CALCIUM CARBONATE BILE

JOSEPH C. ROOT, M. D.

Calcium carbonate bile, or "milk of calcium bile" as it is sometimes referred to, is a condition in which the bile becomes heavily loaded with calcium carbonate and is opaque to the roentgen ray. Because it may be mistaken for a normally functioning gallbladder and because of its relative infrequency, the following case, which presents the typical signs and findings usually found in such a condition, is reported.

The patient was a married, white woman, thirty-one years of age, who was a housewife. The chief complaint was pain in the stomach which had occurred at intervals for the two years previous to our examination. She stated that about two years ago she began to have attacks of cramp-like pain in the epigastrium, which came on after eating and were relieved by vomiting. The attacks were rather frequent at first and lasted for several hours, but were not accompanied by chills or fever. During the preceding year, the attacks had been more frequent and more severe, with continuous vomiting during these times and with inability to retain either food or water. These attacks were not related to the ingestion of food nor to the time of day. The pain was confined chiefly to the epigastrium, but at times it radiated through to the back between the shoulders and often was so severe that a hypodermic would be required to give relief. The patient had been constipated for the past ten or twelve years and used some type of laxative daily. She had noticed that the stool was very light in color at times but there had been no diarrhea or blood in the stools. For the five days preceding our examination, the pain had been very severe and almost constant. A weight loss of fifteen pounds had occurred during the past several months.

The family and past history were essentially negative. The father, mother, and husband were living and in good health; one child was living and well and there was no history of miscarriages. The patient had had no illness except the usual childhood diseases. There had been no symptoms referable to the chest, cardiovascular or genito-urinary systems.

Physical examination revealed a thin, underweight, asthenic woman. The skin was moist and warm with no evidence of jaundice. The eyes were normal except for a slight icteric tinge to the sclera. The tonsils were small, ragged, and embedded; otherwise the mouth and pharynx were normal. The chest was symmetrical and showed good and equal expansion. The lungs were resonant throughout with no râles. The heart was of normal size, shape, and position. The heart sounds and rhythm were normal and there were no murmurs. The abdomen was scaphoid with no masses or spasticity. Tenderness was elicited by pressure over the gallbladder area and over the course of the colon in the right lower quadrant; the tenderness over the gallbladder, however, was the most definite. The remainder of the physical examination gave entirely normal findings.

Laboratory findings: The specific gravity of the urine was 1.024 and there was no albumin, sugar, casts, red or white blood cells. Examination of the blood showed 4,500,000 red cells, 5,000 white cells, and 84 per cent hemoglobin. The blood urea was 24 mg., blood sugar, 79 mg., blood cholesterol, 240 mg., blood calcium, 10.3 mg., and phosphorus, 2.3 mg. per one hundred cubic centimeters of blood. Both the Wassermann and Kahn tests gave negative reactions.

