Primary Lymphoma of the Gastrointestinal Tract:
A Review of 100 Cases

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PRIMARY malignant lymphomas of the intestinal tract are relatively uncommon and in most reports comprise from 1 to 4% of of the malignant neoplasms of the gastrointestinal tract.[4] Since 1932, 100 instances of malignant lymphoma, originating in the gastrointestinal tract, from the stomach to the rectum, have been seen at The New York Hospital. In all cases, the diagnosis was confirmed by microscopic examination.

This comprises 1.7% of all malignant gastrointestinal tumors treated since 1932. The series includes 52 male and 48 female patients. Ages ranged from two to 81 years, average 54 years.

The distribution of these tumors throughout the gastrointestinal tract is listed in Table 1. The stomach is by far the most common site of origin.

Although in most reports the ileum is the most frequently involved site in the small intestine, this was not so in our series.

Clinical Picture

Stomach

In this group of 63 patients, there were 37 men and 26 women. The average age was 56 years with a range of 37 to 81 years. The most frequently encountered complaint was abdominal pain (46 pts.). The duration of symptoms varied from 4 days to 25 years; in most cases significant symptoms were present for 2 to 3 month periods. In almost all instances pain was primarily epigastric and was described as dull and relatively constant. The severity of pain rarely decreased on ingestion of food or alkali. History of weight loss was elicited in 33 cases. In four the chief complaint was dysphagia. Nausea and vomiting were significant symptoms in only 12 patients.

On physical examination all patients were afebrile. An epigastric mass was palpable in 17 patients at the time of admission.

Laboratory tests were of little value in establishing the diagnosis. Thirty patients were anemic to some degree. None had peripheral blood or bone marrow pictures characteristic of leukemia. Stool guaiac examinations were positive in 40 patients. In 11 bleeding was severe enough to warrant preoperative blood transfusions. Gastric analyses were performed in 36 cases. Free acid was absent in all but one. In only ten was acid produced following the administration of histamine. Cytological examinations of gastric washings were performed in 30 patients; in only seven were cells considered suspicious of malignancy.

Esophagoscopy was performed in three patients and gastroscopy in 13 patients. In

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none was the diagnosis of lymphoma established. The diagnosis of carcinoma was considered in 11, benign gastric ulcer in one, esophagitis in two, and in two no lesion was visualized.

Roentgenologic studies were performed on 48 patients. The diagnosis of malignant tumor was made in 39. Other diagnoses included hypertrophic gastritis, chronic duodenitis, benign gastric tumor and normal stomach.

Small Intestine

The small bowel was the site of origin in 25 lymphomas; this group was composed of ten male and 15 female patients. Average age was 42 years with ae range of two to 79 years. All gastrointestinal lymphomas in children were in the small intestine.

The most common complaint on admission was abdominal pain (19 pts.). Over half of the patients had non-specific complaints of malaise, anorexia and fatigue. Symptoms varied from 2 days to 10 months in duration. Pain varied in character and location. In about half it was described as dull and chronic with no area of localization. It was frequently exacerbated by ingestion of food. In three patients pain appeared to be related to recurrent episodes of intussusception and consisted of intermittent attacks of severe lower abdominal "cramps." In four patients pain was related to bowel perforations with subsequent peritonitis. There was a history of weight loss in 13 cases, and a history of vomiting in 12 although none reported hematemesis. Seven patients had recent rectal bleeding, one severe enough to require blood transfusion. Four patients complained of excessive diaphoresis. Five had diarrhea. Three patients with malabsorption syndrome for several years were subsequently found to have small bowel lymphomas.

On physical examination, 11 patients were febrile with temperatures ranging from 38.2 to 40.6 degrees centigrade. Four of these 11 had peritonitis associated with perforated tumors. Seven had palpable abdominal masses at the time of admission.

Laboratory tests showed anemia in six patients. Stool examinations for occult blood were positive in 13. No patient had lymphocytosis.

Roentgenographic studies were performed on ten patients. The diagnosis of lymphoma was made in three. Other diagnoses included cecal tumor, regional ileitis, duodenal ulcer and normal small intestine.

TABLE 1. *Location of Lymphoma Throughout the GI Tract*

Site		No. of Cases
Stomach		63
Small intestine		25
Duodenum	4	
Jejunum	12	
Ileum	9	
Appendix		2
Large intestine		10
Cecum	6	
Rectum	4	
Total cases		100

Appendix

Two cases of appendiceal lymphoma occurred in women and were found incidentally during operation for unrelated diseases.

