CLINICAL ASPECTS AND TREATMENT OF PRIMARY LYMPHOSARCOMA OF THE STOMACH AND INTESTINES

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Malignant neoplasms derived from other tissues than epithelium and affecting the gastro-intestinal tract are, it is true, relatively uncommon, but their occasional occurrence and serious prognosis warrant their study with a view to standardizing so far as possible the methods of treatment. Data from the literature are in a chaotic state, largely because of confusion and looseness in the classification of lesions, whose clinical courses vary greatly according to their type, so that the symptomatology, prognosis and reaction to treatment of one case may have but little resemblance to another, though they are designated by the same name. On account of the rarity of these conditions the experience of any one observer is limited, and the literature therefore consists largely of the recital of single cases, and makes but dull reading.

These tumors, usually loosely included under the term sarcoma, comprise a group sharply demarked in theory from the recognized epithelial tumors, but nevertheless not always clearly defined, since the embryonal origin of the cells of some, such as the endotheliomas, are still the subject of dispute. Moreover, in the case of certain small round-cell tumors, competent pathologists may differ about the classification as between carcinoma or sarcoma. Any of the mature mesoblastic tissues represented in the structure of the gastro-intestinal tract may be the seat of a malignant tumor, which then may be appropriately designated as fibro-, angio-, lipo-, myo-, myxo- and lymphosarcoma, respectively, according to the differentiated type of cell from which it springs. The designation of the tumor according to the morphology of its cells—whether composed of spindle, round or giant cells is not of much significance, since each of these types may occur in tumors springing from any of the mesoblastic tissues; on the other hand, it will be understood that the study of the cellular morphology is necessary for histological diagnosis.

According to Ewing,[1] sarcomas of the gastro-intestinal tract are of three chief groups: (1) Spindle-cell myosarcoma, which are likely to be bulky, more or less pedunculated growths, projecting either within the lumen of the viscus or into the peritoneal cavity, non-infiltrating, late in metastasizing, and apt to become cystic when growth has out-stripped the blood supply; (2) a miscellaneous group of round-cell or mixed-cell alveolar sarcomas, rare and not deserving of classification as a separate variety; (3) lymphosarcoma, which constitutes by far the most numerous and important group, and which requires most careful analysis, on account of the very numerous conditions

which cause hyperplasia of lymphoid tissue. Ewing states that tumors of lymphoid tissue may arise from any of its three normal components: lymphocytes, reticulum and endothelium. Lymphocytic hyperplasia gives rise to a lymphocytoma, which may be due to some irritant, bacterial or otherwise, especially the tubercle bacillus (simple or tuberculous lymphoma), or may be a part of the clinical syndrome known as lymphatic leukemia or pseudo-leukemia, or may be an independent, locally arising tumor having all the characteristics of malignancy—a true malignant lymphocytoma. Reticulum cells undergoing hyperplasia may form tumors which are a local manifestation of myeloid leukemia, or Hodgkin's disease, or may constitute an independent, locally arising malignant tumor which may be designated as large round-cell lymphosarcoma; finally, endothelial cells of lymphoid tissue may proliferate and cause the endothelial hyperplasia of tuberculosis, or a true tumor growth designated as endothelioma. When it is realized that many observers believe that Hodgkin's disease is due to an infection, probably with the tubercle bacillus; that apparently true lymphocytomas have been described in the course of the disease, and that on the other hand in patients with lymphocytoma an excess of lymphocytes similar in all respects to the tumor-cells has appeared in the blood, thus simulating leukemia, it will be realized how difficult and confused is the classification. Mallory[2] prefers to simplify matters by using the term lymphoblastoma to include all lesions variously spoken of as lymphocytoma, lymphoma, lymphosarcoma, pseudo-leukemia, lymphatic leukemia and Hodgkin's disease, believing that these are but different manifestations of the same underlying process. He defines the lymphoblastoma as a tumor of mesenchymal origin of which the cells tend to differentiate into lymphocytes—the type cell is the lymphoblast, which occurs abundantly in the germinative centres in the lymph nodules of lymph-nodes, tonsils, gastro-intestinal tract and spleen. Minot and Isaacs,[3] after referring to the utter confusion in the classification of diseases which have progressive enlargement of the lymphoid tissues as their most prominent feature, suggest the wisdom of recognizing four types depending on age incidence, clinical features, blood picture and pathological histology, as follows: (1) lymphatic leukemia; (2) pseudo- or aleukemic lymphatic leukemia; (3) Hodgkin's disease; (4) lymphoblastoma, having a distinct tendency to invade tissues, to involve tonsils, gastro-intestinal tract and serous membranes, and showing the multiplication of reticulum tissues and lymphoid cells usually called lymphosarcoma.

