 4 Case 1. Surgical specimen of the jejunum. From left to right can be seen atrophic mucosa (*), erosion (thin arrow) and ulceration (thick arrow). Haematoxylin-eosin-saffron $\times 30$.

Fig. 5 Case 1. Necropsy specimen of the colon. It shows cystic dilatation of the colonic glands (arrow) with an adjacent ulceration. Haematoxylin-eosin-saffron, $\times 36$.

stenosis of the distal jejunum, but no obvious ulcerations. At jejunoscopy as far as 40 cm beyond the angle of Treitz, the mucosa appeared erythematous

but not ulcerated; however, four small whitish areas suggesting pseudomembranes were seen in the duodenum. Seven forceps biopsies obtained from

Fig. 6 Case 2. Peroral biopsy of the proximal jejunum before treatment showing total villous atrophy, cuboidal lining epithelium infiltrated with lymphocytes, elongated crypts with numerous mitoses, and a pleiomorphic infiltrate of the lamina propria. Haematoxylin-eosin-saffron, $\times 210$.

Fig. 7 Case 2. Surgical specimen of the mid jejunum showing a chronic ulceration. Haematoxylin-eosin saffron, $\times 210$.

the proximal jejunum and the duodenum (Dr C. Marche) showed a histological picture (Fig. 6) consistent with coeliac disease. A small acute erosion was seen on one duodenal sample.

In January 1977 she presented with severe intestinal obstruction and was operated on: three circular and ulcerated stenosis were found in the distal jejunum; 1 m of mid small bowel was resected. Histologically (Fig. 7) the ulcerations (one of which was fissuring) lay on the muscular or serosal coat and consisted of a superficial layer of necrosis and polymorphs exudate overlying a vascular connective tissue heavily infiltrated with inflammatory cells; the bottom of the ulcerations was occupied by a prominent sclerosis with a few medium sized arteries showing chronic and sometimes obliterative endarteritis; no siderophages could be found; a few lymphoid nodules were scattered throughout the sclerosis and a single tuberculoid granuloma was seen adjacent to a necrotic area; pyloric gland metaplasia was observed on the ulcer edge. In the non-ulcerated areas the mucosa showed normal villi. Mesenteric nodes were unremarkable.

Postoperatively the obstructive symptoms disappeared but she experienced profuse diarrhoea, tetany, and ankle oedema. When first seen at Hospital Saint-Lazare in May 1977, she weighed 39 kg (height 154 cm); physical examination was otherwise unremarkable. One of her nephews was

treated for well-documented coeliac disease. Routine laboratory tests were normal except for hypokalemia (2.1 mM/l); serum gastrin level was normal. Absorption tests are reported in the Table. IgG, A, and M serum levels were respectively 7.5, 2.85, and 1.35 g/l. HLA type was A2, A3, B8, and BW22. Radiographs of the small intestine showed enlarged duodenal folds, slight dilatation of the jejunal loops with moderately thickened and straight valvulae, and markedly widened intervalvular spaces; there was no evidence of stenosis or ulceration. Jejunoscopy down to the third jejunal loop showed no ulcerated areas. Four biopsies from the proximal jejunum and duodenum revealed a picture identical with that observed in the specimens taken at the first jejunoscopy, but without erosions. Rectosigmoidoscopy and rectal biopsy were normal. A gluten free diet alone induced a dramatic clinical improvement (+ 8 kg; normal stool weight) within three weeks. After four months of gluten withdrawal, the patient had put on 20 kg and passed one normal stool per day. The biological improvement is shown in the Table. The patient declined a further jejunal biopsy.

Fig. 8 Case 3. Radiograph of upper gastrointestinal tract showing diffuse narrowing and effacement of the mucosal folds in the proximal small bowel.

