DELTA HEPATITIS IN MALAYSIA

MANGALAM SINNIAH, MARY DIMITRAKAKIS* and DORA S.K. TAN

Division of Virus Research, Institute for Medical Research, Kuala Lumpur, Malaysia.
*Hepatitis Laboratory, Fairfield Hospital, Fairfield, Victoria, Australia.

INTRODUCTION

The Hepatitis Delta virus (HDV), first described in 1977 in Italy (Rizetto, 1983) is an infectious and transmissible agent that depends on the presence of the Hepatitis B virus (HBV) for its expression and replication, Although HDV is an extremely small and defective RNA virus, it is important because of its high pathogenicity to liver cells and its association with acute fulminant hepatitis, which is often fatal and chronic liver disease (CLD). The hepatic damage is believed to occur due to a direct cytopathic action of the HDV virus (Popper *et al.*, 1983) in contrast to the immunological damage caused by the HBV.

The delta virus has been reported to occur worldwide and is endemic in the Mediterranean region, Africa, South America and Middle East. The Arab countries in the Middle East have been reported to have the highest prevalence of HDV infection in the world (Nordenfelt *et al.*, 1983).

As the HDV depends on the HBV for its expression, it is expected that HDV would be common in countries where the carrier rates of HBV are high. However, in the Far East, despite the high Hepatitis-B surface antigen (HBsAg) carrier rates, the prevalence of delta infection has been found to be as low as 1.3% and 7.3% in cases of CLD in Japan and Taiwan respectively (Rizetto *et al.*, 1980).

The transmission of HDV is similar to that of HBV. In endemic areas like Italy, transmission by personal contact is believed to occur. However, in Europe and in the U.S.A. the HDV is transmitted mainly through parenteral inoculation by illicit narcotic use and multiple blood product transfusions (Rizetto *et al.*, 1980).

A previous study carried out in Malaysia did not demonstrate delta virus infection in any of the cases investigated leading the investigators to believe that the delta agent has not yet been introduced into Malaysia (How *et al.*, 1985).

In yet another study carried out between 1984 and 1985, serological evidence of HDV was detected in only 0.5% of 87 Malaysian patients with acute hepatitis B (Dimitrakakis *et al.*, 1986).

The objective of this study was to determine the prevalence of HDV in individuals known to be at high risk for HBV and in medical patients with acute or chronic hepatitis B.

MATERIALS AND METHODS

The patients included intravenous (i.v.) narcotic abusers, male homosexuals, acute hepatitis B cases, asymptomatic HBsAg carriers and cases of chronic HBV liver disease.

Drug abusers: Sera from 106 i.v. drug abusers were collected, of whom 27 were positive only for HBsAg and 79 for anti-HBc IgG alone. All were males consisting of 13 Malays, 14 Chinese, but no Indians, and their ages ranged from 19 years to 54 years (mean 36.4 years).

Male homosexuals: 15 HBsAg positive sera were collected from non-drug using homo-

sexuals who consisted of 11 Malays and 4 Chinese. Their ages ranged from 21 to 32 years and the duration of sexual practice ranged from 1 to 10 years.

Acute Hepatitis B: 16 hospitalized cases of acute hepatitis-B were identified on the basis of history, typical clinical features of type-B hepatitis, presence of HBsAg and abnormal liver function tests. This group consisted of 10 Malays, 2 Chinese and 4 Indians, 12 males and 4 females. Their ages ranged from 6 - 55 years (mean 27.9 years).

The sera of 13 healthy asymptomatic HBsAg carriers were collected; their ages ranged from 10 - 35 years (mean 24.9 years). There were 6 Malays, 5 Chinese and 2 Indians, 8 males and 5 females.

Sera from 9 symptomatic cases hospitalized with chronic HBV liver disease were included for delta screening. Their ages ranged from 38 to 61 years (mean 47 years) and they consisted 4 Malays and 5 Chinese, of whom 5 were males and 4 were females.

All sera were screened for HBV markers viz. HBsAg, anti-HBc IgG, HBeAg and anti-HBe.

Sera from homosexuals were screened for the above markers using reverse passive haemagglutination (RPHA) anti-Hebscell, (PHA) corecell, anti-e-cell Neo and e-Cell Kits respectively, supplied by Green Cross Corporation, Japan.

Sera from all the other groups were tested by the enzyme immunoassay technique (EIA) using commercially available EIA kits supplied by Abbot Laboratories, North Chicago.

The detection of delta antigen and anti-delta antibody in sera was carried out using a microtitre solid phase radio-immunoassay (SPRIA) technique using delta antigen purified from sera of patients coinfected with HBV and HDV (Dimitrakakis *et al.*, 1984).

RESULTS

Of 27 HBsAg positive drug abusers, 4(17.8%) were found to have anti-delta antibodies but none had delta antigen. The positive cases consisted of 3 Malays from a Government rehabilitation centre and one Chinese male, an ex-drug addict currently undergoing treatment for sexually transmitted disease. The prevalence of delta

Table 1

Prevalence of HDV markers in Malaysian patients.

