CARCINOMATOUS CIRRHOSIS OF THE LIVER WITH SARCOMATOSIS OF THE PERITONEUM

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The following case is reported because of the occurrence of two different types of malignant neoplasm with typical portal cirrhosis of the liver. That a pathogenetic relationship exists between Laennec's cirrhosis and primary carcinoma of the liver is generally recognized. Whether the association of a peritoneal sarcoma with the cirrhosis in this case was more than a coincidence seemed an interesting point for discussion.

REPORT OF CASE

E. G., a white Italian male fifty-seven years old, was admitted to the Buffalo General Hospital on the service of Drs. N. G. Russell and A. H. Aaron, Nov. 25, 1934. He died Nov. 29, 1934. All his adult life he had partaken of large amounts of wine and whiskey daily. At the age of seventeen years he had suffered an attack of jaundice of several weeks' duration.

The patient first began to lose weight and strength in 1932 and noticed that his skin was becoming dark. In March 1934 he complained of cramp-like abdominal pain, diarrhea, and bloating. The stools were watery. There was no nausea or vomiting. Upon hospitalization, April 9, 1934, physical examination revealed that the pupils reacted to light and accommodation. The chest was emphysematous; breath sounds were diminished in both bases. The heart was regular; a systolic murmur was heard. The blood pressure was 118/70. The liver and spleen were palpable three finger breadths below the costal margin. The surface of the liver felt irregular but not nodular. No other masses were palpated. Fluid was present in the abdominal cavity. The legs were edematous.

The important laboratory findings included: hemoglobin 70; red blood count 3,970,000 per cu. mm.; white blood count 2800 per cu. mm. with polymorphonuclears 65 per cent, lymphocytes 32 per cent, monocytes 3 per cent; negative Wassermann reaction; blood glucose, 118 mg. per 100 c.c.; urea nitrogen 14 mg. per 100 c.c. Roentgen study of the gastro-intestinal tract, including a flat film of the abdomen, disclosed only a large spleen and a slight lipping of the lumbar spine. The temperature, pulse, and respiration were normal. The diagnosis on discharge, April 14, 1934, was splenic anemia.

From hospital discharge to November 1934 the patient was under the care of his private physician. During this period fluid accumulated rapidly in the abdominal cavity, but under medication this diminished for a time. There was a loss of weight of 25 pounds. Additional laboratory studies in June 1934 disclosed: bile and urobilin in the urine; free acid in the gastric contents but no occult blood; Van den Bergh reaction, positive; bromsulphalein test, 50 per cent retention in five minutes, 10 per cent retention in thirty minutes. In November 1934, a marked increase in the amount of abdominal fluid occurred, with no favorable response to therapy. Concomitantly, abdominal pain, dyspnea, cough, diarrhea, and jaundice appeared. Hospitalization was advised.

Upon admission, Nov. 25, 1934, the abdomen was greatly distended. Abdominal fluid obtained by aspiration was bloody; the specific gravity was 1.016; the Rivalta test weakly positive; cultures were sterile. The sediment contained chiefly red blood cells with a few polymorphonuclear and mesothelial cells; there were no recognizable tumor cells.

1 An abstract of this paper was presented before the Buffalo Pathological Society May 24, 1935.
In a roentgen film of the chest the apices were hazy; the diaphragm was regular. Hilar shadows were large and dense and many small areas of density with considerable increase in lung markings and lung tissue were seen. Death occurred insidiously and unexpectedly Nov. 29, 1934. The clinical diagnosis was atrophic cirrhosis of the liver with hemorrhagic ascites.

**Autopsy Findings**

The autopsy was done two hours after death. It was restricted to the abdominal viscera. The anatomic diagnosis was: Laennec's cirrhosis of the liver with typical small nodular regeneration; chronic splenic tumor (600 grams); varices of lower esophageal veins with recent rupture of one vein; marked gastro-enterorrhagia; slight icterus of skin; multiple carcinomatous nodules in the liver ranging from 3 to 4 cm. in diameter, and showing distinct necrosis and icterus; primary sarcoma of the omentum, mesentery, and entire visceral and parietal peritoneum; hemorrhagic ascites (2000 c.c.); hypertrophy of the median lobe of the prostate; lipoid-poor adrenals; very slight arteriosclerosis of the lower abdominal aorta and iliac arteries; two renal arteries on the left side.

