A CONSIDERATION OF THE PANCREAS AND ITS
DUCTS IN CONGENITAL OBLITERATION
OF THE BILE-DUCTS *

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Congenital obliteration of the bile ducts is a rare disease, but hardly sufficiently uncommon to warrant the report of a single case, unless it presented unusual symptoms, or served as the ground-work for some new conception of the symptomatology, pathogenesis, or pathology of this obscure condition. The excuse offered for this presentation of a case is that the application of a new method of study during life led to a somewhat broader point of view of this pathological condition. In the course of a clinical study, carried on at intervals for about six weeks on an infant afflicted with this condition, the duodenal catheter was frequently employed, in order to obtain information as to the excretion into the intestine of bile as well as of the pancreatic ferments. This catheter has been described in connection with a study of spasm and stenosis of the pylorus,¹ of icterus neonatorum,² and of the flora of the duodenum in infants,³ so that it is not necessary for the technic to be again reviewed in detail. The accompanying cut (Fig. 1) shows the simple apparatus, which consists of an ordinary Nélaton No. 15 (F.) catheter, marked in an appropriate manner, and of a glass aspirating bulb. As has been stated in previous articles, this catheter can be readily and rapidly passed into the stomach, and through the pyloric sphincter into the duodenum, in infants, from the day of birth to the age of about 2 years. By this means bile and the ferments of the duodenum and pancreas may be obtained for examination.

REPORT OF CASE

M. E. was admitted to the hospital Dec. 19, 1911, when 7 weeks old.

Family History.—First child, pregnancy and delivery normal; no history of miscarriages.

Present History.—History of early and increasing jaundice; exact date of onset uncertain; nursed by mother irregularly.

Examination.—At date of admission the infant was markedly yellow, fairly well nourished, weight 9 pounds 4 ounces. Liver at level of umbilicus. Spleen one finger above crest of ilium, edge sharp and soft. Lungs, heart, and general abdominal examination negative. Urine negative, except for large amount of

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*Manuscript submitted for publication May 21, 1912.

1. Hess, A. F.: Am. Jour. Dis. Child., 1912, iii, 133.

2. Hess, A. F.: Am. Jour. Dis. Child., 1912, iii, 304.

3. Hess, A. F.: Jour. Infect. Dis., 1912, x, No. 5.

bile pigment. Stools clay colored. Blood examination showed 6,000 leukocytes, 65 per cent. mononuclear cells, 35 per cent. polynuclears.

December 20. Child being nursed every four hours. To-day traces of blood following rectal irrigation.

Duodenal catheter passed 1½ hours after nursing, and 2 ounces of uncoagulated milk evacuated. Duodenum easily entered, and 3 c.c. of fluid obtained in the course of one hour, slightly acid, and faintly bile-tinged. Stool clay colored with traces of bile.

December 21. Catheter passed a few minutes after nursing. Stomach contents acid, Congo ++. Duodenal contents contain slight amount of bile and food strings (Cannon).

December 22. Jaundice more intense. Catheter passed five hours after nursing. Stomach empty. Duodenum empty after twenty-five minute test.

December 23. Catheter passed three and one-half hours after nursing. Stomach empty. Duodenum empty after a one-half hour test.

December 24. Condition the same. Catheter passed an hour after nursing. Acid, Congo + milk evacuated. Mucoid fluid containing some bile found in duodenum.

Fig. 1.—Infant duodenal catheter.

December 25. Jaundice increased. Infant sleepy. Catheter passed an hour after nursing. About 1 ounce of very acid, Congo + fluid removed from stomach. Small amount of acid mucus obtained from duodenum.

December 26. Condition the same. Some bile tinged mucus aspirated from duodenum.

December 27. Condition worse. Increased jaundice. Some blood in stool, also subcutaneous hemorrhages. Rectal examination showed a considerable amount of dark fluid blood.

Catheter passed three-fourths of an hour after nursing. Congo +++ fluid obtained. About 0.3 c.c. of slightly bile-tinged fluid obtained.

December 28. Coagulation time of blood diminished (15 minutes). Temperature has ranged between 98 and 100 degrees. Weight 9 pounds 2 ounces; that is, only slight loss. Hemorrhages from bowel persist. An operation considered, but thought not advisable.

December 31. Subcutaneous injection of horse serum.

Duodenal catheter passed two hours after nursing. Congo ++ fluid aspirated from stomach, and in ten minutes about 1 c.c. of neutral fluid containing traces of bile obtained from duodenum.

January 2. Child drowsy. Hemorrhages the same. Taken away from hospital against advice.

