Sarcomatous Lesions of the Stomach

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NONCARCINOMATOUS tumors of the stomach comprise only 2% of primary gastric malignancies but they merit attention because they often affect young persons, they tend to occur clinically as very large tumors that may induce massive gastrointestinal bleeding, and, in spite of their average large size, they are resectable in a high proportion of cases with good 5-year survival rates. For practical purposes they include two types—malignant lymphoma and leiomyosarcoma—occurring in the ratio of 4:1.

Material and Methods

This clinicopathologic study is based on tumors found in 270 patients (94 women and 176 men) who were treated at the Mayo Clinic in the 25-year period, 1940 to 1965. Only patients with a biopsy-proved primary lesion were accepted for the study. Patients with gastric metastasis, such as generalized lymphoma with gastric localization, and patients who had been operated on elsewhere and then referred to this clinic for further treatment were excluded. Cases from the earlier portion of this series have been reported.[4, 14]

A detailed analysis of symptoms, physical signs, and laboratory findings was made and every patient was traced either by interview or by letter since January 1969. Thus, the shortest period of follow-up was 6 years and the longest was 30 years (average, 9⅔ years).

All of the microscopic slides were reviewed by one of us (M. B. D.). The lesions were divided into two groups:

1. Malignant lymphoma (218 patients). These lesions were subdivided, according to their cellular composition, into lymphoblastic, reticulum cell, mixed, and Hodgkin's types (Fig. 1). No case of follicular lymphoma was encountered in this series.

2. Leiomyosarcoma (52 patients) (Fig. 2). Although other sarcomatous lesions, such as fibrosarcoma or angiosarcoma, are said to occur in the stomach, we did not have any such cases in this 25-year period.

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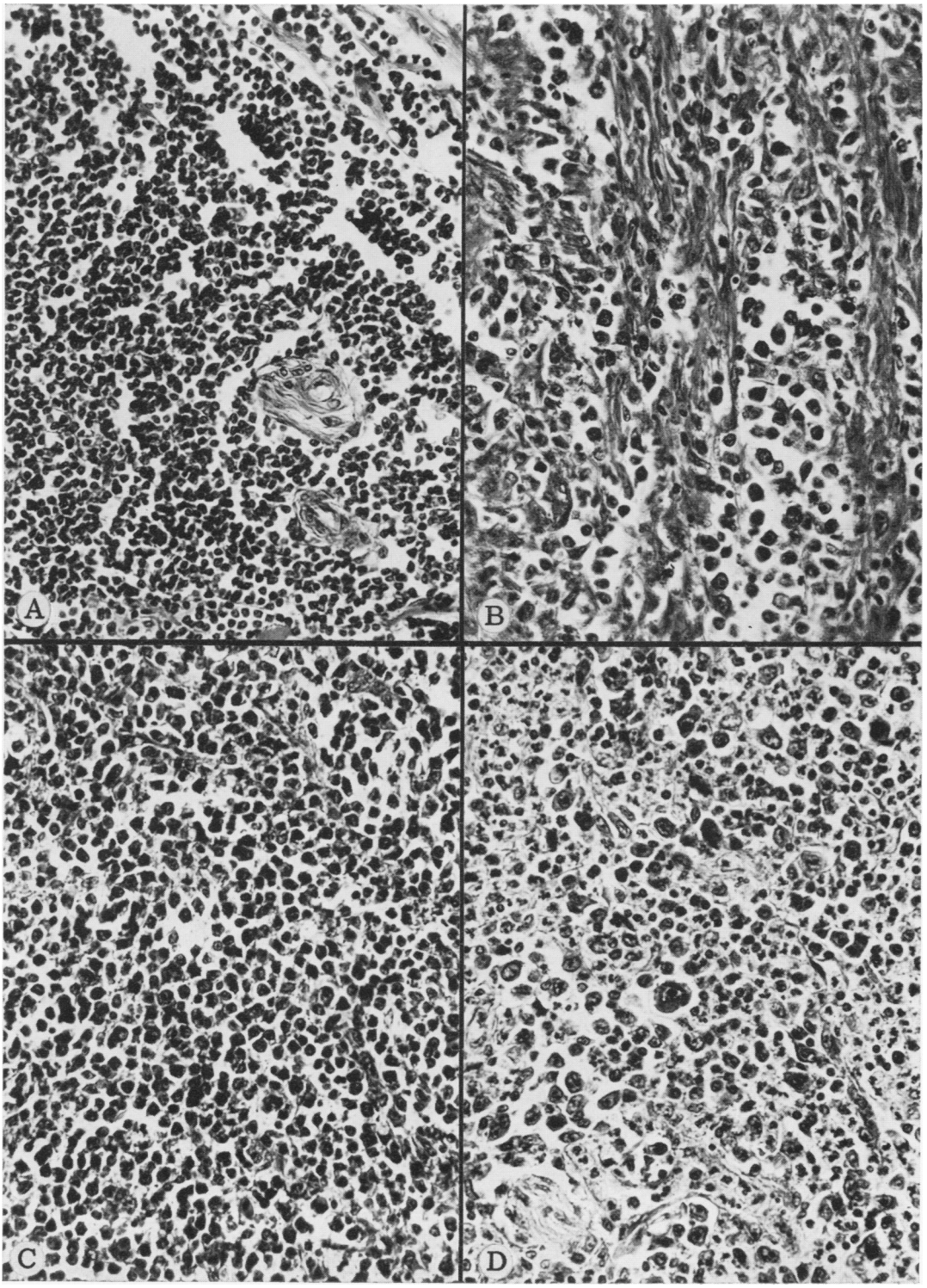
FIG. 1. Malignant lymphoma. *A*, Lymphoblastic lymphoma consisting almost entirely of small, relatively mature, lymphocyte-like cells with little cytoplasm (H & E, ×300). *B*, Reticulum cell (or large round cell) type with large proportion of cells showing prominent nucleoli. Note disruption of invaded muscularis (H & E, ×300). *C*, Mixed type. Some of the cells are lymphoblasts as in *A*. Others are larger with indented nuclei, single or multiple nucleoli, and moderate amounts of cytoplasm (H & E, ×300). *D*, Hodgkin's type with several typical Sternberg-Reed cells (H & E, ×300). (From Stobbe, J. A., Dockerty, M. B. and Bernatz, P. E.: Primary Gastric Lymphoma and Its Grades of Malignancy. Amer. J. Surg., 112:10, 1966. By permission of The Reuben H. Donnelley Corporation.)