**Description of Peritoneal Sarcoma:** Grossly, the omentum, mesentery, and visceral and parietal peritoneum were studded with tumor nodules varying from the size of a pea to that of a cherry. The surfaces of most of these nodules were smooth. Their bases tended to be broad. The consistency was generally firm, the color grayish. Many nodules, however, were pedunculated, highly vascular, and hemorrhagic. Some hemorrhagic nodules floated free in the bloody ascitic fluid. In addition to well formed nodules, the peritoneal surface showed small, flat, gray plaques. Where no nodules or plaques were present, the peritoneum, especially the serosa of the intestines, was for the most part thickened and opaque. The anterior surfaces of the retroperitoneum and pancreas were covered by confluent tumor nodules, a few of which formed almost lump-like structures. Nodules were also seen in the capsule of the spleen. No metastases were found in the abdominal organs, nor in the mesenteric, periportal or periaortic lymph nodes. Palpation of the lung and pleura through the incised diaphragm revealed no metastatic nodules.

Histologically the tumor, just described grossly, proved to be an endothelial sarcoma.
In places the peritoneum appeared practically normal in thickness, though a slight fibrosis of the subserosa could perhaps be made out. In macroscopically thickened and opaque areas, without nodules, there was a distinct proliferation of serosa cells. These were increased in size and formed several layers on the surface. In a few cells the nuclei were hyperchromatic and atypical in shape. The proliferation of serosa cells—where the peritoneal surface was preserved—almost seemed focal in character. The demarcation between serosa and subserosa was not always sharply defined. Cells apparently of serosal origin seemed to have become detached in the outer part of the subserosa. The subserous tissue was distinctly thickened, due to an increase of wavy fibrous tissue, in which lay flat spindle-shaped cells with elongated dark nuclei. Such a picture resembled that seen in the fibrosis of chronic peritonitis.

In some areas, however, the cells in the subserosa were numerous and large. They were fusiform and plump. Their nuclei had blunt ends, took a uniform dark stain, and occupied the mid-portion of the cell. Many dilated lymphatic vessels were seen; some of these were lined with hyperplastic endothelial cells. Scattered throughout were large cells with pale blue-staining cytoplasm that recalled cells of histiocytic origin.

The tumor nodules themselves exhibited different stages of growth. In those with diverse pattern, the cells varied in shape and size. They were predominantly fusiform and polyhedral. For the most part the long axis of the fusiform cells encircled the intestine. The nuclei were uniformly dark. Nucleoli were not present. There were occasional mitotic figures. The cytoplasm was pink-staining and moderately abundant. Cell outlines were not obviously distinct. The ends of the cells faded out into cytoplasmic processes. Uninucleated and multinucleated giant cells were present in abundance. Many endothelial giant cells lined thin vessels. The cytoplasm of a few giant cells was globular and vacuolar. Between the cells was a slight fibrous stroma. With Van Gieson and silver impregnation stains both collagen and reticulum fibers could be demonstrated. Cells assumed a parallel position in relation to fibers.

In the flat plaque-like lesions the histologic structure was identical with that observed in the nodules. In the former, however, proliferation and infiltration were most marked toward the inner coats of the intestinal wall. The muscle layers were invaded; the muscle fibers themselves had become atrophic and were destroyed. In the intestine the submucosa appeared slightly thickened.

In large nodules, the cellular pattern approached some uniformity. The cells were

**Fig. 2. Fibrous Thickening of Serosa with Spindle-shaped Cells and Dilated Vascular Spaces (Medium Power)**

In large nodules, the cellular pattern approached some uniformity. The cells were
large and fusiform. The nuclei were vesicular. Their chromatin material was arranged in
dots. Nucleoli were visible. Cells appeared to run in bundles in a parallel manner. Many
mitotic figures and atypical nuclei were seen. The stroma was scarce. At a general
 glance, the appearance recalled that of a large spindle-cell sarcoma. Some giant cells were
present. Numerous vascular spaces, many of which contained blood, stood out prominently.
An infiltration of neutrophils and round cells was in evidence.

In nodules that were grossly pedunculated and hemorrhagic, many dilated capillaries
were scattered. There was pronounced hemorrhage and necrosis; the picture was one of
hemorrhagic infarction. Psammomatous formations were not seen.

**Description of Hepatic Carcinoma:** The nodules in the liver were rather typical liver­
cell carcinomas. A normal hepatic architecture was not present. The cells stained more
deeply than in the areas of nodular regeneration, and were slightly larger. Their outlines
were indistinct, but they appeared to be chiefly polyhedral in type. For the most part they
were arranged in trabeculae. They also formed tubules containing bile thrombi. Out­
standing features were the nuclear variations, as hyperchromatism, irregularity in size, giant
nuclei, and double nuclei. Occasionally mitotic figures were seen. In some areas there were

![Image](image_url)

**FIG. 3. SARCOMATOUS PLAQUE WITH NUMEROUS FUSIFORM CELLS SHOWING
HYPERCHROMATIC NUCLEI (LOW POWER)**

regressive changes, with granular degeneration and vacuolization of cytoplasm and necrosis.
The stroma was made up of thin capillary vessels which showed distinct leukocytosis. Into
different vessels buds of tumor cells projected; rarely, a tumor cell could be made out in
the lumen.