Whatever the inter-relation of these conditions, and the embryonal or adult origin of their characteristic cells, certain it is that a malignant tumor of lymphoid tissue may appear as an original focus in the gastro-intestinal tract, invade and destroy the structure in which it arises, spread by permeation and by lymphatic and blood metastasis, without the accompaniment of a blood dyscrasia such as lymphatic leukemia, and without the involvement of other lymphoid structures as in pseudo-leukemia, general lymphomatosis or Hodgkin's disease. Such a primarily local, but ultimately invading and

metastasizing malignant tumor closely corresponds to carcinoma in its clinical course, and is theoretically as susceptible of cure by extirpation. It apparently differs from carcinoma, as will be seen, in its markedly greater radio-sensitivity. In spite of theoretical objections the term "lymphosarcoma" conveniently designates these tumors.

This paper attempts to analyze the lymphosarcomas of the gastro-intestinal tract, excluding the rectum, which have been observed at the Peter Bent Brigham Hospital, Boston, since its foundation in 1913.* The diagnosis appears (with the variation "lymphoblastoma" or "malignant lymphoma") twenty-two times, but in four of these instances it is presumptive only, unconfirmed by biopsy or autopsy, while in a fifth a careful review of the histology has convinced the pathologist† that the tumor is in fact a small round-cell carcinoma. A sixth case is that of a fifty-one-year-old woman who died of septicæmia, whose stomach showed at autopsy a small, encapsulated, clinically benign nodule, whose histology was consistent with lymphosarcoma, and was so diagnosed. It seemed possible that a chance discovery at autopsy had revealed a malignant tumor at its early and still benign incipiency. Further pathological study in the course of the preparation of this paper has led to the conclusion that it is a congenital tissue defect, of the type of lymphangioma, and non-malignant in character.

There remain, then, sixteen certified instances of primary lymphosarcoma of the stomach and intestines occurring in a hospital of 240 beds during nineteen years, in the course of which the total number of patients admitted for all tumors of the stomach and intestines was 976, giving a percentage of sarcomas of 1.63. Of the sixteen cases, nine were of the stomach; which among a total of 628 gastric tumors gives a percentage of lymphosarcoma of 1.4; seven were of the intestines, constituting 2 per cent. of all intestinal tumors. These figures correspond with most statements in the literature, that from 0.5 per cent. to 3 per cent. of all tumors of the stomach are sarcomas.[4] Since the jejunum and especially the ileum are the most common situation of intestinal lymphosarcoma, which is much less common in the colon, and since carcinoma—while common in the colon—is exceedingly rare in the jejuno-ileum, it follows that lymphosarcoma of the small intestine, while rare, is by far the most common malignant tumor of that portion of the alimentary tract. Its frequency of incidence seems to increase with its distance from the stomach, being most uncommon in the duodenum and most frequent in the terminal ileum, where it naturally often involves the cæcum. In the Brigham Hospital series of seven cases, the disease was located in the jejunum in two instances, in the jejuno-ileum in two instances,

* For reference, the patients on whom this paper is based are numbered as follows in the Peter Bent Brigham Hospital records: S-3401; S-7322; S-13985; S-14572; S-14737; S-18055; S-21507; S-24969; S-24796; S-26974: S-31823; S-35035; S-38857; M-7428; M-17127; M-19182.

† Dr. S. Burt Wolbach has kindly reviewed the pathological material and his assistance is acknowledged by the writer.

in the distal ileum in two cases, and in the terminal ileum with involvement of the cæcum in one case. There was no instance of primary location in the colon.

Since the etiology is absolutely unknown, there is no object in rehearsing the familiar speculations regarding it. There was nothing to throw light on it derived from the study of this series.

