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LYMPHOSARCOMA OF THE SMALL INTESTINE

Edward Eugene Biever

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INDEX

This paper covers the salient features regarding localized lymphosarcoma of the small intestine. It does not include small intestinal involvement secondary to generalized lymphosarcomatosis. However several authors point out that since lymphosarcoma tends to be a generalized disease, the cases of localized involvement may well be the primary focus of a predestined generalized diseases. (1, 2, 3, 4, 5) It is obvious that the main surgical interest lies in the localized lesion without distant metastasis, and even though with radical surgery and/or roentgenologic therapy the prognosis for this localized disease is grave indeed, it still warrants early diagnosis and strenuous treatment if the numbers of occasional long term survivals are to be increased.

Since there are numerous histologic classifications of the various types of lymphoid malignancies presented by writers on this subject, the all-inclusive term "lymphosarcoma" will be used throughout this paper.

The literature published since 1932, which dealt with lymphosarcoma of the small intestine, has been reviewed; as well as the article by Ullman and Abeshouse which reviewed the literature prior to that time. In addition there is a presentation of five previously unreported cases.

ETIOLOGY: The paucity of information pertaining to the etiology of lymphosarcoma is consistant with the understanding of the subject, for it must be stated that the etiology is at present unknown. Liu(6) points out the possibility that these tumors may well be of embryonic origin, considering the large number of cases that occur during the first decade. Other authors reviewed fail to mention this as a factor. Chont(7) reviews several factors thought to be of etiologic importance in the past but not accepted at present, these include typhoid, colitis, tuberculosis, syphilis, and trauma. Ullman and Abeshouse(8) found a significant number of their cases to be in the working class. Burman and van Wyk(9) mention the incomplete investigation into a possible viral etiology.

SEX: All writers agree that the male is involved more frequently than the female, this is in accordance with the occurence of all types of lymphoma, no matter what body system or systems are involved. The exact ratio of male to female involvement varies somewhat from series to series, but averages are about 2:1. Cameron(10) states that children involved with sarcoma of the small intestine are almost entirely males.

RACE: No valid conclusions can be drawn in regards to racial involvement. Many authors fail to record the race of cases presented, and though there appears to be a predominance of Caucasians, in those cases where race is recorded, one must assume that this same predominance is present in the general admissions to the individual hospitals.

AGE: Ritter(11) in his study of lymphosarcoma of the entire gastro-intestinal tract, found involvement in all ages but a majority in the fourth and fifth decades. This incidence is generally accepted by most authors, whether their studies involved the small intestine alone or the entiregastro-intestinal tract(1, 3, 10, 12, 13, 14, 15, 16, 17, 18, 19). The next age most commonly involved are children in the first decade of life (2, 6, 8, 9, 15, 21, 22). Though primary neoplasms of the small intestine are extremely rare in childhood as compared with adult life, two articles point out that children comprise 10 percent of the patients with primary sarcoma of the small intestine (10, 13). Lymphosarchoma is the most common type of sarcoma in the small intestine (2, 21). Singleton and Moore(22) advise that whenever a neoplastic lesion occurs in a child's intestinal tract, it should be considered lymphosarcoma until it is proven otherwise.

The age incidence is quite important in the differential diagnosis, as lymphosarcoma tends to occur at a younger age than carcinoma (14, 18).

INCIDENCE OF SMALL INTESTINAL INVOLVEMENT: The rarity of lymphosarcoma of the small intestine is mentioned by all writers on the subject, and is dramatically presented by some. McSwain and Beal(17) in reviewing 149,469 hospital admissions between 1933 and 1942, found only 20 cases of lymphosarcoma of the gastro-intestinal tract. During this same period 1,031 cases of carcinoma were found in these same organs, or a ratio of 1:51. Only 3 of the 20 cases of lymphosarcoma were of the small intestine. Raiford(23) was able to find

hospital records of 82 cases of primary tumors of the small intestine, of these 32 were malignant, and 14 were lymphosarcoma. Maxwell et al(16) state that less than two malignant tumors of the small intestine are found per year at the Cleveland Clinic. Between 1922 and 1946 only 13 lymphosarcomas were found in this area. Gillett(24) points out that malignant tumors of the small intestine make up only 3 per cent of all malignancies of the gastro-intestinal tract.

There is a certain disparity in the literature as to whether lymphosarcoma of the small intestine is more frequent, less frequent, or of similar frequency when compared with the stomach and large intestine.

Warren(25) emphasized the fact that tumors, in general, are 10 times as common in the large intestine as in the small intestine. Of 2,3563 malignant lesions of the intestinal tract reviewed by Shields Warren and Lulenski(19) only 53 were of the small intestine; however, the incidence of lymphosarcoma in the small and large intestine were 6 and 8 respectively. Several other writers also found lymphosarcoma to be present in almost equal numbers in the two major portions of the intestinal tract (5, 26). Other authors found lymphosarcoma to be more frequent in the small intestine than in the large intestine (1, 6, 8, 11, 12, 29). McSwain and Beal(17) found in their series seven lymphosarcomas of the large bowel, two of the appendix, and three of the small bowel.

Shields Warren and Lulenski(19) also reviewed 569 malignant lesions of the stomach, and found only 14 lymphosarcomas in this area compared with six in the small intestine. Several other writers

found almost the same incidence for lymphosarcoma in the stomach and small intestine (5, 12, 17). The occurence of lymphosarcoma in several series of cases was found to be almost equal in the stomach and small bowel (1, 11, 22, 26).

In Raiford's(23) studies he found that lymphosarcoma was the most common sarcoma of the small intestine. He also found that other sarcomas were exceedingly rare. The following articles did not differentiate sarcomas as presented in their papers (9, 10, 16, 21, 26, 28, 29). In these papers it was found that the incidence of sarcomas of the small intestine to be one half to one fourth that of carcinoma.

