Adenocarcinoma of the small bowel as a complication of Crohn's disease

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SUMMARY Two cases of adenocarcinoma of the bowel occurring in association with Crohn's disease are described. The first affected the terminal ileum and the second the terminal ileum and caecum. The 28 cases so far described in the world literature are briefly reviewed. It is suggested that adenocarcinoma of the small bowel may be a complication of longstanding Crohn's disease. Eleven patients developed the carcinoma in a surgically bypassed segment of bowel, and it is therefore recommended that where surgery is undertaken excision rather than bypass should be the treatment of choice.

Case 1

Mr L.W. presented in 1957 at the age of 33 with the signs and symptoms of acute appendicitis. At operation the appendix was normal but the terminal 18 in. of ileum was thickened, oedematous, and inflamed. A clinical diagnosis of Crohn's disease was made and an ileo-transverse colostomy performed.

For 13 years he was fairly well with only occasional attacks of diarrhoea and abdominal pain. In December 1970 he presented with abdominal pain, fever, bleeding per rectum, and diarrhoea. Examination revealed a mass in the right iliac fossa. Barium meal and follow-through showed stenosis of the ileo-transverse anastomosis and a grossly contracted terminal ileum between the anastomosis and the caecum. His symptoms settled with conservative therapy but by February 1972 they had progressed and a laparotomy was performed.

At operation a grossly thickened and indurated terminal ileum was found. There was marked fibrosis around the ileo-transverse anastomosis and the ileum proximal to this was dilated. The other viscera appeared normal. A right hemicolectomy was performed, together with excision of the diseased ileum, and the continuity of bowel was restored with an end-to-end anastomosis.

Macroscopically the specimen consisted of terminal ileum (50 cm) with the caecum and colon (30 cm) and an old ileo-transverse anastomosis. There was a stenosing white tumour of the ileum, 2 cm proximal

Fig. 1 Adenocarcinoma infiltrating muscle wall of ileum (haematoxylin and eosin $\times 40$).

Fig. 2 Non-neoplastic chronic ulceration at anastomosis (haematoxylin and eosin $\times 40$).

Fig. 3 Epithelioid follicles in wall of small intestine (haematoxylin and eosin $\times 65$).

to the ileo-caecal valve and extending for 11 cm proximally. On histological examination this tumour was seen to be an adenocarcinoma of the terminal ileum (Fig. 1). No tumour was present at the ileo-transverse anastomosis but there was chronic ulceration with fissuring consistent with Crohn's disease (Fig. 2).

Case 2

Mrs. L.K. presented in 1960 at the age of 42 with subacute, small bowel obstruction and a four-year history of intermittent abdominal pain and diarrhoea. At operation a 6 in. area of terminal ileum was found to be thickened and contracted, and the bowel proximal to this was grossly dilated. A clinical diagnosis of Crohn's disease was made and an ileo-transverse colostomy performed.

In May 1967 she suffered a severe exacerbation of her symptoms and underwent laparotomy. Three skip lesions of Crohn's disease were found, 3 in. and 6 in. from the ileo-caecal valve and 5 in. from the duodeno-jejunal flexure. These were excised and the

ileo-transverse colostomy was disconnected. Histological examination of the resected lesions showed the classical features of Crohn's disease (Fig. 3). She remained in moderate health on conservative therapy until June 1971. She then suffered a relapse and a barium meal at that time showed a filling defect in the medial border of the proximal part of the ascending colon with an abnormal terminal ileum. At operation in February 1972 a hard mass was found in the right iliac fossa which consisted of a grossly contracted and thickened terminal ileum coiled upon itself. It was adherent to an abnormally thickened caecum, and the regional lymph nodes were hard and enlarged. The liver was normal. A right hemicolectomy with end-to-end anastomosis was performed.

Macroscopic examination of the specimen showed that it consisted of colon and caecum (30 cm) and adherent loops of terminal ileum (24 cm). There was a white, hard growth involving the terminal ileum, ileo-caecal valve, caecum, and part of the ascending colon. Histologically there was no evidence of active Crohn's disease. The tumour proved to be an extensive columnar-celled adenocarcinoma involving

Fig. 4 Ileo-caecal adenocarcinoma infiltrating mesenteric fat (haematoxylin and eosin $\times 40$).