Sex seemed to play no part in the incidence, there being four males and five females among the gastric cases, and four males and three females among the intestinal. The average age of all patients was 53.5 years; the youngest was thirty, the oldest seventy-five; the gastric cases averaged 56.2 years and the intestinal 50.1. This is apparently somewhat at varience with common experience, which indicates that sarcoma of the gastro-intestinal tract occurs at an age averaging at least ten years earlier. Balfour and McCann,[5] reporting forty-five cases of sarcoma of the stomach, give the average age as forty-three years, and the preponderance of males over females as more than 2 to 1. Douglas,[6] analyzing the literature, gives the average age as 41.6, and the sexes equally affected. Haggard[7] quotes the average age as about 45.8 years and D'Aunoy and Zoeller[8] tabulate 135 scattered cases whose ages average 36.7 years, with males almost twice as numerous as females. Sarcoma in general is widely recognized as much more prevalent in youth than is carcinoma, and the literature of sarcoma of the gastro-intestinal tract reveals the general opinion that it occurs on the average at a considerably earlier age than does carcinoma—a belief which does not seem to be sustained by the Brigham Hospital series.

Primary lymphosarcoma of the gastro-intestinal tract may have its origin in any nidus of lymphoid tissue, but appears most often to begin in a lymphoid follicle of the submucosa, whence it spreads by permeation along tissue spaces, and by infiltration through the various layers of the viscus, especially the muscularis. Since it does not at first involve the mucosa, ulceration is neither an early nor a characteristic occurrence, in sharp distinction from carcinoma. It has little tendency to penetrate the serosa until late in the disease, when perforation due to ischæmic necrosis is not uncommon. Since the tumor-cells lie in a scanty and very delicate reticulum, instead of being accompanied by the definite and important framework of connective-tissue stroma usually characterizing carcinoma, there is but little tendency for the neoplasm to contract and constrict the visceral lumen; rather does it seem to separate and thus weaken the fibres of the muscularis, or perhaps paralyzes the intrinsic neuromuscular mechanism, so that the viscus, especially if it be the intestine, appears dilated rather than contracted. The infiltrating lymphosarcoma under consideration does not develop the massive semi-pedunculated growths projecting either into the peritoneal or the visceral cavities. Metastasis may be by both blood- and lymph-streams—indeed, the involvement of regional lymph-nodes may be both early and extremely extensive, so that the masses of tumor-nodes in the mesentery or retroperitoneal tissues may quite overshadow the primary growth. Perusal of the literature

reveals much difference of opinion on this point, due usually to confusion of various other histological types with true lymphosarcoma, since it is well known that sarcoma in general, being built on an architecture of new blood-vessels, and perhaps devoid of lymphatics, is much more prone to metastasize by the blood than by the lymph currents. The primary lymph-node invasion is almost certainly by direct permeation rather than by free-cell metastasis. Blood metastases are necessarily through the portal system to the liver.

In gross appearance lymphosarcoma of the stomach cannot be differentiated from carcinoma, especially of the infiltrating "linitis plastica" type. There is diffuse thickening of the wall, of rubber-like consistency, usually without sharp delimitation, often purplish in color and contrasting with carcinoma simplex and malignant adeno-carcinoma by its softer consistency and lack of nodularity. The regional nodes, if involved, are large, smooth, elastic rather than hard, apt to be matted together and to form a tumor mass along the curvatures not separable from the parent tumor. The cut surface is of a uniform grayish or grayish-pink color, without gross evidence of structure. These gross characteristics are not sufficiently distinctive to permit certain differentiation from carcinoma. In the intestine the appearances are similar, the gut appearing enlarged and dilated, and the thickened rubber-like wall justifying the comparison with a piece of garden hose, an appearance quite different from the characteristic sharply delimited annular constricting appearance of the typical scirrhous adeno-carcinoma of the colon. In the cæcum, however, the gross appearances are again very similar to carcinoma. Microscopically, the tumors are composed of varying sizes of small or large lymphocytes, round, oval or polyhedral, with round, sharply outlined nucleus containing chromatin granules often peripherally distributed, scanty, basophilic cytoplasm, and delicate, sometimes scarcely demonstrable reticulum without definite structural arrangement, except for the appearance of thin-walled blood-vessels invaded by tumor-cells. Mitoses are usually numerous and often quite irregular. In some instances the differential diagnosis is scarcely to be made between lymphocytoma and a rapidly growing small round-cell carcinoma, unless secretory vacuoles in the cells of the latter can be demonstrated, and it is undoubted that many cases are reported as lymphosarcomas which are in reality carcinomas.

