

A Study on Relationship between Hepatic Histopathological Changes and Data of Preoperative Liver Function Tests in 151 Patients with Gallstone Disease^{*)}

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ABSTRACT

The relationship between histopathology of liver and preoperative liver functional data was studied in 151 cases with cholelithiasis to clarify how gallstones effect on the hepatic tissues. The results were as follows. 1. Histologically, 80% of all the cases showed hepatic inflammation. 2. The group with cholecystolithiasis had the highest frequency of hepatic parenchymatous changes. 3. The data of liver functions in the group with cholecystolithiasis were found to be almost within normal limits. Conversely, hepatolithiasis group showed to be moderate to severe disorder. 4. Although both groups with stasis and cirrhosis had hepatic functional disorder, the former showed to be moderate to severe, the latter to be normal to mild, in the magnitude of liver functional disorder. As a conclusion, the grade of liver functional disorder in cholelithiasis patients depends upon that of biliary stasis.

INTRODUCTION

Gallstone disease is frequently concomitant of liver disorders which are serious troubles from the therapeutic viewpoint. The grade of liver disorders before the operation greatly affects the prognosis of gallstone diseases. Nowadays it is well accepted that the operation of gallstone disease should be done after the improvement of liver disorder. Therefore, it is important to grasp the preoperative state of liver in a surgical treatment of gallstone disease. Liver disorders accompanied with gallstone disease are separated into two groups. One is a liver damage originated from the result of gallstones. Another is a liver disease supposed to be a cause of gallstone disease, for example, liver cirrhosis is reported¹⁾ to be apt to lead to gallstone disease. In clinical cases, although it is impossible to discriminate them as described above, liver disorders with gallstones are assumed to be mainly composed of the former, that is, the result of gallstone disease. Liver

function tests are made to decide when the operation for gallstone disease should be performed. However, it is uncertain how exactly the routine liver functional data indicate the affected condition of the whole liver. In addition to the routine liver function tests, a histopathological examination of liver would reveal the state of liver more exactly. However, preoperative liver biopsy is inadequate as a routine examination. So it is significant to know how the data of routine liver function tests reflect the hepatic histopathology. The aim of this paper is to study the histopathology by liver wedge biopsy in 151 cases with cholelithiasis and to clarify how gallstones affect liver tissue and how the data of routine liver function tests correlate with the hepatic histopathological change.

CLINICAL MATERIALS AND METHODS

Three hundred and fifty-one patients had undergone the elective cholecystectomy or lithotomy in common bile duct and intrahepatic

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duct for gallstone diseases from 1973 to 1982 in the 2nd Department of Surgery, Hiroshima University Hospital. In 151 patients with historical liver diseases or preoperative abnormality in liver function tests among 351 patients, intraoperative liver wedge biopsies were performed to study hepatic pathology. In location of gallstones, 98 patients (65%) had cholecystolithiasis. Forty-seven patients (31%) had choledocholithiasis. The number of hepatolithiasis was 6 patients (4%). Choledocholithiasis group contained the cases with stones in gallbladder. Hepatolithiasis group included the cases with stones in gallbladder and/or common bile duct (Table 1).

Table 1. Clinical materials with liver biopsies

Location of stone	Number
Cholecystolithiasis	98(65%)
Choledocholithiasis	47(31%)
Hepatolithiasis	6(4%)
Total	151(100%)

Microscopic examinations were evaluated for the presence or absence of lymphocytic infiltration or polymorphonuclear infiltration, bile retention in bile duct, fatty metamorphosis, and cirrhosis. These results were classified into 6 groups on the basis of the histological changes as follows.

1. Normal liver histology: There were al-

most normal or slight changes accompanied with wedge biopsies.

2. Chronic inflammatory change: These biopsies had infiltration of lymphocytes or plasma cells in the portal triads.
3. Acute inflammatory change: These biopsies had infiltration of polymorphonuclear leukocytes in the portal triads.
4. Stasis: There was bile retention in the bile duct.
5. Fatty change: Fatty metamorphosis or fatty liver were present.
6. Cirrhosis: These biopsies had degeneration or necrosis of hepatocytes fibrosis, nodular hepatic regeneration, and rearrangement of hepatic nodules.

The magnitude of liver functional disorders was divided into mildly, moderately and seriously disturbed groups by results of the routine liver function tests as shown in Table 2.

RESULTS

One hundred and ten (73%) out of 151 cases with liver biopsies had some histological changes in liver tissue. Histological changes in liver were shown in all the cases with hepatolithiasis. The group with cholecystolithiasis revealed the lowest percentage (66%) in the histological changes among the three groups (Table 3). In all histopathological changes, infiltration of inflammatory cells in the portal triads was a major change. Parenchymatous changes such as fatty change and cirrhosis

Table 2. Criteria of liver disorder

	Mild disorder	Moderate disorder	Severe disorder
TB (mg/dl)	1.5-1.9	2.0-5.0	5.1 ↑
GOT (U/l)	50-99	100-200	201 ↑
GPT (U/l)	50-99	100-200	201 ↑
Alb (g/dl)	3.7-3.5	3.4-3.0	2.9 ↓
Ch-E (U/l)	2999-2501	2500-2000	1999 ↓

