

## PRIMARY TUBERCULOSIS OF THE GALL-BLADDER

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IT IS obvious that tuberculosis of the gall-bladder is a rare condition when a study of the literature reveals only fifteen reported cases. We think that it is worthy of note that this condition is not mentioned in that comprehensive work, *Gallenwege Chirurgie*, by H. Kehr, published in 1913. Nor have we been able to find any reference to this subject in the American literature for the past twenty-five years, with one exception, to which we refer below. Whether or not the gall-bladder represents the initial tuberculous lesion, or is a secondary point of attack, cannot be determined from the data at hand in most of these cases.

SIMMONDS<sup>1</sup> collected six cases from the German literature in 1908. He fails to note in his article whether or not these cases were thought to be primary tuberculosis of the gall-bladder, nor does he tell us what the authors considered to be the method or route by which the tubercle bacillus gained entry to that organ. He adds a case of his own of a boy, nine months old, dying of acute miliary tuberculosis, in which instance the gall-bladder was believed to be infected from the liver through the bile stream. The mucous membrane of the gall-bladder showed tuberculous ulcerations very similar to those appearing in the urinary bladder in tuberculous nephritis. Simmonds concluded from his own case and his study of the literature that there may be two types of tuberculous cholecystitis: First, a chronic ulcerous cholecystitis, with or without stones, apparently primary or associated with tuberculosis elsewhere in the body; second, an acute tuberculosis of the mucous membrane always secondary, brought by the bile stream from the biliary ducts of the liver, and always a part of a general acute miliary tuberculosis. He thinks the latter type far more frequent in acute miliary tuberculosis than is generally supposed and is unrecognized at autopsy. He mentions that this has been found several times but does not cite cases.

LANCEREAU<sup>2</sup> reports an autopsy in which he found a caseous mass replacing the gall-bladder in a woman thirty-two years old. Tuberculous granulations were found in the common duct; the spleen and mesenteric glands presented many tubercles and the right branch of the pubis was necrosed. He considers this to be a case of primary tuberculosis of the gall-bladder, the bacillus gaining entry through the ampulla of Vater and ascending along the common and cystic ducts. He states that the gall-bladder lesion is clearly the oldest pathologically of any he found and therefore the disease was primary in this organ. Lancereau distinguishes tuberculosis of the extra-hepatic biliary canals and gall-bladder from tuberculosis of Glisson's capsule and from disseminated tuberculosis of the liver. The first condition he thinks is always primary and its mode of entry from the intestine. This type bears no relation to age or sex. This author thinks that tuberculous cholecystitis should always be fairly easy to diagnose, but as he writes from the standpoint of the pathologist this conclusion is not of importance to the clinician. Failure to diagnose tuberculosis of the gall-bladder from other forms of chronic cholecystitis seems to us, in most instances, excusable.

In 1910, GALABRÉE<sup>3</sup> reported two cases of tuberculous cholecystitis, both of which were operated upon by Ténat with one satisfactory recovery, and one death. Chole-

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cystectomy was performed in both instances. In the first case the patient was a woman, thirty-three years old, who had had good health until four years before operation. During this time she noticed dull pains in the right hypochondrium with occasional knife-like pains in the same region and in the right flank. These pains were especially noticeable immediately after eating. Pain had been practically constant for eight months. Six months previous to operation she noticed a tumor at the right costal margin. She showed at the time of operation habitual malaise, emaciation and occasional vomiting, but no jaundice, and no cough. Temperature was 100.4 to 101.4; there was a harsh expiration at the left apex and a few dry râles on deep inspiration. Operation revealed a gall-bladder adherent to the hepatic flexure of the colon and to the pylorus. The adhesions showed granulations, grayish in color, with yellow points. The gall-bladder was hard, its walls greatly thickened and indented, and it was about the size of an adult hand. It contained black viscous matter and two large black stones. There were interstitial nodules the size of a grain of corn in its wall, which on gross section showed dry caseous foci of a puriform, yellowish, thickened substance. The specimen was not examined microscopically, "but, macroscopically there was no doubt as to the tuberculous character." The gall-bladder was removed and the abdomen drained. This patient made a good recovery, the wound healed without fistula, and the patient was dismissed on the thirty-fifth post-operative day. She was well and had no symptoms when seen six years later.

