Neoplasms of the Small Bowel

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Small bowel tumors are unusual lesions exhibiting nonspecific clinical features often diagnosed at an advanced stage. In the cases studied at the Hospital of the University of Pennsylvania nearly all the 32 patients with malignancies were symptomatic whereas in the 34 patients with benign lesions the condition was discovered as an incidental finding in about half of the patients. Weight loss, palpable mass or anemia usually indicated malignancy. Small bowel radiography was the most useful diagnostic aid in the present series. While the etiology of these lesions is unknown, villous adenomas probably bear a relationship to carcinoma. The association between chronic regional enteritis and small bowel tumors is unestablished but suggestive. An analysis of reported series reveals a disproportionate incidence of additional primary tumors in patients with small bowel neoplasms. Surgical extirpation is indicated for curative treatment. In the present series, resection in hope of cure was carried out in 25 of 32 malignant tumors resulting in eight five-year survivals. One of these latter lived nine years with disseminated malignant carcinoid reflecting the occasional indolent course of this tumor.

THOUGH REPRESENTING 75% of the length and over 90% of the mucosal surface area of the alimentary tract, the small intestine is the site of only 3–6% of gastrointestinal neoplasms[1] and approximately 1% of malignant tumors.[8] Only 650 malignant small bowel tumors were recorded in the literature between 1920 and 1965;[18] merely 60 malignancies were found among nearly one million patients admitted to Charity Hospital in New Orleans.[7]

Prompt recognition and expeditious treatment of these lesions are unusual not only as a consequence of their infrequency, but also because of the often vague and non-specific manifestations they produce.

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Improved management of these rare neoplasms depends upon appreciation of their clinical and pathologic features knowledge of which necessarily derives from the combined experience of many institutions.

The present study analyzes the experience with primary small bowel tumors at the Hospital of the University of Pennsylvania.

Clinical Material

Thirty-two malignant and 34 benign neoplasms of the small intestine were diagnosed at the Hospital of the University of Pennsylvania between 1950 and 1970. All lesions included in this analysis were identified histologically following operation or autopsy. Patients ranged 35–79 years of age. Average age at diagnosis was 59.5 years. Patients harboring malignant lesions average 56.8 years compared to 62.2 years for patients with benign lesions.

Malignant lesions were divided equally between males and females, but 23 of the 34 benign lesions were in men.

Thirty of the 32 malignant lesions produced clinical manifestations (Table 1). Weight loss was the most common finding in these patients; it was recorded in 17 instances. Fifteen patients complained of pain evidently related to bowel obstruction or local tumor invasion. Nausea or vomiting occurred in 11 patients, and bleeding, manifest as hematochesis or melena, was reported in eight.

Anemia (hemoglobin less than 10.5 gm%) was the most common clinical sign associated with small bowel malignancy and was encountered in 13 of these patients. Physical examination revealed an abdominal mass in seven and jaundice in two. Obstruction, either partial or complete, was documented in six cases of which two

TABLE 1. *Clinical Manifestations of Small Bowel Tumors*

	Malignant Tumors (32)	Benign Tumors (34)
Symptomatic	30 (94%)	18 (53%)
Weight loss	17 (53%)	6 (17%)
Pain	15 (47%)	14 (40%)
Anemia	13 (41%)	5 (15%)
Nausea or vomiting	11 (34%)	8 (24%)
GI bleeding	8 (25%)	11 (32%)
Mass	7 (22%)	1 (3%)
Obstruction	6 (19%)	7 (21%)
Diarrhea	5 (16%)	3 (9%)
Constipation	4 (13%)	2 (6%)
Jaundice	2 (6%)	0 (0%)
Asymptomatic	2 (6%)	16 (47%)
Autopsy finding	2 (6%)	12 (35%)
Clinical or operative finding	0 (0%)	4 (12%)

were due to intussusception. Two patients were asymptomatic; their lesions were incidental findings at operation for other cause.

Of eight patients with malignant carcinoid, six presented with weight loss, and diarrhea and pain were each reported by five patients. Flushing associated with elevated levels of urinary 5-hydroxy-indole acetic acid occurred in two patients.

In contrast to malignant lesions, 16 of the benign tumors including nine carcinoids were incidental findings at autopsy, operation, or during clinical evaluation of unrelated symptoms. Among symptomatic patients, abdominal pain was the most prominent feature, occurring in 14. Rectal bleeding occurred in ten; one patient presented with hematemesis. Nausea, vomiting, weight loss, diarrhea, and constipation occurred among these patients but infrequently (Table 1).

