Acta Med. Nagasaki 34 : 32－35

Incidence and Correlation between Atrophic Liver Cirrhosis and Hepatocellular Carcinoma in Autopsy Cases at Nagasaki University

Hideo Tsuchiyama, Kiuko Kawai, Kazuto Shigematsu, and Junji Irie

Department of Pathology,
Nagasaki University School of Medicine

It is well known that HB virus is correlated with chronic liver diseases and hepatocellular carcinoma. Nagasaki prefecture generally belongs to hyperendemic area of HB virus, chronic liver diseases and hepatocellular carcinoma [1]. In this report, we examined the incidence and correlation between liver cirrhosis and hepatocellular carcinoma including HB virus carriers in autopsy cases of Nagasaki University.

INCIDENCE OF ATROPHIC LIVER CIRRHOSIS AND HEPATOCELLULAR CARCINOMA

During the period of 1965-1986, 544 out of 8,043 autopsy cases were diagnosed pathologically as having atrophic liver cirrhosis. This rate was 6.8 per cent. Moreover, 381 cases of hepatocellular carcinoma were identified in this series. The rate was 4.7 percent (Table 1). These incidences of liver diseases were significantly higher compared with those of average of autopsy cases in Japan. They were 5.2% and 2.9% respectively [2].

An analysis of chronic liver diseases indicated that 298 out of 544 cases of atrophic liver cirrhosis (54.8%) were associated with hepatocellular carcinoma and that 298 out of 381 cases of hepatocellular carcinoma (78.2%) were associated with atrophic liver cirrhosis. Therefore, relative risk of the development of hepatocellular carcinoma was significantly higher in association of atrophic liver cirrhosis than that of without cirrhosis (Table 2).

The frequency of cancerous changes as a complication of liver cirrhosis varies widely between populations. For example, in Britain and the United States carcinoma of the liver is found at necropsy in from 5 to 10 percent of patients with liver cirrhosis. In Mozanbique, however, hepatic carcinoma is found in 40 percent of patients with liver cirrhosis [3].

SUBTYPES OF ATROPHIC LIVER CIRRHOSIS

Histologically, atrophic liver cirrhosis consists of postnecrotic cirrhosis and portal or Laennec cirrhosis. In Japan, Nagayo's distinc-

Table 1. Incidence of Atrophic Liver Cirrhosis and Hepatocellular Carcinoma between Nagasaki University and Japan (1965-1986).

	Total autopsy cases	Atrophic liver cirrhosis	%	Hepatocellular carcinoma	%
Nagasaki University	8,043	544	6.8*	381	4.7*
Japan	620,841	31,983	5.2	18,063	2.9

* $p<0.05$

Table 2. Incidence and Correlation between Atrophic Liver Cirrhosis and Hepatocellular Carcinoma (1967-1986)

Atrophic liver cirrhosis	Total autopsy cases	%
Without hepatocellular carcinoma	246	45.2
With hepatocellular carcinoma	298	54.8
Total	544	100
Hepatocellular carcinoma	**Total autopsy cases**	**%**
Without atrophic liver cirrhosis	83	21.8
With atrophic liver cirrhosis	298	78.2*
Total	381	100

* $p<0.01$

tion is used to determine the subtypes of atrophic liver cirrhosis. Nagayo's type A generally corresponds with postnecrotic cirrhosis and it shows condensed collagenous connective tissue and lobular collapse, bringing together several portal triads. Nagayo's type B mostly corresponds with portal cirrhosis or posthepatitic cirrhosis by Gall. In this type, liver is composed entirely of pseudolobules and relative narrow bands of connective tissue. The ratio of both subtypes between Nagasaki University and Japan was almost same and about 80 percent of atrophic liver cirrhosis was Nagayo's subtype B (Table 3).

AGE DISTRIBUTION OF LIVER CIRRHOSIS AND CARCINOMA

The age distribution of atrophic liver cirrhosis was mostly from 40 to 60 years. The peak incidence of atrophic liver cirrhosis occurred the 5th decade of life (Table 4). The age distribution of hepatocellular carcinoma was mainly between the age of 40 to 70 years. The peak age for hepatocellular carcinoma was the 5th decade of life as was the case with atrophic liver cirrhosis. Cholangiocellular carcinoma was noted in an older age group than hepatocellular carcinoma (Table 5).

