INTRODUCTION

Benign mesenchymatous tumors of the stomach are considered rare. Various types have been described; myomas occur most frequently. Although related anatomically to myomas of other parts of the gastro-intestinal tract, those of the stomach form a more or less distinct clinical entity.

The first review of the subject, appearing in 1898, was by Steiner (1) who collected all the reported cases of gastro-intestinal myomas beginning with one described by Morgagni in 1765; 21 were in the stomach. Hake (2) in 1912 added 60 cases, 36 in the stomach. A year later, Outland and Clendenning (3), restricting their report to myomas of the stomach, collected 79 cases. The same year Farr and Glenn (4) brought the number up to 84. Nasetti (5) in an accurate review collected 140 cases up to 1914. Eliason, Pendergrass, and Wright (6) in 1925 collected 321 cases; but Nigrisoli (7), writing in 1927, considered not all of these authentic, and cited only 211 cases. Since Nigrisoli's review a total of 108 cases have been reported by the following: Larsén (8), Troell (9), Brayne and Simon (10), McIntosh (11), Millar (12), Mason and Dwyer (13), Willenbacher (14), Lorenz (15), Schneidewind (16), Schosserer (17), Picard (18), Vance (19), Villata (20), Vernengo (21), Anzilotti (22), Domanig (23), Willis (24), Rieniets (25), Morgan (26), Kahn (27), Emmert (28), Baumecker (29), and Davidson (30). The total number of published cases is therefore 319.

The clinical aspects of gastric myomas have been well discussed by many of the above authors. Briefly, these tumors are most frequently found in persons past middle age; the duration of symptoms extends over many years. Hematemesis or melena, followed by severe anemia, is frequent; a number of patients have bled to death from hemorrhage. Obstruction of the pylorus or cardia may occur, or volvulus from invagination of the stomach. Physical examination reveals a mass only if the tumor is large; even then it is very variable. The gastric acidity is usually
unchanged. Roentgen examination is most helpful, especially if the tumor is intragastric or intramural. In recent years many of these tumors have been removed surgically.

Anatomically, gastric myomas are most frequently located on the greater curvature near the cardia, situated externally, intramurally, or internally. They measure from a few centimeters in diameter up to the size of a head. They are frequently ulcerated, occasionally with eroded blood vessels in the floor of the ulcer. Some have been cystic, others degenerated. Multiple myomas have been found (Tilp, 31; Werhahn, 32). Very small single or multiple myomas are not infrequent incidental findings at autopsy (Rieniets, 25).

Microscopically the tumors are either pure myomas or fibromyomas. Adenomyomas have been excluded from this and similar reports because of their different pathological significance.

**Case Report**

H. B., a fifty-year-old white laborer, first entered the University of Illinois Research Hospital, on July 2, 1931. He stated that he had been a heavy drinker, and that after drinking he frequently noticed a pain in the epigastrium, the pain having no relation to food. About three months before admission he had begun to feel weak and dizzy, and to become short of breath on exertion. About one month before, he began to have tarry stools. These symptoms had increased progressively in severity.

At the Research Hospital, neither x-ray studies of the gastro-intestinal tract nor proctoscopic examination showed anything of significance. Blood chemical values were normal; the blood Wassermann reaction was negative; the urine was negative. An examination of the blood revealed: 450,000 red blood cells and 7500 white blood cells per cu. mm.; hemoglobin 18 per cent; color index 0.29; marked aniso- and poikilocytosis; bleeding time, three minutes; coagulation time, one and a half minutes. The fragility test was normal. The patient left the hospital two weeks later.

On July 20, 1931, the patient entered the Cook County Hospital. He was at this time severely ill, with a marked increase in severity of his symptoms. He was exceedingly anemic. Physical examination revealed a systolic murmur at the apex, edema of the lower extremities, a slightly enlarged liver, and the suggestion of an indefinite mass in the abdomen. Roentgen studies of the gastro-intestinal tract were again entirely negative. The stools were repeatedly strongly positive for blood, however, and a diagnosis was made of either a bleeding polyp in the gastro-intestinal tract, or possibly a ruptured esophageal varix secondary to cirrhosis of the liver. Under treatment, including a blood transfusion, the patient responded very rapidly. The red blood count rose to 3,450,000 per cu. mm., and the hemoglobin to 55 per cent. The patient felt so well that on Aug. 17, 1931, he went home against advice.
On Sept. 5, 1931, he returned to the Cook County Hospital with a marked exacerbation of all his previous symptoms. The physical and laboratory findings were essentially as before. The anemia was very severe. A transfusion was advised, but the patient's relatives failed to respond; he gradually became worse and died on Sept. 11, 1931.

