Panel Discussion: (IV) Cholestasis

1. FROM THE ASPECT OF INTERNAL MEDICINE

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It is utmost importance to differentiate the character of jaundice accurately in an early stage, pertaining to the treatment and prognosis of jaundiced patients. From the aspects of clinical signs, liver function tests and peritoneoscopy, studies were made on the difference between hepatocellular jaundice such as hepatitis or liver cirrhosis and extrahepatic obstructive jaundice as caused by carcinoma of head region of the pancreas, and carcinoma or calculosis of the bile duct. The possible alteration of the liver induced by extrahepatic obstruction of the bile duct and the factors contributing to the establishment of such alteration were also discussed.

Incidence of Patients with Jaundice

Number of patients admitted to the First Department of Internal Medicine of Kanazawa University Hospital during the period of 5 years from January, 1961 to December, 1965 was 2,302 in total. Among these, 416 (18.1%) had certain disorders in the liver or in the bile duct. In 227 out of these 416 (54.6%), jaundice was observed with icterus index of more than 11. Extrahepatic obstructive jaundice was encountered in 67 patients; calculosis of the bile duct 20, pancreatic carcinoma 17, carcinoma of the bile duct 10, carcinoma of the gall-bladder 6, primary carcinoma of the liver associated with cirrhosis 2, metastatic carcinoma of the liver 4, carcinoma of the papilla of Vater 3 and miscellaneous 5. On the other hand, intrahepatic obstructive jaundice due to cholangiolitic hepatitis was observed in only 2, obviously being less compared with extrahepatic one. Hepatocellular jaundice was observed in 119 cases; acute hepatitis 69, chronic hepatitis 12 and liver cirrhosis without hepatoma 38. Thirteen cases of primary carcinoma of the liver (with cirrhosis 12 and without cirrhosis 1) and 9 cases of metastatic carcinoma of the liver were equivocal to determine whether jaundice was of obstructive nature due to intrahepatic obstruction by carcinoma, of hepatocellular one due to insufficiency of liver cell function, or of others. Jaundice caused by other origins was seen in 17 cases. Since the number of cases with intrahepatic obstructive jaundice was very small, discussion was made mainly on extrahepatic obstructive jaundice in this paper comparing with hepatocellular jaundice.

Clinical Pictures

In 20 cases with extrahepatic obstructive jaundice due to stone in the bile duct frequent initial symptoms were fever (48.1%), jaundice (44.4%), abdominal pain (44.4%) and pain in the back (29.6%). When extrahepatic obstructive jaundice was due to carcinoma of the pancreas, the bile duct, the gall-bladder and the papilla of Vater, and primary and metastatic carcinoma of the liver, principal onset symptoms of 42 cases were jaundice (46.6%), anorexia (30.2%) and strongly stained urine (27.9%). In 119 cases with hepatocellular jaundice as seen in hepatitis and liver cirrhosis, onset symptoms were jaundice (64.5%), fatigue (57.9%), anorexia (36.1%) and fever (28.5%). Accordingly, it is often difficult to distinguish extrahepatic obstructive jaundice from hepatocellular one at an early stage of the disease solely on clinical symptoms.

In extrahepatic obstructive jaundice due to carcinoma of the bile duct and head region of the pancreas, mean values* of icterus index, alkaline phosphatase activity (Bessey-Lowry) and cholesterol level in the serum were 108.5±15.9 units (32 cases), 19.3±5.3 units (29 cases) and 245.2±30.8 mg/dl (25 cases), respectively, while in extrahepatic obstructive jaundice due to stone 40.0±11.9 units (23 cases), 9.8±4.9 units (20 cases) and 191.6±20.4 mg/dl (17 cases), respectively. Therefore, these values were higher in extrahepatic obstructive jaundice due to carcinoma than in the one due to stone, revealing a significant statistic difference (p>0.05). Ratio of icterus index to alkaline phosphatase activity (MG/Al–P) was 16.6±3.6 in 46 cases of hepatocellular jaundice.

* All mean values in this paper were expressed as confidence limits of 95%.
jaundice, and 8.6±2.0 in 32 cases of extrahepatic obstructive jaundice. The difference between both groups was significant (p<0.05). Ratio of SGO-T activity to alkaline phosphatase activity (SGO-T/A1-P) was lowered frequently below 7 in extrahepatic obstructive jaundice, while in hepatocellular jaundice it frequently exceeded beyond 12. The mean values of SGO-T/A1-P were 37.8±13.3 in 44 cases of hepatocellular jaundice and 7.0±3.0 in 30 cases of extrahepatic obstructive jaundice, respectively. The difference was also statistically significant (p<0.05). Hence, these ratios can be assumed to be useful indicators in making differential diagnosis of jaundice of the two types (Fig. 1).

Fig. 1. MG/A1-P & SGO-T/A1-P in Hepatocellular & Extrahepatic Obstructive Jaundice

Liver cirrhosis is known to be often associated with jaundice and this type of jaundice is generally ascribed to insufficiency of liver cell function, compression upon the intrahepatic bile ducts or ductules by regenerative nodules and others. However, besides above-mentioned factors, it should be carefully taken into consideration that a possible cause of this jaundice might be due to hepatoma developing in the course of liver cirrhosis because in our country a concomitant development of hepatoma with cirrhosis is fairly frequent. In this series, 15 cases of cirrhosis were encountered in which jaundice was ascribed to complication of hepatoma. In two of these 15 cases, jaundice was ascertained to be of obstructive nature due to compression of hepatic bile ducts by carcinoma at the liver hilum, although in the remains, as mentioned already, the cause of jaundice could not be determined. In case of liver cirrhosis associated with hepatoma, both icterus index and alkaline phosphatase activity in the serum continued to increase in parallel with the progress of the disease, compared with the cases with liver cirrhosis alone, but it was often difficult to distinguish liver cirrhosis with and without hepatoma solely from the results of routine liver function tests. Therefore, we suppose that in case of liver cirrhosis showing jaundice, it is indispensable to carry out hepatic scintillation scanning using radio-isotope and/or peritoneoscopic examination.

Accuracy of Clinical Diagnosis

It is extremely important to diagnose and to treat extrahepatic obstructive jaundice in its early stage. Therefore, in order to know to what extent an accurate diagnosis can be made clinically, rate of accuracy in clinical diagnosis was studied in 52 cases of obstructive jaundice (carcinoma of head region of the pancreas 17, carcinoma except head region of the pancreas 24, calculosis of the bile duct 9 and intrahepatic obstructive jaundice due to cholangiolitic hepatitis 2), in which diagnosis was ascertained by laparotomy and/or autopsy (Fig. 2). Time