DIAGNOSIS OF THE KRUKENBERG TUMOR

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Since the time of Krukenberg in 1896, "all ovarian tumors which enlarge the ovaries uniformly without distortion, which present alterations of fibrous areas with mucinous-cell groups, and which propagate along the lymphatics are called Krukenberg tumors" (6). These tumors occur with greatest frequency in women about the age of thirty-five. They are in most instances bilateral and produce a general enlargement of the ovary, which keeps its form and is usually free of adhesions. They are accompanied by ascites; they metastasize early, and are almost invariably fatal.

The original conception of Krukenberg that these tumors were primary in the ovary has been refuted by more recent writers, and most pathologists now agree that pure Krukenberg tumors are always secondary to carcinoma elsewhere. We believe that such tumors are probably of more frequent occurrence than is generally supposed. They are seldom diagnosed before operation or autopsy, and it may be not even then. Solid ovarian tumors are removed at the operating table and unless an autopsy is performed, death is likely to be accredited to recurrence of the ovarian tumor or metastasis from it.

The case here presented illustrates the difficulty of the clinical and even of the autopsy diagnosis of Krukenberg tumors. There is very often a remarkable disproportion between the size and extent of the primary tumor and its subsequent metastasis. Grossly the gastro-intestinal tract may appear negative and only upon detailed search is a small suspicious area found, which in microscopic section enables the pathologist to make a diagnosis.

A review of the literature shows a wide discrepancy in the size of the primary growths. Jarcho (6) reports two cases in which the entire wall of the stomach was infiltrated, another with an ulcer 7 × 5 cm., and still another with a tumor the size of the palm of an infant's hand. Gordon (5) reports a growth on the gastric wall of "fairly large size." Masson (9) cites a case where a "relatively small tumor was removed at operation" and describes another 2 inches in length and a third consisting of a large mass extending upward within 2 inches of the esophagus. Saccone (13) found a large crateriform ulceration infiltrating the stomach wall and extending into the hepatic chain of lymph nodes.

During a laparotomy for removal of an ovarian tumor, Armstrong (1) discovered, by palpation of the stomach, an infiltrating carcinoma the size of a lime. Gordon (5) reports that in one of his cases a careful examination of the stomach was not made at the first operation, but the second laparotomy revealed carcinoma of the pylorus. Greenhill (12) reported an operation on a patient in which all tests to determine a primary lesion of the gastro-intes-

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tinal tract were futile. Death occurred two months later without autopsy. No case appears to have been reported, however, in which the gastric cancer was as minute as in our case.

The patients may complain of vague gastro-intestinal symptoms such as occasional nausea or vomiting, or of indefinite epigastric pain, but these are not sufficient to permit of a diagnosis. Fallas (4) reports a case with a history of vomiting in which roentgen examination of the gastro-intestinal tract was negative. He also mentions a case with a history of gastric hemorrhage, in which an indurated area was palpated at operation and thought to be an ulcer. The diagnosis usually rests with the pathologist at autopsy.

![FIG. 1. A HIGHLY CELLULAR AREA OF THE TUMOR OF THE LEFT OVARY](https://example.com/image1)

The mucus-containing cells lie loosely among the fibroblasts. A capillary filled with tumor cells of the signet-ring type may be seen in the upper right hand corner. Iron hematoxylin and Mayer's mucicarmine stain. × 350.

**CASE REPORT**

A white housewife, aged thirty-three, entered the hospital complaining of swelling of the labia majora of two years' duration. She had been under the care of a physician, and with various local applications the swelling had appeared to subside. The legs had been edematous for the past year. The edema had gradually increased and extended upward to the abdomen and back.

The general health had apparently suffered, and for at least three weeks prior to hospital admission, the patient had been weak and dyspneic, and had coughed without expectoration.

The family history was negative and the patient's earlier history was of little significance. From childhood she had had frequent attacks of severe epistaxis. At the age of eighteen she had had pneumonia. She had one son, five years of age. The delivery had been without complication. There had been one spontaneous abortion.

The menstrual history had been entirely negative until the beginning of her present
illness. For a period of several months some vaginal bleeding had occurred every week or two, but for the past year the periods had been regular.

On physical examination the patient appeared weak, pale, and cachectic, with marked edema and bluish discoloration of the mons pubis, labia majora, abdomen, and back. There was some pain in the left epigastrium upon palpation and a resistance in the lower abdomen as from the pelvis. Roentgen examination of the chest showed costodiaphragmatic pleurisy and hypertrophy of the left heart.