Allen et al(12) found the occurence of lymphosarcoma to almost equal carcinoma in the small intestine. Cheever(1) found that lymphosarcoma although rare in the small intestine, was the most common malignant tumor in this portion of the gastro-intestinal tract.

It is agreed by most writers that the ileum is the most frequently involved, and that the duodenum is but rarely affected. There is an increasing incidence of lymphosarcoma as one progresses from the pylorus to the ileo-cecal valve corresponding with the increase in lymphoid tissue.

It is interesting to speculate as to why there is such a paucity of tumors of the small intestine. It seems strange indeed that this should be the case when one considers the length of this portion of the alimentary canal in comparison with either the stomach or the colon, both of which have a relatively high incidence

of neoplasia. There are several factors which may play a part in this relative immunity enjoyed by the small intestine. There is less physical and chemical irritation in this area; for raw food enters the stomach where it is partially digested and is stored for hours; it then rather rapidly passed through the small intestine, to be stored for many more hours in the colon. The acid gastric juice in the stomach, and the bacterial toxins in the colon, are much more irritating than the alkaline reaction within the small bowel. Since embryologically the entire alimentary canal develops from the primitive gut, there would seem to be essentially the same histogenic factors present in all areas.

SYMPTOMS: It is generally conceded that there is no symptomatology that is diagnostic for lymphosarcoma of the small intestine. In the classical teaching, lymphosarcoma was presented as a non-obstructing lesion (22). Considering the literature reviewed, symptoms of obstruction are present at some time in the course of the disease, in the majority of cases (5, 6, 7, 8, 9, 11, 12, 13, 15, 16, 17, 20, 21, 22, 24, 26, 28, 31, 32, 33). The obstruction may be of almost any conceivable type; partial, complete, intermittent, acute, chronic, or practically any combination of the preceeding. This obstruction may arise from any one of several causes: 1. As an annular mass; 2. as a cylindrical segment; 3. by intrussusception; 4. due to compression by an extraluminal mass; 5. by a sesile or polypoid mass encroaching on the lumen; and 6. by kinking of the bowel due to adhesions (10). Frank et al(13) conclude that when kinking is

seen it is due to an actual "destruction of the bowel wall". Berne et al(30) feel that acute obstruction results from some lesion slowing the fecal stream; this gradually results in distention which increases the intraluminal pressure, this in turn leads to compression of the submucosal vascular plexuses, and the resultant hypoxia causes motor decompensation.

It is generally agreed that most patients experience some type of pain during the course of their illness. In five series of cases, a total of 83 patients, all but four had a history of abdominal pain (1, 5, 15, 17, 20). The character of the pain is by no means absolute; frequently it is colicky, postprandial, and is commonly associated with nausea and vomiting.

Changes in bowel habits are very common; one author states that this is true in all cases (8). Certain other writers found the majority of cases to give a history of constipation and/or diarrhea (9, 15, 16, 20). Constipation was the only disturbance of bowel habits mentioned by other authors (1, 2, 5, 6, 7, 10, 11, 26). McSwain and Beal(17) in their series of lymphosarcoma of the gastro-intestional tract reported only three cases involving the small intestine, all three of these had a history of blood in their stools--one as gross blood, two as tarry stools. Cheever(1) records two cases that had had evidence of blood in their stools--one as gross blood, one as tarry stools. His series included 16 cases. However, in the majority of cases reviewed there had been no gross evidence of gastro-intestinal bleeding.

Weight loss of some degree was a prominent finding in the majority of cases (1, 5, 6, 9, 10, 11, 12, 13, 17, 20, 21, 22, 24, 26, 31, 33, 34, 35, 36). Marked weight loss would appear to indicate a more advanced lesion. Anorexia appears to be present in many cases.

Certain authors record a high incidence of fever in the cases that they reviewed (8, 13, 32, 35, 37, 38). Spellberg and Zivin(26) concluded from their study that fever was a poor prognostic sign.

Three of the articles reviewed stress the importance of a history of jaundice in cases of lymphosarcoma of the duodenum (5, 25, 39).

Perforation of the intestinal wall through the area involved with lymphosarcoma is not uncommon (9, 13, 21, 24, 28, 35, 37). Perforation may be into another portion of the gastrointestinal tract or into the peritoneal cavity with associated peritonitis.

PHYSICAL EXAMINATION: The physical examination is never diagnostic of lymphosarcoma; however, in many cases it may lead one to suspect a tumor of the small intestine or surrounding structures. Even though in most cases an absolute diagnosis cannot be made, there are enough historical facts and physical findings to warrant doing an exploratory laporotomy. Palpation of an abdominal mass is possible in many cases; the percentage of palpable masses as presented by several different authors varies from 50 percent to slightly greater than 75 per cent.(7, 9, 10, 12, 15, 20, 29). In all of the detailed

case reports of lymphosarcoma of the small intestine presented by authors there was a palpable abdominal mass(2, 13, 16, 23, 28, 40). The masses palpated vary greatly in size, shape and consistency. There is also some variation in the amount of tenderness presented by various masses; however, the majority would seem to be nontender. Location of the mass appeared to be constant only when the rather firmly fixed duodenum was involved. When the more mobile jejunum and ileum contained the mass it could be palpated in any abdominal quadrent, or the pelvis, the latter points out the importance of doing an adequate pelvic examination in patients with abdominal complaints. It is not unusual for a mass to be palpable in markedly different areas of the abdomen on various physical examinations; when this happens one can be rather certain that he is dealing with a tumor of the small intestine, jejunal or ileal portions.

Depending on the duration of the tumor, the amount of obstruction, and the severity of any anorexia and/or vomiting the patient may suffer from dehyration, malnutrition or cachexia of varying degrees. This is by no means a constant finding. Pallor and ascities are also inconstant findings.

