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An Adult Case with Congenital Dilatation of Common Bile Duct

—A Study on the Relationship Between Bile Acids and the Cause of Congenital Biliary Dilatation—*)

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ABSTRACT

Although it has been hypothesized that congenital dilataion of the common bile duct is caused by the reflux of pancreatic juice into the choledochus, the etiology of this disease is not yet established. To determine whether bile acids have relations with the cause of congenital biliary dilatation or haven't, we analyzed the choledochal bile in a patient with congenital biliary dilatation. The results showed that the level of lithocholic acid, which has been said to cause bile-stasis was within normal range and that unknown bile acids were not detected in this patient. Therefore, it has been concluded that bile acids have no relations with the etiology of congenital biliary dilatation.

INTRODUCTION

In 1969, Babbitt[1] reported that the etiology of congenitial dilatation of the common bile duct was due to the reflux of pancreatic juice into common bile duct because of the anomalous arrangement of the pancreatico-biliary ducts.

This opinion has been accepted because it is frequent that many patients with congenital dilatation of the common bile duct have the above-described abnormality[10,11]. However, some cases have obviously abnormal pancreatico-choledocho-ductal junction without the common bile duct dilatation[9,19] and the cystic dilatation of the choledochal duct isn't produced in the animal experiments[12]. Thus, only the abnormality of pancreatico-choledocho-ductal junction cannot explain the etiology. Although the congenital factors hypothesized by Yotsuyanagi[20] and Glenn[3] have been recently reconsidered, the cause of this disease has not been established. The lithocholic acid and 3β-hydroxy-5-cholenic acid in primary biliary cirrhosis patients have been considered as important factors in the etiology of the biliary stasis, and close relationship between the biliary bile acid composition and hepato-biliary disorders has been suggested[7,13,14] very recently. In this study, biliary bile acids were analyzed in a patient with the congenital dilatation of the common bile duct accompanied by the anomalous arrangement of the pancreatico-biliary ducts, in order to clarify the relationship between bile acid composition and the etiology of this disease.

CASE REPORT

A previously healthy 27-year-old woman suddenly suffered from epigastralgia and rt-hypochondralgia in February, 1977. Then, she consulted a doctor, but the origin of the pain was not clear. She had been attacked by the same pain three times untill April in 1982, when she was suspected of the congenital biliary

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Table 1. Serum biochemical examination at admission

T-B	4.5 mg/dl	LAP	149 U/L
D-B	3.3 mg/dl	γ-GTP	218 U/L
GOT	589 U/L	ZnTT	5 units
GPT	1011 U/L	Se-Amylase	406 u nits
LDH	599 U/L	ICG(R)	9.3 %
Al-P	368 U/L	ICG(K)	0.165

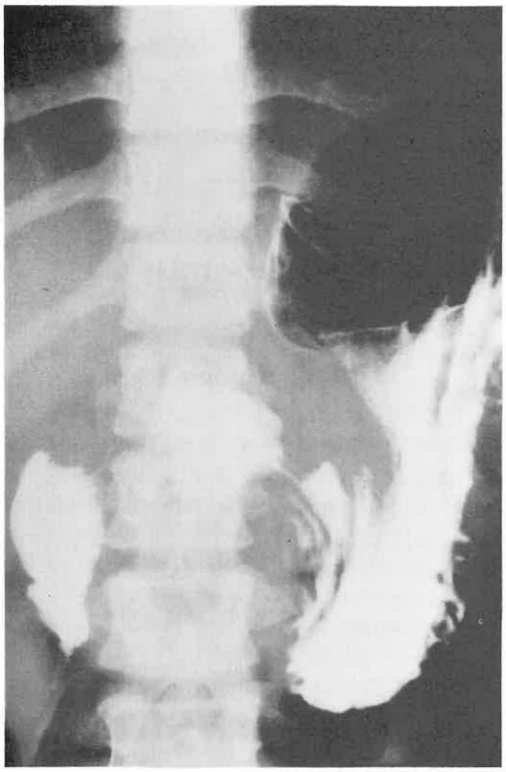

Fig. 1. Defect shadow on the antrum is seen in the gastrofluoroscopy

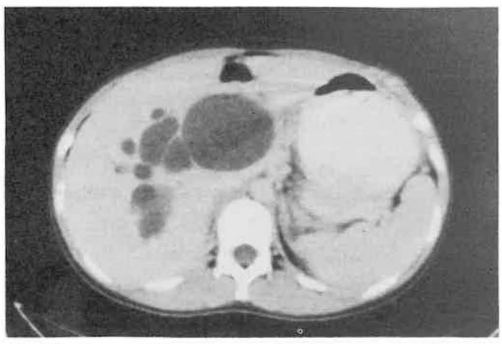

Fig. 2. The whole body computerized tomography shows dilatation of the common bile duct and intrahepatic ducts

