Carcinoma of the Hepatic Duct with the Report of an Additional Case

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The caustic comment of that eminently practical surgeon, John Chalmers DaCosta, to the effect that a very fair number of surgical sea serpents are discovered every year, would seem to be enough to deter even the boldest of medical men from reporting a single case of anything, however unusual he might personally feel it to be. On the other hand, when one may reasonably assume that the single case has been seen not because of lack of experience in clinical medicine but because of the admitted rarity of the disease, then the situation is somewhat different. That is the present status of carcinoma of all the biliary ducts, and particularly of carcinoma of the hepatic duct. Vernon David's experience in operating on two patients with the last-named disease within less than two years is as unusual as is his astuteness in diagnosing the second case at operation because he recalled so vividly the post-mortem findings in the first case.

Carcinoma of the bile ducts has been recognized as a clinical entity for more than half a century, and carcinoma of the hepatic duct was described by Schueppel as early as 1878, but the number of reported cases is still well under fifty. While we have not attempted a thorough search of the literature, which was brought up to date by Wylegschanin in 1927 with the review of 35 collected cases, including one of his own, we have noted since, in addition to the two cases reported by Vernon David, single cases reported by Vander Veer and Nelms, and by Milles and Koucky.1 The rarity of any disease is, of course, a comparative matter; many cases are never reported, many are never recognized at all; but even granting those facts, carcinoma of the hepatic duct is not a frequent condition, and for that reason it has seemed to us proper to report the following case, not only to add to the number of those already on record, but also to point out certain features in which it rather differs from the classic description of the disease.

Case Report

A white male, aged forty-four years, a laborer, was admitted to the surgical service (Ward 109, Maes-Lyons-Lampert-Prejean) of the Louisiana State University Medical Center in Charity Hospital on Nov. 27, 1932, and died Dec. 18, 1932.

1 Since this paper was written (March 1933), there has come to our attention a paper by C. W. McLaughlin in the Canadian Medical Association Journal for March 1933 (28: 255), in which the subject of bile duct carcinoma is fully discussed and in which seven additional cases are reported.

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The patient's story, while rather confused on several points, was essentially as follows: Nine days before admission he had an attack of chills and fever lasting twelve hours, which left him drowsy and listless and unable to resume his regular work. Four days before admission he suffered an agonizing, intermittent epigastric pain which lasted intensely for several hours and which continued in milder form until he entered the hospital. Three days before admission his abdomen began to enlarge, and on the same day his family noticed that he was somewhat jaundiced. There were three small stools after the onset of the pain, none of which contained any blood. Except for vague aching pains in both arms, all other symptoms, including those referable to the gastro-intestinal tract, were specifically denied. The past history was entirely irrelevant.

The patient was a well developed and well nourished white male, with a complexion naturally very dark and further tanned by exposure, so that his jaundice was at first evident only in the sclerae. The temperature was 98.4°F., pulse 80, respirations 18, blood pressure 125/75. There was a slight systolic murmur in the aortic area. The abdomen was symmetrically distended, and in the epigastrium was a tender, hard, slightly movable mass which extended into the right hypochondrium and which was considered to be the liver. The spleen was palpable on the day of admission but could not be made out afterward because of the progressive abdominal distention. Except for a left inguinal hernia, which was apparently not causing symptoms, there were no other positive findings.

The results of laboratory tests were as follows: Wassermann (blood) test negative. Urinalysis negative except for bile, a few granular casts, and some red blood cells. Blood: total red cells 2,365,000; white blood cells, 3,000; hemoglobin 65 per cent; differential count essentially normal. Blood chemistry and fragility test within normal limits. Coagulation time, Dec. 1, 10 minutes plus; Dec. 4, 6½ minutes. Van den Bergh direct immediate. Icterus index 75. Gastric analysis: free acid 0; total acidity 10; laetic acid 0; occult blood present. Fees: occult blood present; no parasites; bile present intermittently.