For reasons related no less to treatment than to the perfection of diagnostic science it would be highly desirable to be able to distinguish clinically between lymphosarcoma and carcinoma of the gastro-intestinal tract. All authorities agree that in the case of the stomach this is usually impossible. Cutler and Smith,[9] reporting in 1922 two instances of lymphoblastoma of the stomach (which are included in the present Brigham Hospital series) state that differential diagnosis is impossible. D'Aunoy and Zoeller[8] stated in 1930 that no case is on record where a clinical diagnosis was established. Pemberton[10] says there is no record of a pre-operative diagnosis. Ruggles and Stone[11] say that X-ray findings are not sufficiently characteristic to permit of a specific diagnosis of lymphoblastoma. Balfour and McCann,[5] report-

ing forty-five cases of proved sarcoma of the stomach occurring at The Mayo Clinic between January, 1908, and July, 1929, say that two were diagnosed before operation as sarcoma, and that in one of these the X-ray diagnosis of lymphosarcoma was correctly made. Presumably the other was some other form of sarcoma, such as myosarcoma, which, in contrast to lymphosarcoma, may present features permitting presumptive diagnosis.

Analysis of the symptoms of the patients in the Brigham Hospital series with involvement of the stomach showed that all complained of abdominal—usually epigastric, pain or discomfort, while some stressed such symptoms as anorexia, dyspnœa, and loss of weight, during a period varying from two weeks to two years before admission to the hospital. The average duration of symptoms was about seven months. Five of the nine cases complained of vomiting, but never of gross blood. Gastric analysis was done in five cases, all but one of which showed low or absent acid values. Occult blood was noted but once. No tarry stools were reported, but tests were positive for occult blood in four of the five cases in which the test was done. An epigastric tumor was felt in seven cases. X-ray examination was made in six instances, in four of which a filling defect was noted, and in two the crater of an ulcer. In one a 100 per cent. six-hour barium residue was reported, and in two a 20 per cent. and a 25 per cent. respectively. The tentative diagnosis was carcinoma in six, ulcer in one, malignancy of the abdomen in one. In all patients but one there was a mild to moderate secondary anæmia.

From this analysis it appears that the typical picture of a patient with lymphosarcoma of the stomach is an individual in the sixth decade, who has complained for seven months more or less of epigastric discomfort or pain, indigestion, moderate loss of weight and strength, and often vomiting. Examination shows an epigastric tumor and moderate anæmia; X-ray shows a filling defect with or without stasis, sometimes with a crater. Gastric analysis shows usually a low or absent hydrochloric acid and occasionally traces of blood. The stools usually show occult blood. It cannot be denied that this description fits perfectly a typical case of gastric carcinoma. Holmes, Dresser, and Camp[12] report X-ray studies of eight cases of lymphoblastoma of the stomach observed at the Massachusetts General Hospital, of which five appear to be true primary lymphosarcoma of the type now under consideration. No correct diagnosis was made in these cases and the authors conclude that the X-ray appearances do not differ from carcinoma except that peristalsis does not seem to be interfered with so much.

Analysis of the symptomatology of the seven cases of lymphosarcoma of the intestine constituting the Brigham Hospital series indicates that the duration of symptoms before admission varied from three weeks to seventeen months, with an average period of six and one-half months. The chief complaint in every case was abdominal pain, noted as epigastric in two instances; subsidiary complaints were vomiting and constipation, each in two instances. All these patients had lost from twenty to thirty pounds in weight. Stools

were noted as bloody by one patient, as tarry by one other. In every instance but one a tumor could be felt. In the four cases in which gastric analysis was done, free hydrochloric acid was absent. X-ray examination was made in six instances and was reported as follows: (1) residue in ileal loops; (2) 100 per cent. gastric residue and dilated duodenum; (3) rigidity of ileocecal valve and slight filling defect of the cæcum; (4) distension and obstruction of the small intestine; (5) filling defect of the sigmoid, not characteristic; (6) filling defect of the cæcum. As already noted, the nature of the infiltrating, non-constricting pathological process is such as not to lead to mechanical obstruction, so that such a picture as is given by the annular constricting carcinoma of the colon is not afforded. The filling defects noted are usually due to extrinsic pressure from large masses of metastatic glands. All patients but one showed a slight or moderate secondary anæmia.

The average clinical picture of a patient with lymphosarcoma of the intestine may be described as follows: a middle-aged or possibly much younger individual who for some months has complained of abdominal pain, situated anywhere but often epigastric, not definitely related to food or bowel action, sometimes but not necessarily accompanied by vomiting; an anæmia of secondary type with otherwise normal blood-picture; an insensitive mass anywhere in the abdomen, either occult or gross blood in the stools, and by X-ray either no striking appearance, or some evidence of dilated loops of small intestine with tendency to local stasis of the barium. An opaque enema would be likely to show a filling defect or deformity, if the disease were located in the colon.