Large Intestine

Ten patients had primary lymphomas of the large intestine, five men and five women. The average age was 54 years with a range of 29 to 68 years.

Symptoms varied with the site of the lesion. Of six patients with cecal tumors, five complained of crampy lower abdominal pain. All had anorexia and weight loss to some degree. Three had rectal bleeding of recent onset. Two complained of diarrhea. In four patients with rectal lesions,

TABLE 2. *Results of Therapy—Stomach*

Definitive resections	48 patients	
a) died post-op	— 2	
b) alive post 5 yrs.	—16	
		a) curative x-ray— 4
		b) other —12
c) died tumor-free post 5 yrs.	— 9	
		a) curative x-ray— 3
		b) other — 6
d) died of lymphoma	— 8	
		a) curative x-ray— 1
		b) other — 7
e) followed less than 5 yrs.	—13	
Unresectable	15 patients	
a) died post-op	— 1	
b) survived 5 yrs.	— 0	
c) died of lymphoma	—11	
		a) curative x-ray— 4
		b) other — 7
d) followed less than 5 yrs.	— 3	

symptoms were related to distal bowel obstruction. All complained of increasing constipation and tenesmus. Two patients had rectal bleeding. Another sought medical aid for hemorrhoids. Two of the four patients had histories of recent weight loss.

On physical examination all six patients with cecal lesions had masses palpable in the lower abdomen. All four rectal tumors were evident on rectal examination. None of the patients was febrile and one displayed lymphadenopathy.

Laboratory tests showed anemia in four patients—two with cecal lesions and two with rectal lesions. Blood counts were otherwise normal in all patients. Stool guaiac examinations were positive for occult blood in six of the ten patients.

Barium enema x-rays were obtained on five patients; the diagnosis of tumor was made in four. One x-ray was described as normal.

Therapy and Results

Stomach

The type of operations performed and additional x-ray therapy varied with the location and extent of the tumors. The most common site of origin of gastric lymphoma was in the area of the greater curvature (22 cases). In some the tumor was too diffuse at the time of operation to identify a primary site.

Definitive resections were performed on 48 patients; procedures included esophagogastrectomy, subtotal and total gastrectomy and segmental gastric resection, combined with splenectomy, partial pancreatectomy or partial hepatectomy when indicated. Fourteen patients were considered unresectable at the time of operation. Eleven of whom underwent only biopsy; three underwent palliative resections or bypass gastroenterostomies. One patient was judged inoperable when metastasis was demonstrated in a supraclavicular lymph node.

Thirty-one patients received no radiotherapy postoperatively, seventeen were given palliative x-ray therapy. In 15 patients "curative" tumor doses of 3,000 rads to 4,000 rads were given. Two received cobalt therapy and one was treated with the 6 MEV machine; all the others were treated with 250 K.V.

Results of therapy of gastric lymphomas are listed in Table 2.

Of 48 patients who underwent definitive procedures (i.e., were "resectable") one died on the first postoperative day of peritonitis. A second died ten days following operation from bronchopneumonia. Of 14 patients judged unresectable one died on the first postoperative day of peritonitis. The operative mortality for the 62 patients undergoing operation was 4.8 per cent.

Forty-seven patients with gastric lymphomas are eligible for follow-ups of 5 or more years. Twenty-five survived for 5 or more years, a survival rate of 53 per cent.

This compares with most other series.[3, 7] Only two of 25 patients surviving more than 5 years thereafter died of lymphoma. In both of these, symptoms of recurrent tumor were manifest by the second postoperative year. The 10-year survival rate is 43% (18 of 42 eligible patients).

All patients surviving 5 or more years underwent definitive resections. No patient judged "inoperable" survived that long a period. The average survival time of patients not "cured" was 5 months.

"Curative" doses of x-ray were administered to 12 of the 47 patients eligible for 5-year follow-up. Of eight with "resectable" lesions, seven survived. Of four patients judged unresectable, none survived five years.

Small Intestine

Twenty-two of 25 patients in this group underwent definitive resections of primary lymphomas with end-to-end anastomosis of the intestinal tract. Three were considered unresectable at operation. In one the lesion was merely biopsied; in two bypass enterostomies were performed.

Fifteen patients received postoperative x-ray therapy. In six "curative" doses of 3,000 rads to 4,000 rads were given. One received cobalt therapy. The remainder were treated with 250 K.V. Nine patients received palliative tumor doses of less than 3,000 rads.