LABORATORY EXAMINATION: There is as yet no laboratory examination, with the exception of cytologic studies, that is diagnostic of localized lymphosarcoma of the small intestine. Anemia has been stressed as a vary frequent finding(1, 6, 8, 13, 16, 24, 34, 41), and it is generally of a mild degree--though rarely it may be severe. This is usually secondary to bleeding from the mucosal surface of the tumor. Massive

hemorrhage is rare, but occult blood is frequently found in the stools. Burman et al(9) and Spellberg and Zivin(26) found in their series totaling 35 cases that anemia was a rare finding. Although one might expect some abnormality in total white blood cell count or differential it is well accepted by practically all of the writers on this subject that the vast majority do not show this. Only two of the articles reviewed mentioned leukocytosis as a frequent finding without abnormality in the differential count (1, 8, 15).

ROENTGENOLOGIC EXAMINATION: It is generally agreed that roentgenologic studies are the most important single diagnostic aid. This is true only to the point that in many cases they allow the diagnosis of some distrubance of the usual pattern of the small bowel as seen roentgenologically. The exact diagnosis of lymphosarcoma of the small intestine is practically never made prior to operation, and many times not until a histologic study is made of the tumor. It must be born in mind that roentgenologic studies of the small intestine are by no means as accurate as in other portions of the gastro-intestinal tract, and that negative findings do not exclude the presence of a lesion (23).

Chont(7) recommends taking a flat plate of the abdomen prior to the administration of an opaque material. This should be performed in both the supine and upright position, and will usually demonstrate intestinal obstruction, partial or complete, if it exists. Maxwell et al(16) feel that roentgenographic study is more reliable if a minimal amount, no more than 2 ounces, of a thin barium suspension is given

orally. In this way the overlaping of barium filled loops of bowel is minimzed, and it is also somewhat less dangerous if the patient has a complete obstruction. Frank et al(13) consider the safest procedure to be the passing of a Miller-Abbott tube, following its progress fluoroscopically, "decompressing the bowel en route", until passage meets resistance. Then a very small amount of opaque material is injected through the tube. This frequently outlines the lesion itself. These tumors may present many different radiologic pictures, dilatation of the proximal bowel, deformity of the lumen, obliteration of the mucosal folds, filling defects, or intussusception. Retention of barium within the small intestine for more than eight hours, or segmentation of barium in the small intestine, both suggest disturbance of motility and warrant further studies(36). Lesions in the terminal ileum are frequently better visualized by performing a barium enema examination than by studies from above(16).

DIAGNOSIS: The most important thing in diagnosing lymphosarcoma of the small intestine is being aware of its existence. It has been stated previously that the diagnosis of this disease is generally not made until the time of operation, and at times not until the tissue has been examined histologically. In most cases a preoperative diagnosis of lymphosarcoma of the small intestine is at best an intelligent guess; however, one case is on record in which an absolute diagnosis was made prior to operation. The tumor involved the distal duodenum and proximal jejunum, and was diagnosed by using exfoliative cytologic examination (39). This type of examination is most applicable to the stomach, and duodenum, and since such a small per cent

of the small intestinal lymphosarcoma are present in this area and this type examination is not performed in many hospitals, it would seem that the number of cases diagnosed in this manner will be small indeed. Rubin et al(42) discuss the method of this type examination adequately.

Chont(7) speaks of a classical triad of symptoms; palpable abdominal mass, occult blood in the stools, and abdominal pain of some type. This would seem to be true in the majority of cases, though all of these factors may not be present at any one time. Symptoms occur earlier in the course of the disease than with carcinoma in a similar area(32, 40). The age of the patient is significant, for one should suspect lymphosarcoma in a younger group than carcinoma. Also, the per cent of palpable lymphosarcomas is greater than the per cent of palpable carcinomas (10). Many authors suggest that the marked response of many lymphosarcomas to a therapeutic trial of irradiation may be used in the differential diagnosis.

Lymphosarcoma of the small intestine has been mistaken clinically as many different conditions eg., various types of appendicitis, regional enteritis, tuberculosis of the small bowel, various types of ovarian tumors, uterine tumors, sarcoma of the mesentery, kidney tumor, mesenteric cyst, anasarca, carcinoma of the head of the pancreas, pancreatic deficency, the sprue syndrome, diverticulitis of colon and pancreatitis.

TREATMENT: It is generally agreed that the treatment of choice for localized lymphosarcoma of the small intestine should consist of

wide surgical excision of the lesion; excision of the lymphatic drainage of the involved portion of bowel; and post-operative x-ray therapy to the involved area.

Many authors point out that in cases where it was found at operation that the lesion was inoperable, one should perform a side-tracking anastamosis, to be followed with radiation therapy.

Various types of therapy have been utilized in the past, only to be abandoned, such as arsenic and other metallic salts, Coley's serum, and radium (8).

Sallow et al(29) indicate in their article that early, radical resection is the treatment of choice, and make no mention of the use of roentgen therapy. Moreton(35) states that since lymphosarcomas react more favorable to irradiation therapy than to any other type of treatment, this should be utilized either alone or following surgery. Other authors feel that irradiation therapy is indicated only when it becomes evident that the surgery performed has not been radical enough, eg., positive lymph nodes, the presence of tumor in the margin of the resected specimen, or the lesion was found to be inoperable(12, 19, 22). Gall and Mallory(3) feel that even though lymphomatous lesions are "strikingly susceptible" to irradiation therapy; that this is but a transitory benefit.

When radiation therapy is contemplated certain points must be born in mind; 1. If an anastamosis of the bowel has been performed radiation therapy should not be started until time has been allowed for the anastamosis to heal; 2. Because of the marked radiosensitivity

of the lymphosarcoma, roentgen therapy should be given in small daily doses, to prevent severe or fatal toxicosis, which may result from rapid absorption of toxic products as the tumor deteriorates (7);
3. Another danger of too intensive radiation therapy is the production of peritonitis or perforation of the bowel if the tumor being irradiated involves the intestional wall (7).

