HIGH PREVALENCE OF DELTA VIRUS INFECTION IN THAI INTRAVENOUS DRUG ABUSERS

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INTRODUCTION

The Hepatitis Delta Virus (HDV) is a unique transmissible, defective hepatotropic RNA virus that depends on the presence of hepatitis B (HBV) for its expression and replication. Delta infections, can therefore occur in patients with HBV infection either concomitantly with an acute HBV or superimposed on a chronic HBV (Rizzetto *et al.*, 1979; Rizzetto, 1983; Redeker, 1983; David *et al.*, 1986). HDV infection is important because of its high pathogenicity to liver cells, its association with acute fulminant hepatitis and chronic liver disease (Popper *et al.*, 1983). Most of the patients who are chronically positive for hepatitis B surface antigen (HBs Ag) and antibody to delta (anti-delta) are chronic active hepatitis (CAH) or cirrhosis cases; a few cases showed chronic persistent hepatitis (CPH) (Jacobson *et al.*, 1985; David *et al.*, 1986). It is endemic in the Mediterranean, parts of Africa, the Middle East and South America (Rizzetto *et al.*, 1980). In Western Europe (Raimondo *et al.*, 1982), Scandinavia (Hansson *et al.*, 1982) and Australia (Hoy *et al.*, 1984) it is confined to intravenous drug abusers and their close contacts.

Since the transmission of HDV is similar to that of HBV, via percutaneous or mucosal exposure to blood and blood products or to serous fluid containing infectious virus (Redeker., 1983; David *et al.*, 1986), a high prevalence of HDV infections is expected in high prevalent area of HBV carriers. However, a low prevalence of HDV, 7.3% was reported from patients with chronic liver diseases in Taiwan (Rizetto *et al.*, 1980), 0.5% of persons with HBs antigenemia in Thailand (Chainuvati *et al.*, 1987), and 0.5% in Malaysian patients with acute hepatitis B (Dimitrakakis *et al.*, 1986). Interestingly, a high prevalence of anti-delta, 17.8% was detected in the intravenous drug abusers who had HB antigenemia in Malaysia (Sinniah *et al.*, 1985), and 78.9% in Taiwan (Lee *et al.*, 1986).

The objective of this study was to compare the prevalence of HDV in selected groups of the population, and in patients with acute and chronic liver diseases in Thailand.

MATERIALS AND METHODS

Sera were obtained from four groups of subjects.

Group 1 comprised of 104 intravenous (IV) drug abusers from Thanyarak and Vajira Hospitals. Sera were obtained during May 1985 to November 1987, from 84 IV drug

abusers who had HBs antigenemia and from 20 IV drug abusers positive for anti-HBc (HBs Ag and anti-HBs were negative).

Group 2 consisted of 38 patients with liver diseases, 18 with chronic active hepatitis (CAH), 2 chronic persistent hepatitis (CPH), 12 cirrhosis and 6 primary hepatocellular carcinoma. These cases were from Siriraj Hospital. They were previously found to be HBs antigenemia. Sera were collected from May to September 1987.

Group 3 comprised of 46 asymptomatic HBs Ag carriers. Sera were collected from 20 asymptomatic HBs Ag carriers; 10 male homosexuals and 10 hospitality girls in May 1985. During May and June 1987, sera from asymptomatic HBs antigenemia cases; 13 males and 13 females, attending routine check-up were also tested.

Group 4 consisted of 51 patients with acute icteric hepatitis B. Sera were collected during January to June 1987.

Hepatitis B surface antigen (HBs Ag) and antibodies to hepatitis B core and hepatitis B surface (anti-HBc and anti-HBs) were tested by ELISA kits from Roche (Switzerland). Sera positive for HBs Ag and anti-HBc or anti-HBc solely were selected for antibody to delta virus (anti-delta) study.

Anti-delta were investigated by ELISA, using competitive sandwich inhibition (Organon Teknika., Belgium). Briefly, the wells of polystyrene microtiter strips were coated with human anti-delta immunoglobulin. The serum sample and a fixed amount of hepatitis delta antigen (HD Ag) were incubated in such a well. The anti-delta in the test sample would compete with the coated antibody for binding with HD Ag. After the washing step, the human anti-delta immunoglobulin which has been labelled with horseradish peroxidase was added. This labelled antibody would bind to the solid phase anti-delta and the serum-HD Ag complex. The plate was washed again and incubated with enzyme substrate. A blue colour of degraded substrate would be shown and turned into yellow after stop reaction with acid. If the tested sample contained anti-delta, a reduced colour would develop when compared to the negative samples.

RESULTS

Of the hepatitis B surface antigenemia cases, anti-delta was found in 55 of 84 (65.48%) IV drug abusers, 2 of 18 (11.11%) patients with CAH and 1 of 12 (8.33%) patients with cirrhosis. The demographic data and anti-delta detection are shown in Table 1. Anti-delta could not be demonstrated in 51 patients with acute hepatitis B, 46 asymptomatic HBs Ag carriers, 6 primary hepatocellular carcinoma and 2 CPH. None of 20 anti-HBc positive drug users had anti-delta.

