Histopathological Studies on Intrahepatic Bile Ducts in the Vicinity of Porta Hepatis in Biliary Atresia

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CHIBA, T., KASAI, M. and SASANO, N. Histopathological Studies on Intrahepatic Bile Ducts in the Vicinity of Porta Hepatis in Biliary Atresia. Tohoku J. exp. Med., 1976, 118 (3), 199-207 — Intrahepatic bile ducts in the vicinity of the porta hepatis were histologically investigated in 9 cases of biliary atresia and the pattern of bile duct was divided into two groups. In the first group, there were a few large bile ducts which had continuity to the extrahepatic bile duct. In the second group, many small bile ducts were histologically observed, but there was no large bile duct at the porta hepatis. This type of abnormal bile ducts was seen in the cases of obliteration of bile ducts at porta hepatis.

Several pathologic studies on the architecture of the intrahepatic biliary tree in biliary atresia have corroborated the existence and patency of intrahepatic bile ducts in the early stage of this disease (Hanai et al. 1967; Oh-i et al. 1969; Ohkuma 1972; Landing et al. 1973; Chiba et al. 1975). However, the bile duct pattern in the hilar region of liver has not been studied. The purpose of this report is to elucidate the pattern of bile ducts passing through the porta hepatis in biliary atresia.

MATERIALS AND METHODS

Nine autopsy cases of biliary atresia at Tohoku University Hospital during the period from 1971 to 1975 (June) were subjected to the present study. The types of biliary atresia and the method of operation for individual cases were briefly summarized in Table 1. The operation disclosed in Cases 1 and 2 cystic dilatation of the common bile duct but no communication with the duodenum (Ia, according Kasai's classification; Kasai 1974). In Case 3, the major intrahepatic bile ducts were demonstrated by intraoperative cholangiography by the injection of contrast medium into dilated portion of porta hepatis. However, the cystic duct and common hepatic duct were found obliterated completely (IIb). Namely, in these three cases luminal continuity between the intrahepatic bile duct and hepatic duct through the porta hepatis and obliteration of the common bile duct were confirmed. Postoperative bile excretion was good in Case 6 and resulted in complete disappearance of jaundice, while other cases showed poor or no excretion of bile after operation. The principal postmortem findings were listed in Table 2. Most of the cases had hepatic cirrhosis and 5 of 9 cases died of hepatic failure.

At autopsy, the liver was carefully taken out together with the tissue of porta hepatis.
TABLE 1. Type of obstruction of extrahepatic bile duct and method of operation

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age at operation (day)</th>
<th>Method of operation</th>
<th>Type of extrahepatic bile duct obstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female</td>
<td>112</td>
<td>D-Y; double-Y hepatic porto-jejunostomy with an external fistula.</td>
<td>$I_x$</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>228</td>
<td>External fistula with common bile duct</td>
<td>$I_x$</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>68</td>
<td>P-J; hepatic porto-jejunostomy.</td>
<td>$II_b$</td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>68</td>
<td>D-Y</td>
<td>Non-correctable (b)</td>
</tr>
</tbody>
</table>
| 5    | Female | 88  | 1) P-J with Witzel-type fistula  
2) Double-barreled jejunalostomy | Non-correctable (b) |
| 6    | Female | 87  | D-Y | Non-correctable (a) |
| 7    | Female | 73  | D-Y | Non-correctable (b) |
| 8    | Male   | 65  | D-Y | Non-correctable (a) |
| 9    | Female | 65  | D-Y | Non-correctable (b) |

D-Y; double-Y hepatic porto-jejunostomy with an external fistula.  
P-J: hepatic porto-jejunostomy.

TABLE 2. Autopsy findings of examined cases

<table>
<thead>
<tr>
<th>Case</th>
<th>Age at death (month)</th>
<th>Cause of death</th>
<th>Weight of liver (g)</th>
<th>Continuity of main intrahepatic bile duct</th>
<th>Bile lake</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>Panperitonitis due to anastomotic leak</td>
<td>450</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>2</td>
<td>8</td>
<td>Hepatic failure and postoperative electrolyte disturbance</td>
<td>400</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>Pulmonary edema and bleeding from digestive organ</td>
<td>350</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>4</td>
<td>7</td>
<td>Hepatic failure and liver cirrhosis</td>
<td>—</td>
<td>+</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>Hepatic failure and anastomotic leak</td>
<td>500</td>
<td>+</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>6</td>
<td>Panperitonitis due to intestinal perforation (strangulated ileus)</td>
<td>—</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>7</td>
<td>23</td>
<td>Hepatic failure and liver cirrhosis</td>
<td>610</td>
<td>—</td>
<td>+</td>
</tr>
<tr>
<td>8</td>
<td>5</td>
<td>Pulmonary bleeding and liver cirrhosis</td>
<td>400</td>
<td>+</td>
<td>—</td>
</tr>
<tr>
<td>9</td>
<td>10.5</td>
<td>Rupture of esophageal varix and liver cirrhosis</td>
<td>350</td>
<td>+</td>
<td>—</td>
</tr>
</tbody>
</table>