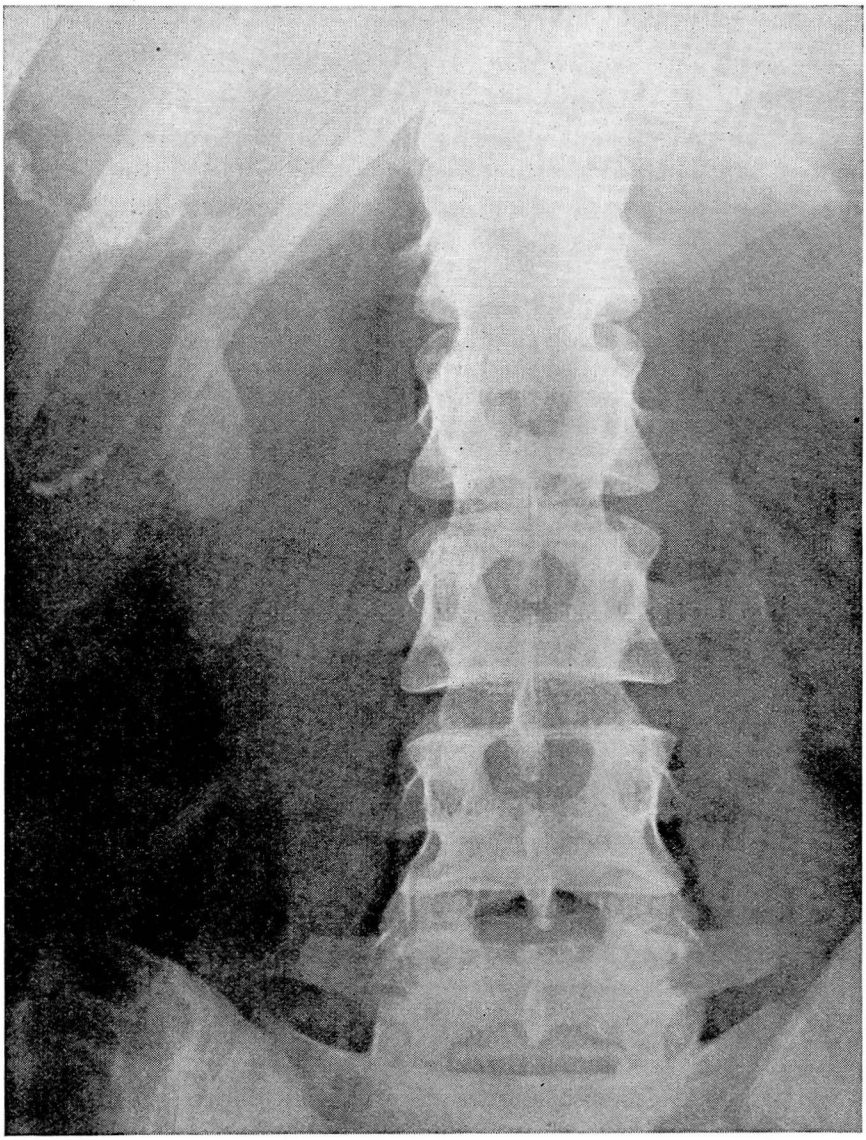

FIGURE 1: Plain film showing shadow simulating a normally functioning gallbladder.

The Ewald test meal showed a free acid of 8 and a total acid of 17. A quantitative examination of the contents of the gallbladder after operation showed iodine to be present to the extent of 5.2 gamma per 100 mg. while the calcium content was 9.2 per cent.

Clinical impression: Chronic cholecystitis and lithiasis; spastic colon; visceroptosis.

Roentgen examination: A roentgenogram of the kidneys, ureters, and bladder showed the lumbosacral spine to be normal, with no suspicious

shadows in the urinary tract. The gallbladder was opaque and well visualized. The right kidney was normal in size, shape, and position. The left kidney was not visualized.

Plain films showed good visualization of the gallbladder and no change was seen after ingestion of the cholecystographic dye. The gallbladder changed shape after a fat meal. The stomach, duodenum, and colon were normal.

Operation: Cholecystectomy and appendectomy were performed under avertin analgesia and ether anesthesia. The common duct was not dilated and no stones could be palpated in it. The duodenum was apparently normal.

Pathological report: The gross specimen consists of a gallbladder and an appendix. The gallbladder measures 10 cm. in length and 2.5 cm. in width. The serosal surface is smooth and pinkish-gray. The wall is moderately thickened. The mucosa is pinkish-gray and granular. Obstructing the cystic duct is a mulberry-shaped calculus measuring 0.6 cm. in diameter. It is soft and is apparently composed of calcium and cholesterin. Free in the lumen of the gallbladder are two similar stones measuring respectively 0.4 and 0.3 cm. in diameter. There is a considerable amount of concentrated bile which has the consistency of soft putty.

Microscopic sections of the gallbladder show thickening of the wall, enlarged mucosal glands, mild inflammatory reaction in all the coats, and fibrosis of the adventitial coat.

Pathological diagnosis: Chronic cholecystitis; cholelithiasis; chronic appendicitis.

The gallbladder as it was first seen during the roentgen examination is shown in figure 1, which is the plain film of the kidneys, ureters, and bladder. This film is made as a routine procedure in all our examinations of the gastro-intestinal tract and is made the day before cholecystographic dye is given. The gallbladder is seen very distinctly on this film and appears much as a normal gallbladder does after cholecystographic dye is administered. The film made 15 hours after ingestion of dye is seen in figure 2. The gallbladder shadow is no more dense here than in the plain film, although the outline has changed somewhat. A fat meal was given this patient but no change in the size of the gallbladder was seen on the film made after the meal.

The diagnosis in this case is quite evident, but a differentiation must be made between opaque bile, a large opaque calculus, and calcification in the wall of the gallbladder. A positive diagnosis of opaque bile may be made if the shape of the gallbladder is seen to change, either on the different films or more especially after the fat meal. Calcification in the wall of the gallbladder generally shows as heterogeneous areas of varying densities, and these shadows will always remain constant in their position.

Calcium carbonate bile, while not rare, is relatively uncommon. Several authors have reported cases similar to ours but we have seen only one report of the frequency with which it may be expected.