Galabré's second case was a woman, thirty-nine years old, who had never been seriously ill until her present illness. One month prior to operation she lost appetite and strength rapidly and had continuous sharp pain in the right side, increased a few minutes after eating. An upper right side abdominal tumor was so large and extended so far posteriorly that she was operated upon by Tédénat with a diagnosis of kidney tumor. Posterior incision was made and a normal kidney was found. Upper right rectus incision was made and a tumor found extending from the liver to the right iliac fossa. This tumefied gall-bladder contained one perforating stone, 50 c.c. of pus, and grayish-yellow adhesions. The wall was one inch thick. It was removed and the abdomen drained at closure. The patient died on the third day. Autopsy was not permitted. Histologically the wall showed many tubercles and tubercle bacilli.

A. LATRONCHE<sup>4</sup> collected four more cases in 1911 and adds one of his own. All of these cases were in women between forty-one and forty-nine years of age. Four of them showed pain as a constant sign; four showed a definite tumor on examination; only one had jaundice, and vomiting was not a pronounced symptom in any. Two of these were treated by cholecystectomy (Braquehay, Tédénat) of which one recovered (Braquehay), and one died (Tédénat). Three cases were treated by cholecystostomy (Riedel, Czerny, Latronche) and all recovered, two with fistula and one without (Czerny). This latter was cauterized at operation with strong zinc chloride solution. Stones were found in all five cases. The gall-bladder was in every case found to be greatly thickened, and contained thick cheesy pus. In only two of these cases was a histological examination made (Braquehay, Latronche). In only one, the author's, was an attempt made to show the relation of the gall-bladder to other tuberculous lesions. In his case there was a definite tuberculous peritonitis, and histological section showed tubercles in the wall of the gall-bladder extending from the serosa inward; from which he concludes that the bacillus was carried by the peritoneal lymphatics and by contiguity to the gall-bladder. Our case was as follows:

RANKIN. CASE NOW REPORTED.—July 12, 1921. Negress, thirty-eight years old, complains of pain and a mass in the right upper quadrant of the abdomen.

*Past History.*—Well as a child; pulmonary tuberculosis seven years ago. Took "the cure" for two years and thinks she made a complete recovery.

*Present Illness.*—Began about five years ago with persistent dull pain in the right hypochondrium. She had some food disturbance evidenced by increase of pain soon

after eating. At first the pain came on at night. For the past two years symptoms have greatly increased and the pain has occasionally radiated to the back on the right side. For past two weeks has been very sore over gall-bladder and has noticed a tumor. She has had some afternoon temperature, no loss of weight, no cough, expectoration, hæmoptysis or nightsweats.

*Physical Examination.*—Well-developed and nourished negress, thirty-eight years of age; does not look acutely or chronically ill; no anæmia; no jaundice of scleræ. Heart and lungs negative. Abdomen somewhat distended; muscles tightened. Mass in epigastrium and right hypochondrium which is fixed and very tender. Vaginal examination negative. Temperature 99, pulse 88, respiration 20. White blood-cells 5000; neutrophils 70 per cent. Urine negative.

*Diagnosis.*—Perforated ulcer of the duodenum with abscess formation.

Operation by Dr. W. Barrow, July 13, 1921. Right rectus incision from costal margin to two inches below umbilicus. Large mass adherent to liver and small intestine. Adhesions separated with free oozing. Mass found to be gall-bladder, adherent to under-surface of liver with extension into liver. Gall-bladder opened, walls about three-quarters of an inch thick. Cavity contained caseous material but no stones. A portion of the wall was removed for diagnosis and rubber tube placed in the gall-bladder with three gauze strips next to the under surface. Layer closure.

The patient left the hospital after an uneventful convalescence. The wound healed without fistula.

*Pathological Examination.*—July 13, 1921. Macroscopic: The specimen consists of a small piece of tissue and caseous material removed from the gall-bladder. Microscopic: Sections from the gall-bladder show the wall to be greatly thickened due to an excess of hyaline connective tissue. It is densely infiltrated with lymphocytes and plasma cells. There are a number of areas of necrosis surrounded by endotheloid and lymphoid cells with a few giant cells. One surface shows a few cells that resemble liver cells. Sections from the caseous material show it to be a granular material with no formed elements.

*Diagnosis.*—Tuberculous cholecystitis.

August 20, 1925, this woman returned for observation. She went back to house work in September, 1921, and has progressed satisfactorily until June, 1925, when her abdomen began to swell. She notices now shortness of breath on exertion and palpitation. Feet and ankles swell at times. Physical examination: Heart and lungs negative. Abdomen: Scar over gall-bladder area, abdomen is prominent and contains fluid; shifting dullness most prominent below navel. Pelvic examination unsatisfactory, perineum and cervix O. K. Fundus and adnexa not felt. Impression Tuberculous peritonitis.

