

DECREASE TREND IN PROPORTIONS OF HEPATITIS B SURFACE ANTIGEN CARRIER IN CHRONIC HEPATITIS, CIRRHOSIS AND CIRRHOSIS WITH HEPATOCELLULAR CARCINOMA

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Abstract: Histopathological analysis was carried out to determine whether hepatitis B surface antigen with the autopsy diagnoses of chronic hepatitis, cirrhosis and/or hepatocellular carcinoma declined between the 1964-1973 and 1974-1983 decades. In this study, the liver specimens from 422 autopsy cases at Nagasaki University Hospital were used. All of the 17 cases of acute hepatitis were hepatitis B surface antigen negative. Hepatitis B surface antigen positive rates in chronic hepatitis and hepatocellular carcinoma showed minor changes during 1964-1983. On the other hand, proportions of hepatitis B surface antigen carriers in cirrhosis and cirrhosis with hepatocellular carcinoma in the recent decade 1974-1983 were found to decrease compared to the last decade 1964-1973. However, the difference of the hepatitis B surface antigen positive rates in cirrhosis with hepatocellular carcinoma between the 2 periods was marginally significant, but not significant in cirrhosis. A possible explanation may be that many cases of posttransfusion hepatitis in the latter decade are not caused by hepatitis B virus.

INTRODUCTION

The most plausible explanation for the increased risk of hepatocellular carcinoma is that the acceleration of cellular replication that occurs in cirrhosis enhances the effects of many carcinogens, including hepatitis B surface antigen. Moreover, the oncogenic potential of hepatitis B virus in the development of hepatocellular carcinoma has been reported (Sherlock *et al.*, 1970; Vogel *et al.*, 1970; Charinuvati *et al.*, 1975; Senba *et al.*, 1984, 1985).

After the discovery of the Australia antigen (hepatitis B surface antigen) by Blumberg *et al.* (1967), the subsequent demonstration by Krugman *et al.* (1967), and Prince (1968) that the Australia antigen was specifically associated with type B hepatitis, it was widely assumed that development of efficient screening tests would detect type B hepatitis infection carriers and make possible the eradication of the problem of posttransfusion type B hepatitis by preventing transfusion of hepatitis B virus positive blood. In Nagasaki University Hospital, hepatitis B surface antigen screening test has been performed since 1974. Therefore, the objective of this study is to see whether hepatitis B surface antigen positive rates in chronic hepatitis, cirrhosis, and cirrhosis with hepatocellular carcinoma have changed or not between the 1964-1973 and 1974-1983 decades.

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MATERIALS AND METHODS

The liver specimens were collected at Nagasaki University Hospital from 422 autopsy cases of various liver diseases, including acute hepatitis (17 cases), chronic hepatitis (40 cases), cirrhosis (177 cases), cirrhosis with hepatocellular carcinoma (170 cases), and hepatocellular carcinoma without cirrhosis (62 cases). The specimens were fixed in formalin, or sometimes in Zenker's formol and embedded in paraffin for histopathologic study. Sections were cut at 5 micron and stained with hematoxylin-eosin, resorcin fuchsin method for elastic fibers, Mallory's method for collagen fibers, silver impregnation method for reticulum fibers, and orcein method for hepatitis B surface antigen (Senba, 1982). The criteria of Leevy *et al.* (1979) and Gibson and Sobin (1978) were applied in assigning the diagnosis of cirrhosis and hepatocellular carcinoma to the tissue.

Statistical calculation was performed using the BMDP (Dixon *et al.*, 1981) on the IBM 4341 system in the Data Center of A-bomb Disaster in Nagasaki University. The statistical method for this study is the Pearson chi-square test for association in contingency table.

RESULTS

Table 1 shows the hepatitis B surface antigen positive results obtained by orcein staining. All of the 17 cases of acute hepatitis were not hepatitis B surface antigen positive. On the other hand, of the 26 chronic hepatitis cases in 1964–1973 and of the 14 in 1974–1983, 4 (15%) and 2 (14%) were hepatitis B surface antigen positive, respectively. As for the cirrhosis cases, 33 (33%) cases were hepatitis B surface antigen positive out of 100 in 1964–1973 and 8 (24%) out of 33 in 1974–1983. As for the cirrhosis with hepatocellular carcinoma cases, 77 (71%) cases were hepatitis B surface antigen positive out of 108 in 1964–1973 and 36 (58%) out of 62 in 1974–1983. Of the 21 and 41 hepatocellular carcinoma cases in 1964–1973 and 1974–1983, 5 (24%) and 11 (27%) were hepatitis B surface antigen positive, respectively.

Results of the statistical analysis on hepatitis B surface antigen, cirrhosis, and cirrhosis with hepatocellular carcinoma are as follows: The Pearson chi-square test for the frequencies of hepatitis B surface antigen positive in cirrhosis between the 2 periods showed Pearson $\chi^2=0.345$; and the Pearson chi-square test for the frequencies of hepatitis B surface antigen positive in cirrhosis with hepatocellular carcinoma between the 2 periods showed Pearson $\chi^2=0.079$, respectively. Thus, the difference of the hepatitis B surface antigen positive rates in cirrhosis

Table 1 Proportions of hepatitis B surface antigen carriers in hepatitis cases, cirrhosis cases, and hepatocellular carcinoma cases

	1964–1973	1974–1983	Total
Acute hepatitis	0/10 (0%)	0/7 (0%)	0/17 (0%)
Chronic hepatitis	4/26 (15%)	2/14 (14%)	6/40 (15%)
Cirrhosis	33/100 (33%)	8/33 (24%)	41/133 (31%)
Cirrhosis with HCC*	77/108 (71%)	36/62 (58%)	113/170 (66%)
HCC*	5/21 (24%)	11/41 (27%)	16/62 (26%)
Grand total	119/265 (45%)	57/157 (36%)	176/422 (42%)

* HCC: Hepatocellular carcinoma

with hepatocellular carcinoma between the 2 periods was marginally significant, but not significant in cirrhosis.

