





## PRIMARY CARCINOMA OF THE GALL-BLADDER.

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THE points of interest in this case are,—

- (1) The early discovery of gall-stones (six and a half months before death).
- (2) The positive recognition of the malignant disease at an early period.
- (3) The absence of jaundice, notwithstanding extensive infiltration and complicated adhesions and distortions.
- (4) The absence of ascites, though there were extensive deposits in the peritoneum.

Mrs. O., housewife, aged 47 years. Previous and family histories negative. About Christmas, 1893, patient fell, and in doing so "felt something give way" in the right side, about three inches to the right of the umbilicus. Since then there has been almost constant dull ache in the same place, with occasional shooting pain passing back to the shoulder. Has never had colicky pain. Somewhat later the patient discovered a "lump" in the locality mentioned. This has remained to the present time, without increasing in size. Aside from the symptoms named she feels very well. Has not lost weight. Appetite is good; bowels rather constipated.

*Status præsens*, April 10, 1894. Small, well-nourished woman; weight, 126 pounds; skin and mucous membranes normal; examination of heart and lungs negative.

The abdomen is above the level of the ribs, the panniculus very thick. Tenderness in the right hypochondrium; the rectus is very tense. Just below the angle of the ribs is a smooth oval tumor about the size of a hen's egg. It is not dull on percussion, does not change its position in respiration, and seems to be formed by the belly of the

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rectus. The liver dulness extends from the upper border of the sixth rib in the nipple line to an inch below the ribs.

There are small external hemorrhoids. Gall-stones have never been looked for.

Urine clear; yellow; acid; specific gravity, 1020; no albumin; no sugar; a few leucocytes and cylindroids.

A small blister was prescribed and the patient directed to look for gall-stones.

After two more visits the abdomen became more tolerant. April 24 we were able to note: a tumor can be felt in the right hypochondrium; sensitive to deep pressure; the size cannot be distinctly made out, but seems to be as large as a small orange; the tumor descends during inspiration; can be moved rather readily; the patient is losing weight, but has less pain and feels better.

May 8, 1894. Examination under ether in consultation with Dr. Nancrede, in the University Hospital. A hard, oval tumor, four inches long and two inches broad, can be felt in the right umbilical region; the tumor is movable; descends on inspiration. By deep palpation crepitus can be felt and made audible.

The patient was advised to undergo an exploratory operation with the object of discovering, if possible, whether the symptoms came from the stones alone or, as the age suggested, whether there was a new growth, the further treatment to be based on the results of the exploration. She consented, but soon after became interested in red-clover tea and withdrew from observation.

On July 7, 1894, I was sent for and told the patient was ready for the operation. She was but slightly emaciated, pale, but not cachectic. For some time there had been attacks of vomiting at intervals of about two weeks. No gall-stones had been found.

The tumor was larger, flatter, and more uneven than before, in the same position, and still movable. In the umbilicus was a small, hard, disk-like mass, beneath the epidermis and adherent to it. A small hard nodule could also be felt in the right iliac fossa.

I at once informed the family of the uselessness of operating, stating that the disease was cancer of the gall-bladder, with secondary growths which would make futile any operation.

For some weeks there was no change in the condition. Bismuth and milk diet made the attacks of vomiting less troublesome. The tumor grew, so that by September 15 it extended downward from the edge of the liver, with which it was continuous, forming a flat oval mass about three inches wide and five long. The surface was uneven, hard; the edges smooth, as was also the edge of the liver. The tumor was dull on percussion, and continuous with the liver dulness. From

this time the tumor became smaller. As emaciation advanced small tumors could be felt near the large one, and by the end of September a long cylindrical body could be felt lying across the abdomen just below the large tumor. This was assumed to be the thickened omentum.

From this time attacks of pain were more frequent and it was necessary to use morphine, which had the beneficial effect so often seen in hopeless cases of malignant disease. By taking at first one-fourth, later one-third, of a grain at night, the patient was kept comfortable, looking after her household duties, and even going out driving, though in bed a large part of the time.