and fixed in 10% formalin. After fixation, the liver was cut into 2-3 mm thick serial slices with an electric ham slicer. In 8 cases, the liver was cut parallel to the inferior liver surface and was cut perpendicular to the inferior liver surface in other case (Case 6). These specimens of the liver were cut into an adequate size for embedding in paraffin or celloidin-paraffin. Serial sections of 4.5 μm in thickness were prepared from every blocks of Cases 3 and 4. In other cases, about 10 sections 6 μm in thickness were cut from each block. All sections were stained with hematoxyline and eosin or Goldner's stain combined with Weigert's stain for elastic fibers. After staining, all sections were projected on tracing paper under high magnification and the bile ducts and ductules were traced. The structure of the bile ducts and ductules was examined by means of graphic reconstruction.
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OBSERVATION

The structure and pattern of main intrahepatic bile ducts in biliary atresia were previously described by the authors (Chiba et al. 1975). The present concern is the pattern of continuity between intra- and extra-hepatic bile tracts. The observations were, therefore, focused on the exits of bile ducts through the porta hepatis.

*Type Ia* (Cases 1 and 2). This type was characterized by cystic dilatation of the common bile duct without communication with the duodenum. In Case 1, a part of both hepatic ducts was obliterated with bile plugs. Intrahepatic bile ducts were visualized by cholangiography with contrast medium injected into the gallbladder in Case 2. Histological sections of the tissue involving the porta hepatis demonstrated a few comparatively large bile ducts (over 1 mm in diameter) with lining of cylindrical epithelial cells on its inner surface (Fig. 1). These bile ducts seemed to be large enough in size to drain bile into the extrahepatic bile ducts. Case 1 had a few bile lakes around the intrahepatic bile duct at porta hepatis. These bile lakes were obliterated by bile mud and by granulation tissue containing inflammatory cells which is further surrounded by dense fibrous tissue (Fig. 2). No bile lakes were seen in Case 2.

*Type II* (Case 3). In Case 3, hepatic ducts were fibrous and measured $6 \times 8$ mm in diameter, while the common bile duct was replaced by fibrous string. Cholangiography through the dilated portion at the porta hepatis displayed the hepatic duct and the intrahepatic bile ducts but did not the common duct. The lumen, however, was not macroscopically identified on the section of the hepatic port at the operation. Histological examinations of the serial blocks of the liver revealed that the interlobular bile ducts were patent over the entire length. In the tissue involving the porta hepatis of this case, several small ducts were

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Fig. 1. Photomicrograph of bile ducts in the vicinity of porta hepatis in Case 2. A comparatively large bile duct is seen in this area, but small bile ducts and proliferated ducts were few in number.
observed along a few large ducts (Fig. 3). These large bile ducts had poorly developed elastic fibers and their epithelial layers were partly destroyed by inflammatory process. Fig. 4 shows the reconstruction of bile ducts at porta hepatis of this case. Many small ducts originating from some large bile ducts were seen in this case. Bile lakes were surrounded by fibrous tissue near the porta hepatis.

**Non-correctable type.** Cases 4 to 9 were classified as non-correctable type by their operative findings. In these cases, the basic findings of the bile ducts penetrating the porta hepatis were similar but modified frequently by postoperative bile passage, infection and other factors. Namely, 4 of 6 cases showed normal structure of the peripheral intrahepatic bile ducts, but there was no large bile duct in the vicinity of the porta hepatis where many small ducts were seen.
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Fig. 4. A graphic reconstruction of bile ducts in the vicinity of porta hepatis in Case 3. Many small bile ducts are separated from interlobular bile ducts.

Fig. 5. A graphic reconstruction of bile ducts in the vicinity of porta hepatis in Case 4. Many small bile ducts are separated from an interlobular bile duct.

These small bile ducts measured 20 to 400 microns in diameter. Detailed histologic examinations of the serial section of this portion revealed that these bile ducts were originating from one or two large lobular bile ducts which ended adjacent to the porta hepatis (Figs. 5 and 6). On the other hand, it had been exhibited by the previous study of extrahepatic bile ducts of biliary atresia that no large bile duct was found in the fibrous tissue replacing the common hepatic duct in almost all cases examined. Fig. 7 shows the fibrous mass surgically removed from the porta hepatis of Case 4 which contains many tiny bile ducts. These findings suggest that the small bile ducts originating from lobular bile ducts are extending in a short distance into the fibrous tissue out of the liver. In Case 6, the fibrous tissue including the porta hepatis had many bile ducts which were dilated enough to drain the bile to the reconstructed intestine (Fig. 8).