Table 3. Incidence of Subtype in Atrophic Liver Cirrhosis between Nagasaki University and Japan (1967-1986)

	Total autopsy cases	Atrophic liver cirrhosis			
		Nagayo-A	%	Nagayo-B	%
Nagasaki University	311	57	18.3	254	81.7
Japan	22,557	4,504	20.0	18,053	80.0

Table 4. Age Distribution of Atrophic Liver Cirrhosis (1967-1986)

Atrophic liver cirrhosis	Age (Yr.)							Total
	20-29	30-39	40-49	50-59	60-69	70-79	80-	
Nagayo-A	4	5	17	18	9	4		57
Nagayo-B	1	10	67	81	62	27	6	254
Total	5	15	84	99	71	31	6	311

Table 5. Age Distribution of Primary Liver Carcinoma (1967-1986)

Primary liver carcinoma	Age (Yr.)							Total
	20-29	30-39	40-49	50-59	60-69	70-79	80-	
Hepatocellular carcinoma	3	10	73	105	84	25	3	303
Cholangiocellular carcinoma			2	8	12	9	4	35
Combined type	1	1	2	3		2		9
Total	4	11	77	116	96	36	7	347

HEPATITIS B VIRUS INFECTION AND CHRONIC LIVER DISEASES

Recent 150 autopsy cases with chronic liver diseases examined to take the frequency of HBs-Ag carriers. Eleven out of 19 cases of atrophic liver cirrhosis (57.8%) and 46 out of 87 cases of atrophic liver cirrhosis with hepatocellular carcinoma (52.8%) were positive to HBs-Ag. On the other hand, hepatocellular carcinoma without atrophic liver cirrhosis occurred in 5 out of 25 cases (20.0%) positive to HBs-Ag. There were no cases of other types of liver cirrhosis and intrahepatic cholangiocellular carcinoma with HBs-antigen carriers (Table 6). Therefore, the frequency of HB virus in patients with atrophic liver cirrhosis of our cases was almost equal to that of liver cirrhosis with carcinoma and it appeared that patients with HB virus tends to become liver cirrhosis and liver cirrhosis with carcinoma more frequently than in patients with hepatocellular carcinoma without cirrhosis.

Toda and co-workers indicated that HBs-Ag in liver tissue by Orcein stain was present at a rate of 47.9% in cases of atrophic liver cirrhosis and that the incidence of HBs-Ag in liver tissue was very high, especially in cases of atrophic liver cirrhosis with hepatocellular carcinoma. Moreover, they pointed out that HBs-Ag was detected in 55.1% of hepatocellular carcinoma tended to be highly dependent on the histology of non-cancerous tissue[4].

Controversies still exists as to whether or not the hepatitis B virus has a direct oncogenic role in the etiology of hepatocellular carcinoma and whether or not a hepatitis B infection causes liver cirrhosis predisponsing patients to hepatocellular carcinoma[5,6].

Recent studies have shown that integration of HB virus DNA is responsible for the activation of just one oncogene, and non-viral factors, such as chemical carcinogens and radiation, might account for the activation of another. Moreover, Okuda suggested that in cirrhosis, liver cell regeneration, hence increased synthesis of DNA, will result in frequent rearrangement or changes in integration site of viral DNA and that cirrhosis itself is carcinogenic, and if the initiation has already taken place, it may be regarded as "preneoplastic"[7]. Our data at present study may suggest this possibility.

REFERENCES

1) Takemoto, T., Sueta, H., Kase, Y.: An observation on natural history of liver diseases in Nagasaki. Acta Med. Nagasaki., 30 : 304-307, 1986.
2) The Japanese Pathological Society : Annual of the pathological Autopsy Cases in Japan, Vol. 7-28, 1965-1986.
3) Weinbren, K. : Factors in the development of primary carcinoma of the liver. In Systemic Pathology edited by W. St C. Symmers, Vol. 3 : 1289-1291, C. Livingstone, Edinburgh, 1978.
4) Toda, Y., Senba, M., Itakura, H. : Further histological study of the role of hepatitis B infection on the development of hepatocellular carcinoma. Tropical Medicine, 26 : 123-136, 1984.

Table 6. Incidence of Autopsy Cases with HBs-Ag Positive Carriers in Liver Disease

Liver disease	HBs-Ag (+)	%	HBs-Ag (−)	Total
Atrophic liver cirrhosis				
Without hepatocellular carcinoma	11	57.8	8	19
With hepatocellular carcinoma	46	52.8	41	87
Other types of liver cirrhosis	0		3	3
Hepatocellular carcinoma				
Without atrophic liver cirrhosis	5	20.0	20	25
Combined with cholangiocellular carcinoma	0		4	4
Intrahepatic cholangiocellular carcinoma	0		12	12
Total	62		88	150

5) Atiyeh, M. and Ali, M.A. : Primary hepatocellular carcinoma in Saudi Arabia : A clinicopathological study of 54 cases. Am. J. Gastroenterol., 74 : 25-29, 1980.
6) Zukerman, A.J. : Symposium on liver carcinoma : Hepatocellular carcinoma and hepatitis B. Trans. R. Soc. Trop. Med. Hyg., 71 : 459-461. 1977.
7) Okuda, K. : Summary of general discussion in proceedings of Japan-China Medical Association, Tokyo, 1986, pp 86-89.