DISCUSSION

The landmark discovery of the Australia antigen (hepatitis B surface antigen) by Blumberg *et al.* (1965) and the linking of this antigen to viral hepatitis (Blumberg *et al.*, 1967) provided the cornerstone for the rapid acceleration on our understanding of viral hepatitis in general, and posttransfusion hepatitis in particular. The hepatitis B surface antigen positive cases were increased by such antigen detection, but false-positive reaction occurred frequently (Hollinger *et al.*, 1973). Further specific methods were developed for recognition of other hepatitis B virus antigens (hepatitis B core antigen and hepatitis B e antigen). The introduction of sensitive assays for hepatitis B surface antigen has resulted in marked reduction in the incidence of posttransfusion hepatitis (Alter *et al.*, 1975). Therefore, in this study, proportions of hepatitis B surface antigen carrier in cirrhosis and cirrhosis with hepatocellular carcinoma in the recent decade 1974–1983 were found to decrease compared to the last decade 1964–1973. The decrease in the hepatitis B surface antigen positive rate from 45% to 36% suggests that infection of type B virus caused by posttransfusion can be prevented in the latter decade. However, the hepatitis B surface antigen positive rates in chronic hepatitis showed minor changes during 1964–1983. A possible explanation may be that high frequency of hepatitis B virus transmission from the carrier mother to her infant has occurred.

REFERENCES

- 1) Alter, H. J., Holland, P. V. and Purcell, R. H. (1975): The emerging pattern of post-transfusion hepatitis, *Am. J. Med. Sci.*, 270, 329–342
- 2) Blumberg, B. S., Alter, H. J. and Visnich, S. (1965): A "New" antigen in leukemia sera, *JAMA*, 191, 101–105
- 3) Blumberg, B. S., Gerstley, B. J. S. and Hungerford, D. A. (1967): A serum antigen (Australia antigen) in Down's syndrome, leukemia and hepatitis, *Ann. Intern. Med.*, 66, 924–931
- 4) Chainuvati, T., Viranuvatti, V. and Pongpipat, D. (1975): Relationship of hepatitis B antigen in cirrhosis and hepatoma in Thailand, *Gastroenterology*, 68, 1261–1264
- 5) Dixon, W. J., Brown, E. L., Frane, J. W., Hill, M. A., Jennrich, R. I. and Toporek, J. D. (1981): BMDP statistical software, University of California Press. Berkeley
- 6) Gibson, J. B. and Sobin, L. H. (1978): Histological typing of the liver, biliary tract and pancreas: International histological classification of tumor No. 20 World Health Organization, Geneva
- 7) Hollinger, F. B., Aach, R. D., Gitnick, G. L., Roche, J. K. and Melnick, J. L. (1973): Limitation of solid-phase radioimmunoassay for HB Ag in reducing frequency of post-transfusion hepatitis, *N. Engl. J. Med.*, 289, 385–391
- 8) Krugman, S., Giles, J. P. and Hammond, J. (1967): Evidence for two distinctive clinical, epidemiological and immunological types of infection, *JAMA*, 200, 365–373
- 9) Leevy, C. M., Popper, H. and Sherlock, S. (1979): Disease of the liver and biliary tract: Standardization of nomenclature, diagnostic criteria and diagnostic methodology, Castle House Publications. Guildford
- 10) Prince, A. M. (1968): An antigen detected in the blood during the incubation period of serum hepatitis, *Proc. Natl. Acad. Sci. USA*, 60, 814–821
- 11) Senba, M. (1982): Staining method for hepatitis B surface antigen (HBs Ag) and its mechanism, *Am*

- J. Clin. Pathol., 77, 312-315
- 12) Senba, M., Nakamura, T. and Itakura, H. (1984): Statistic analysis of relationship between hepatitis B surface antigen, cirrhosis and hepatocellular carcinoma, Trop. Med., 26, 117-122
 - 13) Senba, M., Nakamura, T. and Itakura, H. (1985): Statistical analysis of relationship between iron accumulation and hepatitis B surface antigen, Am. J. Clin. Pathol., 84, 340-342
 - 14) Sherlock, S., Fox, R. A., Niazi, S. P. and Scheuer, P. J. (1970): Chronic liver diseases and primary liver-cell cancer with hepatitis-associated (Australia) antigen in serum, Lancet I, 1243-1247
 - 15) Vogel, C. L., Anthony, P. P., Mody, N. and Barker, L. F. (1970): Hepatitis-associated antigen in Ugandan patients with hepatocellular carcinoma, Lancet II, 621-624

B型肝炎表層抗原の慢性肝炎，肝硬変および肝硬変に伴った 肝細胞癌組織中の陽性率の減少傾向

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1964-1973年と1974-1983年の各年代におけるB型肝炎表層抗原の陽性率を急性肝炎，慢性肝炎，肝硬変，肝硬変に伴った肝細胞癌および肝細胞癌の組織を長崎大学病院の剖検肝臓422例を使用して検索した。B型肝炎表層抗原は急性肝炎の17例の全て陰性であり，慢性肝炎および肝細胞癌の例では1964-1983年の差は小さかった。また，B型肝炎表層抗原は肝硬変および肝硬変に伴った肝細胞癌の例で減少していた。しかしながら，2年代におけるB型肝炎表層抗原の減少は肝硬変に伴った肝細胞癌の例では有意であったが，肝硬変では有意ではなかった。このことは最近の10年間ではB型肝炎ウイルスによる輸血後肝炎がなくなったためと思われた。

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