Results of therapy in patients with small bowel lymphomas are listed in Table 3.

There was one death in the postoperative period. This patient died two weeks following bypass of an unresectable tumor of the terminal ileum, secondary to massive hemorrhage from the tumor. The operative mortality was 4.0 per cent.

Twenty patients with small bowel lymphomas are eligible for 5 year follow-up. Eight survived a survival rate of 40 per cent. This figure is higher than the average reported in most studies.[2]

TABLE 3. *Results of Therapy—Small Intestine*

Definitive resections	22 patients	
a) died post-op	— 0	
b) alive post 5 yrs.	— 7	
		a) curative x-ray—2
		b) other —5
c) died tumor-free post 5 yrs.	— 1	
		a) curative x-ray—1
d) died of lymphoma	— 9	
		a) curative x-ray—1
		b) other —8
e) followed less than 5 yrs.	— 5	
Unresectable	3 patients	
a) died post-op	— 1	
b) survived 5 yrs.	— 0	
e) died of lymphoma	— 2	
		a) curative x-ray—1
		b) other —1

All patients surviving 5 or more years underwent definitive resections. None of the patients who died of lymphoma survived more than 2 years following establishment of the diagnosis. The average survival time was 7 months.

X-ray therapy was administered in "curative" tumor doses to five patients eligible for 5-year follow-up. Of four with "resectable" tumors, three survived for 5 or more years. One patient with an unresectable lesion did not survive.

Large Intestine

The form of therapy in this group varied with the location and extent of the tumor. In six patients with cecal lymphomas, four underwent extirpative resections while two were considered unresectable and underwent bypass procedures. In four patients with rectal tumors, one underwent abdomino-perineal resection while three were treated with x-ray therapy.

Two patients received postoperative x-ray therapy in tumor doses of greater than 3,000 rads using 250 K.V. Four pa-

TABLE 4. *Results of Therapy—Large Intestine*

Definitive resections	5 patients	
a) alive post 5 yrs.	— 1	a) curative x-ray—1
b) died of lymphoma	— 2	a) curative x-ray—0 b) other —2
c) followed less than 5 yrs.	— 2	
Unresectable	5 patients	
a) alive post 5 yrs.	— 1	a) curative x-ray—1
b) died of lymphoma	— 2	a) curative x-ray—0 b) other —2
c) followed less than 5 yrs.	— 2	

tients were treated with palliative doses of x-ray.

The results of therapy in patients with large bowel lymphoma are presented in Table 4.

There were no deaths in the postoperative period.

Six patients are eligible for 5-year follow-up. Two survived for 5 or more years (33%). All patients succumbing died within 2 years of the diagnosis, with an average survival time of 6 months. One 5-year survivor underwent definitive resection of a cecal lymphoma and thereafter received a "curative" dose of x-ray. The other survivor is symptom free 9 years following administration of "curative" x-ray therapy to a rectal lymphoma.

Appendix

In both cases of appendiceal lymphoma, therapy consisted of appendectomy and associated procedures for gynecological conditions which prompted operation. At both operations the appendix was believed to contain a carcinoid tumor on gross examination. No postoperative irradiation was given in either case.

Both patients did well postoperatively and were alive and asymptomatic nine and 28 years following operation.

Pathology

Lymphomas of the gastrointestinal tract generally arise from lymphoid tissue of the lamina propria and extend laterally along the submucosal layer. Tumors may protrude into the bowel lumen forming polypoid masses which tend to ulcerate. They may diffusely infiltrate the bowel wall causing rigidity, loss of peristalsis and aneurysmal dilatation secondary to destruction of the myenteric plexus. Malabsorption may occur if extensive infiltration of the small intestinal wall has occurred and may be the presenting symptom in small bowel lymphoma.[6] Occasionally, infiltration of bowel wall is circumferential forming a "napkin-ring" lesion. An unusual form has been reported in which multiple small lymphomatous polyps permeate the intestinal tract.[5]

Perforation of the intestinal wall is not uncommon in primary lymphomas. In most reported series the incidence of perforation ranges from 1% to 20%.[1] In our series there were nine instances of perforation (9%).