After October 15 all the tumors became smaller. The one in the umbilicus had reached a diameter of two centimetres; it eroded the epidermis and caused hemorrhage occasionally. From this time the patient was unable to take much food on account of the pain, and emaciation progressed rapidly. The skin and scleræ were never jaundiced. The urine was dark, but never contained bile coloring matter.

Death occurred from gradual loss of strength and with intense emaciation, November 25, 1894.

From the autopsy notes I extract the following: Body extremely emaciated, the fat everywhere being almost entirely absent. All the tissues and body cavities very dry.

Heart small; muscle dark-brown; valves normal. The great vessels very small.

Lungs small, anemic.

The omentum is rolled up, forming an irregular cylindrical mass six inches long, one inch wide, and half an inch thick, nodular and uneven, very hard, of a dirty white color, fibrous on section. This mass is adherent to the edge of the liver and to the underlying structures. The mesentery contains large numbers of nodules from the size of a pin-head to that of a cherry. These are all very hard, grayish white. The larger ones have crater-like depressions on one side. Similar nodules, usually not larger than a pea, are scattered over the serosa of the stomach and intestines. A larger one, one and a half centimetres in diameter, at the mesenteric attachment of the lower part of the ileum, has grown through the wall and forms the floor of a smooth shallow ulcer. The cecum is greatly distended. The ascending colon is constricted by a circular mass of new growth in the serosa, which has contracted the lumen so that a finger-tip is barely passable. The transverse colon and some coils of the small intestine are matted together under the omentum, and so firmly fixed that they cannot be separated.

The parietal peritoneum has on it numerous small nodules resembling those already described. Just above the umbilicus is a mass three centimetres in diameter and one centimetre thick, and in the umbilicus another one and a half centimetres in diameter, the outer surface of which is covered by dried blood. The round ligament is not involved, except near the liver.

The diaphragm is densely infiltrated by firm masses of new growth, smooth and white on section, in some places one centimetre thick.

The liver is small, the right lobe globular, the left lobe relatively large. On the upper surface, above the position of the gall-bladder, is a whitish induration six by eight centimetres in extent, with irregular outlines, elevated slightly above the general level. At the anterior edge of the liver this indurated mass is in intimate connection with the omental tumor already described. Deep pressure over the mass gives crepitus.

On section, the liver tissue is pale, bloodless; the acini distinct; the larger bile-ducts are dilated and their walls thickened.

The gall-bladder cannot be found in the normal position. On cutting through the liver from before backward, in the middle of the induration mentioned, a cavity the size of a walnut is opened. This is within the limits of the liver, lying in a mass, the surface of which has been described. The mass is of cartilaginous hardness. It extends into the liver substance without distinct margins. In many places strands of new growth pass out for several centimetres from the main growth, surrounding the walls of the vessels. The cavity contains twenty-eight gall-stones of the common pigment, lime, and cholesterin variety. One of these is roundish, cylindrical in shape, two centimetres in diameter, and two centimetres long; the rest together make about an equal bulk. All of them are so closely fitted together that their adjacent surfaces are quite dry. The walls of the cavity are hard, smooth in some parts, rough in others, but nowhere appearing as a normal mucous membrane. A small amount of thin, yellowish, glairy fluid, containing cholesterin plates, large granular cells, and fat granules, coats the walls of the cavity. No duct can be traced from the cavity. The cystic duct and the hepatic ducts cannot be found in the dense mass under the liver after careful dissection. The orifice of the common duct admits a probe, but its course cannot be traced, being inextricably confused in the dense mass of new growth which surrounds it. The liver does not contain any circumscribed tumors in the interior, but just under the capsule, near the altered gall-bladder, are a few small nodules with umbilicated centres. In the right lobe, between the dense mass surrounding the gall-bladder and the portal fissure, is a calculus, closely fitted in a

smooth-walled cyst. One side of the cyst is made up of new growth ; the other, thin and fibrous, is sharply circumscribed from the liver tissue, from which it easily separates. The stone has the shape of a rounded triangular pyramid, measuring  $3 \times 3 \times 2.5$  centimetres. The surface is white and smooth. The stone is soft ; can be cut with a razor. It is made up of a central body, one centimetre in diameter, of soft granular bilirubin and an outer layer of almost pure cholesterin. The cyst has leading into it one bile-duct two millimetres in diameter. No other pigment-masses or calculi can be found in the liver. The portal lymphatics are entirely fused with the extensive new growth.