A
B
C
D

Survival rates were computed by an actuarial method and compared with survival rates of populations without disease but matched for age and sex.

Findings

Malignant Lymphoma. Males predominated among these patients (148 males and 70 females); age at diagnosis ranged from 12 to 83 years (average, 56 years). Twenty-eight patients were less than 40 years of age.

Anorexia (101 patients) and weight loss (128 patients) were common symptoms. The amount of weight lost was variable and bore no relationship to cell type or duration of symptoms. Pain was an even commoner symptom (173 patients) although this was variable in site and severity. Characteristically, the pain was described as being dull, boring, or aching and was situated in the epigastrium or elsewhere in the upper abdomen.

Bleeding occurred in 54 patients. It usually was manifested as hematemesis, although melena also occurred. Generally, the bleeding was small in amount and was described as "coffee grounds" or by another similar term. Vomiting occurred in 40 patients and abdominal distension, in 39. Vomiting usually was not severe and no patient was dehydrated when first seen. The duration of symptoms was variable, ranging from 3 days to 30 years (average, 18 months). There appeared to be slight differences in duration of symptoms associated with the various cell types, but the sample sizes in these groups were too small for valid statistical comparison.

An interesting finding which may or may not be relevant was that 21 patients had had roentgenologically confirmed peptic ulcers previously and in some cases it was difficult, if not impossible, to ascertain when or if the ulcer symptoms changed to those of gastric lymphoma.

In 129 patients no abnormal physical signs were detected; in 53, an epigastric mass was easily palpable. These masses varied in size and were generally described as being round, smooth, and hard. In an additional 36 patients, abdominal tenderness could be elicited. This too was generally epigastric in location but usually was described as mild, diffuse, or inconstant.

One hundred fifty-five of the 218 patients were anemic (hemoglobin levels < 12 Gm./100 ml.); 20 were severely anemic (hemoglobin levels < 8 Gm./100 ml.). Many of these 20 patients had been admitted on at least a near-emergency basis because of profound anemia.

Gastric analysis was performed in 194 of the patients. The technic varied somewhat over the years, but the results showed that 128 of the patients were achlorhydric. Of the 21 patients in whom a previous peptic ulcer had been demonstrated, 10 were achlorhydric and eight had acid values within the normal range (three had not undergone gastric analyses).