Post-mortem examination was performed by Dr. Jaffe. The skin, mucous membranes, and all the internal organs were very pale. The heart weighed 440 gm. and showed the pale yellow-gray striping of fatty degeneration. The liver also showed fatty degeneration. The spleen weighed 275 gm.

The essential pathology was in the stomach. At the cardia, on the greater curvature, was a tumor mass originating from the gastric wall. It was firm, coarsely lobular, about 9 cm. in diameter and 5 cm. high, extending into the gastric lumen (Fig. 1). It was covered by mucosa except near the center, where there was a crater-like ulcer 2 cm. in diameter and 1.5 cm. deep, filled with coagulated blood. The sectioned surface was a homogeneous gray white.

In the right lobe of the liver was a firm node 2 cm. in diameter, fairly
Fig. 2. Primary Tumor (Mallory Phosphotungstic Acid Hematoxylin, × 1010), Showing the Intracellular Myofibrils

Fig. 3. Metastasis to Liver (Hemalum-Eosin, × 120), Showing Absence of Invasion

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well circumscribed. The sectioned surface was a homogeneous gray white.

Microscopic examination of the tumor of the stomach reveals it to be composed of cells that are long and fusiform and arranged in bundles interlacing in various directions, separated by very little connective tissue and scanty blood vessels. They stain yellow with the Van Gieson method and purple blue with the Mallory phosphotungstic acid hematoxylin method. The nuclei are oval, with rounded ends, distinct nuclear membrane, and fine, evenly distributed chromatin granules. There is practically no variation in the size, shape, or chromatin content of the nuclei. There are very few mitotic figures. The tumor is well circumscribed, and covered by the mucosa and muscularis mucosae. The muscularis propria is displaced and compressed. In the region of the ulcer the tissue is loose and edematous and infiltrated by inflammatory cells and recent extravasations of blood.

The Mallory phosphotungstic acid hematoxylin stain reveals in many of the cells delicate longitudinal intracellular fibrils, the myofibrils characteristic of fully differentiated smooth muscle cells (Fig. 2).
The node in the liver is seen to resemble almost exactly the tumor of the stomach, except that the cells are slightly longer (Figs. 3 and 4). The regularity of the size and structure of the nuclei is striking, and mitotic figures are practically absent. The tumor borders on the liver without limiting membrane, compressing and displacing slightly the adjacent liver cell cords. Short and blunt projections of the tumor tissue extend for a very short distance into the adjacent portal capillaries.

Anatomical Diagnosis: Ulcerated leiomyoma of the stomach; metastasis to the liver; very severe generalized anemia; eccentric hypertrophy of the heart with fatty degeneration of the myocardium; chronic tumor of the spleen.

This is a case, then, of an ulcerated leiomyoma of the stomach, from which the patient bled to death. It is histologically benign and composed of fully differentiated mature smooth muscle cells, but has metastasized to the liver.

Discussion

Benign Metastasizing Tumors: An histologically benign metastasizing tumor is obviously one in which the cells of both the primary growth and the metastasis are fully differentiated and mature, show no anaplasia, have few or no mitotic figures, and show an expansive and not an invasive growth. From this standpoint a study of the reported cases leaves one disappointed. Almost all were reported during the end of the 19th and early 20th centuries, a time when the histologic criteria of malignancy were probably not well established. Hansemann (33) had only in 1893 announced some of the modern ideas of cancer morphology and had coined the term "anaplasia." An important defect of the case reports is their frequent lack of description or illustration. Reviews of the subject cover only the older literature (Hauser, 34; Wolff, 35; Borrmann, 36). Ewing (37) questions the existence of such tumors. Only one recent authentic case can be found, reported by Demel (38) in 1926–28, a myoma of the intestine with metastasis to the liver.