The prevalence of anti-delta was 65.48% in IV drug abusers of HBs Ag carriers compared to 2.22% in the other groups of non drug cases with HBs antigenemia (Table 2). The overall delta infection in the cases studied, with HBs Ag positive sera was 26.48% (58 of 219), and 94.83% (55 of 58) with anti-delta seropositivity were among IV drug abusers.

DISCUSSION

In Thailand, viral hepatitis is one of the major public health problems, approximately 10 per cent of the general population are HB chronic carriers (Thongcharoen *et al.*, 1985). The morbidity per 100,000 was 34.6, and mortality of 0.5% was reported by the Ministry of Public Health in 1985 (Annual Summary, 1985). The studies on HDV as the

Table 1

Demographic data and the prevalence of anti-delta in the selected groups of HBs antigenemia.

Group	No. examined	Sex M	Sex F	Age ($\bar{x} \pm$ SD)	No. positive anti-delta (%)
HBs antigenemia					
Group 1. IV drug abusers	84	84	0	31.32 ± 6.72	55 (65.48)
Group 2. Patients with liver diseases					
Chronic active hepatitis (CAH)	18	13	5	31.18 ± 7.63	2 (11.11)
Chronic persistent hepatitis (CPH)	2	2	0	31.0 ± 5.66	0
Cirrhosis	12	6	6	45.15 ± 12.30	1 (8.33)
Primary hepatocellular carcinoma	6	1	5	52.83 ± 19.79	0
Group 3. Asymptomatic HBs Ag carriers	46	23	23	29.12 ± 8.23	0
Group 4. Icteric hepatitis B patients	51	34	17	30.03 ± 12.68	0
Anti-HBc positive only					
IV drug abusers	20	16	4	30.05 ± 5.7	0

Table 2

Prevalence of anti-delta in IV drug abusers and the non drug cases with HBs antigenemia.

Group	No. examined	Anti delta
IV drug abusers	84	55 (69.48)
Non drug cases	135	3 (2.22)
Total	219	58 (26.48)

etiologic agent of acute and chronic hepatitis are meagre. Burke *et al.*, (1984) could demonstrate 2 cases of acute delta hepatitis in HBs Ag carriers by seroconversion. Both patients had parenteral exposure to blood products within the preceding six months. In their study, anti-delta was not detected in acute hepatitis or asymptomatic carriers, which is similar to our study.

Chainuvati *et al.*, (1987) reported a prevalence of 0.5% anti-delta in a total 200 cases of HBs antigenemia, or 7.69% in 13 CAH patients. The positive case was a young laboratory technician, who did not receive any transfusion. In our study, anti-delta was positive in 11.11% of CAH and 8.33% of patients with cirrhosis. The history of exposure to blood was not recorded. Association between delta virus infection and chronic liver disease due to HBV has been noted in Italy and USA. The prevalence of anti-delta among patients with chronic liver disease due to hepatitis B has been found to be higher than that in asymptomatic HBs Ag

carriers or patients with acute hepatitis B. Patients with CAH or CPH who are chronically positive for HBs Ag and anti-delta were likely to develop cirrhosis or CAH (David *et al.*, 1986). The long term follow-up of the anti-delta positive patients in this study is in progress.

The presence of anti-delta in HBs Ag negative parenteral drug abusers has been reported previously in the patients who were anti-HBc IgG positive (Novick *et al.*, 1985). In our study, we could not detect any anti-delta positivity in 20 IV drug abusers who were solely anti-HBc IgG positive.

This study indicates a high prevalence of HDV infection in the IV drug abusers but low in other groups. The association of HBV infection in CAH and patients with cirrhosis were also demonstrated. It is evident now that HDV is introduced in some groups of the Thai population especially the IV drug abusers. Since the HBsAg carriers in our population are high, we should be fully aware of superinfection or coinfection of HBV and HDV. More information on epidemiological patterns and the natural history of HDV infection should be investigated, so that appropriate intervention could be applied in the prevention and control of this infection.

SUMMARY

The prevalence of antibodies to delta virus (anti-delta) in the selected groups of hepatitis B surface antigenemia population was investigated. The subjects were 84 intravenous drug abusers; 20 chronic hepatitis, 12 cirrhosis, 6 primary hepatocellular carcinoma and 46 asymptomatic healthy carriers. Anti-delta was detected in 65.48% of intravenous drug abusers, 11.11% of chronic active hepatitis and 8.33% of cirrhosis cases. None of asymptomatic carriers had anti-delta. In addition, 51 acute icteric hepatitis B patients who were positive for HBs Ag and 20 IV drug abusers positive for anti-HBc only (HBsAg and anti-HBs negative) were negative for anti-delta.

ACKNOWLEDGEMENTS

The authors would like to thank Miss Poonsri Sakulkoo for technical assistance. This study has been supported by a research grant from Mahidol University, 1985.

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