DISCUSSION

Several reports on the three-dimensional structure of the bile ducts in biliary atresia have appeared to date (Hanai et al. 1967; Oh-i et al. 1969; Ohkuma 1972; Landing et al. 1973; Chiba et al. 1975). Observation on the three-dimensional structure of bile ducts in this disease is particularly important in identifying the developmental process and secondary changes induced by certain exogenous factors such as operation and infection. In order to demonstrate the bile system, postmortalm cholangiography and resin-cast are practically impossible in non-correctable type of biliary atresia, and histological reconstruction is the only technique which meets the requirements. The following characteristics
Fig. 6. Photomicrographs of the liver in Case 4. These pictures show the changing aspects of a main bile duct. “a” was found about 9 mm apart from porta hepatis and “d” was seen at porta hepatis.

have been reported in biliary atresia: 1) The pattern of Hering’s ducts is almost normal (Landing et al. 1973, and 2) main interlobular bile ducts are patent along its entire course through the liver in the early stage (Oh-i et al. 1969; Chiba et al. 1975), intrahepatic bile ducts diminish their number with the lapse of time (Kasai 1974; Landing 1974), the process being called “disappearing bile duct syndrome” by Landing and his co-workers (1973), and 3) the proliferated ductules make a complicated network, forming a labyrinth, and isolated ductules are occasionally observed (Oh-i et al. 1969).

Histologic findings of the porta hepatis have been described by a number of
Fig. 7. Photomicrograph of fibrous mass obtained from porta hepatis at operation.

Fig. 8. Photomicrograph of bile ducts in the vicinity of porta hepatis in Case 6. The form of bile ducts of this area are similar to that of the other cases of non-correctable type. However, some ducts are dilated enough to allow bile passage. This picture shows dilated ducts.

authors from different viewpoints, including the problems on bile lake (Kitahara et al. 1974; Fonkalsrud and Arima 1975), bile containing lymphatic vessels (Kasai 1974; Saito and Ishida 1974) and scanty bile system on a cut surface of the liver (Kasai 1970). Kasai (1970; 1974) observed many small bile ducts as well as the dilated lymphatics in the fibrous tissue of the porta hepatis. However, a three-dimensional approach to the structure of intrahepatic bile ducts arround
the porta hepatis has not yet been attempted. The form and structure of bile ducts in the vicinity of the porta hepatis in this disease is necessary for detailed analysis of developmental and morphological changes.

The models of bile ducts at the porta hepatis were presented from histologic observations of microserial sections of the hilar region of the liver in 9 cases of biliary atresia as shown in Fig. 9. Two types of bile ducts in the region of porta hepatis were discriminated. One group of patients have bile ducts with a large lumen connected with the extrahepatic duct. This pattern was seen in two cases of correctable type of biliary atresia (Ia). The other pattern is made by many small bile ducts presumably originating from large lobular or segmental bile ducts. They usually measured less than 400 microns in diameter. The small bile ducts were lined by columnar epithelium. This pattern was observed in cases of non-correctable type of biliary atresia.

In Case 6, there were several large bile ducts associated with many small ones. These large bile ducts were probably produced by rapid growth of ducts due to active bile flow after operation, because visible bile ducts were not found at porta hepatis during operation. Cholangitis may also affect the histologic findings of bile ducts at the porta hepatis as in Case 3. These findings suggest that the patterns of bile ducts may be modified by some exogenous factors such as postoperative bile flow and ascending cholangitis.

Kasai (1974) classified the forms of extrahepatic bile ducts at the porta hepatis
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into correctable type and non-correctable type according to finding at operation. Microscopically, however, the behaviors of bile ducts in biliary atresia were more complicated. The summarized patterns are as follows. 1) Intrahepatic bile ducts are almost normal, except for the area involving the porta hepatis (Ohkuma 1972; Chiba et al. 1975), 2) two types of bile duct arrangement are observed in the tissue involving the porta hepatis, 3) small bile ducts are seen in the fibrous tissue of porta hepatis in many cases of non-correctable type, and 4) the forms of obstruction of extrahepatic bile ducts are various (Kasai 1974). In view of these complex anatomical findings, it is very important to assess the continuity among these bile ducts by stereographic analysis. Furthermore, we have still to examine the relations between the morphology of bile ducts and some morbid process in perinatal and intrauterine periods such as infection and circulatory disturbance, which may belong to pathogenic factors of biliary atresia.

References