CASE 3

R.Y. attended Hospital Saint-Lazare in October 1975 at the age of 61 years with a four months' history of diarrhoea, abdominal pain, weight loss (10 kg), recurrent leg thrombophlebitis, and fever. Physical examination revealed a new thrombophlebitis and a poor general condition that required immediate treatment by TPN and heparin. Laboratory tests included a haemoglobin of 10.8 g/dl, a WBC of 9900/ μ l with 82% neutrophils, and an ESR of 38 mm/h. Results of absorption tests are shown in the Table. Bacterial overgrowth (*E. coli* 10⁶/ml, *Lactobacilli* 10⁶/ml) was found in the proximal jejunum. Serum IgG, A, and M levels were respectively 8.5, 3.75, and 0 g/l but a few days later IgM was only moderately decreased on immunoelectrophoresis. Search for cryoglobulinaemia was negative and total complement level was normal. HLA type was A1, A9, B13, and B18. Upper digestive endoscopy revealed two minute ulcerations of the second part of the duodenum. Radiographs of the small intestine showed that the barium reached the caecum within 15 minutes; jejunal loops were diffusely narrowed with total effacement of the mucosal pattern (Fig. 8). There were no radiographically visible ulcerations. Ten peroral biopsies were obtained from mid-jejunum to duodenum and showed patchy lesions (Fig. 9): the villous pattern ranged from subtotal villous atrophy to normally tall villi with variable shapes, frequent broadening and distortion; the lining epithelium was normal or cuboidal; crypt arrangement was irregular with clumps of glands in enlarged interglandular spaces. Two crypt abscesses were observed. The lamina propria was infiltrated with numerous plasma cells, neutrophils, and eosinophils. On immunofluorescence the density of IgA-producing cells was greatly increased; that of IgM and IgG cells was moderately increased and normal respectively. On the whole, the lesions did not predominate in the proximal samples and one of the duodenal biopsies had normal villi.

Fifty-three days of TPN improved the nutritional status but did not change small intestinal function and histology. After the failure (Table) of a six-month strict gluten free diet and oral antibiotics (ampicillin, streptomycin) a laparotomy was performed in June 1976. The small bowel, as all other abdominal contents, looked normal. Four full thickness biopsies were taken from proximal and distal jejunum and ileum. Several patterns coexisted on each of the specimens: normal mucosa, scarred ulcerations as shown on Fig. 10; active ulcerations. Granulomas, vascular lesions, and siderophages were absent. Liver biopsy showed only triaditis and mesenteric nodes were normal.

Prednisone (50 mg/day) was then added to previous

Fig. 9 Case 3. (Top). Peroral biopsy taken at the angle of Treitz and showing a dystrophic mucosa with very short and irregular villi and clumps of disordered crypts. (Bottom). Peroral biopsy taken from the duodenum showing a normal mucosa. Haematoxylin-eosin-saffron, $\times 120$.

treatment and the patient soon improved. Six months later (December 1976) laboratory tests showed marked improvement (Table). Serum immunoglobulins were then normal. In May 1977 antibiotics were discontinued and steroids reduced to 15 mg per day. A severe relapse necessitated a new course of TPN, antibiotics, and increased dosage of prednisone (30 mg daily). The attack subsided rapidly but the patient suddenly died on 21 August 1977. At post-mortem examination lesions were limited to the small bowel (except for pulmonary oedema and an inferior vena cava thrombosis) and predominated in the distal jejunum; they consisted of multiple re-epithelialised erosions and ulcerations (identical

with those described on operative biopsies) with rare areas of normal intervening mucosa.