The treatment of lymphosarcoma of the stomach or intestine, until the advent of therapeutic radiation, was exactly as in carcinoma—by an attempt at radical extirpation, and the results have been such as to inspire widespread pessimism. The classic case of Ruppert[13] is widely quoted as the longest reported survival. His patient was a woman of fifty-eight years whose stomach was almost entirely involved in a primary lymphosarcoma accompanied by numerous nut-sized glands in both omenta; a subtotal gastrectomy was done and the patient was reported as living without evidence of recurrence fourteen and one-half years later. In making his report in 1912 Ruppert said that medical literature revealed but twelve radical operations for gastric lymphosarcoma, of which but seven made an operative recovery. The next longest survival, nine years, appears to be that of Finsterer (quoted by D'Aunoy and Zoeller.[8] Balfour and McCann's series[5] of forty-five cases of all types of sarcoma of the stomach afforded thirty-eight resections which survived operation; of those living when last heard from the average duration of life was five years, the longest nine years. This list, however, includes types other than lymphosarcoma. Isolated or small groups of cases are reported with survivals for lesser periods. Approximately the same results have followed surgical extirpation of the disease affecting the intestinal tract. Rankin and Chumley[14] reporting in 1929 eighteen instances of lymphosarcoma of the colon including the rectum, noted

fifteen radical resections with four operative deaths; in five patients the disease recurred, and the remaining six were alive and well for four years and three years and various lesser periods. Weeden,[15] reporting in 1929 twelve cases of lymphosarcoma of the intestine from the New York Hospital, noted six resections with three post-operative deaths, and survival periods of three and one-half years and one year for the two patients who were traced. Graves[16] reports three cases resected with a maximum survival of three years without recurrence. Loria,[17] in 1925, reviewed all reported cases and stated that the prognosis was very poor; he quotes Cornier and Fairbanks[18] as analyzing ninety-six cases, with only one patient surviving as long as eight years. There are numerous isolated reports in the literature, which give the impression that on the whole the prognosis of the disease is even less favorable in the intestine than in the stomach.

The well-known radiosensitivity of undifferentiated cells in general and of lymphocytes and lymphoblasts in particular offers ground for hope that radiation may be effective in the relief of lymphosarcoma. Ruggles and Stone[11] say that X-ray therapy has a good deal to offer and on this account stress the desirability of diagnosis without exploratory operation, while regretfully admitting that it seems to be impossible. They present an analysis of eleven cases but do not mention the result of X-ray treatment. Matas, discussing a paper by Loria,[17] stated in 1925 that deep X-ray therapy and radium have proved unavailing. Gunsett and Oberling[19] report a remarkable case of a forty-eight-year-old man with an extensive annular neoplasm of the stomach, adherent to and involving the pancreas, extending upward on the lesser curvature to the cardia, with extensive glandular involvement along both curvatures—hopelessly inoperable. Biopsy of a gland showed lymphoblastic sarcoma; the cells were round or polyhedral with large nucleus containing one or two nucleoli and a delicate chromatin network, cytoplasm staining pink with eosin; mitoses were frequent and often irregular in type. The patient was given X-ray therapy in seventeen sessions during three weeks and at the end of five years was living and without symptoms if he avoided indigestible food; X-ray examination then showed that most of the stomach seemed to have disappeared! Strauss[20] reports the instance of a man of sixty-two with an inoperable tumor of the duodenum; biopsy showed lymphosarcoma. He received deep X-ray therapy and two years later had gained forty pounds, was in excellent health and showed no evidence of recurrence. Freeman[21] reports a striking case of a man sixty years of age upon whom he performed resection of the stomach—the lines of section passing through tumor tissue. The pathological diagnosis was variously reported as carcinoma, lymphosarcoma, inflammatory tissue and chronic granuloma, but subsequently pathologists of The Mayo Clinic and Columbia University rendered a verdict of lymphosarcoma. The patient had X-ray treatment (inadequate on account of his objection) and small doses of Coley's fluid, and was reported as well eighteen months later—the stomach appearing normal by X-ray except for reduction in size.