Barium meal x-ray examination of the stomach revealed lesions in 203 of the 218 patients; in 170 the roentgenologic diagnosis was carcinoma of the stomach and in 20 it was benign gastric ulcer. In only 13 was the correct diagnosis made. All patients underwent laparotomy.

Histopathologically, the lesions were classified as lymphocytic-lymphoblastic type in 88 cases, reticulum cell type in 85, mixed in 26, and Hodgkin's type in 19.

Of the 94 patients in whom the lesion was confined to the stomach, 80 underwent partial gastrectomy, nine were treated by total gastrectomy, two had local resection of small gastric lesions, and three had biopsy only with later treatment by x-ray.

Of the 69 patients with local extension of the lesion beyond the confines of the stomach, 19 had "palliative" partial gastrectomies, four had total gastrectomies, two had local resections, and 10 had some other form of palliative procedure (for example, gastroenterostomy without resec-

tion). In the 34 other cases, biopsy alone was performed.

There were 76 patients with obvious nodal involvement; 28 also had local extension of the lesion. Of these, 38 underwent partial gastrectomy and 11 underwent total gastrectomy with hope of cure. In both these groups an attempt was made to remove as many of the regional nodes as possible. Six had some form of palliative surgery, and in 21 no surgical procedure other than biopsy was performed.

Two patients had hepatic metastases at the time of laparotomy, and four had both lymph node and hepatic metastases. One patient had distant metastasis believed not to be associated with obvious generalized lymphoma. No surgical procedure other than biopsy was performed in any patient with hepatic or distant metastasis.

Postoperatively, 161 of the patients were given a course of deep x-ray therapy; 116 of these had had what was thought to be complete removal of involved tissue at operation and the remainder had had no surgical procedure or a purely palliative one. Seven patients with "inoperable" lesions were given a course of nitrogen mustard, and another seven were given chemotherapy and radiotherapy; four patients who had undergone palliative surgery also were given a course of chemotherapy and radiotherapy.

Of the 218 patients, 146 had died by the time of follow-up. Death was due to lymphoma in 118 cases and to some unrelated cause in 28 cases. None of the 72 survivors had evidence of recurrence when last seen.

The survival curves for the various types of malignant lymphoma show that in all groups there was a rapid decrease in the number of survivors over the first 1 to 2 years (Fig. 3). The deaths in the first year include those in the first 30 days (14 patients), which is the operative mortality (6.4%). After this time the survival curves are almost parallel to the survival curve for matched normals, indicating that by

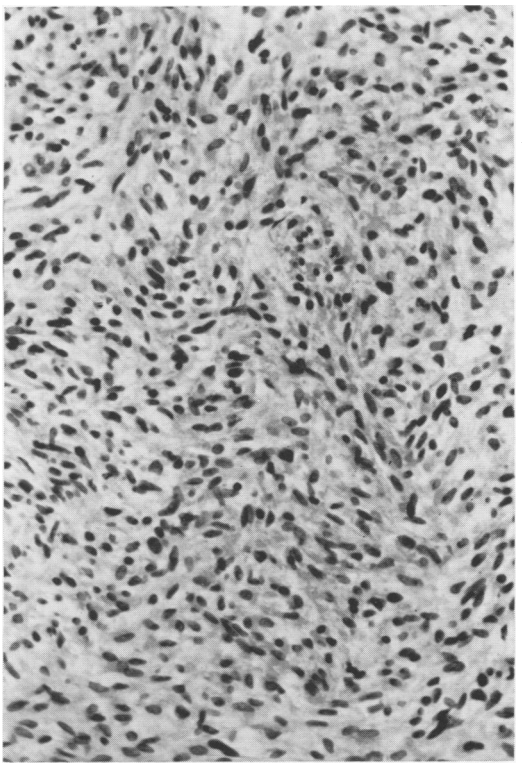


FIG. 2. Grade 2 gastric leiomyosarcoma. This cellular spindle cell neoplasm features granular "myogenic" cytoplasm and mitotic figures (H & E, ×320).

then the patients were dying at the same rate as the corresponding normals. The crude 5-year survival rate was 50%, and the 10-year survival rate was 32%. If only patients who had resection with hope of cure are considered, the 5- and 10-year survival rates were 64 and 44%, respectively.