Year	Author	Age at Diagnosis of Carcinoma	Sex	Symptoms (yr)	Tumour	Crohn's	Diagnosis	Outcome after Operation
1956	Ginzburg <i>et al</i>	30	M	19	Jejunum	Jejunum	Postoperative	Died 6/12, metastases
1957	Kornfield <i>et al</i>	36	F	8	Jejunum	Jejunum	At surgery	Died 6/12, metastases
1958	Crohn and Yarnia	—	—	—	Jejunum	Jejunum & ileum	—	—
1958	Bersack <i>et al</i>	26	M	9	Duodenum, jejunum, colon	Ileum	Necropsy	Died 4/52
1958	Lear	—	—	—	Ileum	Ileum	Postoperative	—
1959	Buchanan <i>et al</i>	47	M	28	Ileum	Ileum	Postoperative	—
1959	Weingarten <i>et al</i>	44	F	27	Jejunum ¹	Jejunum	Postoperative	Died 4/12, metastases
1960	Weingarten and Weiss	28	F	5	Ileum ¹	Jejunum & ileum	At surgery	Died 3 years, metastases
1960	Zisk <i>et al</i>	61	F	1/52	Ileum	Ileum	Postoperative	Died 2/52, pulmonary embolism
1960	Zisk <i>et al</i>	62	F	25	Ileum ¹	Ileum	Preoperative	—
1960	Steele and McNeely	38	M	15	Ileum ¹	Ileum	Necropsy	—
1960	Almond <i>et al</i>	48	F	15	Ileum	Ileum	Postoperative	—
1963	Hoeffert <i>et al</i>	40	M	1.5	Ileum	Ileum	Postoperative	Died 2 years, metastases
1964	Berman and Prior	51	M	25	Ileum	Ileum	Postoperative	Alive & well immediately after operation
1968	Cantwell <i>et al</i>	60	M	31	Ileum	Ileum	Postoperative	Died 4 days, metastases
1968	Shiel <i>et al</i>	40	F	5	Ileum	Ileum	Postoperative	Died 16/12, metastases
1968	Morovitch <i>et al</i>	41	M	22	Ileum	Ileum	Postoperative	Died 4/12, metastases
1969	Tyers <i>et al</i>	32	M	12	Jejunum ¹	Jejunum & ileum	Postoperative	Died 3/12, metastases
1969	Wyatt	31	M	7	Ileum	Ileum	Postoperative	Died 1 day, bronchopneumonia
1969	Magnes and Bell	71	M	11	Ileum	Ileum	Postoperative	—
1970	Farmer <i>et al</i>	43	M	9	Jejunum ¹	Jejunum	Postoperative	Died 7/12
1970	Farmer <i>et al</i>	61	F	7	Jejunum	Jejunum	Postoperative	Died 3/12, metastases and pulmonary embolism
1970	Brown <i>et al</i>	55	F	25	Ileum ¹	Ileum	Postoperative	Died 1/12
1970	Goldman <i>et al</i>	21	F	9	Jejunum	Jejunum & ileum	Postoperative	—
1970	Schuman	48	M	7	Ileum	Ileum	Postoperative	—
1970	Rha <i>et al</i>	38	M	5/12	Ileum	Ileum	Postoperative	Alive and well, 6/12
1972	Schofield	20	M	7	Ileum	Ileum	At surgery	Died 2 years, metastases
1972	Schofield	20	M	4	Ileum ¹	Ileum	At surgery	Died few months, metastases
1972	Frank	48	M	15	Ileum ¹	Ileum	Postoperative	Alive and well, 3/12
1972	Frank	55	F	16	Ileo-caecal ¹	Ileum	Postoperative	Alive and well, 3/12
1973	Frank and Shorey present series							

Table I Recorded cases in the literature of small bowel adenocarcinoma associated with Crohn's disease

¹Bypassed segment of bowel

the ileo-caecal region and infiltrating the mesenteric fat (Fig. 4).

Discussion

The first case of an adenocarcinoma of the small bowel occurring in association with Crohn's disease was reported by Ginzburg, Schneider, Dreizin, and Levinson in 1956, 24 years after the original description of the disease as a pathological entity (Crohn, Ginzburg, and Oppenheimer, 1932). Over the past 16 years there has been a progressive increase in the number of cases appearing in the literature (Table I), possibly because there is now a greater awareness that an association may exist between these two diseases. The reported incidence of this association is almost certainly low, due to the fact that a small carcinoma may easily be overlooked. Multiple sections must be taken and the specimen examined thoroughly before a case of longstanding Crohn's disease is labelled 'no sign of malignancy'.

The diagnostic signs and symptoms of an adenocarcinoma of the small bowel are usually masked by those of Crohn's disease and thus a preoperative diagnosis is virtually impossible. It appears that only Zisk (Zisk, Shore, Rossoff, and Friedman, 1960) has suspected the diagnosis before operation, and his suspicions were aroused because of a previous encounter earlier in the year with a patient in whom the two diseases coexisted.

Significant differences exist in the natural history, pathology, and prognosis of small bowel adenocarcinoma arising in otherwise normal small bowel and adenocarcinoma arising in small bowel which is also the site of Crohn's disease. Table II shows that the latter disease affects a much younger age group, has a worse prognosis, and no five-year survivors have, as yet, been reported. In addition, adenocarcinoma of the small bowel arising in patients with Crohn's disease occurs twice as frequently in the

ileum than in the jejunum. This is in contrast to adenocarcinoma occurring in patients with otherwise normal small bowel in whom the jejunum is three times more commonly affected than the ileum (Darling and Welch, 1959; Pagtalunan, Mayo, and Dockerty, 1964).

Adenocarcinomas have arisen in bypassed segments of bowel in nine out of the 28 cases so far reported and in both patients described in this paper, although the bypass was disconnected in the second patient five years before the carcinoma was discovered. It appears, therefore, that where surgery for Crohn's disease has to be undertaken, and there are no contraindications to resection, excision of the affected area should be the treatment of choice.

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	Small Bowel Adenocarcinoma Alone	Small Bowel Adenocarcinoma with Crohn's Disease
Average age at diagnosis	55 yr	43 yr
Duration of symptoms	14 mth	12 yr
Site of carcinoma	Jejunum/ileum 3'5/1	Jejunum/ileum 1/2
Reported average postoperative survival	32 mth	8 mth
Reported five-year survival	20%	0 recorded cases (inadequate follow-up)

Table II Comparison of small bowel adenocarcinoma and small bowel adenocarcinoma associated with Crohn's disease

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