These patients frequently present the problem of dehydration, avitaminosis, anemia or edema and an attempt should be made to correct these conditions prior to operation (16). Debilitated persons tend to demonstrate some degree of chronic shock, and may tolerate anesthesia and surgery poorly, therefore early blood transfusion may be necessary (43). Normally there is as much as five liters of intestinal content that pass the upper ileum each day even in the absence of oral intake(30). Since the majority of cases of lymphosarcoma of the small intestine present with some type of intestinal obstruction, there tends to be distention of the proximal bowel. It is therefore wise to intubate with an intestinal tube, which may be used for decompression of the small bowel (43, 44). This same tube may be utilized in the x-ray examination of the patient, which has been previously discussed.

Unlike the stomach or colon, complete extirpation of the small intestine is incompatible with life (45, 46). Experimental evidence indicates that the distal portion of the small intestine is primarily concerned with glucose absorption (45, 46). Assuming that this is the case in human beings, and since the majority of lymphosarcomas of the small intestine are found within the ileum, it is understandable that

many patients have difficulty maintaining their weight post-operatively. Lepore(46) recommends large dosage of anticholinergic drugs post-operatively to slow intestinal motility and allow more time for absorption of food products by the small intestine. He also suggests using a high protein, moderately low fat diet, with no excess starch, but containing simple sugars and fruit sugars. When steatorrhea is present. Sorlate, (Tween-80), and pancreatic extract is frequently useful. Vitamin deficiencies are quite common, especially folic acid, B_{12}, K, and D, and this must be handled appropriately. Occasionally iron deficiency anemia is present requiring either oral or intravenous iron (46).

Shinkin et al(47) conclude that life is prolonged by treatment even in cases in whom the treatment does not eradicate the disease.

PROGNOSIS: Even though there are cases on record of long-term survivals following treatment, the majority of patients have a very poor prognosis. Burman et al(9) feel that the prognosis of treated cases is generally so poor that a five-year survival merits a report in the literature. The surgical results compare very unfavorably with those for large bowel malignancy (29). The prognosis is however better for lymphosarcoma than for carcinoma involving a similar area of small bowel (29, 32, 35). There is much disagreement in the literature as to what information should be utilized in prognosticating any one case. McSwain and Beal(17) feel that survival is influenced more by the extent and location of the growth than by the age of the patient or the histologic type of the neoplasm. Shallow et al(29) found that

the prognosis was most favorable when the duodenum was involved. Marcuse and Stout(15) found no correlation between the clinical and pathological findings and the prognosis of their case.

Burman et al(9) have found the highest mortality in infants and children. In those cases which have a sprue-like clinical picture, once the diarrhea caused by intestinal involvement starts, the average life expectancy is a little over a year.

Allen et al(12) record a five year survival rate of 33 per cent, excluding operative deaths. Ullman and abeshouse(8) in their series of 103 cases record an immediate operative mortality of 17.6 per cent, and there were only 30 patients that lived more than one year, 12 lived 5 or more years, and 2 lived 10 or more years. Faulkner and Dockerty(20) in reporting on a series of 33 cases of lymphosarcoma of the small intestine, report a 12 per cent operative mortality rate, 4 patients died in the immediate post-operative period, 2 died while receiving post-operative roentgen therapy; 10 patients lived 2 years and 3 patients lived at least 5 years. Marcuse and Stout(15) present 13 cases: 5 lived less than six months; 3 were alive at 5 years; one was living and well 14 years and 4 months post-operatively. Charach(48) in 1943 was able to find 404 cases of intestinal lymphosarcoma in the literature and only 103 of these had adequate follow-ups, in these the average duration of life was 16.7 months.

PATHOLOGY: There is some disagreement as to where these localized lymphosarcomatous lesions arise in the intestine, but most authors agree that the majority arise from the submucosal lymphoid follicles.

Certain authors feel that many of these lymphosarcomas arise primarily in the abdominal lymph nodes, and that the bowel wall is involved secondarily (30, 35, 35prime, 22). From the submucosal area the tumor infiltrates the surrounding tissues (2, 5, 9, 13, 22, 29, 32, 34). The spread of the tumor is peripherally along the long axis of the bowel, and there is gradual invasion and replacement of the muscular layers, at which time the tumor becomes sub-serous (9). The serosal surface becomes irregular and some of the many nodules penetrate the serosa (9). Serosal involvement is a late manifestation (1, 18, 32). Singleton and Moore(22) state that usually all layers of the bowel are invaded except the serosa. Faulkner et al(20) found that there was a "tendency to dissect under, rather than to burst through, the peritoneal and mucosal barriers". The separation of the muscular fibers may cause them to become weakened and paralyses of the intrinsic nervous mechanism may explain the dilatation, rather than constriction, seen in some of the involved segments of bowel (1, 8). Since there is generally an absence of a well-developed fibrous stroma, in contradistinction to carcinoma, the "napkin-ring" type constriction seen in the latter is indeed rare in lymphosarcoma of the small bowel (2, 9). The two main types of gross involvement are diffusely infiltrated bowel and polypoid growths. Faulkner et al(20) found in their series of 33 cases that the lesions in the area of the terminal ileum tended to be of polypoid type, whereas the lymphomas of the upper ileum and jejunum tended to be of the diffuse type with ulceration. Either type of lesion may be multiple, but multiple polypoid lesions are

common; therefore, when one lesion is found at operation, the rest of the bowel must be carefully examined (8, 18). There appears to be a tendency for the diffusely infiltrating type lesion to become ulcerated on its mucosal surface (11, 12, 20). There is a strong tendency for intraluminal polypoid lesions to initiate some degree of intussusception. This is aptly shown by Faulkner et al(20) in their series which included nine polypoid lesions, eight of which demonstrated varying degrees of intussusception. It appears that hemorrhage is quite a common finding; however, it is seldom massive and perforation may be seen due to ischemic necrosis within the tumor mass. Obstruction is very common, the causes of which will be found in another portion of this paper. The vast majority of cases present regional lymph node involvement. Burman et al (9) hasten to point out that this does not preclude a successful therapeutic result, for there are cases of five year cures on record following resection of the involved bowel and lymph nodes. Warren and Littlefield(5) found that only 50 per cent of the nodes palpable at operation in their series of 49 cases of malignant lymphomas of the entire gastro-intestinal tract, contained tumor cells. Adjacent structures may be involved either by direct extension or by adhesions devoid of tumor.