Intussusception, when it occurs, is usually associated with the polypoid form of tumor, as was the situation in two of 25 small intestinal lymphomas. In some series the incidence of small bowel intussusception is reported as high as 50%.[8]

Ulceration is common in most gastric lymphomas, regardless of the morphologi-

TABLE 5. *Gross Morphology of GI Tract Lymphomas*

Site		Polypoid	Diffuse	Annular
Stomach		18	45	—
Small intestine		9	9	7
Appendix		—	2	—
Large intestine		8	1	1
Total cases	100	35	57	8

TABLE 6. *Histological Patterns of GI Tract Lymphomas*

Site	Lympho sarc.	Retic. Cell	Hodg. D.	Giant Foll.
Stomach	35	21	6	1
Small intestine	12	9	4	—
Appendix	2	—	—	—
Large intestine	8	2	—	—
100 total cases	57	32	10	1

cal type. It was present to some degree in 40 of the 63 cases (63%).

Gross classification of lymphomas as to polypoid, diffuse or annular, together with distribution throughout the gastrointestinal tract, are listed in Table 5.

Lymphomas have been classified into four histological variants: 1) lymphosarcoma, 2) reticulum cell sarcoma, 3) Hodgkin's disease, and 4) giant follicular lymphoma. These variants are not always distinct, and in some instances the differential diagnosis of reticulum cell sarcoma and Hodgkin's disease is difficult, but these have have been classified as Hodgkin's disease whenever definite Reed-Sternberg cellls are identified. The distribution of lymphomas throughout the gastrointestinal tract according to histological grouping is listed in Table 6.

Prognosis did not appear related to the microscopic pattern of the tumor. Table 7 compares the histological groups of lymphoma with survival rate.

Discussion

The diagnosis of primary lymphoma of the gastrointestinal tract is difficult to establish prior to surgical exploration. Clinical findings do not differ significantly from those of other GI tract neoplasms. A large palpable mass in an otherwise asymptomatic patient may suggest lymphoma rather than carcinoma.

Roentgenographic studies were diagnostic of neoplasm in 80% of patients with gastric lymphomas and raised the possibility of tumors in an additional 8 per cent. In the small intestine the diagnosis of neoplasm was made in 30%; the possibility of neoplasm was raised in another 20 per cent. Roentgenograms of the large intestine made the diagnosis of tumor in 80% of the cases in which x-rays were taken.

Several features were repeatedly present in those patients in whom the diagnoses of lymphoma was made preoperatively. These included: 1) large mass in relation to the duration and severity of symptoms, 2) multiple polypoid lesions on x-ray, and 3) extremely large ulcerated gastric neoplasm on x-ray.

The longest survivals occurred in those undergoing definitive resection of lymphoma followed by a "curative" tumor dose (3,000 rads to 4,000 rads) of x-ray; 11 of 13 patients in this category were alive and asymptomatic after 5 years. Of six patients treated solely by x-ray in this dose range, only one survived for 5 years.

The over-all 5-year survival rate was

TABLE 7. *Comparison of Histological Patterns of Lymphoma to Five-Year Survival*

Site	Lymphosarc.	Retic. Cell	Hodgkin's D.
Stomach	15/30 (50%)	8/13 (61%)	2/4 (50%)
Small intestine	6/11 (55%)	1/5 (20%)	1/4 (25%)
Appendix	2/2 (100%))	—	—
Large intestine	2/5 (40%)	0/1 (0%)	—
Total cases	25/48 (52%)	9/19 (47%)	3/8 (38%)

49% (37 of 75 eligible patients). Recurrence following therapy invariably produced symptoms within 2 years. Most of these patients died within 6 months of the initial diagnosis. Of 24 patients followed for more than 10 years, none developed recurrent tumor. The prognosis 5 years or more after therapy in an asymptomatic patient, appears excellent.

Summary

One hundred cases of primary lymphoma of the gastrointestinal tract are reviewed. The clinical findings do not differ substantially from those of other GI tract neoplasms. Five-year survival rate was 49 per cent. The highest survival rate (85%) was in those patients in whom definitive resections of the lesion were performed, following which x-ray therapy in a tumor dose of 3,000 rads to 4,000 rads was administered. Of six patients treated by x-ray alone in tumoricidal doses, only one survived for more than 5 years. Prognosis did not appear related to the microscopic pattern of the lymphoma or to the site of origin in the GI tract. Recurrence invariably produced symptoms within 2 years of therapy. Average survival time for patients not "cured" was 6 months. Twenty-four patients survived for periods of from 10 to 30 years. None of these developed recurrences. The prognosis, therefore, 5 years or more after therapy in an asymptomatic patient, is excellent.

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