Leiomyosarcoma. There was not the same male predominance as observed with malignant lymphoma (24 females and 28 males). The age at diagnosis varied from 9 to 78 years (average, 54 years). Six patients were less than 40 years of age. The duration of symptoms on average was a little shorter (10 months) than in the lymphoma group but the wide range (2 days to 8 years) makes the difference of little importance.

The symptoms, however, showed some marked differences from those of the lym-

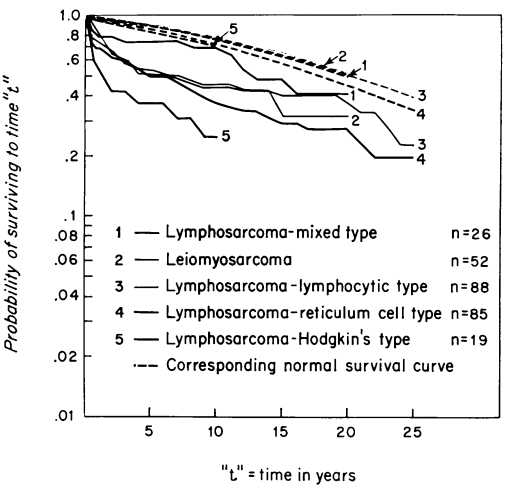


FIG. 3. Survival curves of patients with noncarcinomatous malignancy of stomach, according to cell type of lesion. In this and following figures, survival curve of general population of same sex and age distribution is superimposed for comparison. (Calculated by the method of Berkson, J. and Gage, R. P.: Calculation of Survival Rates for Cancer. Proc. Staff Meet. Mayo Clinic, 25:270, 1950.)

phoma group. Anorexia (11 patients) and weight loss (14 patients) were less common whereas bleeding (33 patients) was relatively more frequent. The bleeding tended to be copious and often repeated; the blood was bright in color. Pain was much less common than in the lymphoma group and, when present, was less severe. It usually was epigastric but was described as "slight," "like indigestion," and so forth.

Five of the patients had noted the presence of an epigastric mass and seven others complained of abdominal distension. Three of the patients had had roentgenologically proved previous "peptic ulcer."

In contrast to the lymphoma group, a palpable epigastric mass was common (38 patients). This mass usually was described as rounded, firm, and often mobile. Abdominal tenderness was common and in some cases may have interfered with detection of a palpable abdominal mass.

In view of the typical history of bleeding it was not surprising to find that anemia was common: 39 of the 52 patients had hemoglobin levels <12 Gm./100 ml. and in six the level was <8 Gm./100 ml.

Of the 50 patients who had undergone gastric analysis, 35 were achlorhydric, 11 had normal acid values, and four had high acid values. Of these latter four, two reported a history of previous peptic ulcer.

Barium meal x-ray examination revealed the lesion in 40 cases. In 20 it was thought to be carcinoma and in the other 20 it was thought to be a benign mass, probably leiomyoma.

In 37 patients, laparotomy revealed the lesion to be confined to the stomach; partial gastrectomy was performed in 21 of these patients; total gastrectomy was done for a high-lying lesion in four, and local resection was carried out for smaller growths in 12. In 11 patients, huge lesions had extended beyond the stomach by direct invasion of surrounding areas. In three of these patients no curative surgical procedure was attempted and in two a palliative procedure was performed; local resection was done in one and partial gastrectomy, in five. Five patients had metastases to the liver (one also had local extension of the lesion) and had either a palliative procedure or no definitive operation. One patient had lymph

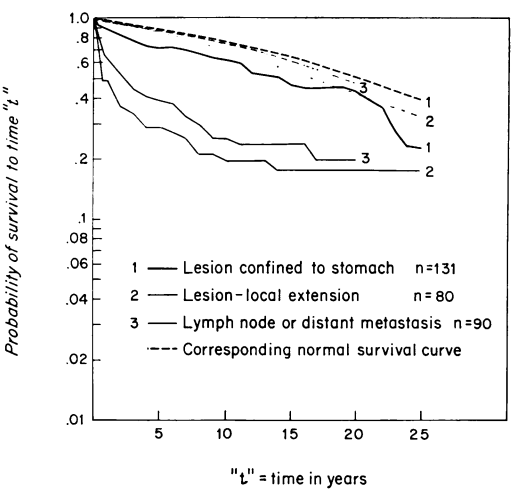


FIG. 4. Survival curves of patients with noncarcinomatous malignancy of stomach, according to extent of lesion.

node metastasis as well as local extension of the lesion and was treated by radical subtotal gastrectomy with removal of nodes.