The gross appearance of lymphosarcoma, at operation, is sufficiently different from carcinoma that it may be identified or at least suspected. Lymphosarcoma tends to feel firm and rubbery, in contradistinction to the hardness of carcinoma (22, 34). Lymphosarcoma usually involves the entire circumference of the bowel, and much longer segments of bowel

than does carcinoma (4, 30, 34). The cut surface of the tumor is light grey to light yellow, is glistening and has homogeneous appearance of lymphoid tissue (12, 30, 34).

MICROSCOPIC PATHOLOGY: There is no universally accepted histologic classification of lymphosarcoma as it relates to the small intestine. Numerous classifications have existed in the past, and still do exist. Some terms that have been used by the various pathologists are as follows: Lymphocytoma, lymphoblastoma, intestinal Hodgkin's, chronic inflammatory tumor, lymphoid granulation tumor, granulomatous pseudoleukemia, reticulum-cell sarcoma, lymphosarcoma, small round cell lymphosarcoma, large round cell lymphosarcoma, nodular lymphosarcoma, macrofollicular lymphoma and giant follicular lymphoblastoma. Many of the preceeding terms are used interchangably. The classification as presented by Gall and Mallory(3) with minor deviations is becoming rather widely used. Gall and Mallory(3) classify these tumors according to the cell from which they arise, i.e., from the stem cells or the parenchymal cells of the lymphoid tissue. The components of their classification are as follow; lymphocytic lymphoblastoma, lymphoblastic lymphoblastoma, stem cell lymphosarcoma, clasmatocytic lymphosarcoma, Hodgkin's sarcoma, and giant follicular lymphoblastoma (3).

Certain authors point out that it is not uncommon for several or all microscopic types of lymphosarcoma to be demonstrated if enough sections of a given tumor are examined (9, 22).

Symmers(49) states that many of the examples of "Primary" Hodgkin's

disease of the gastro-intestinal tract are actually granulomatous lesions resulting from foreign particles, tuberculosis, and reginal ileitis.

Cheever(1) is of the opinion that"--the differential diagnosis is scarcely to be made between lymphocytoma and a rapidly growing small round-cell carcinoma--" unless secretory vacuoles are demonstrated in the cells.

PRESENTATION OF CASE REPORTS

CASE-M.V.W.:

This 59 year old, white, male, shoe cutter, entered the hospital on 10-15-55 with the chief complaints of: (1) Stomach ache for over one year. (2) Very hungry but lost weight over the last year. (3) Gross hematemesis today. He had previously been in this hospital in January of 1955 for weight loss of 8-10 lb., pain in epigastrium on eating, gas and belching, and excessive appetite 3 months duration. At that time an exploratory laparotomy was performed and reported as being negative except for adhesions due to an appendectomy done in 1938. He did fairly well in the interum, but continued to have the same complaints. On the day of admission he became nauseated and vomited about 3 pints of blood. He had one tarry stool about 2 months prior to this admission.

Physical Findings: The patient was slightly emaciated and looked chronically ill. Abdomen was slightly distended, the liver was palpable as irregular, and hard just below the right costal margin. No other abdominal masses were palpable. The rest of the physical examination was within normal limits.

Laboratory and X-ray: Hemoglobin 13.1, and red blood cells 4.2 million, no study was made of the white blood cells. No x-ray examination was performed.

Clinical Diagnosis: Gastric ulcer with gastric hemorrhage, severe.

Operation: 10-16-55 After entering the abdomen a gastrotomy was performed which revealed no abnormalities. Palpation revealed fixation

of the jejunum with a rather large, firm mass projecting from the retro-peritoneal space, and involving the first portion of the jejunum approximately six inches from the ligament of Treitz. Perforation was noted in the area of the mass. A wide excission of the involved portion of bowel and its mesentery was performed, followed by an end-to-end anastamosis.

Post-operative Diagnosis: Tumor, retro-peritoneal involving upper jejunum with erosion and perforation of the jejunum.

Post-operative Course: Somewhat stormy. The abdominal cavity had to be opened on 11-8-55 because of a sub-diaphragmatic abscess. After this his hospital course was uneventful and he was dismissed on 12-27-55.

Pathology: The wall of the jejunum was edematous and contained areas of hemorrhage. On the serosal surface, and connecting it to another segment was a brown necrotic area with a thick fibrous reaction surrounding it. The attached segment of bowel was encircled by this necrotic tissue. There were many large lymph nodes in the mesentery and the serosal surface had a gray granular appearance.

Microscopic examination: The mucosa of the ileum contained an infiltrate of plasma cells and lymphocytes. The muscularis mucosae remained, but the muscularis proper had disappeared in most areas. It was replaced by a granulmatous type tissue in which there were areas of necrosis, a pleomorphic infiltrate of lymphocytes, plasma cells, histiocytes and neutrophils. Occasional cells had large nuclei and a few of these had the multinucleated appearance of Reed

Sternberg cells. The large nodes in the mesentery showed marked reticuloendothelial and germinal center hyperplasia but did not show the same tumor pattern as the mass in the mucosa or in the mesentery of the intestine.

Diagnosis: Hodgkins disease involving upper jejunum.

Follow up: The only information available is that this patient died in July of 1956. Whether he had recurrance or metastesis of his disease is not known, nor is the the cause of death.

CASE-C.W.S.

This 30 year old, white, male, assistant physical director at a YMCA, entered the hospital on 1-5-53 complaining of vomiting and weight loss. He had suffered with intermittent vomiting about five hours after eating, especially at night after retiring, for 2 months duration. This had been aggrevated by a large meal. He had a feeling of fullness after meals. There was no desire to eat for periods as long as 24 hours. He had lost 15 pounds in the last two weeks prior to admission, and had lost a total of 23 pounds over an undetermined length of time. Had had no change in bowel habits, and no evidence of blood in his stools.