CASE 4

This case has been already reported in detail elsewhere (Belaiche *et al.*, 1977) and will be summarised here. N.K., a 28 year old Algerian male, complained of frequent diarrhoea and vomiting since the age of 10 years without detectable aetiology despite numerous investigations in several other hospitals. Multiple therapeutic trials (gluten free diet for three months, oral tetracycline and metronidazole) had been unsuccessful. When first seen at Hospital Saint-Lazare in November 1974, he was in a poor nutritional state (33 kg; 160 cm) and had digital clubbing. Laboratory values were haemoglobin 9.4 g/dl, WBC 6300/ μ l with a normal differential, ESR 35 mm/h. Other routine biological investigations were normal. Results of absorption studies are reported in the Table. Pancreatic enzymatic response to a Lundh meal was normal and fasting jejunal fluid was sterile. Serum gastrin was normal. Immunoelectrophoresis using a monospecific antiserum to IgA ruled out α -chain disease and serum levels of IgG, A, and M were normal. HLA type was A9, ADa25, BW5, and B12. Radiographs of the small intestine showed total effacement of the mucosal pattern without ulcerations. Oesogastroduodenoscopy and colonoscopy were normal. Multiple duodenal, jejunal, and colonic biopsies showed no abnormalities. Fifty-six days of TPN greatly improved the patient's nutritional status but absorption tests remained unchanged. At laparotomy (January 1975) the distal small intestine wall was thickened along its mesenteric insertion and there were several ileal stenoses: 90 cm of ileum were resected. On opening the bowel multiple ulcerations were found to be located exclusively along the mesenteric attachment. Histological examination (Fig. 11) revealed non-specific active ulcerations lying on the submucosa, which was very vascular, infiltrated with inflammatory cells, and underlined by sclerosis. At the edge of the ulcerations villi were irregular but not atrophic and a few crypts showed antral metaplasia. A few re-epithelialised ulcerations were also seen. Vascular abnormalities, granulomas, and siderophages were absent. The intervening mucosa was normal and mesenteric nodes showed non-specific stimulation.

After a slight improvement the patient returned to his preoperative status; he received successively oral prednisone (40 mg/day for two months), oral tetracycline (2 g/day for six weeks) without any benefit (Table). In August 1977 he developed a peripheral neuropathy predominating in the legs, and the aetiology of which remained obscure: there was no alcoholism, normal B12 and folate serum levels,

Fig. 10 Case 3. Surgical biopsy from the mid jejunum showing a re-epithelialised ulceration. Haematoxylin-eosin-saffron, $\times 35$.

Fig. 11 Case 4. Ileal resection. Chronic ulceration surrounded by dystrophic mucosa. Haematoxylin-eosin-saffron, $\times 14$.

unspecific abnormalities of peripheral nerves without inflammatory infiltrate or evidence of vasculitis or amyloidosis at neuromuscular biopsy, and normal CSF. High doses of intramuscular vitamin B1 and B6 induced a questionable improvement.

Discussion

Our patients had in common a malabsorption syndrome and anatomically documented multiple ulcerations of the small bowel (and of the colon in

case 1). None of the known causes of chronic ulcerations of the small bowel (Bayless *et al.*, 1967; Wayte and Helwig, 1968) could be found despite extensive investigations. In case 2 the familial history of coeliac disease, the total villous atrophy in the proximal jejunum and the dramatic response to a gluten free diet rule out Crohn's disease, in spite of the presence on the resected specimen of one fissure and a single tuberculoid granuloma. Patient 1 had been on low doses of corticosteroids for four days, a few weeks before the clinical relapse due to ulcera-

tions. Yet there is no convincing evidence in the literature that steroids are able to induce chronic intestinal ulcerations, as discussed elsewhere (Modigliani, 1977). Our cases can thus be classified as chronic non-specific ulcerative duodenojejunoileitis (CNSUDJI). Since the first report by Nyman (1949) 39 such cases, including these, have been reported with some detail in the English and French literature. Major clinical features of this syndrome are chronic diarrhoea, malabsorption, exudative enteropathy, abdominal pain, fever, and surgical complications (stenosis, perforation, and bleeding) leading frequently to repeated operations and eventually death. The following discussion will focus on three points which are well illustrated by our cases: the difficulty in diagnosis, the relationship of this syndrome with coeliac disease and the management of CNSUDJI.

