

Hepatitis B Virus and polymyalgia rheumatica: a search for HBsAg, HBsAb, HBcAb, HBeAg, and HBeAb

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SUMMARY Forty-three consecutive patients with polymyalgia rheumatica were studied for serological markers of actual or previous hepatitis B virus infection. Signs of active virus replication, which include HBsAg supported by the presence of HBeAg and anti-HBc in high titres, were not found in any cases. Anti-HBs, a serological sign of previous hepatitis B virus exposure, was present in 16.8%. The prevalence of anti-HBs is strongly age-dependent in the normal population, and its prevalence in polymyalgia rheumatica was not significantly different from the incidence found in other hospital patients. No significantly raised incidence was found in any subgroups, including patients with or without giant cell arteritis treated or not treated with prednisone and patients with or without liver dysfunction. These results do not support the concept that current or previous hepatitis B virus infection plays any role in the pathogenesis of the majority of cases of polymyalgia rheumatica.

Polymyalgia rheumatica (PMR) and giant cell arteritis are closely related diseases of unknown aetiology. During a search for a virus aetiology Bacon *et al.* found an increased incidence of hepatitis B virus antibody.¹ This may be an important finding, as some reports during the last few years have demonstrated a link between hepatitis B virus infection and later development of vasculitis (polyarteritis nodosa, essential cryoglobulinaemia).²⁻⁴ However, the normal serological events in the course of hepatitis B virus infection are characterised by the occurrence of several antibodies and antigens, of which the e/anti e system are indicators of chronicity.^{5,6}

We decided to look for these serological markers in PMR and the results of a search for HBsAg, HBsAb, HBcAb, HBeAg, and HBeAb in the first 43 patients are presented here.

Patients and methods

Forty-three consecutive patients were studied. Thirty-six showed classical symptoms of PMR:

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muscle aching, extreme tiredness, weight loss, fever, raised erythrocyte sedimentation rate (ESR), and anaemia, and 7 showed mostly signs of temporal arteritis.

Controls comprised 684 patients aged 50-89 years admitted consecutively to a general hospital.

In all but 8 cases a biopsy of a temporal artery was performed. Hgb, ESR, se-fibrinogen, alkaline phosphatase, and immunoglobulins were estimated by routine methods. Antinuclear antibodies (ANA) and rheumatoid factors (latex, Waaler-Rose) were tested for at the State Serum Laboratory. HbsAg was studied by an enzyme immunosorbent technique (Hepanostica, Organon Technica). Anti-Hbs was determined by a radioimmuno precipitation assay previously described.⁷ Anti-Hbc was detected by counterimmunoelectrophoresis⁸ and by radioimmunoassay (Core-AB, Abott). Anti-Hbe was studied by an immunodiffusion technique.⁵

Results

The youngest patient was 51 and the oldest 86 years old, mean 69 years; 77% were female. Table 1 shows the clinical findings. At the time of investigation 19 patients were on prednisone treatment and 24 had not received any treatment except

analgesics. Ten had had their disease less than 1 month, 6 between 1 and 3 months, and 27 over 3 months. The range was 2 days to 10 years.

Giant cell arteritis was found in 48% of 35

Table 1 *Clinical findings in 43 patients with polymyalgia rheumatica*

<i>Prednisone</i>		
Treated		19
Not treated		24
<i>Temporal arteritis</i>		
+		17
0		18
Not tested		8
<i>Mean ESR</i>		97 (44-144)
<i>Duration of disease</i>		
< 1 month		10
> 1 month < 3 months		6
> 3 months		27
<i>Sex</i>		
Male		10
Female		33
<i>Mean age</i>		68.7 (51-86)
<i>Alkaline phosphatase</i>		
Raised		20
Not raised		15
Not tested		8

Table 2 *Hepatitis B associated antigens and antibodies in 43 patients with polymyalgia rheumatica*

<i>Patients with polymyalgia</i>	<i>Number studied</i>	<i>HBs</i>		<i>HBc</i>	<i>HBs</i>	
		<i>Ag Positive</i>	<i>Ab</i>	<i>Ab Positive</i>	<i>Ag</i>	<i>Ab</i>
Untreated	24	0	5 (20.8%)	2*	0	0
Treated with prednisone	19	0	2 (10.5%)	2*	0	0
Total	43	0	7 (16.8%)	4	0	0
Control patients	684		55 (12.4%)	NT		

*Also positive for anti-HBs.