Physical findings: The physical examination was within normal limits except for slight tenderness to deep palpation on the left side of the abdomen adjacent to the unbilicus. No palpable abdominal masses.

Laboratory and X-ray: Hemoglobin, white blood count and differential were all within accepted normal limits. An upper gastro-intestinal series of x-rays taken on 1-6-53 showed partial obstruction of the duodenal-jejunal junction.

Clinical Diagnosis: (1) Diverticulum of duodenum at duodenal-jejunal junction. (2) Tumor of small bowel or retroperitoneal tumor (lymphoma). (3) Nonspecific enteritis.

Operation: 1-7-53 On opening the abdomen a small tumor nodule was found in the jejunum just beyond the ligament of Treitz, with fixation and kinking of the jejunum against the posterior abdominal wall including left colic artery and vein. Frozen section was interpreted as reticulum cell sarcoma. The infiltrating mass and involved jejunum were excised and an end-to-end anastamosis performed.

Post-operative Diagnosis: Reticulum cell sarcoma, first portion of jejunum.

Post-operative Course: Uneventful. Dismissed on 1-16-53.

Pathology: On the inferior surface of the portion of small intestine removed, there was a firm 25 mm. tumor mass involving the muscularis and subserosa, but not the mucosa. The intestine was acutely angulated at that point, and the upper portion dilated. Microscopic examination: The tumor consisted of masses of neoplastic reticulum type cells which had invaded and destroyed the muscularis, the submucosa and part of the adjacent fat. The tumor cells were variable in size, but they tended to be relatively small, slightly vesicular nuclei in older hyalinized areas and larger vesicular nuclei with macronucleoli in the more solid areas. In general the cytoplasm of the tumor cells was scanty and the cell boundaries are indistinct. Mitoses are fairly frequent and there were occasional tumor giant cells.

Diagnosis: Reticulum cell sarcoma involving small intestine at duodenojejunal junction.

Follow Up: After dismissal the patient received a course of x-ray therapy to the involved areas. Following this he returned to work and was able to hold down two jobs. He re-entered the hospital 8-17-53 because of fatigue of six weeks duration and recent jaundice. Diagnosis at that time: Hepatitis. He was again admitted to the hospital on 12-19-55 because of fatigue, general malaise, fever and chills, and nausea and vomiting of about four days duration. Physical examination at that time was well within normal limits, except for minimal tenderness to deep palpation in the right upper abdominal quadrent. Upper gastro-intestinal x-ray examination showed no evidence of recurrent new growth at the site of anatomosis.

The last information available was that he was alive and working in another city in 1957.

CASE-A.K.:

This 60 year old, white, male, farm laborer, entered the hospital on 11-4-57 with the chief complaint of a 20 pound weight loss over a two month period, and an intermmitant right lower quadrant abdominal pain of six weeks duration. The pain was present at infrequent intervals and lasted one to two days. He had had no change in bowel habits, no nausea or vomiting, and no evidence of gross blood in his stools.

Physical Findings: Essentially negative except for abdominal examination which showed extreme tenderness in the right lower quadrant and a 3 x 3 cm., tender, nonmovable mass in this area. The liver was palpable 2-3 cm. below the right costal margin on deep inspiration was slightly tender.

Laboratory and X-ray: Hemoglobin - 11.4 gms., red blood cells - 3.9 million, white blood cells - 7,700 with a normal differential. A barium enema examination on 11-5-57 demonstrated narrowing of the lumen with dilatation of the proximal portion of one of the terminal ileal loops which appeared to involved by an inflammatory mechanism, there were also changes in the normal mucosal pattern.

Clinical diagnosis: Granuloma of the terminal ileum.

Operation: 11-7-57 On opening the abdomen a tumor was visulized approximately 20 cm. proximal to the ileo-cecal junction. This mass was adherent to the lateral parietal peritoneum, also the ascending and transverse colons were densely adherent to the mass. Massive nodes were present in the mesentery of the small bowel. The terminal ileum, mesentery, cecum and ascending colon were excised and an ileo-transverse colostomy was performed. The liver was free of metastasis.

Post-operative Diagnosis: Lymphoma of the terminal ileum.

Post-operative Course: Uneventful. Dismissed on 11-16-57.

Pathology: 13 cm. in diameter tumor, with ulceration on the mucosal surface, narrowing of the lumen, and thickening of the ileal wall. The ascending colon and the cecum appeared normal. Microscopic examination: The tumor cells tend to be pleomorphic and vary moderately in size. They had large nuclei and scanty cytoplasm. The nuclear chromatin tended to be irregular and clumped. Mitoses were frequent and many were atypical. Little stroma accompanied the tumor and the cellular pattern was similar in all sections

taken from the ileum. Section of regional mesenteric lymph nodes showed replacement of the normal architecture by similar tumor.

Diagnosis: Reticulum cell sarcoma involving ileum, mesenteric lymph nodes and abdominal wall.

Follow Up: Patient admitted to another hospital on 2-13-58 because of vomiting of six days duration, and frequent black stools since his operation on 11-7-57. He felt tired and weak, and had been aware of an abdominal mass which had been increasing in size for two weeks. Physical examination revealed a tender 13 x 13 cm., firm mass in the right side of the abdomen. Patient was operated on 2-10-58 and an extremely large nodular mass was found involving the mesentery of the terminal small bowel, which was densely adherent and probably invading into the anterior abdominal wall of the right upper abdominal quadrent. The mass appeared to be causing almost complete compressive obstruction of the duodenum. Anticolic gastrojejunostomy was performed. Pathologic diagnosis of biopsy material obtained at operation was probable reticulum cell sarcoma. The patient had received x-ray therapy to the abdomen during this hospital admission prior to operation, and the response had been disappointing. On 2-13-58 an x-ray of the chest revealed bilateral basilar bronchial pneumonia, and bilateral free air under the diaphragm suggesting recent operation.