DIAGNOSIS

The diagnosis of this syndrome is difficult. (1) The clinical, biological, and radiological picture is aspecific. The ulcerations have been detected radiologically in only four patients (Bayless *et al.*, 1967; Neale, 1970; Stuber *et al.*, 1971; Seliger *et al.*, 1973). (2) Except on one occasion (Patterson *et al.*, 1966), blind biopsies of the small intestine have never documented the ulcerations even if taken at multiple levels (cases 1, 3, and 4) and from areas ultimately proved to be involved by the disease (cases 1 and 3); however, the dystrophic pattern of the mucosa (variability of villous shape and height, irregularity of crypt distribution, sclerosis of the lamina propria) may be suggestive of scarred ulcerations as in case 3. (3) As proved by two recent case reports (Lotsberg *et al.*, 1976; Cerf *et al.*, 1977), enteroscopy with guided biopsies represents a major advance in the diagnosis of CNSUDJI but does not preclude the need for laparotomy to establish the nature of the ulcerations. (4) Indeed, in all but one patient (Lotsberg *et al.*, 1976), the diagnosis has been ascertained only after laparotomy (or necropsy) and histological examination of full thickness biopsies or resection specimens. The serosal surface may look normal at operation (Seliger *et al.*, 1973; Cerf *et al.*, 1977; Gouffier *et al.*, 1977; our case 3); peroperative enteroscopy might thus be of value to locate ulcerations and guide surgical sampling (Gouffier *et al.*, 1977). Thus a laparotomy with peroperative endoscopy and biopsies is presently the most reliable diagnostic procedure.

RELATIONSHIP WITH COELIAC DISEASE

The relationship between CNSUDJI and coeliac disease is not clear (Bayless *et al.*, 1974). Although a universally agreed definition of coeliac disease has not been achieved (Cooke and Asquith, 1974;

Booth, 1974), it can be considered as a condition in which a malabsorption syndrome and a typical pathological pattern of the proximal small bowel are associated and which improves on a gluten free diet (Trier, 1973). When discussing the relationship of this disease with CNSUDJI one is faced with problems concerning both the morphological and therapeutic criteria: (1) patchy villous atrophy with completely flat mucosa next to normal villi is frequent in CNSUDJI (Jeffries *et al.*, 1968; our case 3); a single peroral biopsy showing total villous atrophy may thus falsely suggest coeliac disease; multiple peroral biopsies are, in fact, crucial, as illustrated by case 3 in which three out of 10 mucosal samples showed a completely flat mucosa, whereas the presence of normal villi in other samples, one of which was duodenal, ruled out the disease. (2) A trial of a gluten free diet implies a sufficiently prolonged period of complete gluten exclusion with, at best, a morphological documentation of its effect; associated steroids may obscure the interpretation of this trial. These morphological and therapeutic requirements are rarely fulfilled and the lack of relevant information precludes further discussion of some of the published cases (Nyman, 1949; Himes *et al.*, 1957; Smitskamp and Kuipers, 1965; Moritz *et al.*, 1971; Seliger *et al.*, 1973). With these limitations in mind, patients with chronic ulcerations of the small bowel and malabsorption can be classified under three headings with respect to their relationship to coeliac disease:

Proven CD (fulfilling histological and therapeutic criteria) associated with ulcerations

Six such cases (Bayless *et al.*, 1967; Davidson, 1969; Neale, 1970; Dowling, 1972; Jones and Gleeson, 1973; Klaeveman *et al.*, 1975) have been already fully reported, to which our patients 1 and 2 can be added. Two similar cases are briefly mentioned by Hindle and Creamer (1965). Among the eight cases published with some detail the ulcerative process revealed coeliac disease by a surgical complication in two patients (Davidson, 1969; our case 2), was discovered at the same time as (Jones and Gleeson, 1973), or a few months after coeliac disease (Neale, 1970; Dowling, 1972; Klaeveman *et al.*, 1975) in four instances; in two cases (Bayless *et al.*, 1967; our case 1) a gluten free diet had been strictly followed for several years and the mucosa had returned to normal when ulcerations occurred; furthermore, in our case 2, the ulcerations developed in the distal jejunum, an area where the intervening mucosa had normal villi. These findings suggest that the ulcerative process of coeliac disease is not gluten-induced and does not require villous atrophy to develop. The presence of an obliterative arteritis in the ulcerations

of case 2 is probably a secondary phenomenon. The involvement of the colon in the ulcerative process, as in case 1, is a rare but already reported possibility (Dowling, 1972).