Signs of obstruction were present in seven patients with benign lesions. Intussusception was responsible for the obstructive picture in two of these instances and caused the mass palpated in one patient. Five individuals were anemic.

Of 48 symptomatic patients, 27 reported symptoms of at least six months' duration. Eighteen of the 27 had malignant lesions. Among symptomatic patients, nine malignancies and six benign neoplasms were symptomatic over one year prior to diagnosis (Table 2).

The preoperative diagnosis of small bowel neoplasm was made in 28 cases in this series. Accurate preoperative diagnosis was made in 17 (53%) of the patients harboring malignancies. In 15 of these 17 cases, barium studies of the upper gastrointestinal tract including the small bowel ("long GI series") revealed the lesion. Two additional malignant lesions were diagnosed by identifying the features of the carcinoid syndrome. Nine symptomatic and two asymptomatic patients with benign lesions were diagnosed preoperatively by means of long GI series. Two other patients had abnormalities described in long GI series (mass, partial small bowel obstruction), but the diagnosis of small bowel tumor was not entertained. Nineteen additional patients had films interpreted as showing a normal small bowel pattern. Thus, 26 of 41 long GI x-ray examinations revealed the lesion. Barium enema examination revealed an ileal lesion by reflux of barium into the ileum in two cases.

The histologic and anatomic distribution of the lesions encountered in this series is presented in Table 3. The 32 malignancies were distributed generally throughout the small bowel. However, over half of the 19 adenocarcinomas were duodenal. Three-quarters of the malignant carcinoids were located in the ileum. A wide variety of benign lesions was identified, but leiomyomas and benign carcinoids accounted for one-third of the lesions. Nine of the ten benign carcinoids were found in the ileum.

Thirteen of the patients in this series had 14 other primary tumors outside of the small bowel. The small bowel lesion in seven of these patients was carcinoid (Table 4).

Treatment and Prognosis

Twenty-one patients with benign small bowel lesions had an operative procedure. The procedures performed included 13 wedge resections, four polypectomies, one

TABLE 2. *Duration of Symptoms*

	Malignant Tumors (30)	Benign Tumors (18)
0–5 days	5	5
5 days–2 months	3	1
2 mos.–6 mos.	4	3
6 mos.–1 year	9	3
More than 1 year	9	6

TABLE 3. *Histologic and Anatomic Distribution of Small Bowel Tumors*

	Total	Duodenum	Jejunum	Ileum
Adenocarcinoma	19	10	5	4
Malignant carcinoid	8	0	2	6
Leiomyosarcoma	4	1	2	1
Lymphosarcoma	1	0	0	1
Malignant tumors	32	11	9	12
Leiomyoma	12	4	7	1
Benign carcinoid	10	1	0	9
Hemartoma	3	2	1	0
Inflammatory polyp	2	0	0	2
Lymphangioma	2	1	1	0
Lipoma	2	0	1	1
Brunners gland polyp	1	1	0	0
Endometriosis	1	0	0	1
Leiomyoblastoma	1	0	1	0
Benign tumors	34	9	11	14
All tumors	66	20	20	26

gastrectomy for carcinoid of the first part of the duodenum, and one right hemicolectomy for an ileal carcinoid. A duodenal leiomyoma and a duodenal lymphangioma were incidental findings in gastrectomy specimens in two patients operated upon for peptic ulcer disease.

The treatment and survival data for patients with malignant lesions are tabulated in Table 5. Of 11 patients with duodenal malignancies, nine underwent treatment intended to cure. Three adenocarcinomas were extirpated by wedge resection and three by polypectomy. Two patients were treated by radical pancreaticoduodenectomy (Whipple operation). No five-year cures were achieved. An additional patient had a palliative bypass and another had no operative procedure. A leiomyosarcoma of the duodenum was managed by pancreaticoduodenectomy. This patient died four years postoperatively free of disease.

Seven jejunal malignancies, including one malignant carcinoid, four adenocarcinomas and two leiomyosarcomas were treated by wide wedge resection for cure. Two patients with adenocarcinoma and one with leiomyosarcoma survived five years. Two patients underwent palliative resection. One patient with malignant carcinoid with metastases survived nine years following a palliative resection, the latter six years with the carcinoid syndrome.