X-ray examination of the abdomen and lower chest on the day of admission showed no free air beneath the diaphragm and no fluid levels. Gastro-intestinal study with a barium meal was negative except for a slight cecal stasis at forty-eight hours and an irregularly filled appendix at twenty-four and forty-eight hours.

The diagnostic possibilities considered were malignancy of the head of the pancreas, hemolytic jaundice, cholelithiasis, malaria, syphilis and Hodgkin's disease.

During the investigation of the patient the treatment was chiefly symptomatic, directed toward the relief of the progressive distention. It is a curious fact that, although the distention was promptly recognized, and although careful daily examinations were made of the abdomen by members of the staff and by a consultant, fluid was made out positively only on the night before operation. After admission an irregular temperature developed, ranging from 100 to 101°F., but the pulse was usually below 90 and the respirations were usually below 24. No method of treatment caused any abatement of symptoms, and operation was therefore done as soon as the necessary preparations could be made, on the diagnosis of an obstructive jaundice of undetermined origin.

Operation was done Dec. 5, the ninth day after admission, under spinal analgesia supplemented by a small amount of ethylene (Drs. Lyons-Lampert-Prejean). When the peritoneum was opened, bile-stained fluid escaped, and it was estimated that approximately a gallon was removed, the quantity being surprising in view of the difficulty, above referred to, of eliciting its presence at all. The intestines were much distended. The liver was rather large, and of the hob-nailed type, but the pancreas was grossly normal. The gallbladder was thick, edematous, and distended, and contained thick, blood-stained, mucoid fluid; no stones could be made out in it, or in the cystic or common ducts. Palpation of a structure assumed to be the common duct showed it to be thick, dilated, and edematous, but the cystic duct was grossly normal. Further investigation was not possible, as the patient's condition at this point became alarming, and cholecystostomy was therefore quickly done, with the idea of relieving the jaundice, though it was fully realized that it could be only a palliative procedure. Closure was exceedingly difficult, partly because of the abdominal distention, partly because the peritoneum was very friable, and en masse sutures were finally resorted to.

The immediate postoperative reaction was reasonably good. On the second day
there was an elevation of temperature to 103° F., and profuse drainage from the wound began, the fluid seeming to pour directly out of the abdominal cavity. Thereafter the patient's course was steadily downhill. The temperature ranged around 100° F., the pulse averaging about 100 and the respirations about 24. The abdominal distention became progressively more marked, being only slightly relieved by paracentesis on alternate days and by the constant profuse drainage from the wound. At no time was there any drainage from the catheter in the gallbladder, and the jaundice continued until death, which occurred on the fourteenth postoperative day, after some forty-eight hours of coma.

![Gross Specimen, Showing Malignant Tumor in the Hepatic Duct](image)

Note that the proximity to the liver substance precludes any possibility of radical surgery.

The autopsy protocol reveals the following important findings. The peritoneal cavity contains approximately 700 c.c. of a cloudy, brownish fluid. There is considerable leakage all through the surgical wound, especially around the tube. The field of operation shows a slight inflammatory reaction, with some recent adhesions covering the anastomosis of the tube with the gallbladder.

The liver weighs about 1600 gm., is firm in consistency, and is of a dark, greenish-brown color. The surface of the organ shows numerous nodules, ranging in size from 2 mm. to 2 cm.; some of these nodules consist of white, firm tissue and apparently represent a metastatic malignancy; others are greenish-brown in color. The surface of the liver shows a marked dilatation of the bile ducts, the walls of which appear to be thickened and which are filled with thick, dark bile. The periportal fibrous tissue is markedly increased. There are numerous white tumor nodules scattered through the substance.

The gallbladder is normal in size, with thickened walls, and contains a light, greenish-stained, mucous material and a soft concrement. The common and cystic ducts show no apparent pathologic changes. The hepatic duct is greatly dilated, and is obstructed by a large tumor mass just above its junction with the cystic duct. This mass is brown in color and is adherent to the wall of the hepatic duct by a peduncle. Grossly it closely resembles a polyp; on section it is seen to be composed of very friable tumor tissue. The lymph nodes at the hilum of the liver are enlarged and firm, as are the glands in the hepatic ligament, though to a lesser degree.
CARCINOMA OF THE HEPATIC DUCT

On the basis of the tumor mass obstructing the hepatic duct, a pathologic diagnosis of primary carcinoma of the hepatic duct was made, with multiple metastases in the liver and the regional lymph nodes. In view of the rarity of this disease, a meticulously careful search was instituted of the abdominal cavity and of each of the abdominal organs, to be certain that the primary focus of the malignancy was not located elsewhere. No other deviations from the normal were found, however, except an enlargement of the spleen.

