Biopsy of the Tissue of the Liver

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Since Iversen and Roholm¹⁾ introduced needle biopsy technique to clinical medicine, histologic examination of the liver obtained by biopsy has been regarded as one of the most important procedures to make diagnosis and estimate prognosis of the liver diseases. However, the histologic diagnosis on the liver specimen obtained by biopsy are not infrequently controversial as yet. Beside this problem, needle biopsy technique has diagnostic limitation in cases of circumscribed liver diseases and in some cases of cirrhosis because of the tiny specimen obtained. Furthermore, clinical application of biopsy technique occasionally reveals discrepancy between histologic changes of the liver and liver function tests.

Observation was made to clarify these problems such as differential diagnosis, correlation between histologic changes and liver function tests, limitation of biopsy technique and incidence of liver diseases in Japan, based on histologic examination of 1,600 biopsy specimens obtained since 1952.

I. Differential diagnosis

To make differential diagnosis between extrahepatic biliary obstruction and intrahepatic cholestasis, 29 cholestatic cases with total serum bilirubin of over 15 mg./dl. were studied (Table 1). Dilatation of bile duct lumen and cholangitic abscess were characteristic for extrahepatic biliary obstruction. Feathery degeneration and bile infarcts were mainly found in this condition, whereas hepatocellular degeneration such as acidophilic bodies, balloon cells, and Kupffer cell mobilization were prominent in intrahepatic cholestasis. Regarding the histologic features of intrahepatic cholestasis caused by virus and drugs, single cell necrosis, acidophilic bodies, Kupffer cell mobilization, mononuclear infiltration and fibroblastic proliferation in the portal tracts were much more frequently encountered in viral cases.

Persisting inflammation in the portal tracts associated with Kupffer cell mobilization was regarded as a morphologic characteristic of chronic hepatitis of both inactive and active types²⁾. In chronic inactive hepatitis, portal inflammation showed nodular accumulation of inflammatory cells but no perivascular infiltration. On the contrary, chronic active hepatitis was characterized by fibrosis, occasionally resulting in fibrous linkage with the adjacent portal tracts. Inflammatory cells around the vessels and ductular proliferation were prominent. In advanced cases of chronic active hepatitis

Table 1

**Histologic Features in Extrahepatic Biliary
Obstruction and Intrahepatic Cholestasis**
(29 cases with total serum bilirubin of over 15^{mg}/dl)

Histologic features	Extrahepatic biliary obstruction (12 cases)	Intrahepatic cholestasis	
		Viral hepatitis (10 cases)	Drug- induced (7 cases)
<u>Portal tracts:</u>			
Inflammation	+ 4	+ 4	+ 4
Neutrophiles	+ 4	+ 3	+ 3
Mononuclears	±	+ 4	+ 1
Eosinophiles	±	+ 2	+ 3
Cholangitic abscess	+ 1	0	0
Fibroblastic proliferation	+ 4	+ 2	±
<u>Interlobular bile ducts:</u>			
Bile thrombi	+ 2	+ 1	0
Luminal dilatation	+ 3	±	0
Periductal lamination	+ 4	0	+ 1
Ductular proliferation	+ 3	+ 3	+ 4
<u>Hepatic cells:</u>			
Pleomorphism	±	+ 3	+ 3
Balloon cell	+ 1	+ 2	+ 3
Single cell necrosis	+ 1	+ 3	±
Acidophilic bodies	0	+ 3	+ 1
Multiple nuclei	±	+ 3	+ 1
Kupffer cell mobilization	+ 1	+ 3	+ 1
Central vein inflammation	+ 1	+ 3	+ 2
Feathery degeneration	+ 3	+ 1	±
Bile infarcts	+ 2	0	0

+ 4: Over 90% of cases + 1: 10 ~ 39% of cases
+ 3: 60 ~ 89% ± : below 10%
+ 2: 40 ~ 59%

lobular disorganization and so-called collapse fissures were detectable. Though these features may represent pre-cirrhotic changes, they should be strictly differentiated from cirrhosis, in which complete pseudolobulation and nodular hyperplasia are found throughout the liver.

II. Correlation between histologic changes and liver function tests

Twenty-two to 29.3 percent of clinical diagnosis was corrected following histologic findings on biopsy specimens³⁾. This is due to the fact that no specific liver function tests fit to make diagnosis of liver diseases such as amyloidosis, fatty liver and granulomatous hepatitis, on the one hand, and due to discrepancy between histologic changes and liver function test occasionally found in chronic hepatitis, cirrhosis and even in acute hepatitis, on the other hand.

