Case report

Acute delta superinfection in a previously unrecognised HBsAg carrier with transient loss of HBsAg simulating acute non-A, non-B hepatitis

C M CHU AND Y F LIAW

From the Liver Unit, Chang Gung Memorial Hospital, Chang Gung Medical College, Taipei, Taiwan, Republic of China

SUMMARY An 18 yr old previously well male Taiwanese was admitted with malaise, anorexia, and jaundice for two weeks. Results of liver tests were compatible with acute hepatitis. On day 1, he was seronegative for HBsAg, IgM anti-HAV, IgM anti-HBc, IgM anti-CMV, and IgM EBV capsid Ab, but positive for anti-delta in association with anti-HBc and anti-HBs. At follow up on day 5 HBsAg converted to positive with decreasing titre of anti-HBs. On day 19, the titre of HBsAg increased concomitantly with loss of anti-HBs. The results of these serological profiles indicated that this patient was a previously unrecognised HBsAg carrier, who developed acute hepatitis delta virus superinfection with transient loss of HBsAg. This phenomenon should be kept in mind in the serodiagnosis of acute viral hepatitis, especially in areas of high HBV prevalence.

The aetiology of acute viral hepatitis includes acute type A hepatitis, acute type B hepatitis, acute non-A, non-B (NANB) hepatitis, and acute cytomegalovirus (CMV), and Epstein-Barr virus (EBV) infections. In areas endemic for hepatitis B virus (HBV) infection, a significant proportion of patients with acute viral hepatitis are previously unrecognised hepatitis B surface antigen (HBsAg) carriers superimposed with other forms of acute hepatitis, such as acute exacerbation of underlying chronic HBV infection or superinfection with other non-B virus(es).¹⁻⁴ Studies in man and in animals have shown that non-B virus superinfection in chronic HBsAg carriers may transiently or persistently suppress the production of HBsAg.⁵⁻⁹ It is conceivable that, if a previously unrecognised HBsAg carrier was superinfected with other non-B viruses and the synthesis of HBsAg was suppressed to an undetectable level, the serological findings may show acute viral hepatitis seronegative for HBsAg simulating acute non-B hepatitis. The

case reported here emphasises this possibility and should be kept in mind in the serodiagnosis of acute viral hepatitis, especially in areas of high HBV prevalence.

Case Report

An 18 year old previously well Taiwanese man was referred to our unit with general malaise, anorexia, nausea, and vomiting for two weeks and progressive jaundice for four days. He denied any past history of hepatobiliary or systemic disease, alcoholism, blood transfusion, homosexuality or intravenous drug addiction. On admission, physical examination revealed that there was marked yellowish discoloration of his skin and sclera. The liver size was 13 cm along the right middle clavical line with 2 cm palpable below right costal margin. The consistency of the liver was soft. The spleen was impalpable. There was no spider angioma, nor palmar erythema. The results of liver biochemical tests were compatible with severe acute hepatitis with low serum albumin (33 g/l, N>35), high AST (1802 U/l, N<40), ALT (2790 U/l, N<40), and bilirubin (316 µmol/l, N<17). With

Address for correspondence: Chia-Ming Chu, MD, Liver Unit, Chang Gung Memorial Hospital, 199, Tung Hwa North Road, Taipei, Taiwan, 10591, Republic of China.

Received for publication 16 February 1988.

supportive treatment, the patient's clinical symptoms and biochemical test improved gradually. The serological hepatitis markers on admission day 1 failed to detect HBsAg, IgM anti-HAV, IgM anti-HBc, IgM antibody against CMV (IgM anti-CMV), and IgM antibody against EBV capsid antigen (IgM EBV capsid Ab), but anti-delta was incidentally found to be positive (1:10) in association with anti-HBc and anti-HBs. On day 5, serum HBsAg converted to positive with decreasing titre of anti-HBs. On day 19, the titre of HBsAg increased concomitantly with loss of anti-HBs. Anti-delta was persistently positive at the same titre. The clinical course and the sequential changes in the titres of HBsAg and anti-HBs are shown in the Figure.

Serum HBsAg, anti-HBs, anti-HBc, anti-delta, and IgM anti-HAV were assayed with radioimmunoassay (Ausria II-125, Ausab, Corab, anti-delta, and HAVAB-M, Abbott Laboratories, Chicago, Ill, USA). IgM anti-HBc was assayed with solid phase u-antibody capture radioimmunoassay (Core-IgMK, Sorin, Italy). IgM anti-CMV was assayed by EIA (CMV stat M, MA, Maryland, USA). IgM EBV capsid Ab was assayed by indirect immunofluorescence (EBV IgM, Gull, Utah, USA).

Discussion

It seems obvious that the acute viral hepatitis in this case could not be attributed to acute HAV, HBV, CMV, or EBV infection. It is noteworthy that the patient was incidentally found to be seropositive for anti-delta without detectable HBsAg on initial serological studies. As it is usually not necessary to test anti-delta in the absence of serum HBsAg,¹⁰ this patient thus might have been diagnosed as acute NANB hepatitis initially if anti-delta was not tested.

There are several relatively rare occasions in which anti-delta was detected without serum HBsAg: (1) Acute coinfection of HBV and hepatitis delta virus (HDV) with early clearance of HBsAg. De Cock *et al*¹¹ have reported such a patient who developed acute hepatitis seropositive for IgM anti-HBc and anti-delta but without circulating HBsAg. (2) Past infection with HBV and HDV. These patients might have recovered from infection of HBV and HDV, and they were positive for anti-delta in association with anti-HBc and anti-HBs.¹² (3) Acute HDV superinfection in chronic HBsAg carrier with suppression of HBsAg below the detectable levels.^{5,6} The initial serological profile of our patient therefore suggested that he might have had past infection of HBV and HDV and the current episode of acute viral hepatitis was probably caused by acute NANB hepatitis, or that he was a previously unrecognised HBsAg carrier who developed acute HDV superinfection with sup-

Figure Clinical course and the sequential changes in the titres of HBsAg and anti-HBs in a previously unrecognised HBsAg carrier with acute hepatitis delta virus superinfection. Normal values for bilirubin, AST and ALT were <17 μmol/l, <40 U/l, and <40 U/l respectively. HBsAg and anti-HBs were positive when S/N >2.1.

pression of HBsAg. The demonstration of the reverse seroconversion from anti-HBs to HBsAg in this patient strongly indicated that he contracted HDV superinfection with transient loss of HBsAg because of viral interference of HDV.

Rizzetto *et al*⁷ have shown that there is a transient suppression of the production of HBV-associated antigens when HBsAg carrier chimpanzees were superinfected with HDV. Several clinical studies also showed a transient or persistent loss of HBsAg with seroconversion to anti-HBs in HBsAg carriers with HDV superinfection.^{5,6} A similar phenomenon also has been reported when HBsAg human carriers were superinfected with HAV or when HBsAg carrier chimpanzees were superinfected with NANB viruses.^{8,9} It thus should be kept in mind that acute superinfection of HAV, NANB viruses, or HDV in previously unrecognised chronic HBsAg carriers might serologically simulate acute type A or NANB hepatitis, or present as acute viral hepatitis seropositive for anti-delta without circulating HBsAg, as seen in the present case, if the production of HBsAg was suppressed to an undetectable level. We therefore suggest that in areas of high HBV prevalence retest of HBsAg during the convalescence period is recommended for cases presenting as acute non-B hepatitis.

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