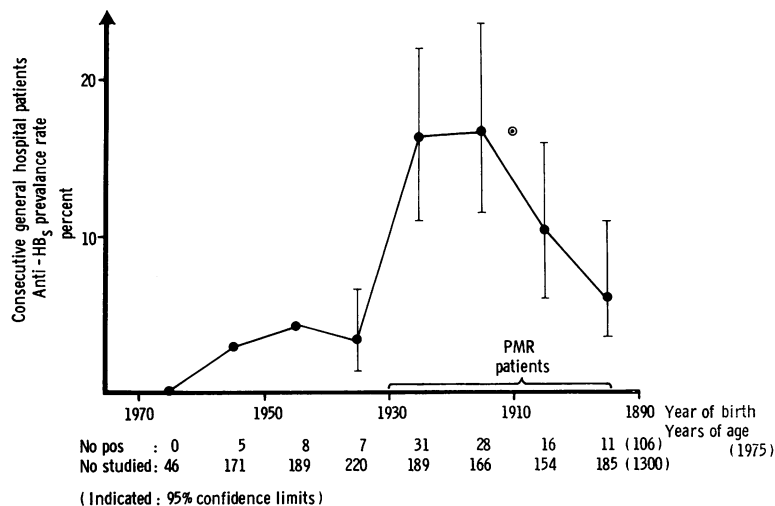


Fig. 1 *Anti-HBs prevalence rate in 1300 consecutive general hospital patients*

patients investigated. The mean ESR before treatment was 97 mm in the first hour range (44-144).

Elevated alkaline phosphatase levels were observed in 57% of 35 patients investigated. No other biochemical signs of hepatic dysfunction were found (normal results for aspartate amino transferase, bilirubin, prothrombin). Two patients had a history of previous hepatitis 10 and 20 years before investigation, and 1 had cirrhosis of the liver.

Table 2 shows the occurrence of hepatitis B virus surface antigen and antibody (HBsAg, HBsAb), hepatitis B core antibody (HBcAb), and the e antigen and antibody. HBsAg was not found in any patient. In the whole group 7 sera were positive for HBsAb, and 4 of these were also positive for anti-HBc. None of the sera reacted in the e/anti-e system. The prevalence rate of anti HBs was 20.8% in the untreated group and 10.5% in patients treated with prednisone ($P > 0.05$), corresponding to 16.8% in the whole group. When compared with the prevalence rate in 684 inpatients of the same age (12.4%) (Fig. 1) the overall frequency of anti-HBs was not significantly raised among PMR patients ($\chi^2 = 0.67$).

Table 3 shows an analysis of various patient subgroups and the occurrence of hepatitis B virus (HBV) antibodies. No relation was found to age over or below 70 years, to raised alkaline phosphatase levels, treatment with prednisone, mean ESR, or giant cell arteritis.

The duration of disease before investigation was lower in the seropositive group, but the range was considerable. In the 5 untreated seropositive patients the mean duration of disease was 89 days as compared with 98 days in untreated seronegative patients.

Table 3 Clinical data on 43 patients with and without serological signs of hepatitis B virus infection

Seroreactions for HBV infection	Number studied male/female	Temporal arteritis Pos./Neg.	Mean age years	Duration of disease before investigation	Alk. phosphatases not raised	Maximum ESR (mean)	Treated with prednisone ±	
Positive	1/6	2/4	66	<1 month	1	4 (57%)	67	2/5
				>1 <3 months	0			
				>3 months	6			
Negative	9/27	15/14	70	<1 month	9	16 (44%)	94	17/19
				>1 <3 months	6			
				>3 months	21			

Discussion

The normal sequence of serological events in the course of hepatitis B infection is now well characterised. Signs of active virus replication include HBsAg supported by the presence of HBeAg and anti-HBc in high titres.⁶ In agreement with Dickson *et al.*⁹ and other investigators¹⁰ we did not find HBsAg in any sera in the present series. This is further supported in the present report by the lack of HBeAg.

From the sensitive test used in the various investigations it can be concluded that signs of active hepatitis B virus replication such as are seen in some cases of polyarteritis nodosa and other types of vasculitis is *not* a feature of polymyalgia rheumatica or giant cell arteritis.

Nor does the present report support the concept of any relationship between previous hepatitis B virus infection and subsequent development of polymyalgia rheumatica in the majority of patients, as proposed by Bacon *et al.*¹ and Müller-Schoop *et al.*¹¹ Serological signs of previous hepatitis B virus replication include anti-HBs with or without lower titres of anti-HBc, with the modification based on the recent report of Spero *et al.*¹² that the presence of anti-HBc may signify ongoing intrahepatic HBV infection. We have found evidence of previous hepatitis B exposure in 16.8% of patients with polymyalgia rheumatica. However, since the prevalence of anti-HBs is strongly age-dependent^{13 14} and shows an excess prevalence in older age groups (Fig. 1), the prevalence in polymyalgia rheumatica is similar to the incidence in other hospital patients.

This strange age-dependent distribution of anti-HBs antibodies—which is probably a cohort phenomenon and found in most Scandinavian countries—strongly influences the interpretation of previous reports, the data in which are not based on age-corrected control populations.

Our data show a prevalence rate twice as high in the untreated group as in the steroid treated, which may imply, as proposed by Bacon *et al.*,¹ that prednisone decreases the antibody titre effectively.

Our data do not disprove the evidence for hepatitis B virus association in some cases of PMR, but provide evidence that the advocacy of this virus as the major cause of PMR is greatly overstated. PMR as a syndrome may be a final common pathway for a variety of antigen-antibody complex interactions.

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