Microscopic study of the polypous mass in the hepatic duct showed it to be a malignant growth, adenocarcinomatous in type. Numerous metastases of the same type of tumor tissue were found widely distributed in the liver, which showed also a moderately progressive type of atrophic cirrhosis. The regional lymph nodes revealed similar typical metastases.

COMMENT

While carcinoma of the gallbladder occurs very much more frequently in women than in men, the proportion is reversed in carcinoma of the bile ducts, although the preponderance is not so overwhelming. Why either ratio should exist is not clear. The age incidence of carcinoma of the ducts is that of carcinoma of the gallbladder, between fifty and seventy years. In Musser’s series the average age was 56.6 years, in Rolleston’s it was 55.5, and in Judd’s (composite) it was 57.1. Our patient was just forty-four years old, decidedly younger than is usual, and, for that matter, just within the age limit ordinarily set for malignancy, although we have long doubted the wisdom of emphasizing an arbitrary age limit for any sort of malignancy; there are too many exceptions to make the rule safe.

The etiology of bile duct malignancy has never been definitely settled. Rolleston mentions the possibility of its being superimposed upon a previous ulcer, as in gastric malignancy, but, aside from the grave doubt with which many pathologists view such a transition, the evidence is insufficient. Zenker considers that the malignancy may begin as a papilloma, and various observers agree that Rolleston’s case seems to support such a theory, but one swallow does not make a summer. The theory of gallstones as an etiologic factor is plainly untenable, for cholelithiasis was noted in less than 20 per cent of the reported cases. Ewing’s suggestion of migrating calculi is no more helpful, and the etiology remains an unsolved problem. In our own case no etiologic or predisposing factor is apparent. The patient was a man in vigorous, robust health, who steadfastly denied any premonitory symptoms, and whose history, however carefully it is scanned, furnishes not the slightest clue to the development of his disease.

Lord Moynihan has said that there is no one living who is infallible in the differential diagnosis of obstructive jaundice. He might well have gone farther and said that there is no one living who, even if he suspects bile duct malignancy, can determine before operation—and perhaps not then—in which one of the ducts the malignancy is located. Experience, however, does make one suspicious. We personally suspected very strongly that a female patient recently admitted to the surgical service of this school after an emergency operation for obstructive jaundice of undetermined origin by Dr. W. O. Moss, of the Charity Hospital House Service, had carcinoma of the bile ducts, because the
Clinical history, the operative findings, and the postoperative course so strongly resembled those of our patient. Autopsy revealed malignancy of the common duct. A similar patient, also operated on by Dr. Moss, is now under observation.

The first symptom of bile duct carcinoma is generally agreed to be jaundice, and this is what might be expected, for the location of the tumor is almost bound to give rise to obstruction, and to give rise to it early. As a rule, the jaundice is dark green, very intense, and steadily progressive, but the onset may be insidious, and the change in the color may pass unnoticed until the patient's attention is called to it. Itching is an almost constant accompaniment, though our patient did not complain of itching at any time. On first inspection his jaundice was overlooked by a very careful intern, undoubtedly because his skin was naturally dark, but during hospitalization it became progressively deeper.

Absence of pain is commented upon by many writers as a very striking feature of the disease, and such pain as does occur, except for attacks simulating biliary colic, is supposed to be due to metastatic carcinoma of the head of the pancreas (Rolleston). This patient had pain, at times very severe, shortly after the onset of his illness, and the pain remained more or less constant, although both grossly and microscopically the pancreas was found free from disease.