Table 3. Percentage of histological changes by liver biopsies

	No. of cases	No. of cases with histological changes
Cholecystolithiasis	98	65(66%)
Choledocholithiasis	47	39(83%)
Hepatolithiasis	6	6(100%)
Total	151	110(73%)

Table 4. Hepatic histopathology by liver biopsies

	No. of cases	Chronic inflammatory change	Acute inflammatory change	Stasis	Fatty change	Cirrhosis
Cholecystolithiasis	65	55.4%	19.3%	3.6%	13.3%	8.4%
Choledocholithiasis	39	57.6%	23.7%	10.2%	6.8%	1.7%
Hepatalithiasis	6	37.5%	37.5%	12.5%	12.5%	0%
Total	110	55.3%	22.0%	6.7%	10.7%	5.3%

Table 5. Results of liver function tests in the cases with liver biopsies

	No. of cases	Normal	Mild disorder	Moderate disorder	Severe disorder
Cholecystolithiasis	98	81(82.6%)	4(4.1%)	9(9.2%)	4(4.1%)
Choledocholithiasis	47	23(48.9%)	4(8.5%)	7(14.9%)	13(27.7%)
Hepatalithiasis	6	0(0%)	2(33.3%)	3(50.0%)	1(16.7%)
Total	151	104(68.9%)	10(6.6%)	19(12.6%)	18(11.9%)

were found more frequently in liver tissues with cholecystolithiasis as compared with choledocholithiasis and hepatalithiasis (Table 4).

One hundred and four (69%) out of 151 cases with intraoperative liver wedge biopsies had normal values in the routine liver function tests. Most of the cases with cholecystolithiasis showed normal data in liver function tests. However, 13 (28%) of 47 cases with choledocholithiasis showed severe functional disorders, although the results of liver function tests in half of choledocholithiasis were within normal limits. Hepatalithiasis group accompanied mild and moderate functional disorders in the major parts (Table 5).

In a relationship between histological changes and liver function, although most of the cases with normal finding in hepatic histology had normal liver functional data, more than half of the cases with abnormal hepatic histology

Table 6. Relationship between histological changes and liver function

		Liver functional data	
		Normal	Abnormal
Hepatic histology	Abnormal findings	65(43.1%)	45(29.8%)
	Normal findings	39(25.8%)	2(1.3%)
	Total	104(68.9%)	47(31.1%)

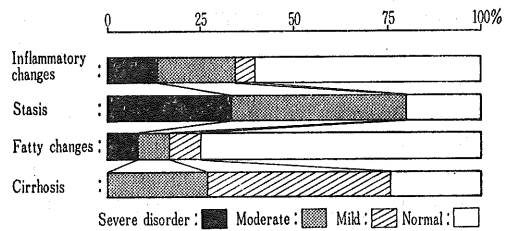


Figure: Grade of liver disorders in each histological change

showed normal functional data (Table 6).

The Figure shows the proportion of liver functional disorder in each histopathological change. Almost all of the cases with inflammatory or fatty change in hepatic histology demonstrated normal liver functional data. Although most of the cases with cirrhosis had normal or mild liver disorder, liver function in the stasis group was moderately or seriously disturbed.

DISCUSSION

In this study, about 80% of all the cases histologically showed hepatic inflammation. Other investigators likewise reported^{3,6)} to be predominant changes in gallstone diseases. Among the groups with cholecystolithiasis, choledocholithiasis and hepatalithiasis, there was no difference in the ratio of patients with positive inflammatory change. However, the percentage of acute inflammatory change showed the high-

est frequency in the group with hepatolithiasis. This may suggest that impairment of bile flow is responsible for the acute hepatic inflammatory changes. Interestingly, in the group with cholecystolithiasis the percentage of parenchymatous changes such as fatty change and cirrhosis was higher than in choledocholithiasis and hepatolithiasis groups. Parenchymatous changes in cholecystolithiasis may be relevant to the etiology of gallstone to some extent.

Abnormal values of liver function tests in gallstone diseases were showed in all the cases with hepatolithiasis. Furthermore, the magnitude of liver disorders in hepatolithiasis group were found to be moderate to severe disorder, whereas in the group with cholecystolithiasis liver functional data were almost within normal limits. These results imply that the grade of liver disorders demonstrated by data of liver function tests depends upon the impairment of bile flow by gallstones. This is supported by the result that stasis of bile is sensitively reflected in liver function tests as shown in the Figure.

Most of the cases with normal finding in hepatic histology showed normal liver functional data. However, all the cases with abnormal finding were not always found to be abnormal liver functional values (Table 6). A discrepancy between histological changes and liver function was found in this study. In our previous report⁴⁾, we described the difficulty in differentiating liver diseases only by liver function tests. In many other papers^{2,5,7,8)}, it was reported that biochemical investigations were not useful in predicting histological appearance of liver tissue. In any case, there is either overestimation of histopathological examination in liver biopsies or underestimation of liver function tests in relationship between hepatic histology and functional tests. In hepatic histopathological changes, since the groups with inflammatory or fatty change in liver almost showed normal or mild

disturbed liver function, they might be overestimated in histopathological examination. In the same way, the cases with stasis in hepatic histopathology might be underestimated in liver function tests. In the future, it should be necessary to study which examination out of liver function tests accurately represents hepatic histopathological change on the development of successful surgical treatment in gallstone diseases.

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