Malignancy and adult coeliac disease

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The suggestion has been made that malignancy anywhere in the body may be accompanied by intestinal mucosal changes similar to those found in adult coeliac disease (Creamer, 1964). The following case report indicates that characteristic jejunal mucosal changes, once reverted to normal by a gluten-free diet, do not reappear if a malignancy develops, providing that the gluten-free diet is maintained.

CASE REPORT

E.T., a woman aged 63 when first seen (29 June 1963), complained of losing 28 lb in weight over the previous 18 months and of bone pains for four years. Three months before she developed oedema of the ankles, began to pass loose, pale stools once a day, and complained of epigastric discomfort. At another hospital, she had been found to have steatorrhoea (11 g/24 hr), abnormal intestinal radiographs, histamine-fast achlorhydria, and occasional positive stool tests for occult blood. She had been on a gluten-free diet for one month. On admission to the General Hospital, Birmingham, she weighed 101 lb and was thin with pitting oedema of the ankles. She had

a moderately distended abdomen, clubbing of the fingers, no glossitis, and a blood pressure of 98/65 mm Hg. Laboratory investigations are detailed in Table I. Radiological examination of the intestinal tract and skeleton showed a normal stomach and a persistent abnormality in the first part of the jejunum. The bones showed generalized demineralization but no evidence of osteomalacia. Jejunal biopsy produced two specimens which showed moderately severe histological abnormalities (grade II of Roy-Choudhury, Cooke, Banwell, and Smits, 1967) and were not diagnostic of adult coeliac disease. A presumptive diagnosis of reticulosarcoma was made and laparotomy advised. At operation, the stomach was normal on inspection and palpation: the small intestine was moderately distended and injected from the gastroduodenal junction distally. Biopsies were taken from the liver, pancreas, jejunum, and a mesenteric lymph node. No histological abnormalities were present except in the jejunal biopsy (Fig. 1) which was characteristic of adult coeliac disease.

She gradually improved on a gluten-free diet. However, her weight and serum albumin showed little improvement until milk was removed from her diet in addition to gluten. She was admitted for review nine months after laparotomy. Jejunal biopsy showed minor abnormalities

TABLE I
LABORATORY FINDINGS

Date	Weight (lb)	RBC $\times 10$ (cmm)	Hb. (g/100 ml)	PCV	MCV	MCHC	Serum Proteins (g/100 ml)		Ca (mg/100 ml)	P (mg/100 ml)
							Albumin	Globulin		
29. 6.63	100	3.95	11.4	38	96	34	1.9	2.4	7.4	2.4
15. 7.63	Laparotomy									
4. 9.63	101	4.34	13.1	42.5	96	31	2.2	2.3	7.9	2.4
29.11.63	109	4.10	13.2	42	102	32	3.8	2.7	8.3	2.0
30. 1.64	106	4.59	13.8	43.5	95	32.5	4.2	2.9	8.9	2.6
10. 4.64	108	4.72	13.4	43	92	32	4.5	2.8	8.8	2.5
4. 6.64	114						4.0	2.4	9.7	3.6
2.10.64	119	4.60	13.4	40	86	34.5			9.2	3.4
29. 4.65	116	4.53	13.4	40	88	34	3.7	2.0	9.3	3.9
21. 4.66	126	4.32	12.8	39	90	33	4.4	2.3	9.1	3.7
13.10.66	123	3.59	11.1	30	84	36	4.1	2.9	11.2	4.0
26. 1.67	120	4.12	11.2	35	85	32	3.3	3.2	8.5	3.3
3. 2.67	Laparotomy									
18. 3.67	Death									

in the three specimens obtained. Faecal fat excretion was still increased and the folic acid excretion test (Cox, Meynell, Cooke, and Gaddie, 1958) was abnormal. Calciferol, 1.25 mg daily, was given in view of the persistently raised serum alkaline phosphatase levels, low urinary calcium (15 mg/24 hr), and an iliac crest biopsy with increased osteoid.

Her health and weight continued to improve until October 1966 when a slight reduction in haemoglobin was noted (Table I). She felt well and had no complaints. In January 1967 she began to complain of epigastric pain. She had lost 3 lb in weight, the serum albumin had dropped from 4.1 to 3.3 g/100 ml, and the alkaline phosphatase had risen from 8 to 45 K.A. units. Examination showed guarding and tenderness beneath the left costal margin. X-ray studies showed destruction of the gastric mucosa of the body of the stomach from the fundus to the incisura. The area was abnormally rigid. The findings were those of gastric malignancy and lymphoma could not be excluded. At the second laparotomy a malignant perforated ulcer was found and she had a total gastrectomy and splenectomy. A biopsy of the jejunum from immediately adjacent to the site of the previous laparotomy biopsy was taken (Figure 2). Histological examination of the surgical specimen of the stomach revealed 'malignant granuloma' in the form of diffusely infiltrating reticulum cell sarcoma associated with necrotizing changes in the vessels. Secondary deposits were identified in one of the gastric lymph nodes. She died following a severe intestinal haemorrhage six weeks later (18 March 1967).