There is, other than jaundice, itching, and absence of pain, no typical group of symptoms for carcinoma of any of the bile ducts. The disease may be preceded by vague digestive symptoms, and it may have an insidious or, as in this case, an apparently acute onset. After the development of the jaundice, there may be gastro-intestinal symptoms of various sorts: constipation or diarrhea or alternating constipation and diarrhea, furred tongue, foul breath, and a progressive loss of weight and strength. The pulse is approximately normal, as it usually is when jaundice is present, and the temperature is normal or subnormal. Death occurs from cholemia, from an overwhelming biliary toxemia, or from exhaustion and cachexia. Our patient had no gastro-intestinal symptoms of any sort before his admission to the hospital and none of any consequence during his illness. He exhibited the progressive downhill course of a patient suffering from toxemia, and the actual cause of death was probably exhaustion as much as cholemia. The temperature was normal on admission, and the subsequent slight elevation we may interpret, in the light of the autopsy findings, as due to an associated cholangitis.

The findings at operation are usually fairly characteristic, and, as David points out, provided one knows what to look for, the firm, fibrous consistency of the hepatic duct, like dense scar tissue, ought to suggest the diagnosis immediately. The gallbladder, as a rule dilated from backward pressure when the tumor involves the common duct, is usually small in carcinoma of the hepatic duct. Stones are seldom found. The duct is normal below the lesion and dilated above it. Metastases, while they may be found in the gastro-hepatic ligament, the pancreas, the liver, the portal vein and the retroperitoneal glands, are relatively
rare; they occur in not more than 20 per cent of the reported cases, and in only one case (Delafield) was there extension beyond the abdominal cavity. The liver is likely to be quite large, in contradistinction to its size in carcinoma of the gallbladder, but ascites is not marked except as a terminal phenomenon.

Again the case we are reporting differs in several particulars from the classic picture. The hepatic duct was not palpated at operation, partly because the patient's condition did not warrant a prolongation of the operative procedure, partly because it was located too high to be readily accessible, but chiefly because no suspicion was entertained that it was the site of the primary pathology. The gallbladder was distended and filled with bile-stained, mucoid material, this being a rather general finding when the malignancy involves the common duct, but a distinctly unusual one when it involves the hepatic duct. It should be emphasized, too, that bile-stained fluid was found in the gallbladder at autopsy, although at no time had there been any drainage from the cholecystostomy tube, the mechanics of which were apparently quite satisfactory. The findings in the common duct at operation and at autopsy are difficult to reconcile. At operation the structure which was assumed to be the common duct was found thick and dilated, whereas at autopsy it was perfectly normal, as it should have been, for there was no obstruction in it and therefore no reason for the dilatation.

Metastasis to the liver had already occurred, as well as to the regional lymph nodes, in spite of the very short duration of the disease, or, to be more correct, of the exhibition of symptoms, and there was, in addition, a definite cirrhosis of the liver, which, after repeated careful study, the pathologists diagnosed as of the portal type instead of the more usual biliary type. The ascites, which increased progressively from the day of admission until death, was undoubtedly due to the cirrhosis of the liver rather than to metastasis, as is ordinarily the case, and its control, in spite of the profuse drainage through the abdominal wound, was a constant problem; it overshadows all the other symptoms and caused the patient intense distress.