The first tumors of this type were chondromas, reported as early as 1855 by Paget, Virchow, and others. Ernst (39) collected 20 cases up to 1900. Borrmann (40) reported 2 cases in 1923. Lubarsch (41) considers these tumors not infrequent. Pathologists are familiar with the benign appearing skeletal chondromas, really chondrosarcomas because of their great tendency to invade, recur, and metastasize.

In 1876 Cohnheim (42) described a metastasizing nodose
colloid goiter. Numerous cases have since been reported, but they have not been accepted as benign metastasizing tumors. Although Wegelin (43) considers 14 authentic, Boyd (44) points out that none have been proved. Graham (45) showed that carcinomas of the thyroid frequently cannot be differentiated histologically from benign nodes or benign epithelial hyperplasia; he considers invasion of blood vessels as the chief diagnostic factor. Warren (46) considers even the latter an insufficient criterion.

Benign metastasizing angiomas were described by Borrmann (36) and others. Wolff (35) considers them to be angiosarcomas. Jaffe (47) points out that the existence of such tumors is doubtful; although they show no anaplasia, yet, because of their infiltrative growth and their stroma of undifferentiated mesenchyma, they cannot be considered histologically benign.

Less important benign metastasizing tumors reported are a myxolipoma (Waldeyer, 48), obviously malignant; an ovarian cyst; an “amyloid” tumor, etc.

Benign metastasizing leiomyomas have been the most frequently reported of this type of tumor. The first was described by Krische (49) in 1889 in a uterus. Langerhans (50), Minkowski (51), Schlagenhaufer (52), and a number of others soon followed with similar tumors. Several cases have been reported in the intestine, and several in the stomach (Hansemann, 53; Eising, 54). A study of the reports shows that a number of these tumors are undoubtedly malignant. Others may have been authentic, but the published reports are incomplete and therefore questionable. Ewing (37) states that no case has been fully studied in which definite variations from the usual structure of leiomyoma were wanting, although in several instances these variations have not been very pronounced. Hansemann’s case in the stomach is such a one; that of Eising is definitely malignant. A source of error lies in the fact that no clear distinction was made by the older writers between mature myomas, immature myomas, and myosarcomas. Because of the weight of Ribbert’s contention that sarcomas arise only from the connective-tissue stroma, the term “malignant myoma” was used for all myoblastic tumors with metastases. Some of these tumors present so little anaplasia that the term does seem suitable, yet modern pathologists would not hesitate to call them myosarcomas. R. Meyer (55) in 1907 first contended that, because of the slight degree of anaplasia, cellular immaturity, lack of myofibrils, abundance of mitoses, and invasive powers, these
tumors show they are in reality myosarcomas. He reserved the term “malignant myoma” for those fully mature histologically benign myomas with metastases. Yet two years later Ghon and Hintz (56) retained the term for myosarcomas. It has continued to be used by many authors (Ballin and Vaughan, 57; Proper and Simpson, 58; Schreiner, 59), and is still used by MacCallum. Williams used the term “myoma sarcomatodes”; Mallory uses “leiomyoblastoma.” However, Aschoff, Kauffmann and others name these tumors correctly, myosarcomas (58).

Most of the benign metastasizing myomas are composed of active immature and undifferentiated cells, although without anaplasia or invasive properties. This is the type figured by Ribbert (60) and others as the typical metastasizing myoma, the ability to metastasize being due to the immaturity of the cell. Metastasis of such tumors would not be surprising; but metastasis of a completely mature and differentiated benign tumor such as is here presented is rare.

**Histologic Grading of Malignancy:** The complete discrepancy between the histologic appearance and the malignancy of these tumors is so striking that they deserve consideration with regard to the recent attempts at the histologic grading of malignant tumors. Since Hansemann’s time occasional attempts have been made to correlate the malignancy of tumors with the degree of anaplasia. The first serious attempt at tumor grading was made by Broders (61) in 1920, who, working with MacCarty at the Mayo Clinic studied a series of squamous-cell carcinomas and developed a system based on the degree of cellular differentiation. Martzloff (62) in 1923 devised a similar method based on cell types. MacCarty (63) in 1924, after a series of studies of carcinomas of the breast, rectum, stomach, etc., considered the degree of lymphocytic infiltration, fibrosis, and hyalinization as important. Greenough (64) in 1925 developed a somewhat different method. Hueper (65) and his co-workers in 1926 devised a method of reporting a number, the “malignancy index,” which would represent the degree of malignancy; this number was derived at first from 9, later from 20 different histologic factors, the “malignogram.” A number of workers have since made similar attempts at tumor grading (see reviews by Plaut, 66, and Hueper 67).

