HEPATITIS B VIRUS INFECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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ABSTRACT

Sera from 76 patients with systemic lupus erythematosus (SLE) were examined for HBsAg, anti-HBsAb and total anti-HBcAb by radioimmunoassay. Fifteen patients (19.7%) had one or more of these serological markers of HBV infection. This is comparable to the sero-prevalence in 100 sex- and age-matched healthy individuals (19%). There was no significant difference in the prevalence of HBV infection in patients who had received immunosuppressants compared with those who had not. Patients who had received transfusion of blood or blood products had a higher prevalence of serological markers but this was not statistically significant.

Keywords: systemic lupus erythematosus, hepatitis B virus.

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INTRODUCTION

Hepatitis B virus (HBV) causes acute and chronic hepatitis. The clinical manifestations and outcome following acute liver injury associated with HBV infection are determined by the immunologic responses of the host[1]. Patients with defects in cellular immune competence are more likely to remain chronically infected rather than clear the virus. During acute hepatitis, immune-complex mediated injury appears to play a major pathogenic role in the extra-hepatic manifestations[2]. About 5-10% of patients develop the prodromal serum sickness-like syndrome that mimics rheumatologic diseases. In patients who become carriers of HBsAg following acute hepatitis, other immune-complex diseases such as glomerulonephritis with nephrotic syndrome may be observed[3]. Polyarteritis nodosa (PAN) develops in less than one percent of patients with HBV infection but 20-30% of patients with PAN have HBsAg in their sera[4].

The association of HBV infection with systemic lupus erythematosus (SLE) has been studied since the early 1970s[5-8]. The relationship is still unclear. Some studies found a higher prevalence of serological markers of HBV infection in lupus patients[7-9], while others do not[5,6,10,11].

Hepatitis B virus infection is endemic in Singapore and the surrounding region. In 1982, Looi and Prathap[12] studied the prevalence of HBsAg in renal biopsy specimens and found that 30 of 47 specimens from patients with SLE had HBsAg in glomerular immune complexes. They suggested that HBV may have a role in the pathogenesis of SLE. More recently, a study from Hong Kong[11] did not support an increased prevalence of HBsAg in sera and renal biopsy specimens of lupus patients. However, the numbers studied were small. In view of these discrepancies, we undertook a study to evaluate the prevalence of HBV infection in our SLE patients.

PATIENTS AND METHODS

Seventy-six patients, all of whom fulfilled four or more of the revised classification criteria (1982) for SLE, were studied. The majority of the patients attended the rheumatology clinic at Tan Tock Seng Hospital. A few were from Toa Payoh Hospital, a general hospital. All were female with an age range of 16 to 45 years and a mean age of 31 years (SD $\pm$ 7.8). Their mean duration of SLE was 5.2 years (SD $\pm$ 5) with a range of one month to 25 years. There were 65 Chinese (85.5%), 7 Malays (9.2%), 3 Indians (3.9%) and one Eurasian (1.3%) (Table I).

The patients' blood, taken from a peripheral vein (after informed consent), was spun down and the sera immediately stored at -70°C before analysis within the week. The sera were

Table I - Demographic profile of patients and controls

	SLE patients n=76	Controls n=100
Sex	Female	Female
Age range (year)	16-45	18-40
Mean age (SD) (year)	31 (7.8)	27 (5)
Racial distribution (%)		
Chinese	85.5	85
Malay	9.2	8
Indians	3.9	6
Others	1.3	1

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Table II - Results of serological markers of HBV infection

	SLE Patients no. (%)	Controls no. (%)
No positive marker	61 (80.3)	81 (81)
One or more positive markers	15 (19.7)	19 (19)
Serological marker		
HBsAg	1 (1.3)	6 (6)
Anti-HBsAb	12 (15.8)	12 (12)
Anti-HBcAb	11 (14.5)	16 (16)

Table III - Relationships of seropositivity to immunosuppressive therapy and transfusion

	At least one positive marker no. (%)	No positive marker no. (%)
Previous transfusion		
Yes	4 (28.6)	10 (71.4)
No	10 (17.9)	46 (82.1)
Unknown	1	5
Use of immunosuppressants		
Yes	6 (20)	24 (80)
No	9 (20)	36 (80)
Unknown	0	1

tested for the presence of HBsAg, anti-HBsAb, and total anti-HBcAb using radioimmunoassay technique.

The following data were obtained from the patients'charts: history of tranfusion, the use of prednisolone and immunosuppressants both in the past and at the time of study. Quantitative immunoglobulin levels done within 3 months of the study were recorded, if available.

One hundred sex- and age-matched healthy volunteers were used as controls. These also had their sera tested for HBsAg, anti-HBsAb and total anti-HBcAb.

All the patients and healthy controls never received hepatitis B vaccination.

RESULTS

Fifteen SLE patients (19.7%) were found to have one or more serological markers of HBV infection (Table II). This result is comparable to the prevalence of HBV infection in the age and sex-matched control group in which 19% had one or more markers of infection.

Only one SLE patient was positive for HBsAg and she was also positive for total Anti-HBcAb. Of the 11 patients with anti-HBsAb, only 2 had a titre of less than 10 mIU/ml, 6 had titres of more than 100 mIU/ml.

Seventy-five patients had received steroids and thirty had received immunosuppressants (azathioprine or cyclophosphamide). There was no significant difference in the prevalence of HBV infection in patients who had received immunosuppressants compared with those without immunosuppressants (Table III). The group of patients who had received transfusion in the past had a higher prevalence of positive serology compared to those without a history of transfusion but this was not statistically significant. Of the 14 patients who had a history of transfusion, 9 also gave a history of use of immunosuppressants and of these 9 patients, only 2 were positive for any of the markers of HBV infection. Eleven patients had quantitative immunoglobulin measurement and this was abnormal in 2; one had selective IgA deficiency, the other had low IgM. These 2 patients did not have any marker of HBV infection.

DISCUSSION

Hepatitis B virus infection is endemic in Singapore. Infection is frequently acquired in the perinatal period and childhood.

Our study did not reveal any increase in the prevalence of HBsAg, anti-HBsAb and total anti-HBcAb in SLE. These findings are in agreememt with results from Bonafede et al[10], Panush et al[5], Shorey et al[6] and Lai et al[11]. Studies by Alarcon-Segovia et al[7], Ziegenfuss et al[8] and Permin et al[9] however showed a sero-prevalence of 25% to 75%. The higher prevalence in earlier studies may have been due to non-specific reactions or false positive readings related to the technique used. Permin et al[9] however used a standard radioimmunoassay.

Our study suggests that seroprevalence of HBV infection is unrelated to the therapy of SLE. There is no difference between those who had received immunosuppressants and those without immunosuppressants. History of transfusion of blood or blood products was associated with a higher prevalence of positive serology. This, however, was not statistically significant. This data is reassuring since patients with SLE may occasionally require transfusion for problems of thrombocytopenia or pulmonary haemorrhage.

In the 2 patients who were found to have abnormal immunoglobulins, one with selective IgA deficiency and the other with low IgM, none had any positive marker of HBV infection. Alarcon-Segovia et al[7] reported the appearance of high titres of hepatitis-associated antigen with the disappearance of IgA in a patient. Both the IgA deficiency and antigenemia persisted in this patient described by the authors. Because of the small number of patients with IgA deficiency, its significance as a risk for HBV infection is unknown.

In conclusion, we have shown that HBV infection is not increased in patients with SLE. Steroid and immunosuppressants do not increase the risk of infection.

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