The child was not seen again for about one month. On February 5 I was sent for and saw it at its home. Although it had lost weight it looked comparatively well and the hemorrhages had ceased. The child was being fed on condensed milk every three hours.

February 7. Doing poorly; has been vomiting; vomiting expulsive in nature. Stool still clay colored. Catheter passed; Congo +++ fluid evacuated from stomach. Marked cardiospasm, and great difficulty in entering stomach. (Probably food has not entered stomach.) Also difficulty in entering duodenum; "accessory method" has to be resorted to. Duodenal feeding with whey.

February 8. Still vomiting, as yesterday. Stool brown (starvation). Catheter passed. Cardiospasm the same, pylorospasm less. Duodenal feeding. Patient readmitted to hospital.

February 9. Doing poorly. Vomiting continuous. Cardia and pylorus less spastic. Duodenal feeding.

February 10. Exitus.

Clinically, the case was clearly one of congenital obliteration of the bile-ducts, showing intense jaundice, marked enlargement of the liver and spleen, and subcutaneous and intestinal hemorrhages. The urine contained a large amount of bile; the stools, although clay colored, also showed traces of bile. The duodenal catheter was frequently passed and determined the presence of bile in the duodenum, and also of the pancreatic ferments in the fluid which was aspirated. The infant did fairly well for three months and then suddenly developed vomiting which was followed by inanition and death. The cause of this vomiting could not be definitely ascertained. Possibly it was due to some error in feeding. It was markedly expulsive in nature, and characterized by cardiospasm, pylorospasm, and a hypersecretion and hyperacidity of the gastric juice.

An autopsy was performed by Dr. Eli Moschcowitz, whom I wish to thank for the following report:

AUTOPSY PROTOCOL

MACROSCOPIC

No. 2764. Heart and lungs not removed.

The liver weighs 170 gm. (formalin). Contour normal; consistency firm. Stained deeply bile-green. Surface roughened. On section the liver is deeply bile-stained; the cut surface shows green lobules with narrow, white spaces intervening. The lobules are slightly elevated; the white portions appear fibrous, and are situated at the periphery of the lobules in the portal spaces. The gross picture corresponds to that of a typical periportal cirrhosis. The remains of the ductus venosus enters the liver through a deep fossa hollowed out of the anterior border. There is a corresponding fissure on the under surface.

The fissure for the gall-bladder is at its normal site, and is occupied by a rather thick mass of fibrous tissue. In this mass there is a small cavity (the gall bladder) running longitudinally for a distance of about 2 cm. The lumen admits a narrow probe, and contains a few drops of clear watery fluid. The finest bristle passed from the gall-bladder in the direction of the cystic duct fails to find an exit.

The ducts of the liver are completely obliterated, and are represented by dense strands of fibrous tissue. The right and left hepatic ducts are impervious

up to the point where they emerge from the liver, as well as the common hepatic duct.

The strand representing the common bile duct is somewhat thicker than the others, and passes to the posterior surface of the duodenum.

On the intestinal wall corresponding to the attachment of this strand, is a small papilla within the lumen (to be described below).

The portal vein and the hepatic artery occupy their normal situations, and show no abnormality in size. There are a number of small lymph-nodes at the base of the fissure for the gall-bladder.

The duodenum is normally situated. Within the lumen and on the posterior aspect are two papillae. The lower one, wider and deeper, is found to be the opening of a pancreatic duct, and into this a fine bristle can be passed. The upper papilla is situated about 2 cm. distant and corresponds to the attachment of the fibrous remnant of the common duct, above described. This papilla is impermeable to the finest bristle.

The stomach, intestines, spleen, mesentery, kidneys, genito-urinary tract and the adrenals are normal; except for rather intense bile staining.

Anatomical Diagnosis: Complete obliteration of all the extra hepatic bile ducts and the papilla of Vater. Hypoplasia of the gall-bladder. Bile pigmentation of the liver, with periportal cirrhosis. Anomalous insertion of the ductus venosus. Anomalous position of accessory pancreatic duct (Santorini) below papilla of Vater.

MICROSCOPIC EXAMINATION

Liver: Under the low power the liver presents the typical appearance of rather advanced periportal cirrhosis. The connective tissue is abundant, loose, moderately infiltrated with round cells, and surrounds many of the lobules completely.

Interspersed in this connective tissue are abundant newly formed bile ducts, similar to those found in the cirrhosis of Laennec.

These ducts are very narrow, anastomose, and in only a few instances can a lumen be demonstrated; the lumen is empty.

Distinct transitions between the liver trabeculae and the newly-formed bile ducts can be demonstrated in many instances.