The patient's course continued downhill, and died 2-22-58. No autopsy was performed.

CASE-M.P.

This 66 year old, white, housewife entered the hospital on 2-1-49 with the chief complaint of anorexia for two months. During this time she was unable to eat solid foods because is would cause severe cramping, epigastric and left lower abdominal quadrant pain, and occasional vomiting. During this same period she was extremely constipated, being unable to pass any stools without enemata. For the last two weeks there had been tarry stools with each enema. She had experienced diarrhea for the last 2-3 days. There had been approximately two pounds of weight loss in the last two months. The preceeding November the patient had the "flu", at which time she had noticed lumps in her stomach that were crampy and associated with severe pain. She had had a constant stomachache since one month prior to admission, epigastric in nature, and worse at night.

Physical Findings: Patient was slightly emaciated but well-developed. Abdominal examination revealed generalized protuberance, a 7 x 10 cm. slightly moveable, pulsating mass in the upper left abdominal quadrant, another slightly moveable, tender, firm, smooth, mass palpable 10 cm. to the right of the umbilicus. The remaining portions of the physical examination were within normal limits.

Laboratory and X-ray: Hemoglobin - 11.9; red blood cells - 4.9 million; white blood cells - 12,300 with a differential count that was within normal limits. Stool examination for occult blood was positive. Barium enema revealed the palpable right lower quadrant mass was causing apparent extrinsic pressure on the inferior pole of the cecum.

Clinical Diagnosis: Carcinoma of the cecum.

Operation: 2-14-49 On entering the abdomen the cecum was visulized, showing a large mass estimated to be 8 cm. in its greatest diameter completely surrounding the ileo-cecal junction, with the greater portion of the mass surrounding the ileum. The mass was not fixed to the parietal peritoneum in the iliac fossa. Large lymph nodes were palpated near the base of the mesentery of the small bowel and some extended superiorly along the aortic chain. The terminal ileum, cecum, about 25 cm. of the ascending colon, and the involved mesentery were extirpated. An end-to-end ileocolostomy was performed.

Post-operative Diagnosis: Hodgkin's disease of terminal ileum, cecum and mesenteric nodes.

Post-operative Course: Patient recovered from operation quite well. Deep x-ray was given 7 times to the abdomen before the patient was dismissed on 2-14-49. Patient expired 6-2-49 at home. No autopsy was performed.

Pathology: The distal 7 cm. of the terminal ileum and the adjacent portion of cecum were involved in a firm elastic grayish-white mass of tissue which had partially occluded the lumen of the ileum and which was also encroaching on the lumen of the cecum. Bowel mucosa appeared essentially normal except in the region of the tumor mass. The tumor involved the medial half of the cecum and the distal 7 cm. of the terminal ileum, and narrowed but did not occulde the ileo-cecal valve. The surface of the tumor was rough and irregular. On cut section it had a grayish, granular, homogeneous appearance. The

tumor tissue was adherent to and invading the mesentery of the distal 30 cm. of terminal ileum. Microscopic examination: Sections of cecum and terminal ileum revealed clumps and masses of highly anaplastic tumor cells. The individual cell showed much variation in size, shape and staining reaction. Nuclei for the most part were large and vesicular but were hyperchromatic. Unevenly distributed throughout the tumor were numerous giant cells with single or multiple nuclei which were deeply lobulated and had a deep staining cytoplasm. Moderate numbers of mitoses were present. The tumor tissue seemed to invade but not completely destroy the mucosa, however, the tumor invaded and separated the muscularis and extended through the serosa. Several mesenteric nodes were examined, in some there was considerable hyperplasia of reticulo-endothelial elements and mixed with large bizarre, frequently multinucleated anaplastic tumor cells.

Diagnosis: Hodgkin's disease of terminal ileum, cecum and mesenteric nodes.

CASE-M.J.:

This 68 year old white, female entered the hospital on 7-18-56 with the chief complaints of upper abdominal pain for two months, and a 40 pound weight loss over the last three months. The patient had been previously admitted two months before for gastro-intestinal studies, and had been told then that she had gall stones. Patient had marked anorexia. The pain occured mainly on arising in the A.M., and was slightly releaved by "anacin". Pain was in the left epigastium, and occasionally also on the right side of the abdomen.

Physical Findings: Moderately jaundiced sclera, dry skin, but no jaundice of skin. Marked tenderness to palpation of the abdomen especially on the left side, and right upper quadrant. A tender mass palpated in the left lower quadrant was thought to be sigmoid colon.

Laboratory and X-ray: Hemoglobin 10.8; red blood cells 3.9 million; white blood cells 7,400 with a normal differential count. Examination of the feces for occult blood was positive. Barium enema examination revealed diverticulosis of the transverse, descending and sigmoid colon. Upper GI series showed a large ovoid zone of barium accumulated on the posterior gastric wall compatible with active ulcer niche, and the possibility of presence of this niche within a central area of new growth could not be excluded. A small paraesophageal hiatus hernia and a diverticulum of the second duodenal segment were also seen.

Clinical Diagnosis: Carcinoma of the stomach.

Operation: 7-26-56 The abdominal cavity was entered and a lesion 4 cm. in diameter was palpated in the posterior surface of the midportion of the stomach. No nodules were palpable in the liver. Approximately 45 cm. from the ligament of Treitz a partially annular lesion of the jejunum was noted, and several large lymph nodes were present within the adjacent mesentery. The duodenum was transected immediately distal to the pylorus, and approximately 50 per cent of the stomach was removed. A wedge of jejunum was excised including the adjacent mesentery. Appropriate anastamosis was performed.

Post-operative Diagnosis: Lymphoma of the stomach and jejunum with regional lymph node metastasia.

Post-operative Course: She did well until x-ray and nitrogen mustard therapy was begun, at which time she developed abdominal pain, nausea and vomiting. She also developed a severe cystitis. She was dismissed as improved on 9-8-56.