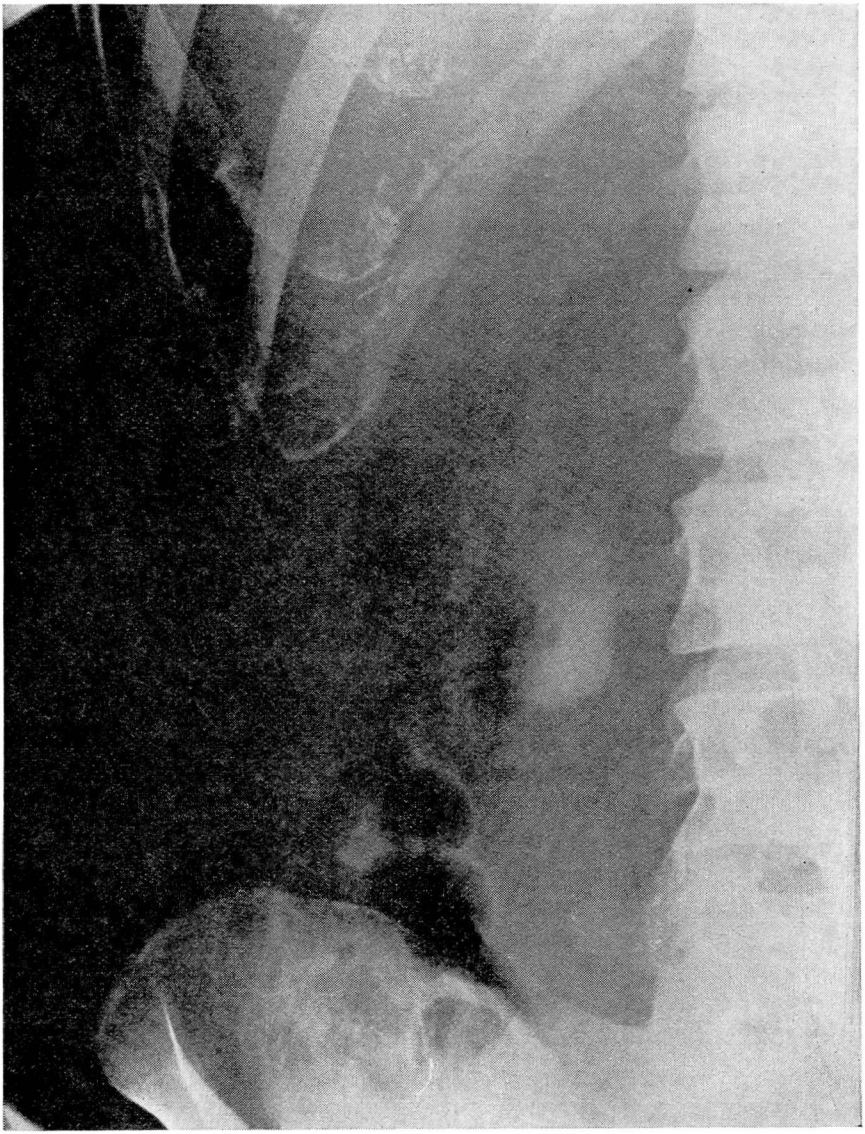

FIGURE 2: Cholecystogram after administration of dye. No change is seen in the density of the gallbladder shadow.

Mathews, in a discussion of a paper by Phemister et al[1], stated that, in the examination of 6700 gallbladders, he had recognized only one of this sort. We have found this condition to be more common, however, since in the last 1700 examinations of the gallbladder which have been made at the Cleveland Clinic, we have seen two which contained opaque bile. One of these, the present case, was proved at operation. Operation

has not yet been performed in the second case, but the same findings were revealed in a subsequent recheck examination of the gallbladder.

The chemical analysis of the contents of the gallbladder in this case is interesting, since in other reported cases we have not seen a quantitative report of the amount of calcium present in the thick, putty-like substance. In some of these cases it was simply reported that a high percentage of calcium was found. In the case under consideration the calcium content of the dried mass was found to be 9.2 per cent. The total amount of inorganic salts in normal bile is about 0.65 per cent, which includes other compounds as well as calcium. It is readily seen that in the contents of this gallbladder there is a tremendous increase over the normal amount of calcium, thus accounting for the very dense gallbladder shadow which was seen in the original plain film. A roentgenogram of the surgical specimen is shown in figure 3, the gallbladder having been opened and the calculi and calcium carbonate removed. The opaque nature of the bile in comparison to the density of the calculi and the gallbladder itself will be noted. A qualitative chemical examination of the thickened bile was not made since it is quite generally conceded that the calcium salt found in these cases is calcium carbonate.

The formation of calcium gall stones and the thick milk of calcium bile are probably very closely related. Since, in this case and others reported, there has always been an obstruction of the cystic duct, it would seem that this is a necessary factor for the formation of calcium products within the gallbladder. The obstruction in most cases has been due to a calculus, although any obstruction, such as may be the result of a neoplasm, will produce a similar result.