Ewing's description of the gross anatomy and histopathology of malignant tumors of the bile ducts may be accepted as it stands. Such tumors, he says, are villous, nodular, or diffuse. Villous growths, which may be single or multiple, fill and distend the duct, and although it may give rise to extensions, the original tumor remains small. In the nodular variety, masses, seldom very large, appear in the sub-mucosa and in the muscularis; they encircle the duct and constrict its lumen, giving rise to a cicatricial stenosis; malignancy is apparent on microscopic examination. The diffuse variety extends along the duct, converting it into a rigid tube, from the inner surface of which numerous small cancerous projections protrude into the lumen. Histologically the malignancy is usually adenocarcinoma, with cylindric cells and mucus production. Occasionally, however, the alveoli are small and the lining cells cuboidal or spherical. The case we are reporting is of the adenocarcinomatous type.
Practically all writers on carcinoma of the bile ducts take the position that the tumor, because it is small and because it metastasizes late, should be considered among the comparatively favorable malignant neoplasms, provided the correct diagnosis is made promptly. We grant that operation should always be done, however hopeless the outlook may seem, on the ground that every individual has a right to his chance of life, slim though that chance may be, but we cannot accede to the point of view that the disease is in any way favorable. Indeed, we believe, from our experience in this case and from our study of the reported cases and of the literature on the subject, that this type of malignancy is distinctly unfavorable. In the first place, a surgical cure depends upon other factors than size and period of metastasis. The part involved must be at least relatively accessible for extensive resection, which the bile ducts, particularly the hepatic duct, frequently are not. The tumor must be so located and so small that adequate resection is possible, as well as satisfactory anastomosis of the resected ends of the duct, conditions which again very frequently cannot be met. In the second place, we question whether the apparently slow metastasis in this disease is not really due to the fact that the patient dies of his biliary obstruction and toxemia before sufficient time has elapsed for extension to occur. Finally, early diagnosis, unfortunately, is, just as it so often is in other malignant conditions, an ideal to be aimed at rather than a fact to be achieved. In our own case the patient was dead within a month after his symptoms developed, and the autopsy showed that he had rather extensive metastases, while the primary malignancy was located so near the liver substance that radical surgery could not have been considered. Moreover, as Bastianelli has pointed out, the diagnosis of rare diseases is likely always to show a high percentage of error, chiefly because the diagnostic refinements suggested after operation or autopsy are mostly the consequence of theoretical or so-called logical considerations which are seldom adaptable to practice. It would naturally profit us to remember at all times that the unusual is decidedly more frequent than we think, but while the human equation remains what it is, it is too much to expect that the individual surgeon will always consider all the possibilities while he is making his diagnosis, however obvious the condition may seem after the event.

Theoretically, therefore, while resection of the duct is a perfectly possible procedure, at least in certain circumstances, if the diagnosis is made early enough, practically it seems to us to be usually an inapplicable one, and the cases reported in the literature seem to bear out our contention. Palliative operations, such as simple cholecystostomy or the establishment of biliary continuity by some method of biliary intestinal anastomosis, are likely, as a rule, to serve the patient’s interests as well, and, particularly if cholecystostomy is the procedure selected, are likely to be associated with a far lower primary mortality. The risk of postoperative hemorrhage, to which many writers call attention, can usually be controlled by the employment of the proper preoperative measures. In our own case preoperative preparation consisted chiefly
of infusions of glucose and Hartman's solution and of glucose and calcium chloride, and hemorrhage was not a factor.

We grant frankly that the diagnosis was missed in this case. The cholecystostomy was done not with any idea of relieving permanently the primary condition, for the origin of the disease was not discovered until autopsy, but empirically, with the idea of relieving the jaundice by the standard procedure under the circumstances. Even had the tumor been identified, its location, as we have pointed out, would have prevented satisfactory extirpation, and we question whether the attempt would have prolonged the patient's life at all; indeed, we are rather inclined to believe that we should have hastened his end, quite aside from the fact that, even had surgery been temporarily successful, the hepatic and glandular metastasis which had already occurred would have made it a useless and unnecessary procedure.

SUMMARY

1. Carcinoma of the biliary ducts is a relatively rare disease, the etiology of which is still undetermined.

2. The age and sex incidence, symptomatology, clinical course, and gross and histologic pathology of bile duct carcinoma are briefly reviewed.

3. A case is reported of primary carcinoma of the hepatic duct in which the diagnosis was missed until autopsy, and which differs in many respects from the classic picture of the disease.

NOTE: We are grateful to Dr. Shirley C. Lyons for the privilege of reporting this case from his ward service; to the Department of Pathology of the Louisiana State University Medical Center and of Charity Hospital for their cooperation in the study of this patient; and to Mr. Joseph Patterson of the Department of Medical Art of the Medical Center, who is responsible for the illustration.

BIBLIOGRAPHY