Curative resection, including two right hemicolectomies, was performed in nine patients with ileal malignancies. Five-year cure was achieved in two of four malignant carcinoids, one of three adenocarcinomas and in the sole instance of lymphosarcoma. The latter was treated by right hemicolectomy and postoperative irradiation. Hemicolectomy for an ileal adenocarcinoma failed to eradicate the disease.

TABLE 4. *Other Neoplasms in Patients with Small Bowel Tumors*

Small Bowel Tumor	Other Primary Tumor
Benign Carcinoid (ileum)	Carcinoma of Esophagus
Benign Carcinoid (ileum)	Carcinoma of Cervix
Benign Carcinoid (ileum)	Leiomyoma of Stomach
Benign Carcinoid (ileum)	Carcinoma of Gall bladder
Malignant Carcinoid (jejunum)	Carcinoma of Rectum
Malignant Carcinoid (ileum)	Papillary Carcinoma of Bladder
Carcinoma (duodenum)	Carcinoma of Cervix
Carcinoma (duodenum)	Carcinoma of Colon
Lipoma (jejunum)	Carcinoma of Lung
Leiomyoma (duodenum)	Carcinoma of Colon
Leiomyoma (duodenum)	Carcinoma of Prostate
	Retroperitoneal liposarcoma
Leiomyosarcoma (jejunum)	Carcinoma of Prostate

Thus, 25 patients with malignancy were subjected to operation intended for cure: 17 wedge resections, three radical pancreaticoduodenectomies, three polypectomies, and two hemicolectomies. Seven five-year cures were achieved. An additional patient died at four years free of disease, and another died nine years following palliative resection.

Discussion

Reported series indicate that small bowel tumors are rare lesions which generally occur later in life, the median age of diagnosis being in the sixth decade. There is a slight predominance of occurrence in males.[7,14,15,19]

TABLE 5. *Malignant Tumors: Treatment & Survival*

		Operation				
	Total	Curative	Palliative	None	5 Year Survival	Lost to Followup
Adenocarcinoma						
Duodenum	10	8	1	1	0	2
Jejunum	5	4	1	0	2	0
Ileum	4	3	1	0	1	0
	19	15	3	1	3	2
Malignant Carcinoid						
Jejunum	2	1	1	0	1*	0
Ileum	6	4	2	0	2	0
	8	5	3	0	3	0
Leiomyosarcoma						
Duodenum	1	1†	0	0	0	0
Jejunum	2	2	0	0	1	0
Ileum	1	1	0	0	0	0
	4	4	0	0	1	0
Lymphosarcoma						
Ileum	1	1‡	0	0	1	0
All Malignancies	32	25	6	1	8	2

* Patient had palliative resection, lived 9 years with metastases.
† Patient died at four years free of disease.
‡ Patient received radiotherapy postoperatively.

Clinical Features

A wide variety of protean manifestations occur with these lesions. Abdominal pain, nausea, vomiting, weight loss, palpable mass, and anemia are the commonest and most characteristic symptoms.[5–7,14,15,19] Dorman[7] identified cramping abdominal pain, weight loss, and a palpable mass as a "diagnostic triad of paramount importance." Peripapillary lesions frequently produce jaundice. Weight loss and a palpable mass, when present, tend to distinguish malignant from benign lesions;[5] however, a mass was recorded in only five of 77 patients with malignancies at the Lahey Clinic.[1]

Diagnosis

Although over 90% of malignant tumors produce symptoms[1,8,19] diagnosis is frequently delayed for long periods. A correct preoperative diagnosis was made in 53% of symptomatic patients reported by Strauch[24] and in only 21% reported by Ostermiller.[14]

Preoperative diagnosis was made radiographically in about 50% of patients with malignancy in the present series. Small bowel radiography revealed abnormalities in 14 of 19 studies in patients subsequently shown to have malignant lesions at Johns Hopkins Hospital.[8] In addition to the characteristic x-ray findings in obstruction and intussusception, Good has identified several radiographic patterns seen in barium contrast studies of the small bowel.[9] Local filling defects in the barium column may be 1) intraluminal, 2) mucosal or ulcerating, or 3) intramural. Intraluminal filling defects are most commonly caused by adenomatous polyps, but other lesions such as leiomyomas may become pedunculated and produce this picture. Mucosal or ulcerating defects are often caused by adenocarcinoma or lymphomas. Lesions arising intramurally such as lymphomas or sarcomas may encroach upon the lumen but the mucosa remains intact. In contrast, such lesions growing outward, rather than compromising the lumen, may produce a clinically palpable mass which correlates radiographically with displacement of adjacent small bowel loops.[1,6,9,18]