The results of treatment in the Brigham Hospital series are as follows: of the nine cases of lymphosarcoma of the stomach two died on the medical service shortly after admission, and autopsy showed in each inoperable primary lymphosarcoma of the stomach with metastases, and with terminal perforation. Two patients were explored, found inoperable (one had perforative peritonitis) and died a post-operative death. One patient explored and found inoperable, made an operative recovery and died three months later after having been admitted for X-ray treatment to another hospital, whose records, however, fail to show whether she was treated or not. One patient, No. S-31823, a man of seventy-one, had an exploratory laparotomy which revealed a large tumor mass occupying most of the stomach and adherent to and involving the left lobe of the liver; he made an operative recovery and had two X-ray treatments before discharge; the tumor diminished rapidly in size but the general condition did not improve and he died four months later. The biopsy of this tumor showed it to be composed of rather large round cells containing large nuclei, a rim of dark-staining cytoplasm and many mitoses, and it was designated lymphoblastoma. One patient, No. S-38857, was explored, found inoperable, given X-ray treatment and restored to apparently perfect health. Her story will be examined presently. Only two patients could be subjected to radical resection—one (No. S-14572) operated on by Dr. E. C. Cutler in 1921, had a resection of the pyloric third of the stomach with tributary involved nodes, made a normal convalescence but died of recurrence one and one-half years later, without having had supplementary X-ray treatment; the other (No. S-21507) operated on by the writer in 1924, had a segmental resection of the middle third of the stomach for an ulcerated lesion of the posterior wall, made a good recovery and was given two X-ray treatments on discharge from the hospital, but failed to report for later therapy. Six years later she wrote that she was "in better health than for years and had no stomach symptoms." Since then it has been impossible to trace her. The histological structure of the tumor showed "lymphoid tissue infiltrating the connective tissue and smooth muscle of the muscularis mucosa and submucosa; the cells are of lymphoid type with round nucleus of sharp outline and peripherally distributed chromatin, the amount of cytoplasm is small; there are occasional larger cells with basic staining cytoplasm; the growth is distinctly invasive and could not be confused with inflammation; there are many mitoses; the diagnosis is lymphosarcoma." (S. B. Wolbach.)

The treatment of the seven patients with lymphosarcoma of the intestines constituting the Brigham Hospital series resulted as follows: one died on the medical service shortly after admission, of metastases and perforation; three had exploratory laparotomy (two with palliative anastomoses) for inoperable tumors with extensive glandular metastases, followed by X-ray treatment; these patients died after intervals of four, seven and ten months respectively; three patients had resection (two by Dr. John Homans and one by the writer) without mortality; one of these could not be traced after his discharge; one

died of recurrence about one and one-half years later, and the third patient lived in perfect health for more than four years and died of angina pectoris —his physician reporting that he noted a palpable mass in the abdomen. Neither of these cases had X-ray therapy.

The history of one patient may be given in more detail, since it seems to point the way to a rational treatment of these cases.

L. M. G., No. S-38857—a woman sixty-three years of age, previously well, had complained for two years of unaccountable anorexia, indigestion and occasional nausea, and for ten months of increasing epigastric discomfort, loss of weight, pallor, asthenia and occasional vomiting without blood. Examination showed a mass in the epigastrium; the blood showed hæmoglobin of 65 per cent., red cells 4,600,000, white cells 5,850 and

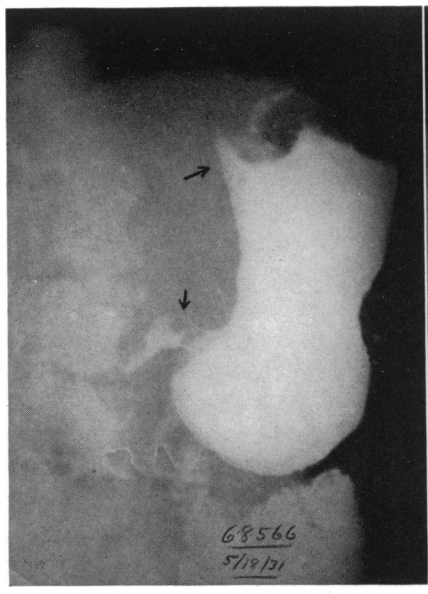

FIG. 1.