Limited postmortem examination showed no abnormality in the heart, lungs, and genito-urinary system. Permission was not granted to examine the neck or central nervous system. The abdominal cavity contained two abscess cavities communicating with the anastomotic

site. A blood vessel in one of the cavities had ruptured. Four ulcerated metastatic lesions, three in the jejunum and one in the ileum were identified, the largest 5 cm in diameter. Metastatic tumour tissue was identified in the mesenteric and para-aortic lymph nodes. The liver showed 'nutmeg' change.

Histological examination of the necropsy material revealed secondary deposits in the para-aortic and mesenteric lymph nodes. The liver showed early infiltration of the portal tracts and minute deposits were identified in bone marrow preparations. The wall of the abscess cavity near the tail of the pancreas was also infiltrated by reticulum cell sarcoma. Dissecting microscopy of the intestinal mucosa from jejunum to ileum showed digitate and leaf villi with occasional ridges and early convolutions (Figure 3). The histological appearances ranged from normal to grade I with occasional small areas of grade II. Slight autolysis was present but residual surface epithelium appeared normal. Calcified and uncalcified sections of bone showed osteoporosis. There was no evidence of osteomalacia.

DISCUSSION

The evidence in favour of the initial diagnosis of adult coeliac disease in this patient was the presence of steatorrhoea, a characteristic jejunal biopsy, low serum levels of folic acid, and biochemical evidence of osteomalacia and therapeutic response to calciferol. In confirmation of this diagnosis was the clinical and biochemical response to a gluten-free and milk-free diet and the reversion of the abnormal jejunal histology to normality. She had symptoms and signs of osteomalacia and of adult coeliac

TABLE I—continued
LABORATORY FINDINGS

Date	Alkaline Phosphatase (K.A. units)	Folic Acid L. casei (ng/ml)	B ₁₂ (pg/ml)	Fe (μg/ml)	TIBC (μg/ml)	Faecal Fat (g/24hr)	Treatment
29. 6.63	16	0.1	165	27	235	23	Folic excretion test 2.8/0.1. Glucose tolerance 90, 100, 115, 115, 120
4. 9.63	22						Gluten-free, milk-free diet
29.11.63	30	6.6	225				
30. 1.64	26						
10. 4.64	27	12.6	285	21	217	7.4	Folic excretion test 1.98/0.50. Glucose tolerance 95, 150, 155, 125, 115. ⁵⁵ CoB ₁₂ hepatic uptake 2037/μc/min
4. 6.64	24	4.3	170				Calciferol, 1.25 mg daily
2.10.64	12	5.3	150				
29. 4.65	8	13.7	205	106	279		
21. 4.66	8						
30.10.66	8						
21. 6.67	45			25	141	10.6	Calciferol, 0.5 mg daily

FIG. 1A.

FIG. 1B.

FIG. 1. A Surgical biopsy of jejunum showing the flat biopsy characteristic of adult coeliac disease $\times 20$.
B Higher-power view of area marked in A $\times 60$ showing cuboidal surface epithelium.

FIG. 2. A Surgical biopsy of jejunum at site of previous biopsy shown in Figure 1 $\times 10$.

B Higher-power view of surgical biopsy showing restoration of surface epithelium and grade 1 histological findings $\times 40$.

FIG. 2B.

FIG. 2A.

FIG. 3. *Dissecting microscopy* $\times 8$. A characteristic appearance of the upper small intestine seen at necropsy.

disease for approximately seven and a half years before her death. Three and a half years before death the stomach had appeared normal on radiology and was macroscopically normal at laparotomy.

Harris, Cooke, Thompson, and Waterhouse (1967) have presented evidence that there is a significant increase of gastrointestinal malignancy in adult coeliac disease. The patient reported here was included in the 202 patients surveyed (case number 72) and developed malignancy after that report had been completed.

The possibility cannot be excluded that the gastric reticulosarcoma was present at the time the initial flat biopsy was obtained. However, if a malignancy was then present, it is evident that the jejunal mucosal lesion responded to a gluten-free diet and if it was not present, the subsequent development of reticulosarcoma with metastatic involvement of the jejunum and ileum did not result in a flat mucosa. We believe that in this patient the primary lesion was adult coeliac disease of long duration, and that this was complicated by reticulosarcoma. Since the mucosal lesion was responsive to a gluten-free diet and not influenced by extensive malignancy, it provides some evidence that the presence of a flat mucosa in patients with malignant lesions indicates adult coeliac disease complicated by malignancy, rather than the mucosal lesion is produced by the malignant neoplasm.

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