Gynecological examination revealed a small uterus and on the left a large tumor filling the lower abdomen and extending to about two fingers below the umbilicus. Another smaller tumor could be palpated in the right lumbar region.

A diagnosis of cystadenoma of the ovary or myoma of the uterus was made. In spite of transfusion the course was rapidly downhill and death ensued three weeks after admission to the hospital.

**Autopsy:** The body was that of an emaciated female with severe edema of the lower extremities, swelling of the genitalia and a greatly distended abdomen.

The abdominal cavity contained over 3 liters of opalescent fluid. The peritoneal serosa was smooth and transparent. Large tumors involved both ovaries, the surfaces consisting of irregular, yellowish-white nodules. On section the tissue appeared somewhat gelatinous with several whitish areas of more compact consistency. A few cystic cavities, the largest the size of a pea, were seen in the cortex.

The mesentery appeared somewhat thickened and contained distended lymph vessels. The mesenteric lymph nodes were enlarged throughout. There were a number of small areas of fat necrosis within the pancreas.

The gastro-intestinal tract showed no changes except on the smaller curvature of the stomach, near the pylorus, where there was a slightly bulging, inconspicuous, superficially ulcerated area about 2 cm. in diameter.

The left pleural cavity contained about three-quarters of a liter of clear, sanguineous fluid; the right cavity was entirely obliterated by fibrous adhesions. The left lung, on cut section, showed a peculiar network of whitish markings, apparently due to distended lymphatics, filled with tumor tissue. The same was seen on the pleural surface and to a lesser degree in the right lung.

The heart was of normal size. A small wart-like excrescence was found on one aortic cusp.

The bone-marrow of the femur, the sternum, and the vertebral bodies was largely replaced by whitish tumor areas, containing considerable amounts of newly formed bone tissue.

**Microscopic Study:** In both ovaries (Fig. 1) the structure was quite characteristic of the Krukenberg tumor. The stroma for the most part had a very loose, myxoma-like texture but without demonstrable intercellular mucin. Numerous tumor cells lay in small clusters among the fibroblasts. The cells were large and round, with a very clear protoplasm and small, deeply staining, somewhat shrunken, and generally eccentrically situated
nuclei. The sections stained with Mayer's mucicarmin show protoplasm filled with fine deep red granules.

In the subcapsular portions of the tumor, the stroma was much more cellular and the mucus-containing cells were very numerous. There were also large areas of highly cellular tumor tissue in the deeper layers, where the mucus stain of the tumor cells often appeared less deep and frequently visible as only a faint pink tint.

A few fairly well preserved primitive follicles and ripening graafian follicles were seen widely scattered by the tumor tissue. There was also a recent hemorrhagic body and in one ovary a well developed corpus luteum.

In the stomach (Fig. 2) a slightly bulging area, about 2 cm. in diameter, was seen in the prepyloric mucosa. In this the mucosa was entirely replaced by tumor tissue, which consisted of epithelial cells of irregular shape, those in the central portions being somewhat closely packed to form solid bands, separated by capillaries. Elsewhere they were more loosely scattered among fibroblasts and inflammatory cells. This was especially true of the borders of the affected area, where there were numerous isolated tumor cells lying between the gastric crypts or even replacing the epithelium. Most of these isolated cells were found to be filled with mucus (Fig. 3).

From the mucosa the tumor penetrated directly into the submucosa. The muscularis mucosae was almost entirely destroyed, only a few distorted bands of muscle remaining. In the submucosa the tumor tissue appeared still looser, owing to the accumulation of free mucus in which small clusters of cells or even isolated signet-ring cells were suspended. Besides this, there were small band-like groups of cells growing between the bundles of fibrous tissue. These cells contained rare small droplets of mucus.

The growth was confined rather sharply beneath this and did not penetrate into the muscularis propria. Several small lymphatic vessels and small veins packed with neoplastic cells were seen at the borders of the tumor. No single artery was found to be blocked with tumor emboli.

In the lungs there were numerous lymph vessels along the bronchi and arteries greatly distended by tumor cells (Fig. 4). Several small arteries and capillaries contained tumor

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**FIG. 3. PART OF THE TUMOR OF THE STOMACH**

cell emboli. Some of the larger arteries showed a cellular proliferation of the intima, with narrowing and partial occlusion of the lumen. Small nests of tumor cells could be seen in this cellular layer. Occasionally a hyaline thrombus blocked the residual lumen. Almost all of the tumor cells gave a strongly positive reaction for mucin, which made even the smallest tumor nests quite conspicuous.