August 20, 1925: X-ray of chest for tuberculosis, negative.

August 24, 1925: Operation (Rankin). Upper right rectus incision through old scar. There was quite a lot of free fluid in the abdomen. The peritoneum, pelvis, broad ligaments and serosa of the bowel were studded with tubercles. The right upper abdomen contained densely adherent masses of viscera in the neighborhood of the gall-bladder and it was with difficulty that separation was made down to this organ. There was a small, thickened, nodular gall-bladder. All of the fluid was evacuated and the abdomen was closed without drainage.

*Pathological Report.*—Macroscopic examination: The specimen consists of a small piece of tissue from the peritoneum.

*Microscopic Examination.*—The sections show rather loose œdematous connective tissue with no evidence of acute inflammation.

September 4, 1925: Convalescence uneventful, all sutures out, wound healed by primary union. This patient was advised to consult her home doctor for paracentesis and to return for X-ray treatment.

December 4, 1925: Patient returns for X-ray treatment. She has had seven paracenteses since operation; was "tapped" four days ago, but abdomen is distended.

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Treatment K. V. 190; M. A. 5. Distance 50 cm. Filter  $\frac{1}{2}$  cm. i al. Time 25 minutes. Area 25 x 25 cm. Location—anterior abdomen.

December 5, 1925: Same treatment.

January 18, 1926: Some nausea and vomiting after second half of previous treatment. General condition improved. Eating and sleeping better. Has been "tapped" once since last treatment. Treatment same.

January 25, 1926: Nausea and vomiting following treatment a week ago. Feeling O. K. now. Length of treatment reduced five minutes.

March 9, 1926: Patient had "flu" in February, in bed two weeks. Feeling fairly well again. Slight cough persists. Abdomen soft, little or no fluid. Was "tapped" a month ago and only a few ounces obtained.

March 9, 1926: Twenty-five minutes' treatment. March 11, 1926: Twenty minutes' treatment.

We do not think that laparotomy in August, 1925, was an important factor in the great improvement this patient has shown. We are rather inclined to the opinion that the X-ray treatments should be given the credit, though this method of treatment has only occasionally been of material benefit in tuberculous peritonitis. Of course, the case is too recent to form conclusions in regard to any therapeutic method.

This is too short a series, and the details in all but a few cases are too meagre to draw any satisfactory conclusions, but there are some similarities and differences in those cases in which we have more detailed accounts which warrant emphasis in a brief discussion. The rarity of a tuberculous lesion in the gall-bladder, even in acute general tuberculosis, may be due either to failure of the pathologist to recognize the condition, or to a special resistance of this organ to the tubercle bacillus. We are rather inclined to the latter opinion, because it has been shown by Hanot and Létienne<sup>5</sup> that the cystic bile of patients dying from tuberculosis failed to show tubercle bacilli in all but one case. And the work of Sergent<sup>6</sup> shows that tubercle bacilli flourish in the bile of guinea-pigs and dogs but do not produce lesions of the gall-bladder unless this organ has been injured, or the common duct has been injured or ligated. The presence of stones in eleven out of sixteen cases and chronic disease in four,\* we believe a significant factor in lowering the gall-bladder resistance. There is no report to show the presence of tubercle bacilli in the stones themselves, and it is extremely doubtful that they can be the primary cause for lithiasis, which is assumed to be the case for the typhoid and colon bacilli at times. Is it possible that the fat-splitting and fat-soluble properties of the bile and pancreatic fluid are factors in this resistance, possibly attacking the waxy coat of the bacillus itself?

The mode of entry of the bacillus into the gall-bladder is in most cases purely a matter of conjecture. It may be brought by the blood from a distant focus by the hepatic artery or portal vein. If carried through the hepatic artery the bacillus may infect the gall-bladder directly, or secondarily through the liver, being brought to the gall-bladder in the bile after the hepatic biliary ducts have become involved. It may ascend from the intestine directly through the bile duct, though this is hard to understand in the case of a non-

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\* In Lancereau's case the gall-bladder was completely caseous, which made histological determination of its structure and type of inflammation impossible.

motile bacillus in a fluid flowing in the opposite direction, unless there is injury to the duct by existing inflammation. The gall-bladder may be the seat of tuberculosis secondary to the liver, which in turn has become infected from an active tuberculosis in the lower part of the right lung, the bacillus travelling through the diaphragm along the course of the lymphatics (Oberling<sup>7</sup>). The gall-bladder may become involved from a generalized tuberculous peritonitis by lymphatics of the peritoneum and by contiguity as in Latronche's case. In our case it seems reasonable to suppose that a gall-bladder already chronically diseased furnished a weakened site for a blood stream infection originating in the lung. The gall-bladder in this case appears to be almost certainly the primary abdominal focus of tuberculosis and for this reason the title, "Primary Tuberculosis of the Gall-bladder," has been chosen. In only five of the other cases in this series can be found stated an opinion in regard to the location of the primary focus. Galabré<sup>3</sup> thinks the gall-bladder was primarily affected in both of his cases, and Lancereau<sup>2</sup> seems certain that this is true in his case. Latronche<sup>4</sup> and Simmonds<sup>1</sup> clearly show the condition to be secondary in their reports.