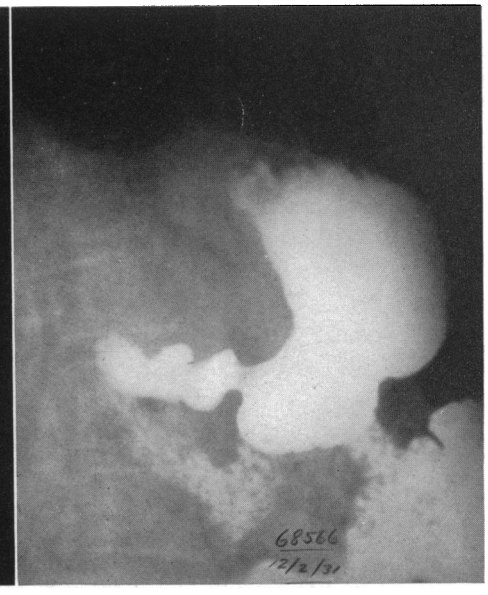

FIG. 2.

FIG. 1.—Before radiation. Note the extensive filling defect of the antrum, the rigid appearing and irregular lesser curvature, and the defect caused by extrinsic pressure near the cardia.

FIG. 2.—Seven and one-half months after radiation. Note the disappearance of the filling defect, the normal-appearing lesser curvature, and the absence of evidence of extrinsic pressure from masses of neoplastic glands.

normal cytology; X-ray (Fig. 1) showed an extensive filling defect of the pyloric antrum with rigidity of the whole lesser curvature, 25 per cent. six-hour residue, and evidence of extrinsic pressure near the cardia. No gastric analysis was made. The pre-operative diagnosis was carcinoma, probably inoperable. At operation by the writer on May 23, 1931, under avertin and supplementary ether anæsthesia, there was found an infiltrating tumor mass involving the whole antrum and the whole lesser curvature to the cardia; there was direct adhesion to and apparently involvement of the pancreas, and extensive glandular involvement along the lesser curvature with especially large masses about the cardia and celiac axis. The liver was uninvolved. Nothing unusual was noted about the tumor except that the diseased nodes were unusually large, rounded and elastic. Tissue was taken for immediate diagnosis and reported as probable small round-cell carcinoma. Convalescence was exceedingly stormy on account of inability to take nourishment and a moderate pneumonic or atelectatic complication. Paraffin sections of the tissue showed

"cells with scant basic cytoplasm whose boundaries are not distinct; there are many degenerating cells with small dense nuclei (pyknosis). There are many mitoses with peculiar dense, small, compact spindles of the nuclei; there are accompanying fibres simulating stroma formation but no arrangement into columns or glands and no secretory vacuoles are seen. The diagnosis is lymphosarcoma." (Figs. 3 and 4.)

X-ray treatment was begun on the fourteenth day. After a brief period of toxic manifestations necessitating mild and divided dosage, the response was most favorable, the nausea and vomiting ceased and nourishment began to be taken without discomfort. Six months later a barium X-ray (Fig. 2) showed complete disappearance of the filling defect of the stomach, including the evidence of extrinsic pressure from involved nodes near the cardia, the stasis had ceased, and no trace of a pathological process remained except a slight narrowing of the antrum as though by scar tissue. Fourteen months after the operation the patient writes that she has gained thirty pounds in weight, is

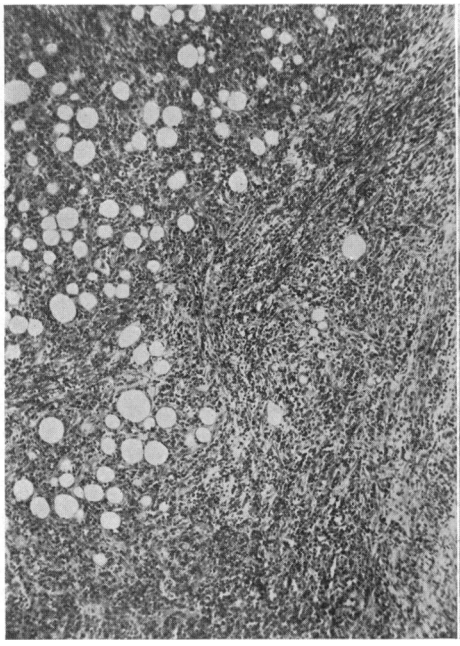

FIG. 3.