Several arteries in the capsule of the suprarenals were blocked by embolic tumor tissue, which may account for the widespread hemorrhagic necrosis affecting large portions of both the medulla and the cortex. The sinuses of the gland also contained tumor cells. The structure of the pulp cords of the medulla was partly obliterated by granulation tissue, studded with single tumor cells, most of which had the signet-ring form.

Both the afferent and efferent lymph vessels of the mesenteric nodes were filled with tumor cell masses and afferent lymph stasis was apparent.

**Fig. 4. Tumor Growth in the Periarterial Lymphatics of the Lung. × 13**

**Discussion**

The question may arise as to whether the relatively small, seemingly recent growth found in the stomach was the primary tumor or a metastasis. We believe that it was the primary tumor. The microscopic structure was of the type that is rather common in primary carcinoma of the stomach. It was apparent that the neoplasm originated in the mucosa with changes limited to the mucosa and the submucosa. The muscle and serosa showed no malignant cells and the growth appeared quite definitely confined to the inner layers of the gastric wall. Metastatic involvement of the gastric mucosa in carcinomas of other origin is extremely rare. Nor were any further tumor foci found in the adjacent portions of the gastric wall that might be interpreted as emboli, either through blood vessels or through the lymphatics.

The disproportion between the small size of the primary tumor and the
widespread metastasis is to be sure a rather uncommon feature. It is, however, duplicated by sporadic observations in carcinomas of other organs, such as the lungs, thyroid, or prostate.

One might assume that the gastric tumor represented an early stage of growth, but the clinical history shows definite signs of a metastatic involvement of the genital organs of at least two years' duration.

The path of transmission of the tumor cells from the primary growth in the gastro-intestinal tract to the ovaries has long been debated. Three possibilities have been advanced: (1) implantation, if the gastric carcinoma has already reached the serosa; (2) blood metastasis; (3) retrograde lymphatic communication between the stomach and ovaries.

Frankenthal (6), as well as Saccone and Gordon (13), believe that the clinical history, gross pathology, and microscopic findings indicate that the tumor originates in the stomach, infiltrates the peritoneum, and is transmitted to the ovaries by implantation of wandering tumor cells.

Major's case (8) established the possibility of the blood route, as typical Krukenberg tumor cells were found in the pulmonary blood vessels. We have recently autopsied a case in our clinic with late extensive bone metastasis.

There is, however, much evidence pointing to the lymphatic route, suggested by Amann, as the most plausible one. This theory is based upon the involvement of the retrogastric and superior lumbar nodes. A blockage of the lymph stream may thus be produced with retrograde migration by way of the ovarian lymphatics. "Weight has been added to this theory or hypothesis in the shape of these secondary tumors, which, even when large, almost invariably conform to the original form of the ovary as though the invasion were through the medulla rather than the cortex" (Fallas, 4).

Jarcho collected evidence of propagation of the tumor by the retrograde retroperitoneal lymphatic route. Armstrong and Wolfe (1) and Vazzoler (16) report cases which led them to the same conclusion.

In our case the involvement was far too extensive and too general to afford definite conclusion as to the path of transmission. We believe that it was by way of the lymphatics and blood stream. The involvement of the mesenteric lymph nodes and vessels establishes the possibility of spread from the primary tumor via the lymph system as far as the ovaries. This view finds additional support in the long-standing edema of the external genitals, which gives evidence of high-grade lymph stasis. The lymphangitis in the lungs also adds weight to our conclusion that most of the spread was by way of the lymphatics. Blood stream metastasis, perhaps late, was also apparent, however, from the presence of embolic tumor cells in the arteries of the lungs and the suprarenals and the widespread bone metastases.

**Conclusion**

The fact that pure Krukenberg tumors are always secondary to carcinoma elsewhere should make this tumor as important to the gastro-enterologist as to the gynecologist. The gastro-intestinal tract should be examined at every operation for ovarian tumor. The primary growth is sometimes so small, however, that its presence cannot be determined at operation, regardless of
careful search. Because of this variability in size of the original tumor and the difficulty in its determination, we feel that many Krukenberg tumors are not diagnosed as such. The diagnosis frequently rests upon a careful post-mortem study.

**Summary**

In a case of typical Krukenberg tumor, with widespread involvement of mesenteric lymphatics, lungs, bone marrow, and suprarenals, a very small primary carcinoma about 2 cm. in diameter, and limited to the mucosa and submucosa, was found in the stomach. Such an inconspicuous tumor could with difficulty be recognized at operation and might be overlooked even post mortem. Some examples of supposedly primary Krukenberg tumor found in the literature may have been due to the non-recognition of the primary neoplasm.

**Bibliography**