Pathology

Sarcomas, lymphomas, and carcinoids increase in incidence progressively from the duodenum to ileum. In contrast, adenocarcinomas are nearly evenly distributed between the duodenum, jejunum, and ileum with perhaps slight predominance in the duodenum.[2,18] Twenty per cent of duodenal adenocarcinomas are peripapillary; the remainder are divided evenly between supra- and infra-papillary locations.[18]

Adenocarcinoma is the most common variety of malignant tumor affecting the small bowel, representing nearly one-half of such lesions.[18] Excluding carcinoids, lymphomas follow adenocarcinoma in frequency of occurrence.[12] Lymphosarcoma, reticulum cell sarcoma, and Hodgkin's disease occur in decreasing order of frequency. Of 48 lesions studied at the Mount Sinai School of Medicine,[13] there were 31 lymphosarcomas, ten reticulum cell sarcomas, and seven cases of Hodgkin's disease. The age, sex distribution, and clinical manifestations of these lesions were similar to the general features of small bowel lesions described above.

Leiomyosarcomas are characterized by their intramural origin, the large size they attain, and their vascular nature producing a high incidence of bleeding.[6,10]

Etiology

In general, the etiology of small bowel neoplasms is unknown. However, the multiple polypoid hamartomas of the Peutz-Jeghers syndrome are inherited as a Mendelian dominant trait.[6]

Small bowel villous adenomas appear to bear the same relationship to carcinoma as colonic lesions.[11,22] In a review of the literature from Cleveland Clinic, 27 cases of small intestinal villous adenomas were collected.[11] Of 20 duodenal lesions, five contained invasive adenocarcinoma, two focal carcinoma, and one *in situ* carcinoma. Among seven jejunal villous adenomas two contained invasive carcinoma and one "superficial" carcinoma.

Whereas a clear association exists between long standing ulcerative colitis and subsequent colon carcinoma, the relation between chronic inflammatory disease and malignancy of the small bowel is unestablished. However, recent reports suggest such an association may exist.[3,4,17,21,25] Twenty-five cases of small bowel adenocarcinoma complicating chronic regional enteritis have been reported. Nine of these tumors have occurred in segments of small bowel previously bypassed because of Crohn's disease. Tyers[25] and Steiger[21] point out that adenocarcinomas arising in patients with regional enteritis differ from the usual lesions in that they occur at an earlier age (average 42.9 years), their distribution parallels that of the inflammatory disease (69% in ileum), and the prognosis is grave (no five-year survivals).

A high incidence of additional primary tumors occurs in patients with small bowel neoplasms. Reyes and Talley[16] reported an incidence of second primary neoplasms outside the small intestine of 17.7% compared to 0.33% noted in the average population. In that series, 11 of 62 patients had 13 second primary tumors including three basal cell carcinomas and three rectal adenocarcinomas. Second primary malignancies occurred in 10 of 60 patients, in 12 of 61 patients, and in six of 47 patients in series reported by Dorman,[7] Ostermiller[14] and Strauch[24] respectively.

Treatment

Curative treatment for malignant lesions entails wide resection with the adjacent mesentery. In McPeak's view[10] adequate management requires pancreaticoduodenectomy for duodenal lesions and right hemicolectomy for distal ileal lesions. Opinions regarding the adjuvant role of radiotherapy in lymphomas vary. Sternlieb[23] recommends it; Weaver[26] questions the value of radiotherapy in patients in whom lymph nodes are negative and the tumor has been removed.

Patients with metastatic carcinoid appear to benefit by the reduction in tumor burden achieved by palliative resection of primary and metastatic tumor. Brookes[2] reports a 33% five-year survival rate after palliative surgery.

Prognosis

The prognosis for adenocarcinoma is grim. Five-year survival figures range from 16.4 to 32% in reported series.[2,7,15,19] Corresponding figures for lymphoma range between 31–40%.[13,15] A 48% five-year survival rate following resection of leiomyosarcoma was reported by Pagtalunan.[15]

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