The symptoms in cases of tuberculous cholecystitis are mainly those present in any case of chronic disease of the gall-bladder, with or without stones, and therefore vary widely. The history of discomfort and pain may range between one month and fifteen years in duration. Pain is an almost invariable accompaniment, being absent but once in the cases reported. It may be sharp and agonizing in character, or dull and persistent; sometimes little more than a feeling of heaviness and discomfort after eating; it may be localized in the right hypochondrium or epigastrium or appear in the right lower quadrant of the abdomen, or even in the region of the right kidney. It is usually increased immediately after eating. Constipation is always present, usually extremely persistent, according to Latronche.<sup>4</sup> This symptom was absent in our observation. Vomiting is notably absent. The absence of jaundice, which was present in but one case, is not remarkable if we accept as correct Bland's<sup>8</sup> estimation that it is present in but ten per cent. of all cases of disease of the gall-bladder and biliary tracts. The sex is in every instance female, and the age lies in the fourth and fifth decades, except in acute miliary tuberculosis. Loss of strength and appetite, emaciation, and cachexia are usually present, but mainly where the disease is far advanced elsewhere in the body.

The presence of a tender tumor has been noted in every case where details have been given. Latronche<sup>4</sup> says, "A tumor in the right hypochondrium, consisting of the hypertrophic gall-bladder, is found always during the course of tuberculosis cholecystitis." Fever may or may not be present. It was absent in several cases in this series.

The diagnosis had not been made before operation or autopsy except in the case reported by Lancereau.<sup>2</sup> Several times even at operation tuberculosis has not been considered. Riedel<sup>9</sup> reported his as sarcoma; Braquehay and Latronche thought the condition was possibly carcinoma until the histological

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examination was made. Other diagnoses have varied between cholelithiasis, the prevailing one, kidney tumor and ruptured duodenal ulcer. Obviously the true condition can be justly suspected only in cases with signs of general (miliary) or far advanced tuberculosis in other areas.

The specific post-operative complications may be a permanent fistula, tuberculous peritonitis, or both. Czerny<sup>10</sup> states that the persistence of a permanent fistula following operation for gall-bladder disease should lead one to suspect the presence of tuberculosis. In the six cases operated on in this series a fistula remained in two (Riedel, Latronche) of the four patients treated by cholecystostomy, and there was no fistula following cholecystectomy in the two cases which recovered (Braquehay, Galabré).

We think it is rather strange that tuberculous peritonitis has not been mentioned as a complication in any but the authors' case, except where this condition was, with the gall-bladder, a part of a generalized tuberculosis. When one considers the frequency with which this condition is associated with other active tuberculous lesions, both intra-abdominal and pulmonary, we would expect to find it appearing more often in our series. Holmes<sup>11</sup> reported a case in 1906 in which he operated for tuberculous peritonitis and distended gall-bladder. The gall-bladder and peritoneum showed no tubercles, but there was a large amount of free fluid in the abdomen. The ascites he attributed to pressure on the portal vein by the greatly distended gall-bladder. This case is not included in our series because histological examination showed no tubercles in the gall-bladder, though doubtless it shared in the condition of general tuberculosis found later to be present. Autopsy five weeks later showed diffuse miliary tuberculosis and tuberculous peritonitis. He thinks the operation stirred up the condition and the ascites facilitated its spread. Our case showed no peritonitis at the time of the first operation, but this appeared four years later.

The treatment of tuberculosis of the gall-bladder must of necessity be decided by the case. Acute miliary tuberculosis need not be considered. In conditions secondary to far-advanced active tuberculosis elsewhere, the surgical treatment of the gall-bladder should be palliative. In those cases where local and general conditions permit, we feel that a cholecystectomy should be done, but in saying this we are not unmindful of the figures in this short series, including our own case; namely, that of four cholecystostomies, there were four recoveries, two without fistula, while of four cholecystectomies done there were but two recoveries.

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