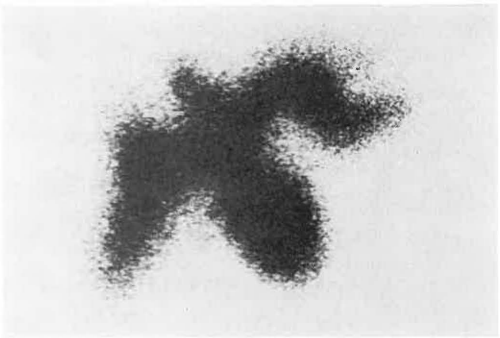

Fig.3. The scintigraphy of the biliary tree shows the cyst-like shape in the common bile duct.

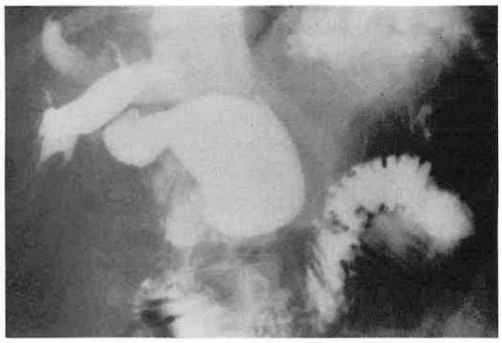

Fig. 4. Choledochal dilatation and anomalous arrangement of pancreatico-biliary duct on ERCP

dilatation from the results of cholangiography and ERCP in a certain hospital. She consulted our department for the operative treatment.

EXAMINATIONS: Laboratory data showed mild jaundice, high GOT, GPT, Al-p, LAP and γ-GTP values. Serum amylase level was 406 units (normal : 69–219) (Table 1). The antrum of the stomach was deformed by neighbouring lesion in the gastrofluoroscopy (Fig. 1). Intrahepatic ducts were remarkably dilated, and common bile duct showed the cyst-like shape in the whole body computerized tomography (Fig. 2). Any stones were not present in choledochal duct, intrahepatic duct and gallbladder. The scintigraphy of the biliary tree showed dilatation of intrahepatic and common bile duct (Fig. 3).

In ERCP, common bile duct was just like a cyst and showed anomalous arrangement of pancreatico-choledocho-junction (Fig. 4). At this point, this patient was confidently diagnosed of Alonso-Lej I type of congenital biliary dilatation with abnormal pancreatico-choledocho-junction.

OPERATION : After the improvement of the liver function, cholecystectomy and choledocho-jejunostomy were completed. Choledochal cyst and gallbladder didn't have either any stone or malignant change, but their walls showed serious inflammatory changes. The level of bile amylase aspirated from the choledochal cyst during the operation showed very high value, 10900 units.

ANALYSIS OF BILIARY STEROLS

METHODS: Biliary sterols of the contents of choledochal cyst and gallbladder were analyzed. Bile acids and choleserol were quantitated by gas-liquid-chromatography (GLC) as previously described[4]. Phospholipid quantitation was carried out by enzymatic method[16].

RESULTS: Very small amounts of unusual bile acids were found in GLC with 3%OV-17 column, the retention times of which were 26. 49 minutes and 30. 16 minutes respectively (Fig. 5). They were tentatively identified as 7-ketolithocholic acid and 7-ketodeoxycholic acid from the relative retention time and authentic samples. Analyzed bile acid composition was shown in Table 2. Any difference in the bile acid composition wasn't found between the contents of choledochal cyst and gallbladder. Table 3 shows the molar concentration and percentage of bile acids, cholesterol and phospholipids. The concentration of cholesterol and phospholipids was higher in gallbladder contents than in choledochal cyst contents, but the concentration of bile acids was reverse. Lithogenic index by Thomas and Hofmann[18] was 0. 97 in choledochal bile, 1. 30 in gallbladder bile, respectively (Table 3).