As is well known, the grading of carcinomas is being given serious attention, is influencing therapeutic procedures, and is being applied to the determination of radiosensitivity (Quick and
Cutler, 68, and others). Although in a general way correlation seems to exist, even the most ardent exponents admit that many discrepancies and disappointments occur. Differences of opinion are being voiced from many sources (Plaut 66, Reimann, 69). Tumors of identical histologic appearance may run entirely different clinical courses. Radiosensitivity can be only approximately determined, and there are many exceptions (Haagensen, 70; Phillips, 71). Windholz (72) reported an adenocancroid of a uterus which had been heavily irradiated before surgical removal. Here, almost as in a controlled experiment, the two elements can be assumed to be of equal malignancy, yet the squamous-cell element had undergone far more regressive changes than the glandular. Finally even MacCarty (73) in 1931 concluded that the matter is of greater academic than practical importance. Most of the 15 factors he presents in evaluation of malignancy are clinical and gross features; only 4 are histologic.

There has been no real proof of the underlying ideas involved. First, clinical malignancy involves many factors, namely rapidity of growth, recurrence, occurrence and nature of metastases, cachexia, response to radiation, etc. If the duration of life alone is considered, many other factors are involved, such as the age and condition of the patient, the location of the tumor, complications of a mechanical nature, such as obstruction, compression, or perforation of vital organs, associated infection, etc. Also, radiosensitivity includes two factors not sufficiently distinguished, namely primary regression and definitive cure.

Second, the histologic criteria used in the determination of malignancy have not been well established. Cell types are sometimes almost impossible to determine; the polymorphic character of squamous-cell carcinoma is remarkable. The number of mitotic figures is inconstant, and may depend on variable physiologic factors. There may be a definite rhythm in cell division. There is growing evidence that amitosis, or possibly a shortened form of mitosis, is of great importance in tumor growth. Furthermore, a small portion of a tumor removed for study may not be representative of the growth as a whole; the character of a tumor frequently changes as time goes on; and metastases may appear much different from the primary growth.

Third, the patient, the host, has been entirely neglected. Under the microscope two tumor cells may appear identical, yet in different individuals, even in different organs, they probably
behave quite differently. The spleen, the great blood filter, probably receives many embolic tumor cells, yet it is singularly immune to metastases. Normal blood has the power to dissolve carcinoma cells in vitro; blood of cancer patients has not this property (Freund and Kaminer, 74). Tumor immunity and resistance are beginning to receive more attention. The reticuloendothelial system may be of importance in such immunity (Jaffé, 75).

It may be that the future will reveal finer cytological characteristics of tumor cells not yet known. Cytological studies of tumor cells are few. Perhaps morphology here ends and physiology begins. With the present state of knowledge the explanation of the metastasis of a benign tumor such as is here presented can be only a speculative one, but must take into consideration the status or the resistance of the individual. The older writers on the subject adhered to such a theory (Ribbert's tissue tension theory) rather than postulating a new cell race. Benign tumors by their expansive growth can produce pressure atrophy and break into blood vessels. Normally the embolic tumor cells are immediately destroyed. However, if in their new environment the cells find "favorable circumstances," whatever these may be, they conceivably will continue to grow. This conception of the resistance or status of the individual is perhaps of importance in a consideration of the etiology of tumors.

SUMMARY

A review of the published cases of myomas of the stomach is presented. The case reported is an ulcerated leiomyoma of the stomach from which the patient bled to death. It was histologically benign and composed of fully differentiated smooth muscle cells, and metastasized to the liver. A review of the subject of benign metastasizing tumors is followed by a consideration of the present status of the histologic grading of tumors.

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