Supplementary (2) Serum Lipids and the Pattern of Lipoproteins in Cholelithiasis and Their Relation to the Compositional Change of Bile and Bile Acids

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Serum lipids and the pattern of lipoproteins were estimated in patients with gallstones and the relation of hyper or normolipidemic state to the abnormality in composition of bile and bile acids in bile was investigated.

There were no differences in serum concentration of cholesterol between cholelithiasis and healthy controls both for males (201 ± 29 vs 197 ± 28 mg/dl) and females (217 ± 49 vs 210 ± 55). However, the serum concentration of triglycerides was significantly higher in patients with gallstones than in controls, especially for male subjects (157 ± 73 vs 111 ± 47 mg/dl, $P < 0.05$). The frequency of the cases with triglyceride level higher than 200 mg/dl was 31% for males (vs 8% of the control) and 17% for females (vs less than 1% of the control).

The lipoproteins were separated into α and ($\beta + \text{pre } \beta$) fractions by heparin-manganese ion precipitation method. Distribution pattern of serum lipoproteins was also determined by cellulose acetate membrane electrophoresis. The serum concentration of cholesterol in ($\beta + \text{pre } \beta$)-fraction was almost the same for the patients and the control subjects, while the concentration of cholesterol in α -fraction was significantly decreased in patients with gallstones both for males (33 ± 11 vs 49 ± 12 mg/dl) and females (45 ± 13 vs 62 ± 18). The distribution ratio, $\beta + \text{pre } \beta / \alpha$, of cholesterol was markedly increased in cholelithiasis, compared with the control subjects who had the same level of total serum cholesterol. An abnormality in lipoprotein metabolism was strongly suspected in cholelithiasis even if the serum lipid concentration was in nor-

mal range.

Analysis of lipids and lipoproteins on 42 patients (16 males and 26 females) showed the appearance of hyperlipidemia and allied disorders in 45% (8 males and 11 females), including 4 cases of Type IIa, 4 cases of Type IIa', 2 cases of Type IIb and 9 cases of Type IV. Type IIa' is referred to the lipoprotein abnormality which shows an elevation of the distribution ratio of cholesterol, $\beta + \text{pre } \beta / \alpha$, with the total cholesterol level being in normal range.

Bile was collected through a duodenal tube after an overnight fast and the composition of bile was analyzed for cholesterol, phospholipids and bile acids. Composition of bile acids in bile was also determined on GLC.

The patients were divided into a) hypertriglyceridemics with serum triglyceride concentration no less than 200 mg/dl and b) normotriglyceridemics. There was a significant decrease in the ratio of bile acids to cholesterol in normotriglyceridemics (6.43 ± 1.70 vs 12.10 ± 1.35 of the control), while the ratio was not significantly decreased in hyperlipidemic patients (9.56 ± 3.01) with a half of the cases remaining in normal range.

The bile acid composition was compared for the patients with hypertriglyceridemia who had a normal ratio of bile acid to cholesterol in bile (Group I), the patients with hypertriglyceridemia who showed a decrease in the ratio of bile acids to cholesterol (Group II), and the patients with normotriglyceridemia (Group III). The percentage of cholic acid plus deoxycholic acid in total bile acids in bile was significantly higher in Group I compared with Group II

and III (73.0 ± 5.1 for Group I vs 58.4 ± 8.9 for II, and $54.1 \pm 15.2\%$ for III, $P < 0.02$). The data show that the synthesis of cholic acid was increased in hypertriglyceridemics, so that the relative concentration of total bile acids in bile was kept in normal range. The present results are in good agreement with the results of Einarsson et al (J Clin

Invest 54: 1301, 1974), which showed an increased pool size of cholic acid in hypertriglyceridemia. The cause of the frequent occurrence of cholelithiasis in Type IV hyperlipidemia (European type of cholelithiasis) must be different from the mechanism working for normotriglyceridemic patients (American Indian type cholelithiasis).

(7) Hepatolithiasis—Clinical Findings and Cholangiographic Features

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By using percutaneous transhepatic cholangiography (PTC) and endoscopic retrograde cholangiography (ERC) in practice, hepatolithiasis has been exactly diagnosed without surgical help. Surgical procedures have not yet shown a sufficient effectiveness to cure the disease.

Clinical features and pathogenesis of hepatolithiasis have been studied on the basis of cholangiographic findings by PTC and ERC.

Gross findings of hepatic calculi and their chemical composition

All hepatic calculi of 14 patients showed a brown coloured amorphous structure. They belonged to pigment- calcium stones from chemical composition.

Incidence of hepatolithiasis

Hepatic calculi were found by cholangiography in 5.5% of the patients of gallstone diseases. When the patients previously underwent cholecystectomy were excluded from the group, the rate of incidence became 3.2%.

Clinical symptoms and laboratory findings

Fever and jaundice in hepatolithiasis appeared more frequently and intensively than those in cholecystolithiasis and choledo-

cholithiasis. Disturbed liver function and inflammatory findings were also evidenced more frequently by various clinical laboratory examinations.

Clinical features of hepatolithiasis

(1) Causes of postcholecystectomy symptoms

Hepatic calculi were found in a high incidence, 21.5% of the patients with postcholecystectomy symptoms who underwent roentgenologic examinations by PTC and ERC.

(2) Mortality due to gallstone disease

Mortality rate of hepatolithiasis was 23.5% and far higher than 0.3% of cholecystolithiasis and 2.2% of choledocholithiasis.

(3) Repeated surgical procedures of the biliary system

Most of the mortal patients due to hepatolithiasis had undergone repeated surgical laparotomies of the biliary system before the death.

Classification of hepatolithiasis

According to cholangiographic findings by PTC and ERC, hepatolithiasis is divided into two types, primary and secondary (Figs. 1 and 2).

The primary type of hepatolithiasis has a saccular or cylindrical segmental dilatation of main intrahepatic bile ducts where