DISCUSSION

The role of bile acids on congenital dilatation of the common bile duct is unclear. Since it

Table 2. Bile acids analysis

	choledochal cyst	gallbladder
CA	56.8%	57.8%
CDC	38.3%	39.4%
DC	2.3%	2.8%
LC	0.7%	—
7-Keto	1.9%	—

CA : cholic acid
CDC : chenodeoxycholic acid
DC : deoxycholic acid
LC : lithochlic acid
7-Keto : 7-ketodeoxycholic acid+7-ketolithocholic acid

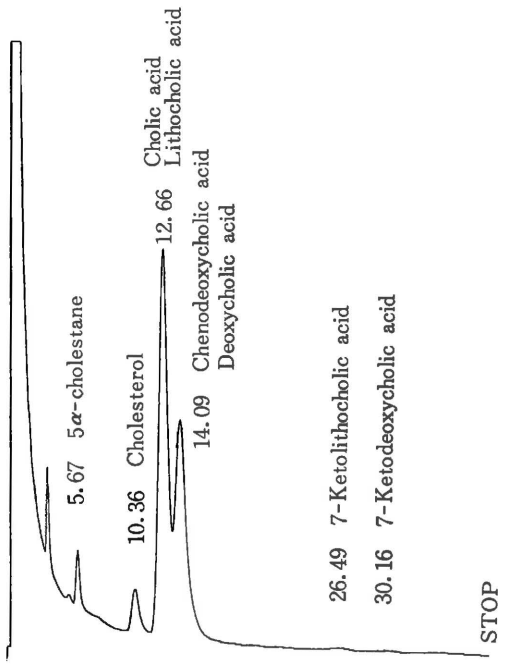

Fig. 5. Bile acids analysis in the choledochal cyst on GLC with ov-17(270°C), TMSi

Table 3. Biliary lipids analysis

	choledochal cyst	gallbladder
Bile acids	24.716 mmol/L 91.094 mol%	6.143 mmol/L 68.164 mol%
Phospholipids	0.825 mmol/L 3.040 mol%	1.713 mmol/L 19.007 mol%
Cholesterol	1.592 mmol/L 5.866 mol%	1.156 mmol/L 12.829 mol%
Lithogenic index[18]	0.97	1.30

has been suggested that lithocholic acid and 3β-hydroxy-5-cholenic acid are intensively related to some of hepatobiliary diseases[7,13,14], the relationship between this disease and bile acids should be investigated. Therefore, the bile acids in a patient with common bile duct dilatation were examined in this study. 7-keto-lithocholic acid and 7-ketodeoxycholic acid were found even in low amounts as unusual bile acids in this patient. The pathological significance of them is still unknown. It is considered that they are not initiators in this disease because keto-bile acids are present in some of other hepato-biliary diseases[2,5,15].

In the composition of bile acids, about 39% of total bile acids was occupied by chenodeoxycholic acid. This is a almost same number as in Japanese average[6]. But in this patient, the percentage of cholic acid in total bile acids was higher, compared to Japanese average[6] (about 57% in this patient vs. 50% in Japanese average). On the other hand, deoxycholic acid was lower than Japanese average[6] (about 3% in this patient vs. 13% in Japanese average). This means that very little bile acids are excreted to duodenum in this patient, that is to say, the stasis of the choledochal bile and gallbladder bile. Because cholic acid is dehydroxylated to deoxycholic acid by the intestinal bacteria. The percentage of lithochnlic acid is considered to be an important factor for bile stasis[7,13,14], was very low in this patient (0.7% vs. 2% in Japanese normals[6]).

Therefore, it has been concluded that the cause of congenital dilatation of the common bile duct has no relations to bile acids, for unknown bile acids were not detected and lithocholic acid was within normal level.

Tanimura[17] reported that the patients with choledochal cyst frequently complicated cholelithiasis. There was no complication of gallstones in this case, but it was found that this patients is in precondition to form cholesterol gallstones from the aspect of lithogenic index of gallbladder bile (LI=1.30). So, to be interested, it was predicted that this patient has much more possibility to develop in forming cholesterol gallstones, although it has been described[8,17] the type of the gallstones complicated in congenital dilatation of the common bile duct was pigment one.