Six of the patients who underwent no surgical procedure other than laparotomy and biopsy received a course of postoperative radiotherapy, as did another five patients who had had palliative surgery.

At follow-up, 20 of the patients were alive and free of recurrence. Of the 32 dead, 30 had died either postoperatively or from the tumor.

The survival curve for these patients again shows the rapid decrease over the first 2 years (7.5% operative mortality) and then the flattening of the curve to almost parallel that of a matched population (Fig. 3). The crude 5-year survival rate was 50% and the 10-year survival rate was 45%. For those patients who underwent resection with hope of cure, the 5- and 10-year survival rates were 62 and 45%, respectively.

Factors Influencing Survival. When the survival curves for all the patients are arranged according to histologic type of the lesion, there is no statistically significant difference between the curves. However, when the curves are arranged according to the anatomic extent of the lesion, when the lesion is confined to the stomach the survival is almost identical to that of a normal matched population (5-year survival rate, 71%) (Fig. 4). Extension of the lesion to local lymph nodes or to nearby organs worsens the prognosis significantly (5-year survival rates, 39 and 29%, respectively).

There was no significant difference in survival between males and females. Advanced age at the time of operation increased the operative risk but did not alter prognosis in regard to death from the sarcomatous lesion.

Patients treated by different types of operations had marked differences in survival (Fig. 5). Those patients in whom the lesion could be treated by local resection or

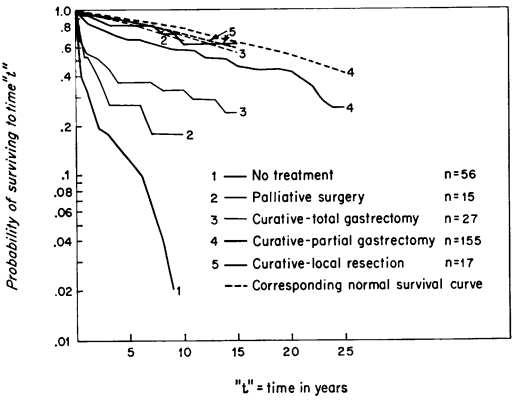


FIG. 5. Survival curves of patients with noncarcinomatous malignancy of stomach, according to type of resection.

partial gastrectomy had a survival little worse than that for a normal population (5-year survival rate, 82 and 68%, respectively). With total gastrectomy the outlook was poorer (5-year survival rate, 37%), and palliative surgery or irradiation alone gave poor results (5-year survival rate, 27 and 12%, respectively).

However, those patients treated by total gastrectomy, palliation, or irradiation alone also had more extensive lesions, which undoubtedly played a major role in the worsened prognosis.

Discussion

The higher proportion of males than females that we noted in our lymphoma group, but not in our leiomyosarcoma group, has also been noted in most series in the literature.[5, 7-10] The reason for this sex distribution is unknown as is the etiology of these tumors in general.

There was a striking contrast in the clinical presentation of the two main groups, with pain, weight loss, and anorexia characterizing the lymphoma group and bleeding and the presence of an epigastric mass being associated with leiomyosarcoma. Therefore, lymphosarcoma is impossible to differentiate from carcinoma clinically and it may be almost as difficult to tell the two lesions apart roentgenologically.[2, 13] Indeed

Bernatz [1] has shown that in certain instances it may be difficult to differentiate sarcoma from carcinoma even histopathologically.

In our series, achlorhydria was commonly associated with both malignant lymphoma and leiomyosarcoma. Several other workers have recorded similar findings.[5, 7, 9, 12] Loehr and associates [7] in particular noted that 35 of 36 patients had no free hydrochloric acid present. However, Nicoloff, Haynes, and Wangensteen [10] and Marvin and Walters [8] did not find such a striking incidence of achlorhydria. In view of the low acid levels reported, it is of great interest to note the frequency of previous peptic ulcer disease in these patients, both in our series and in the literature.[4, 5, 9] It has been suggested by Lemon and Broders [6] that these tumors may arise from the irritated connective tissue adjacent to the ulcer. However, in several patients we did not note a change in peptic ulcer symptoms which might have given a clue that the lesion had changed in its malignant potential. Although we cannot say that a lesion was not in fact malignant from the beginning, when histories longer than 20 years are being considered it seems likely that Lemon and Broders' suggestion may be pertinent.