Possible CD associated with small bowel ulcerations

This group includes 11 patients with total or subtotal villous atrophy of the proximal jejunum but in whom gluten withdrawal had no effect (Shiner, 1963; Goulston *et al.*, case 2 and 3, 1965; Stuber *et al.*, 1971; Corlin and Pops, 1972; Armstrong *et al.*, 1973) or was unappreciable (London *et al.*, 1961; Cerf *et al.*, 1977); a gluten free diet was not prescribed in three of them (Goulston *et al.*, case 1 and 4, 1965; Lotsberg *et al.*, 1976). None of our patients belonged to this group. Search for a family history of coeliac disease, HLA typing and organ culture of jejunal biopsy specimen (Klaeveman *et al.*, 1975) might be helpful in these difficult cases.

Chronic ulcerations of small bowel and no coeliac disease (true idiopathic CNSUDJI)

In this group of 10 patients the histological picture rules out coeliac disease, as it shows either entirely normal villi (Patterson *et al.*, 1966; Case Records of the Massachusetts General Hospital, 1969; Karz *et al.*, 1971; Gouffier *et al.*, 1977; our case 4) or a patchy villous atrophy with adjacent areas of entirely normal and flat mucosa (Jeffries *et al.*, 1968; Gouerou *et al.*, 1977; our case 3). Our case 4 is unusual because of (1) its protracted evolution extending over 18 years; (2) the location of the ulcerations only along the mesenteric border of the intestine; and (3) the recent occurrence of a peripheral neuropathy of unknown aetiology but apparently different from the neurological disorder which may complicate the course of coeliac disease (Cooke and Smith, 1966; Bernier *et al.*, 1976).

TREATMENT

Treatment of CNSUDJI is difficult for the following reasons.

Many of these patients come to surgery because of stenosis, haemorrhage, or perforation: out of 12 patients who were followed up after resection of the whole (or supposedly so) abnormal area, five died (Goulston *et al.*, case 2, 1965; Case Records of the Massachusetts General Hospital, 1969; Neale, 1970; Karz *et al.*, 1971; Armstrong *et al.*, 1973), two did not improve until they were put on steroids (Klaeveman *et al.*, 1975) or a gluten free diet (our case 2), and one remained unchanged (our case 4). The four remaining subjects had a favourable outcome but received a gluten free diet immediately after surgery (Hindle and Creamer, 1965; Davidson, 1969; Moritz *et al.*, 1971).

Gluten withdrawal is beneficial (sometimes dramatically, as in case 2) to a few patients with villous atrophy of the proximal small bowel but only after the ulcerative process has been controlled by steroids (Jones and Gleeson, 1973) or surgery (Hindle and Creamer, 1965; Davidson, 1969; Moritz *et al.*, 1971; our case 2). A gluten free diet does not seem to influence or prevent the ulcerative process itself.

Corticosteroids are useful in a limited number of patients with ulcerations and proven coeliac disease (Jones and Gleeson, 1973; Klaeveman *et al.*, 1975), possible coeliac disease (Goulston *et al.*, case 4, 1965; Lotsberg *et al.*, 1976), and no coeliac disease (Jeffries *et al.*, 1968; our case 3).

Exclusive parenteral feeding can overcome severe nutritional distress, as in our cases 3 and 4, but failed in these patients to improve small intestinal function and morphology, though prolonged for 53 and 56 days respectively.

The general prognosis of CNSUDJI is poor, as 17 of the 30 patients whose follow-up has been published are dead at the time of publication. Six of the survivors come from the coeliac disease group: four are well on a gluten free diet alone (Hindle and Creamer, 1965; Jones and Gleeson, 1973; our case 2); one needs maintenance corticotherapy (Klaeveman *et al.*, 1975) and the last had a second perforation after giving up a gluten free diet (Davidson, 1969). None of the four survivors of the group with possible coeliac disease has fully recovered (Goulston *et al.*, case 4, 1965; Corlin and Pops, 1972; Lotsberg *et al.*, 1976; Cerf *et al.*, 1977). The third group seems to carry the worst prognosis, as only three out of 10 patients were alive at the time of publication (Patterson *et al.*, 1966; Gouffier *et al.*, 1977; our case 4).

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