Pathology: The stomach revealed on its posterior surface an ulcer 4 cm. in diameter, with firm rolled edges, and a central necrotic area. In the mid-portion of the jejunum there was a 30 mm. band of tumor which encircled the entire jejunum and extended into the mesentery. The surface of the tumor was ulcerated. The tumor was grayish-white and firm, and it extended into the muscularis and into the serosa. Microscopic examination: The normal gastric mucosa ended abruptly at the border of the tumor which replaced the mucosa and extended into the muscularis, and into the serosal surface. The tumor was rather solid in character, composed of cells with irregular vesicular nuclei and prominent nucleoli. Fairly frequent mitoses were present. The cytoplasm was moderate in amount and faintly acidophilic to neutrophilic in staining quality. Many of the cells assumed a somewhat elongated shape with reticulum like cytoplasmic processes. The lesion in the jejunum was essentially similar. The lymph nodes were entirely replaced by cells which were similar to those seen in the stomach and jejunum.

Diagnosis: Reticulum cell sarcoma of the stomach, jejunum, and lymph nodes.

Follow Up: The patient was readmitted on 10-2-56, because of a progressive deterioration over the previous three weeks. She died three to four minutes after arrival in the hospital. Autopsy revealed metastasis to the liver, spleen, adrenal glands, and stomach. The immediate cause of death was due to myocardial insufficiency.

TABLE I

FIVE NEW CASES

CASE	AGE	SEX	INVOLVED AREA	SYMPTOM	PX	LABORATORY	X-RAY	RX	SURVIVAL
MVW	59	M	Jejunum	Pain in stomach Weight loss Tarry stools	Cachexia	Hbg. 13.1	None	Excision	Approx.9 months
CWS	30	M	Jejunum	Vomiting Weigh loss	Tenderness in abdomen	Normal	Partial obstruction at duo-jejunal junction	Excision	1. & w. approx. 5 years
AK	60	M	Term ileum	Weight loss Abdominal pain Anorexia	Tenderness Palpable mass	Hbg. 11.4 RBC 3.9	Barium enema showed ileal involv.	Excision X-ray	Approx. 2½ months
MP	66	F	Term ileum & cecum	Anorexia Cramping in abdomen Vomiting	Abdominal mass	Hbg. 11.9 RBC 4.9 WBC 12,900 Diff.normal Pos. occult blood	Barium enema showed external mass compressing cecum	Excision X-ray	Approx. 3½ months
MJ	68	F	Jejunum	Abdominal pain Weight loss Anorexia	Tender, palpable abdominal mass	Hbg. 10.8 RBC 3.9 Pos. occult blood	Upper GI IMP. Ca of stomach	Excision X-ray Nitrogen mustard	Approx. 2½ months Myocardial insufficiency Much metastasis

SUMMARY: Review of the literature since 1932 and of Ullman and Abeshouse's article which reviewed the literature prior to 1932 yield the following information regarding lymphosarcoma of the small intestine. The localized lymphosarcomatous lesions arise in the submucosal lymphoid follicles, or in the abdominal lymph nodes with early involvement of the submucosal lymphoid follicles. The tumor then invades peripherally along the long axis of the bowel and gradually replaces the muscular layers of the bowel wall. The serosa and mucosa may be involved late in the disease. The etiology is as yet unknown. Males are involved about twice as frequently as females. The majority of cases occur during the fourth and fifth decade, and the first decade is the next most frequently involved age. The incidence of lymphosarcoma in the small intestine is extremely small when compared with all other malignancies of the gastro-intestinal tract. The ileum is more frequently involved with lymphosarcoma than any other portion of the small bowel. There are no symptoms which are pathognomonic, however most cases have some sort of obstructive symptoms at sometime in the course of the disease. Pain is present in most cases, weight loss is usually present, and changes in bowel habits are common. Frequently there are no abnormal physical findings, though there may be cachexia, dehydration and/or a palpable abdominal mass. Laboratory examination may show a mild anemia, but the white blood cell count and differential are usually within normal limits. When the stools are checked for occult blood it is frequently found. Roentgenologic examination is the most important single diagnostic aid. Diagnosis

prior to operation is very infrequent. The treatment of choice is wide surgical excision followed by x-ray therapy. The prognosis in these cases is extremely poor in the majority of cases, however, due to the occasional long-term survival strenious treatment is indicated.

CONCLUSIONS: (1) The findings in the five cases presented in this paper generally agree with findings of other authors. There was a preponderance of involvement in the male of 3:2. The average age in this series was 56.6 years, with only one case (30 years) below 59 years of age, this is somewhat higher than most series.

(2) In previous series of cases the majority of cases were in the terminal ileum. In this series the jejunum was involved in three cases, in one of these there was also a seperate lesion in the stomach; the ileum was involved in only two cases and in one of these there was also involvement of the cecum.

(3) As would be expected from previous reports four cases had had abdominal pain, and four had had weight loss. Three of these cases had had anorexia, and one had had a tarry stool.

(4) Physical examination was essentially negative in all cases except for tenderness in the abdomen on palpation in three cases, and a palpable abdominal mass in two.

(5) In accordance with previous findings the hemoglobin was below 12 grams per cent in three cases, but was above 10.8 in all cases. The white blood count was within normal limits in all cases except one in which it was 12,300, the differential white count was within normal limits in all cases. Stool examination for occult blood

were positive in two cases.

(6) Concurring with previous series, abnormalities were noted on x-ray examination in four cases.

(7) The treatment employed in this series was radical excision in all cases. In addition x-ray therapy was used in two cases and x-ray therapy plus nitrogen mustard in one. The only long term survival resulted from excision alone.

(8) The survival period once the patient was operated upon was generally quite short. One would expect this from reviewing the literature. Three of these cases had died within three and one half months. One in nine months, and one patient is living and apparently free from disease five years after his treatment.

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