Sections of the round ligament one centimetre from the abdominal wall show no infiltration.

The stomach is small ; contains a small quantity of black watery fluid (bismuth) ; the mucosa thin and smooth.

The small intestine is narrow, the mucous membrane smooth, the cavity empty. The cecum and rectum contain hard, dark, fecal matter.

The spleen is small, bloodless, firm ; the connective tissue prominent. The capsule is the seat of several small, hard, whitish tumors.

The kidneys are small, anemic.

The wall of the bladder is very thin ; it contains a number of small whitish nodules.

The pancreas is small ; contains nothing abnormal except a soft, white, circumscribed tumor one and a half centimetres in diameter near the tail. The nodule is finely reticular on section.

Microscopic examination shows the growths to be cylinder-celled carcinoma. The soft mass in the pancreas appears as an adenoma, with roundish alveoli lined by cylinder cells in a single layer, with scanty stroma. In all other parts the growth has the structure of scirrhous, varying in different parts. The wall of the gall-bladder is made of dense fibrous and fibroid tissue with few nuclei. In parts the inner surface is necrotic, either homogeneous and hyaline, with nuclei which do not stain, or else granular. Farther out is a zone of sclerotic tissue with a few alveoli, lined by cylinder cells, which here, as elsewhere, have the appearance of those lining the normal gall-bladder. Interspersed in this zone are necrotic areas of carcinoma with alveoli filled with cells, with relatively scanty stroma. These areas take no nuclear stains at all, and stain faintly with eosin. Still outside this is a zone of dense scirrhous character, with alveoli usually smaller than those in other parts. This zone passes into the liver tissue for a considerable distance, in the capsule of Glisson, which is greatly thickened thereby. The acini here are small, the outer rows of liver cells lying in the new growth. The liver cells show an excess of pigment ; protoplasm and nuclei stain well.

In the mesentery the alveoli are long and oval, lying between the

bands of connective tissue, which are spread out in fan-like manner. In many of the mesenteric tumors, as in the liver, the remarkable power of contraction of the growth is clearly shown.

That the growth was primary in the gall-bladder I do not think can be questioned. The history of gradual onset, pain, and absence of jaundice, as well as the relations found post mortem, make the course clear. The only alternative could be primary cancer of a gall-duct within the liver, with early and general implication of the gall-bladder.

As to the cause of the disease itself, the case bears out the prevailing idea of the assisting action of gall-stones. The history seems to point to a change in the position of gall-stones in December, 1893, nearly a year before death. Certain it is that the stones were present more than six months before death, and although the gall-bladder was probably cancerous then, it is hardly likely, I think, that the new growth was present six months earlier than that.

It might be thought that the presence of so large a stone in the liver would weaken the idea as to the relation of calculus to cancer. This I do not think bears on the case. The stone in the liver began as a pigment calculus from stoppage. A dilatation cyst formed around it, and from the walls of the cyst cholesterolin was secreted. No importance can be placed on the relative hardness of the stones, for it is most probable, as Naunyn has pointed out, that most gall-bladder stones are formed rapidly.

Although I agree with the idea expressed above that the stones antedate the cancer, I must also say that I think the question can only be positively settled by examinations of cases in which operations are made during life early in the disease.

The case illustrates the remarkably contractile power of such growths, the large tumor formed by the gall-bladder being ultimately entirely retracted, so to speak, into the liver. That in the course of all the infiltration and distortion occlusion of the ducts did not occur is an interesting fact of some clinical value. Before the section I had predicted that the growth would be largely in front of the common duct, as in a case I reported some years ago,<sup>1</sup> but this proved not to be the case.

The distant metastases, especially those in the bladder and the one in the umbilicus, are interesting, the latter being due to transport, and not to continuous growth, as I have once seen in a case of secondary cancer of the liver, when the growth followed the round ligament to the abdominal wall. Inclusions in the epithelial cells are rare and do not suggest parasites.

<sup>1</sup> Transactions of the Philadelphia Pathological Society, Vol. XIV, p. 47.