The hepatic artery and the portal vein in the capsule of Glisson are normal, but no well formed bile-duct is present. There are nowhere evidences of cystic dilatations of the bile-ducts. The cells of the liver trabeculae stain well; the nuclei are distinct and reticular. The intra- and intercellular bile-capillaries are everywhere dilated and filled with green bile. These dilatations are especially prominent in the central portions of the lobule. A noteworthy picture is the occasional appearance of a trabecula of the acinus gland type; the cells are arranged concentrically in a single row around a blood capillary. Such formations are few in number.

Section of the hypoplastic remnant of the gall-bladder reveals merely a dense fibrous structure, lined by a single layer of low cuboidal epithelium which is thrown up in low folds.

There is no structure corresponding to the submucosa or muscle fibers of the wall.

Section of the fibrous strands of the obliterated ducts shows nothing in any way suggestive of epithelium or lumen. These strands consist merely of dense fibrous tissue, with a few nerves and small blood-vessels.

Section of the upper papilla reveals this to be a small accessory pancreas in the wall of the duodenum. Serial sections reveal no evidence of a lumen, or of inflammatory tissue.

Sections of the other organs reveal nothing noteworthy. Pancreas normal; no cirrhosis.

DISCUSSION OF AUTOPSY REPORT

The autopsy therefore confirmed the clinical diagnosis of congenital obliteration of the bile ducts. All the extra hepatic ducts were found obliterated. The usual changes in the liver following marked stasis were present. The only notable features were the very exceptional site of entrance of the accessory pancreatic duct (Santorini) in the duodenum, which was below instead of above the papilla of Vater, and the accessory pancreas found in the wall of the duodenum at the site of the papilla of Vater (Fig. 2, a). On opening the duodenum this was seen as a small nodule, resembling one of the solitary lymph-nodes commonly found in the lower intestine. Its true nature was not suspected. It was submitted to serial section with the purpose of ascertaining whether inflam-

Fig. 2.—Obstruction of common bile-duct and pancreatic duct. a, accessory pancreas at site of papilla of Vater; b, opening of accessory pancreatic-duct (Santorini) below papilla of Vater; c, connective tissue representing common bile-duct; G. B., rudimentary gall-bladder; L, liver; St., Stomach; Sp., spleen; D, duodenum.

matory tissue could be found at this point, as it is still an undecided question in the pathogenesis of this disease, whether the obliteration of the bile-ducts is due to a fetal inflammatory process, or to a developmental anomaly. No sign of inflammatory tissue was found on microscopic examination. The glandular arrangement of some of the liver strands, called attention to by Finkelstein,⁴ is also worthy of mention.

4. Finkelstein, H.: *Lehrbuch d. Säuglingskrankh.*, 1912, Part II, p. 438.

EXAMINATION OF DUODENAL FLUID

In the clinical report mention has been made of examinations for pancreatic ferments carried out on the fluid aspirated from the duodenum. Quantitative and qualitative tests were made for the presence of trypsin, 5 per cent. gelatin being used for this purpose; for the tests for amylase a 1 per cent. starch solution was used, and after forty-eight hours the mixture was titrated for sugar by means of Fehling's solution; neutral ethyl butyrate was used to test for lipase, and after twenty-four hours the acidity was determined by means of titrating with twentieth-normal sodium hydroxid. All solutions were rendered alkaline by means of sodium hydroxid, and sterile by the addition of toluol. It does not seem necessary to describe these methods in detail, as an article soon to be published treats of a large series of tests made on infants by this means. It was found in this case that all three pancreatic ferments were being excreted into the duodenum. The trypsin was in considerable quantity as it digested gelatin within twenty-four hours. The amylase was likewise found not insufficient compared with the results obtained on normal infants. The lipase was, however, found to be diminished. Whether this was due to the lack of bile in the duodenum, which, as is well known, intensifies the action of the pancreatic fat-splitting ferment, or whether there was, in fact, a deficiency of lipase, it is difficult to say without further study. The stool contained a large amount of fat, as is the case in all instances of obstructive jaundice.

Cases with obliteration of the common bile-duct usually have been classified according to the obstruction of the hepatic ducts, the cystic duct, or the presence or absence of the gall-bladder. It would seem that this classification can possess no clinical or pathological significance where the common bile-duct is absolutely impervious. It would appear, however, by no means of purely academic interest to ascertain whether the pancreatic ducts are patent or likewise obstructed. In view of the fact that when the common duct is obstructed by a biliary calculus situated at the papilla of Vater, the pancreatic duct frequently is also obstructed, resulting in acute or chronic pancreatitis, it is remarkable that in the pathological condition which we are considering no attention whatsoever has been paid to the pancreas. In a rather extensive review of the literature I have not met with an instance in which the pancreas has been described at autopsy or later examined microscopically. For example, in Thomson's⁵ excellent monograph, published in 1892, which carefully reviewed forty-nine cases, in Beneke's⁶ report of 1907, which considered seventy-four cases, in reports of cases by Murchison,⁷

