Postgraduate Medical Journal (February 1982) **58**, 80–81

The clinical course of acute type A hepatitis in chronic HB_sAg carriers—a report of 3 cases

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Summary

The clinical, virological, and biochemical course of 3 chronic HB_sAg carriers who developed acute hepatitis A is described. Two of the patients had pre-existent chronic active hepatitis. The clinical course in each case was benign with resolution within one month, and there was a marked fall in HB_sAg titre in one of the patients with chronic active hepatitis.

Introduction

It is now recognized that the hepatitis A virus (HAV), and hepatitis B virus (HBV) are antigenically and morphologically distinct (Dane, Cameron and Briggs, 1970; Feinstone, Kapikian and Purcell, 1973) and there are reports of patients who have had repeated attacks of hepatitis owing to exposure to the different viruses (Mosley *et al.*, 1977). It is not surprising, therefore, that chronic HB_sAg carriers do not appear to be protected against infection with epidemic HAV (Dietzman *et al.*, 1972), and sporadic non-A, non-B agents. As the outcome of these double infections is unclear and documented attacks of acute HAV infection in chronic HB_sAg carriers with biopsy-proved liver disease are rare, the authors present the clinical and virological course of 3 chronic HB_sAg carriers who contracted an acute HAV infection.

Case reports

Case 1

This 25-year-old male homosexual was found to be HB_sAg positive when he attended a venereology clinic in June 1979. Liver function tests at that time were abnormal (bilirubin 8 μmol/l, alkaline phosphatase 85 u/l, alanine aminotransferase (ALT) 184 i.u./l. Liver biopsies were carried out in September 1979, and again in October 1980 because of persistently abnormal liver function tests, and showed chronic active hepatitis with piecemeal necrosis and bridging fibrosis. Orcein staining showed an occasional positively stained hepatocyte. Throughout this period he was HB_eAg positive by radio-immunoassay (RIA) (Abbott Labs) and the HB_sAg titre by reverse passive haemagglutination (Wellcome Labs) was 1 : 25 000. On 30 March 1981 the patient became nauseated and a few days later presented with pruritus, fever and dark urine. Liver function tests during the acute attack and after resolution are shown in Table 1. Viral studies showed the presence of an IgM anti-HAV antibody confirming acute infection with HAV. His clinical course was unremarkable and both clinical and biochemical resolution occurred within 4 weeks, with return of the alanine aminotransferase to pre-infection concentrations.

Case 2

This 34-year-old male heterosexual had been a chronic HB_sAg carrier since 1974 when he was detected at a blood donor session. Throughout the years 1974–1981 his liver function tests have remained normal. His HB_sAg titre was 1 : 3600 and he had anti HB_e antibody by RIA. On 27 February 1981 he presented with anorexia, and became jaundiced 3 days later. Liver function tests are shown in Table 1. Acute HAV infection was confirmed by detection of the anti-HAV IgM antibody. He made a complete clinical and biochemical recovery within 4 weeks and there was no significant change in his HB_sAg status.

Case 3

This 27-year-old male homosexual was found to be an HB_sAg carrier on routine screening at a venereology clinic in January 1979. His liver function tests at that time showed bilirubin 24 μmol/l, alkaline phosphatase 57 u./l, alanine aminotransferase 132 i.u./l. Liver biopsies performed on May 1979 and June 1980 showed chronic active hepatitis and many orcein-positive HB_sAg-containing cells. Throughout this period he has been HB_sAg positive with an HB_sAg titre of 1 : 32 000. The serum alanine

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0032-5473/82/0200-0080 $02.00

aminotransferase fluctuated between 67 and 186 i.u./l, until 3 April 1981, when he presented with nausea, pruritus and dark urine. Liver function tests are shown in Table 1. IgM anti-HAV antibody was detected. By 28 April 1981 he was feeling well and his liver function tests had returned to levels lower than before the acute hepatitis. In addition the HB_sAg titre was negative by reversed passive haemagglutination and was positive only by radioimmunoassay. Liver biopsy carried out 3 weeks later showed chronic persistent hepatitis and orcein staining was negative.

TABLE 1. Liver function tests in 3 Hb_sAg carriers before, during, and after acute type A hepatitis

	Case 1	Case 2	Case 3
Before acute hepatitis			
Bilirubin (μmol/l)	8	4	6
Alk. phosp (u./l)	85	57	50
ALT (i.u./l)	300	16	270
During acute hepatitis			
Bilirubin (μmol/l)	140	160	195
Alk. phosp (u./l)	128	149	128
ALT (i.u./l)	2890	3160	5820
Following recovery			
Bilirubin (μmol/l)	30	7	7
Alk. phosp (u./l)	128	50	114
ALT (i.u./l)	287	19	48

Alk. phosp = Alkaline phosphatase; ALT = alanine aminotransferase.

None of these 3 cases has received any drug therapy either before or during the course of the attack of acute viral hepatitis.

Discussion

The 3 patients described each developed acute type A hepatitis on top of chronic hepatitis B virus carriage. In all 3, the clinical course was benign, even in the 2 patients with biopsy-proved chronic active hepatitis, and liver function tests returned to pre-attack levels in each patient. On the other hand, acute viral hepatitis may have a much more serious and even fatal course in patients with pre-existent established cirrhosis (Theodossi *et al.*, 1979).

The fall in HB_sAg titre in case 3 from 1 : 32 000 to undetectable concentrations by reverse passive haemagglutination in successive tests, a highly significant reduction, is of great interest particularly because the HB_sAg titres are usually constant in patients with chronic active hepatitis (Heijtink *et al.*, 1980). This phenomenon would support the theory of viral interference (Dulbecco and Ginsberg, 1973) which suggests that simultaneous infection with 2 viruses results in inhibition of multiplication of one of them. In addition, it has been suggested (Heijtink *et al.*, 1980) that the introduction of a foreign antigen results in interferon production and consequent reduction in viral particle synthesis, a view supported by the results of parenteral interferon administration in this group of patients (Greenberg *et al.*, 1976).

The finding that 2 of the 3 patients are homosexuals is consistent with the high incidence of both HAV (Corey and Holmes, 1980) and HBV (Coleman, Waugh and Dayton, 1977) infection in these patients, and that HAV attacks in this particular social group tend to occur in mini-epidemics (Mindel and Tedder, 1981).

Acknowledgments

L. A. Viola is in receipt of a grant from the University of Buenos Aires, Argentine; I. G. Barrison is in receipt of a grant from the Trustees of Charing Cross Hospital.

Addendum

Case 3 remains negative for HB_sAg by reverse passive haemagglutination and has developed anti-HB_s antibodies (Sept. 1981). His liver function tests are now normal.

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