**COMMENT**

The combination of two different malignant blastomas, such as we have
described, in a case of Laennec's cirrhosis is exceptional.

That carcinoma of the liver is linked pathogenetically with hepatic cir­
rhosis has been proved by the statistics and histologic studies of many authors. Ewing (1) summarizes the generally accepted belief by stating that "the
tumor process appears to be the direct sequel of, or essentially connected with
the cirrhosis." In this case the question arises as to whether the development
of a peritoneal sarcoma can also be dependent upon the presence of cirrhosis. The
temptation is great to look for some pathogenetic relationship between the
primary sarcoma of the peritoneum and chronic ascites from portal obstruc­
tion.

In chronic ascites from portal obstruction distinct thickening of the vis­
ceral and parietal peritoneum, so called plastic peritonitis, is usually observed.
(We have also seen such an occurrence in ascites from other causes.) It is
FIG. 4. SECTION OF SARCOMATOUS NODULE, SHOWING FUSIFORM CELLS WITH HYPERCHROMATIC NUCLEI, MULTINUCLATED AND ENDOTHELIAL GIANT CELLS, MODERATE STROMA (HIGH POWER)

FIG. 5. SECTION OF SARCOMATOUS NODULE, SHOWING FUSIFORM CELLS WITH VESICULAR NUCLEI, VERY SLIGHT STROMA, RARE GIANT CELLS (MEDIUM POWER)
believed that the proliferation of the mesothelial and subserous mesenchymal cells is a resorptive effect of chemical irritation, rather than merely a mechanical result of pressure from a large volume of fluid. The finding of a peritoneal sarcoma in this case impels us to consider the possibility that prolonged irritation of the surface of the peritoneal cavity may be one factor in bringing about not only mere inflammatory and hyperplastic thickening of serosa and subserosa but a true blastomatous proliferation as well.

Experimentally several workers have investigated the response of subserosal (endothelial and fibroblastic) and surface cells of the peritoneum to chronic irritation. In 1921 Foot (2) demonstrated that endothelial cells in capillaries of the omentum in frogs and rabbits can change with aseptic injury and acquire an embryonic character. They differentiate in three directions.

Some cells penetrate vessels, assume wandering and phagocytic properties, and develop syncytia. Others become converted apparently into fibroblasts and take part in formation of fibrous tissue. Still others form new capillary vessels. Foot believed that the stimulating substance which causes the reversion to an embryonal type of tissue is associated in some way with blood.

Ranvier, Cornil, Marchand and Roloff, and others, quoted by Cunningham (3), were of the opinion that during mild inflammation serosa cells and fibroblasts of the omentum are morphologically and functionally interchangeable. Cunningham disagreed with the assumption. Later (4) he pointed out that remarkable changes in peritoneal cells may occur from long continued low-grade irritation, even that brought about by physiologic saline. Progressive stages of hyperplasia of surface cells followed intraperitoneal injections of laked or whole blood in rabbits. When irritation was increased in degree, or was long continued, proliferation of underlying connective tissue with pushing

Figs. 6 and 7. Carcinomatous Nodule in Liver

Fig. 6 (left) shows the distinction between the carcinomatous nodule and the adjacent liver cells (low power). Fig. 7 is a section through the carcinomatous nodule, showing the trabecular arrangement, variations in nuclei, and capillary vessels in stroma (medium power).
out of tufts was noted. The changes were most marked on the surfaces of parenchymatous organs.

In 1929 M'Gowan (5) made repeated intraperitoneal injections of powdered glass, and tar in liquid paraffin, in fowls. Following this he observed uniform peritoneal thickening; isolated round, smooth nodules; adhesions, and hemorrhagic ascites. The thickening and adhesions were due to scar tissue. The nodules represented fibroid mesoblastic tumors which were identical with spontaneous fibromas of fowls, and which were interpreted as expressions of a perverted repair process. M'Gowan believed that the tumors belonged to the macrophagic lineage of the reticulo-endothelial system. He also cited the production of granulomas and tumors by intraperitoneal injections of kieselguhr in dogs, rabbits, and guinea-pigs, and rarely of sarcomas by injection of tar.

Grossly and histologically the endothelial sarcoma here described resembles in certain respects the endothelial tumors of the peritoneal cavity reported by Miller and Wynn (6) Crowdy (7), and Geschickter (8). Failure to find lymphogenous or hematogenous metastases is of interest.

BIBLIOGRAPHY