Serum Immunoglobulin Levels in Hepatitis Non-A, Non-B: A Comparison with Hepatitis A and B

Introduction

The development of serological methods for the diagnosis of hepatitis A and hepatitis B infections has revealed a third type of viral hepatitis without the serological markers of hepatitis A or B in serum. This new type is presently called hepatitis non-A, non-B. In recently published clinical studies on hepatitis non-A, non-B, certain clinical differences between the two classical types of hepatitis and the new type have been found (1).

The patterns of immunoglobulins in presumed hepatitis A and in hepatitis B have been documented (2, 3, 4), while little is known about hepatitis non-A, non-B in this respect. In the present study the serum levels of IgA, IgG and IgM during the early acute phase of infection were compared in patients with hepatitis A, B and non-A, non-B.

Materials and Methods

Patients: The material consisted of 86 patients with viral hepatitis (23 females; age 18 to 57 years), admitted consecutively to the Department of Infectious Diseases, East Hospital, Göteborg, Sweden, during 1976 and 1977. Onset of illness was defined as the first day of dark-coloured urine or jaundice. Blood samples were obtained within two weeks of onset of illness. A serum alanine-aminotransferase (S-ALAT) level at least five times the upper normal level was criterion for the diagnosis of viral hepatitis.

Hepatitis A was serologically diagnosed by a solid phase radioimmunoassay (5). A fourfold or greater increase of anti-HAV titer in paired serum samples occurred in 16 patients. In six patients with detectable anti-HAV in serum, but without a significant increase in titer, anti-HAV of the IgM class was demonstrated (6). Thus in all, 22 patients were serologically classified as cases of hepatitis A infection.

Hepatitis B was diagnosed in 50 of the 86 patients. HBsAg was transiently demonstrable by radioimmunoassay (Austria II, Abbott Laboratories) in 46 patients. Four other patients with anti-HBc (Corab, Abbott Laboratories) in acute phase serum samples, who developed anti-HBs during convalescence, were also classified as cases of hepatitis B infection.

In patients without serological evidence of hepatitis A or hepatitis B, paired serum samples were analysed for the presence of IgM antibodies against cytomegalovirus (CMV) by the immunofluorescence technique (7). The ox-cell haemolysin test (8) for heterophile antibodies was used to diagnose Epstein-Barr virus (EBV) infection.

Fourteen patients lacking serological evidence of infection with hepatitis A or hepatitis B, were classified as cases of hepatitis non-A, non-B. About half of the patients in each of the three types of hepatitis were drug addicts.

Immunoglobulin levels: The levels of IgA, IgG and IgM were determined in fresh serum samples by the single radial immunodiffusion technique (9). Fisher's permutation test (10) was used for the comparison of the serum immunoglobulin levels in the different groups of patients.

Summary: The serum levels of IgA, IgG and IgM were determined by the single radial immunodiffusion method in 86 patients with acute viral hepatitis serologically differentiated by radioimmunoassays. The levels of IgA and IgG were similar in patients with hepatitis A, B and non-A, non-B, while differences in IgM levels were observed between the three groups. The hepatitis non-A, non-B group had significantly lower levels of IgM than both the hepatitis A and hepatitis B group, a finding which may be diagnostically useful if hepatitis A serology fails.


Received: 2 July 1979

Dr. G. Norkrans, Dr. M. Wahl, Prof. S. Iwarson, Department of Infectious Diseases, University of Göteborg, East Hospital, Göteborg, Sweden;
Dr. L. A. Nilsson, Institute of Medical Microbiology, University of Göteborg, Göteborg, Sweden;
PD Dr. G. Frösner, Max-von-Pettenkofer-Institut, University of Munich, Pettenkoferstr. 9a, 8000 Munich 2, West Germany.
Figure 1 a, b und c: Serum levels of immunoglobulins A, G, and M in 86 cases of hepatitis differentiated serologically into hepatitis A, B and non-A, non-B. Males (M) and females (F) have been indicated separately. Mean values and standard errors are given at the bottom of each figure. The normal range in healthy adults in Sweden is indicated by the shadowed areas.

and females have been indicated separately. No statistically significant differences were noted between the three types of hepatitis for the serum levels of IgA and IgG. Marked differences were however observed for the IgM levels. The mean IgM value in the hepatitis A group was significantly higher than that of the hepatitis B (p < 0.02) and the hepatitis non-A, non-B (p < 0.001) group. The mean IgM value in the hepatitis B group was also significantly higher than that of the hepatitis non-A, non-B group (p < 0.01).

Eighteen hepatitis A patients (82%) and seventeen hepatitis B patients (34%) had IgM levels which exceeded the highest observed value in the non-A, non-B group, which was 2.95 g/l.

Discussion
The serum levels of IgA, IgG (3, 4) and IgD (11) have been shown to be similar in HBsAg positive and HBsAg negative hepatitis patients. This finding was confirmed for IgA and IgG in the present series. Previous studies on