REFERENCES

1. **Babbitt, D. P.** 1969. Congenital choledochal cysts. new etiological concept based on anomalous relationships of common bile duct and pancreatic bulb. Ann. Radiol. **12** : 231-240.
2. **Brown, E.** 1963. Evidence for a ketonic acid in human bile. J. Lab. Clin. Med. **61** : 629-632.
3. **Glenn, F. and Mcsherry, D. K.** 1973. Congenital segmental cystic dilatation of the biliary ductal system. Ann. Surg. **177** : 705-713.
4. **Harada, M., Kodama, M., Ezaki, H. et al.** 1982. Bile acid dynamics after relief of biliary obstruction. J. Hiroshima Med. Ass. **35** : 910-915.
5. **Hoshita, T., Yashima, H., Okada, S. et al.** 1968. Stero-bile acids and bile alcohols. Isolation of 3α, 7α-dihydroxy-12-oxo-5β-cholanoic acid from the bile of patients with hepatobiliary diseases. Hiroshima J. Med. Sci. **17** : 105-113.
6. **Izumi, K.** 1965. Studies on the chemical composition of gall bladder bile and gallstone; especially on the difference between cholesterol stone and pigment stone. Fukuoka Acta. med. **56** : 488-523.
7. **Javitt, N. B. and Emerman, S.** 1968. Effect of sodium taurolithocholate on bile flow and bile acid excretion. J. Clin. Invest. **47** : 1002-1004.
8. **Komi, N. and Udaka, H.** 1982. Congenital biliary dilatation; composition between pediatric cases and adult cases. The biliary tract and Pancreas **3** : 327-332.
9. **Konishi, T., Nagakawa, T., Jinno, M. et al.** 1981. Four cases of anomalous arrangement of pancreaticobiliary duct associated with gallbladder cancer. The biliary tract and Pancreas **2** : 435-442.
10. **Nakazawa, S., Naitho, Y., Kimoto, A. et al.** 1982. Problems in difinition of congenital dilatation of the common bile duct. The biliary tract and Pancreas **3** : 305-313.
11. **Oi, I. and Hara, T.** 1977. Abnormal connection between the choledochus and the pancreatic duct in case of congenital choledochal cyst examined by endoscopic pancreatico cholangiography. Jap. J. Pediat. Surg. **9** : 1121-1129.
12. **Ohkawa, H., Sawaguchi, S., Yamazaki, Y. et al.** 1981. Research on animal models of the anomalous pancreatico-biliary ductal union. J. Jpn. Soc. Pediat. Surg. **17** : 13-21.
13. **Palmer, R. H.** 1972. Bile acids, liver injury, and liver disease. Arch. Intern. Med. **130** : 606-617.
14. **Schaffner, F. and Popper, H.** 1969. Cholestasis is the result of hypoactive hypertrophic smooth endoplasmic reticulum in the hepatocyte. Lancet **2** : 355-359.
15. **Shimazutsu, S.** 1974. Basic and clinical studies on bile acids iff the human bile. Hiroshima J. Med. Sci. **22** : 477-496.
16. **Takayama, M., Itho, S., Nagasaki, T. et al.** 1977. A new enzymatic method for determination

of serum choline-containing phospholipids. Clin. Chim. Acta **79** : 93-98.

17. **Tanimura, H., Takahashi. Y., Mukaibara, S. et al.** 1982. Incidence of gallstone in the dilated bile duct. The biliary tract and Pancreas. **3** : 343-350.
18. **Thomas, P. J. and Hofmann, A. F.** 1973. A simple calculation of the lithogenic index of bile. Expressing biliary lipid composition on rectangular coordinates. Gastroenterology **65** : 698-700.
19. **Uchimura, M., Mutho, Y., Waki, S. et al.** 1982. Association of carcinoma with congenital dilatation of the bile duct. The biliary tract and Pancreas. **3** : 333-342.
20. **Yotsuyanagi, S.** 1936. Contributions to the aetiology and pathology of idiopathic cystic dilatation of the common bile-duct with report of these cases, a new aetiological theory based supposed unequal epitherial proliferation at the stage of the physical epitherial occulusion of the primitive choledochus. Gann **30** : 601-605.