When the obstruction of the duct is established and a certain amount of infection is present, there is a thickening of the gallbladder wall with a subsequent change in its physiology. With these changes, there probably occurs an increase in the excretion of the calcium-bearing mucus from the walls of the gallbladder. Certainly, obstruction of the cystic duct alone is not sufficient to cause this condition, as is shown by those cases of obstruction and hydrops in which no increase in the calcium content is noted. It would seem, then, that the correct amount and severity of inflammation and obstruction must be present before calcium-containing substance is formed within the gallbladder.

Various attempts have been made to reproduce such phenomena. Wilkie[2] was able to produce both calcium and the cholesterol calculi in rabbits. In his experiments, cholecystitis was induced in each animal, and in some the cystic ducts were ligated. He found that if the cystic duct were not obstructed, cholesterol calculi resulted, whereas, if the cystic duct were ligated, stones rich in calcium were produced.

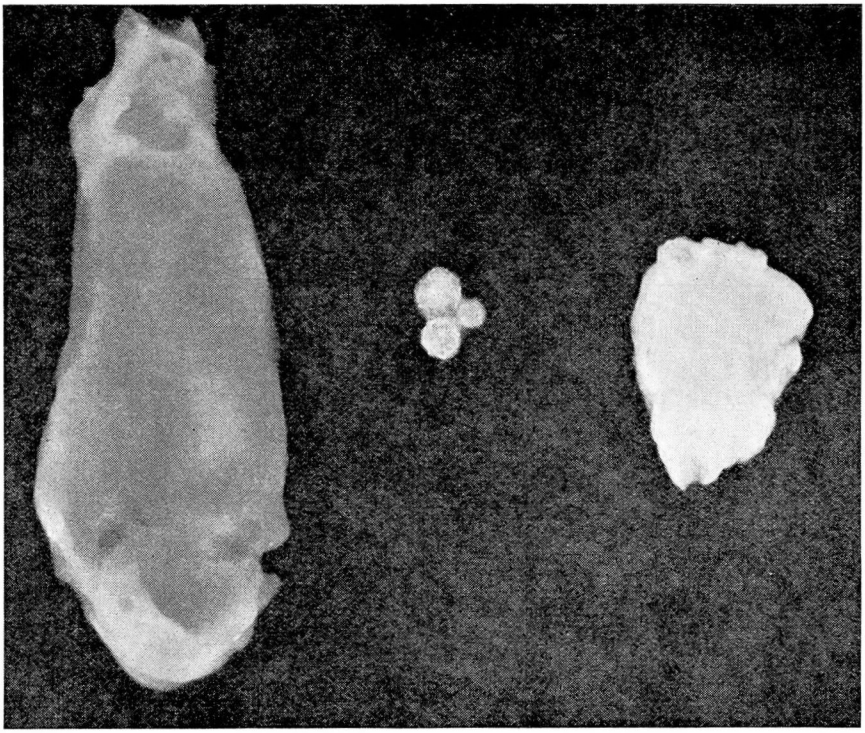

FIGURE 3: Roentgenogram of opened gallbladder and contents.

The acidification of the bile in the gallbladder is perhaps one of the important factors which prevent the formation of calculi within the gallbladder. The hydrogen-ion concentration of bile in the normal liver is 8.2, while that in the gallbladder ranges from 5.8 to 6.0 and is strongly acid to litmus. The solubility of any salt, calcium carbonate as an example, is certainly influenced by the fluid in which it is contained. In the acidified bile the calcium is not precipitated; hence no calcium stones are formed. On the other hand, if any process, such as an inflammatory change in the gallbladder wall, interferes with or changes the normal physiology, we may expect the bile to become more alkaline and to approach the hydrogen-ion concentration of liver bile. This would be a factor favoring the precipitation of calcium and the formation of opaque calculi or calcium carbonate bile.

The possibility of the presence of opaque bile is of major importance to the roentgenologist if he is to avoid error in the interpretation of cholecystograms. The roentgen examination must be complete and should include plain films as well as the usual films made after the ingestion of the gallbladder dye. In the case under discussion, the gallbladder was so well visualized on the plain film that one might easily

believe it to be a normally functioning gallbladder containing dye and to report it as such.

The fat meal is of value in certain cholecystographic examinations to rule out shadows of the gallbladder and to differentiate between calcification in the wall or the presence of opaque bile as in the present case.

The formation of calcium carbonate bile is probably dependent upon a combination of obstruction and inflammatory changes, with a subsequent change in the physiology of the gallbladder.

References

1. Phemister, D. B., Rewbridge, A. G., Rudisell, H.: Calcium carbonate gall-stones, and calcification of gallbladder following cystic-duct obstruction, Ann. Surg., 94:493-516, (October) 1931.

2. Wilkie, A. L.: Bacteriology of cholecystitis, clinical and experimental study, Brit. J. Surg., 15:450-465, (January) 1928.