5. Thomson, J.: Congenital Obliteration of the Bile Ducts, 1892.

6. Beneke, R.: Kongenitale Atresia d. grossen Gallengänge, Marburg, 1907.

7. Murchison: Diseases of the Liver, 1885, p. 422.

Schueppel,⁸ Henoch,⁹ Rolleston,¹⁰ and many others, no attention has been paid to the pancreas or its ducts. Indeed, the only mention which I have found on this subject was one by Wilks¹¹ in a report published in 1862, which states that "in the duodenum the opening of the bile-duct was found as usual and a probe passed freely into the pancreas." In almost all of these cases the obliteration of the common bile-duct included the papilla of Vater, which is known generally to harbor the outlet of the pancreatic duct as well as of the bile-duct. In these cases, unless there existed another duct from the pancreas to enable it to pour its ferments into the intestine, there must therefore have been in addition to an obstruction of the bile an obstruction of the external secretion of the pancreas. It is difficult to state in just what percentage of cases an accessory pancreatic duct, the duct of Santorini, enters the intestine separately. Opie¹² dissected 100 cases in order to investigate this subject and came to the practical conclusion that "in at least a third of all individuals the duct of Santorini cannot act as an accessory outlet when the duct of Wirsung is occluded."

CONCLUSIONS

In the pathologic condition termed congenital obliteration of the bile-ducts, the common bile-duct has been found almost invariably obliterated in the greater part of its course, including in almost every instance the duodenal end and the papilla of Vater. Into this papilla the main pancreatic duct almost always enters, and accordingly is subjected at the same time to absolute obstruction, so that it would seem preferable to term this disease congenital obliteration of the common bile-duct and pancreatic duct. A classification from a clinical point of view better than the purely anatomical one generally made use of would seem to be to divide this pathologic condition into two main groups of cases: (1) where associated with the obliteration of the common bile-duct there is an obliteration of pancreatic duct, which, however, is compensated for by the fact that the accessory duct, the duct of Santorini, is present and able to excrete the pancreatic ferments into the duodenum;¹³ another group (2) where the obliteration of the excretory apparatus of the pancreas is total and complete, as not only is the duct of Wirsung absolutely obstructed, but no accessory pancreatic duct exists. Cases of congenital obliteration of the common bile-duct and pancreatic duct can, therefore,

8. Schueppel: *Arch. f. Heilk.*, 1870, p. 78.

9. Henoch, E.: *New Syd. Soc. Tr.*, i, 28.

10. Rolleston, H.: *Diseases of the Liver*, 1905.

11. Wilks: *Tr. Path. Soc. London*, 1862, p. 119.

12. Opie, E.: *Am. Med.*, 1903, p. 996.

13. Under this group would come those exceptional cases in which the common bile-duct and the duct of Wirsung enter the duodenum separately and at different levels.

be divided into those with compensated or with uncompensated pancreatic obstruction. The case described in the foregoing pages was of the compensated variety, which comprises the larger group. During life the three pancreatic ferments, trypsin, amylase, and lipase, were repeatedly found in the duodenal fluid obtained by means of aspiration with the duodenal catheter, and the diagnosis of compensated pancreatic obstruction was substantiated after death by finding the main pancreatic duct obliterated and the accessory duct patent.

It is of interest to note that notwithstanding the absolute closure of the common bile-duct, bile was demonstrated in the duodenal fluid and in the stool, proving the probable excretion of bile from the circulation through the intestinal wall. The infant lived for three months, and died as the result of inanition brought on by an acute attack of vomiting accompanied, as tests by means of the catheter showed, by cardiospasm, pylorospasm, and hyperacidity and hypersecretion of the gastric juice. This complication may bear no relation to the underlying pathologic disturbance; reference to the literature in regard to this point, however, shows that marked vomiting has been an important intercurrent symptom in many cases, so that attention should be directed to this complication in the future.

It is probable that it will be found that the cases of congenital obliteration of the bile-ducts associated with uncompensated obstruction of the pancreatic ducts are the more serious, and that infants in this group survive for a shorter period than those in whom the ferments gain entrance to the duodenum by an accessory duct. A test of all cases by means of the duodenal catheter will permit of a clinical classification during life of the compensated and the uncompensated cases, and the data obtained by this means should be carefully correlated with the results of post-mortem examination, especially with the pathological condition of the ducts and parenchyma of the pancreas, an organ which has been absolutely disregarded in the consideration of this disease.

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