	HBs-Ag positive	Anti-HBc IgG pos.but HBsAg neg.	Delta-Ag positive	Anti-delta antibody pos.	% delta markers in HBsAg pos.
I.V. drug abusers	27	79	0	4	17.8
Homosexuals	15	0	0	1	6.7
Acute hepatitis B cases	16	0	1	1	12.5
Healthy carriers	13	0	0	0	0
Chronic hepatitis B cases	9	0	0	0	0
Total	80	79	1	6	8.75

Table 2

Details of the seven hepatitis delta virus positive cases.

Patient Code		Age & Sex	Race	HBV Markers				
				HBsAg	HBeAg	Anti-HBe	Delta-Ag	Anti-delta antibody
Drug Abuser	(1)	31 M	Malay	+	+	−	−	+
	(2)	34 M	Malay	+	−	+	−	+
	(3)	54 M	Chinese	+	−	+	−	+
	(4)	31 M	Malay	+	−	−	−	+
Homosexual	(1)	30 M	Malay	+	−	−	−	+
Acute hepatitis B								
Patient	(1)	29 M	Malay	+	÷	+	+	−
	(2)	22 M	Indian	+	−	−	−	+

M = male, (+) = positive, (−) = negative.

markers was found to be higher in Malay drug abusers (23% or 3/13) as compared to Chinese drug abusers (7% or 1/14).

In the group of 79 drug abusers who were negative for HBsAg but positive for anti-HBc IgG no evidence of delta infection was detected. Of 15 HBsAg positive homosexuals, only one Malay male (6.7%) had anti-delta antibody.

Of 16 acute hepatitis B cases only 2 (12.5%) were positive for delta markers. One patient had anti-delta antibody while another was found to be carrying the delta antigen. The former was a 22-year-old intravenous heroin addict and the latter was a 29-year-old sexually promiscuous male. Of 13 healthy HBsAg carriers and 9 chronic hepatitis B cases, none showed evidence of superinfection with delta virus.

DISCUSSION

It is apparent from this present study that the intravenous drug abusers had the highest prevalence rate of delta markers (17.8%) followed by homosexuals (6.7%) while asymptomatic HBsAg carriers and chronic hepatitis-B cases had the lowest prevalence rates (0%). This indicates that in Malaysia, as in other non-endemic regions, HDV transmission occurs mainly via the parenteral and sexual routes.

It is interesting to note that in the group hospitalized with acute hepatitis B, the only delta positive patients were an i.v. heroin addict (who had anti-delta antibody) and a sexually promiscuous male who had delta-antigen. In other words delta markers were not detected in those acute hepatitis B patients who did not belong to high risk groups.

There was no evidence of delta infection in any of the asymptomatic HBsAg carriers or chronic hepatitis B cases in this study. Although the sample of these two groups was small, the findings are similar to those of two previous studies where delta infection was not demonstrable in chronic HBsAg carriers in Malaysia (How *et al.*, 1985, Dimitrakakis *et al.*, 1986).

This study indicates that the delta prevalence rate is low in homosexuals as compared to drug abusers, although the homosexual HBsAg carrier rate of 14%,(Mangalam, 1986, unpublished) is higher than that of drug abusers (Mangalam *et al.*, 1986). Reports from Britain and the U.S.A. have also indicated a similar trend.

It appears from this study that HDV has been introduced only into certain populations in Malaysia and that a reservoir of HDV exists in intravenous narcotic abusers, male homosexuals and probably also in sexually promiscuous heterosexuals. The HDV has not as yet been introduced into the normal population as evidenced by the absence of delta-markers in individuals not in the above risk groups.

It is therefore evident that the HDV does exist in Malaysia and the notion that the delta infection is uncommon in this region is due probably to the sparcity of information owing to a relative lack of studies carried out on HDV. It is therefore suggested a continuous monitoring programme for HDV isneeded that would include larger numbers, and a wider section of the Malaysian population with particular emphasis on groups known to be at high risk for HBV.

SUMMARY

Sera from one hundred and fifty nine Malaysian individuals were screened for the prevalence of delta markers. These included 15 HBsAg positive homosexuals, 16 acute hepatitis B cases, 9 chronic hepatitis B patients, 13 healthy HBsAg carriers and 106 intravenous (i.v.) drug abusers, of whom 27 were positive for HBsAg only and the rest were anti-HBc IgG positive but HBsAg negative. The prevalence of delta markers in the homosexuals was found to be 6.7%, in the HBsAg positive drug abusers 17.8%, in acute hepatitis B cases 12.5%. No evidence of delta infection was detected in healthy HBsAg carriers, chronic hepatitis B cases and HBsAg negative i.v. drug abusers.

With reference to i.v. drug abusers, the prevalence of delta markers was higher in Malays (23%) than in Chinese (7%) although the latter had a higher HBsAg carrier rate. Although the HBsAg carrier rate in the homosexuals was high, their delta prevalence rate was low as compared to drug abusers.

In Malaysia, as in other non-endemic regions, hepatitis delta virus transmission appeared to occur mainly via the parenteral and sexual routes.

This is the first time in Malaysia that a reservoir of delta infection has been demonstrated in certain groups of the population at high risk for hepatitis B.

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