To investigate this kind of discrepancy in acute viral hepatitis 48 cases were examined. SGPT was estimated once a week during each 2 weeks before and after the time of biopsy. Fluctuation mode of SGPT was divided into 5 groups following its fluctuation pattern and range as listed in Table 2. Histologic diagnosis

Table 2

Correlation between Fluctuation Mode of SGPT during 4 Weeks and Histologic Diagnosis of the Liver obtained in this period (48 cases of acute viral hepatitis)

Fluctuation pattern of SGPT	Fluctuation range of SGPT	Histologic Diagnosis			Total cases
		Diagnostic viral hepatitis	Suggestive viral hepatitis	Nonspecific reactive hepatitis	
①	> 50 μ	10 cases	0	0	10 cases
②	> 50 μ	9 cases	2 cases	5 cases	16 cases
③	> 50 μ	10 cases	0	1 case	11 cases
④	< 50 μ	2 cases	5 cases	2 cases	9 cases
⑤	within normal value	1 case	0	1 case	2 cases

Bp↓: time of biopsy

was classified into diagnostic viral hepatitis, suggestive viral hepatitis and nonspecific reactive hepatitis according to Chung's study⁴. Twenty among 21 cases (95%) whose fluctuation mode of SGPT belonged to either the first or third group (i.e. linear rise of SGPT over 50U. or fluctuation of that over 50U. for period of 4 weeks) showed diagnostic viral hepatitis, revealing close relation between SGPT value and histologic changes. However, cases with other fluctuation mode did not show any correlation between the two. Moreover, it is noteworthy to point out that one case showed diagnostic viral hepatitis histologically despite completely normal SGPT value for 4 weeks.

III. Limitation of histologic diagnosis on biopsy specimens

Though highly accurate diagnosis in liver diseases has been obtained by needle biopsy³, misleading of cirrhosis is occasionally followed when the specimens are obtained from hyperplastic nodules⁵. Another misleading is related to circumscribed hepatic disorders such as hepatic tumors and granulomas.

In our series 195 cases of hepatobiliary diseases were examined both by biopsy and peritoneoscopic examination. As a result, 84 percent of total cases were diagnosed by histologic findings alone and 83 percent of the cases were diagnosed peritoneoscopically. Moreover, when these two techniques were applied at the same time, 94 percent of the total cases were diagnosed correctly, pointing out that this kind of combined technique could improve diagnostic accuracy of biopsy, especially in circumscribed liver diseases and chronic hepatic disorders.

IV. Incidence of hepatic diseases revealed by biopsy

In order to clarify the incidence of hepatic diseases in Japan, 884 cases in which histologic diagnosis was obtained by biopsy since 1960 were classified as listed in Table 3. Incidence of fatty liver was not so low as might be expected before in this country. Acute, subacute, chronic viral hepatitis and intrahepatic cholestasis caused by virus were found in 328 cases (37%), revealing high incidence of viral hepatitis and its sequelae.

Table 3. Histologic Diagnosis of 884 Liver Specimens Obtained by Needle Biopsy (Sept. 1960-Dec. 1966)

Histologic diagnosis	No. of cases
Acute hepatitis:	123 (13.9%)
viral	122
others	1
Intrahepatic cholestasis:	26 (2.9%)
viral	17
others	9
Subacute hepatitis	3 (0.3%)
Chronic hepatitis	186 (21.0%)
Cirrhosis	59 (6.7%)
Hemochromatosis	2 (0.2%)
Extrahepatic biliary obstruction	13 (1.5%)
Cholangitis or Pericholangitis	22 (2.5%)
Fatty liver	55 (6.2%)
Carcinoma:	26 (2.9%)
primary	11
secondary	15
Granuloma	1 (0.1%)
Dubin-Johnson syndrome	11 (1.2%)
Portal fibrosis	86 (9.7%)
Miscellaneous	173 (19.6%)
Normal	65 (7.3%)
Inadequate specimens	33 (3.7%)

References

- 1) Iversen, P. and Roholm, K.: Acta med. Scandinav., 102: 1, 1939.
- 2) Ichida, F., Sasaki, H. and Wakisaka, G.: In "Progress in Liver Diseases". Vol. II. H. Popper and F. Schaffner (Eds.). Grune and Stratton, New York, p. 416, 1965.
- 3) Schiff, L. and Gall, E. A.: In "Diseases of the Liver". L. Schiff (Ed.). J.B. Lippincott Comp., Philadelphia, p. 179, 1963.
- 4) Chung, W.K. et al.: Arch. Int. Med., 113: 535, 1964.
- 5) Braunstein, H.: Arch. Path., 62: 87, 1956.