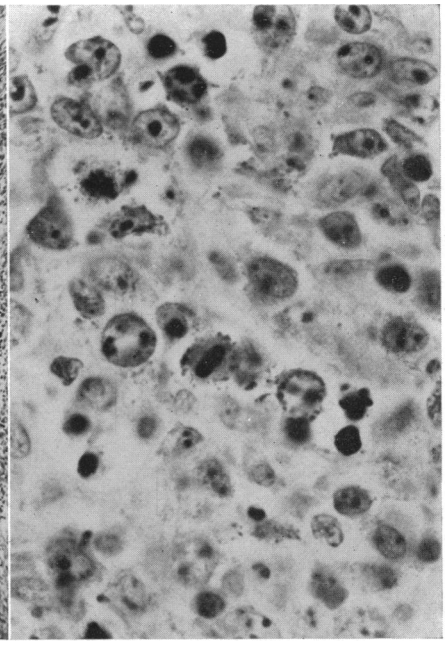

FIG. 4.

FIG. 3.—Tumor-cells invading fat tissue of the omentum, low power (magnification = 112). Case No. S-38857.

FIG. 4.—Tumor-cells; high power (magnification = 1500). Case No. S-38857.

regularly attending to her former clerical occupation, and is eating a liberal mixed diet without discomfort or symptoms of any sort.

Review of this material from the Brigham Hospital clinic confirms the general impression that lymphosarcoma of the gastro-intestinal tract is an uncommon condition and one carrying the gravest prognosis. It is as insidious as carcinoma, and seems to offer no greater probability of reaching the surgeon in an early and operable stage. In the stomach its radical operability is extremely low—in this series only 22.2 per cent., and its differential diagnosis from carcinoma, in the writer's opinion, absolutely defies the skill of the diagnostician, except in the rare instances where it occurs

in individuals so young that carcinoma would be a clinical curiosity. It is realized that these statements as to low rate of operability and gravity of prognosis are at considerable variance with views expressed by some authorities, but they are based on all the instances of the disease observed in a hospital of 240 beds during a period of nineteen and one-half years, on the medical and surgical services and in the autopsy room. In comparing the published evidence, the reader must again be warned as to the utter confusion which he will encounter, due to the failure of many writers to differentiate consistently or at all between the various types of "sarcoma" either in reporting their cases or in summarizing the literature, whereas, as has been noted, true lymphosarcoma differs widely in symptomatology, operability and prognosis from the fibro-, myo-, lipo-, myxo-, angio-sarcoma group—almost as widely, perhaps, as does true malignant osteogenic sarcoma of bone from giant-cell "sarcoma." When the intestine, especially the small bowel, is the seat of the disease, there appears to be probability of earlier diagnosis reflected in an operability in this series of 42.8 per cent., though the ultimate prognosis appears to be quite as grave as in the stomach.

Unless our conception of primary lymphosarcoma of stomach and intestine as originally a local disease is quite erroneous, radical cure by total extirpation is possible, and this should be the goal of general practitioner and surgeon alike, to be attained by early diagnosis and prompt operation. But it is amply evident that in therapeutic radiation we have a powerful substitute, if surgical removal is impossible, and in any case an important aid. Of the Brigham Hospital series, the gastric cases most benefited were No. S-21507, who had a resection followed by X-ray treatment and who reported herself six years later to be in perfect health, and No. S-38857 who had X-ray therapy for an inoperable lesion and who shows no clinical evidence of the disease after fourteen months, whereas No. S-14572—an apparently favorable case, had a resection without X-ray therapy and died of recurrence in eighteen months. An unfavorable result, but one in whom not much could be expected, was No. S-31823, an old man with extensive involvement of the liver, who lived but four months after exploration and X-ray treatment. The intestinal cases do not permit of dependable deductions; three very advanced inoperable cases who had X-ray were possibly benefited, and two patients with resection but without X-ray died with evidence of recurrence after one and one-half and four years. It may be believed that they would have survived longer if they had had the benefit of X-ray therapy.

In conclusion, the writer, on the strength of this survey of a group of patients with lymphosarcoma of the gastro-intestinal tract, wishes to urge the importance of exploratory operation and biopsy even in patients where the clinical evidence points strongly to inoperability, in order that the occasional case of lymphosarcoma may be identified and receive the benefit of X-ray therapy. It may be objected that this is unnecessary since radiation may be used in any event as a therapeutic test; the drawback to this plan is the usually uncomfortable and sometimes serious reaction of a debilitated patient

to X-ray therapy, but above all it seems important that adequate evidence should be accumulated as to the exact histological type of neoplasm which can be benefited by this means.

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