The treatment of these lesions is rewarding compared with that of carcinoma of the stomach, although Naqvi and associates [9] and Garvie [3] reported only 29 and 22% 5-year survival rates, respectively. Nicoloff and co-workers [10] reported 40%, Joseph and Lattes [5] 58.7%, and Loehr and associates [7] 53%, all similar to our 50% 5-year survival. It is rewarding to note how few patients die of sarcoma after having survived 5 years from the time of operation.

Stobbe and co-workers [14] reported that gastric lymphosarcoma tends to push into the tissues with minimal fibrous reaction as compared with the infiltration and scirrhous reaction to a carcinoma, and this helps explain why, despite their large size, many of these lesions can be excised.

At this clinic it has been thought that all patients with lymphosarcoma of the stomach should be treated aggressively surgically and then be given a course of radiation therapy.[11] Even if some of the lesion must be left behind surgically, this philosophy is sound because prognosis still may be favorable. Finally, it is important that, when any patient appears to have inoperable carcinoma of the stomach, biopsy proof of the diagnosis should be obtained because confusion with a curable sarcoma would be a tragedy indeed.

Summary

Two hundred seventy cases of primary noncarcinomatous malignancies of the stomach were reviewed. Two hundred eighteen patients were diagnosed as having malignant lymphoma, manifested clinically by epigastric pain, anorexia, and weight loss. Anemia and achlorhydria were common, and barium meal x-ray examination usually was thought to demonstrate carcinoma. Fifty-two patients were diagnosed as having leiomyosarcoma, manifested clinically by severe, persistent bleeding and an abdominal mass. Anemia and achlorhydria were again common, and the roentgenogram usually was thought to show a benign lesion.

All of the patients underwent laparotomy and biopsy proof of the diagnosis was obtained. The lymphosarcomatous lesions were surgically resected when possible and later given a course of radiotherapy. The crude 5-year survival rate was 50% and the 10-year survival rate was 32%. For those patients surgically treated with reasonable hope of cure, the 5- and 10-year survival rates were 64 and 44%. Leiomyosarcoma was resected more "locally" and did not require irradiation. The crude 5- and 10-year survival rates were 50 and 45%, respectively. If only those patients undergoing resection with hope of cure are in-

cluded, the 5- and 10-year survival rates were 62 and 45%.

Acknowledgment

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Discussion

Dr. J. Lynwood Herrington, Jr. (Nashville): This is an extremely impressive series of patients, probably unmatched by any institution in the country, and there is nothing with which I can disagree.

During a 20-year period, only 14 cases of lymphomas were encountered at St. Thomas Hospital and 39 of these combined cases were seen at Vanderbilt University Hospital. At Vanderbilt, 28 cases of primary lymphoma involved the stomach. Twenty were lymphosarcomas, seven were Hodgkin's disease, and one was of the reticular cell type. The over-all 5-year survival rate in this group of patients was 31%, and the 10-year survival was 14%.

On the other hand, of 11 leiomyosarcomas the over-all 5-year survival in this group of patients was increased to 60% whereas the 10-year survival rate was 80%.

Most lymphomas were treated by radical subtotal resection of the stomach or by total or extended total gastrectomy plus radiation. I would like to ask Dr. ReMine if, in inoperable cases, he has had any long survivals following radiation therapy alone?

Leiomyosarcomas in our small group were treated by radical gastrectomy if they were located in the distal portion of the stomach. A total gastrectomy was reserved for huge, bulky lesions that occupied an extensive portion of the stomach.

A lesion in the stomach that was described in 1962 by the late Arthur Purdy Stout, the so-called leiomyoblastoma, has been reported less than 100 times in the literature. Fortunately, we have encountered two such cases during the past 5 years. The patient usually has pain, or massive bleeding, and at operation the patient is believed to have a leiomyoma.

(Slide) We operated upon this patient at Vanderbilt several years ago. He was bleeding massively, during which a G.I. series was performed. He was transferred immediately to undergo operation. The smooth defect which is located on the greater curve of the stomach we felt represented the garden variety of leiomyoma.

(Slide) This patient underwent a 65% resection of the stomach and the pathologic report showed not a leiomyoma but a leiomyoblastoma. None of the elongated smooth muscular cells were present in the microscopic study; a huge conglomeration of round cells and polygonal cells, with a clear vacuolated cytoplasm were present. Most of these tumors are benign, but a small per cent of them are malignant. They metastasize and can cause death.