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The Seroepidemiological Pattern of Acute Viral Hepatitis

An Epidemiological Study on Viral Hepatitis in the Hannover Region

Summary: The natural incidence of the etiologically distinct types of viral hepatitis was determined by investigating acute phase sera of symptomatic hepatitis cases occurring in the Hannover area in 1975 for the presence of hepatitis B surface antigen, antibodies to hepatitis A, hepatitis B core and surface antigens, and by measuring the IgM serum levels. Fourteen different seroepidemiologic patterns were recognized. Although there was a high prevalence of hepatitis A antibody in the population, the frequency of hepatitis A was low (n = 56) suggesting that the hepatitis A virus does not play a major role in symptomatic hepatitis in the Hannover area at present. Spread of the hepatitis A virus was mostly associated with person-to-person contact or tourist travel in southern Europe. Hepatitis B was the predominant type of hepatitis (n = 211). Hepatitis non-A, non-B was observed infrequently (n = 62). A high percentage of patients with hepatitis B and hepatitis non-A, non-B reported parenteral exposure to potentially contaminated materials. No other findings, however, suggested an infectious etiology of hepatitis non-A, non-B.

Introduction

The detection of the hepatitis B surface (HBs-Ag) and core (HBc-Ag) antigens, and the demonstration of their corresponding antibodies provides a serologic tool for distinguishing hepatitis B from other types of hepatitis (1, 2, 3, 4). There is substantial evidence that an infection with the hepatitis A virus may be recognized by demonstrating the presence of antibody to the hepatitis A antigen (HA-Ag), a virus-like particle which is seen in stool specimens obtained prior to and in the early acute phase of hepatitis A (5, 6, 7). Applying these antigen-antibody systems, prospective studies on post-transfusion hepatitis have revealed that most cases can be attributed neither to the hepatitis A virus nor to the hepatitis B virus (8, 9, 10). This type of hepatitis has been referred to as hepatitis type non-A, non-B, which can only be recognized by exclusion of an infection with either the hepatitis A or the hepatitis B virus. Therefore, the etiologic differentiation of viral hepatitis on strictly epidemiologic grounds must be made with caution. Far more cases of sporadic hepatitis than previously thought were found to be HBs-Ag positive when tests for HBs-Ag were applied routinely (11, 12). Recent studies have indicated that in Costa Rica hepatitis A affects a majority of the population during childhood, while in the USA and Germany the prevalence of antibody to HA-Ag (anti-HA) did not reach 50–60% until the fourth decade (13, 14).

This study presents the results of an epidemiologic investigation on viral hepatitis in the Hannover area comprising a total—mostly urban—population of one million people in the northern part of the Federal Republic of Germany. All cases were clearly differentiated by means of serologic data thus demonstrating the seroepidemiologic patterns and the natural incidence of hepatitis A, hepatitis B and hepatitis non-A, non-B.

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Materials and Methods
Details about the organization of this study have been reported elsewhere (11, 15). In 1975 blood samples from 329 patients with acute viral hepatitis were collected within a period of 45 days after onset of clinical symptoms. A second serum sample was obtained from 275 patients between 2 and 5 weeks later. The diagnosis of acute viral hepatitis was accepted only if confirmed by the physician taking care of the patient, and if serum transaminase activities were above 200 U/l during the course of the disease. All sera were tested for the presence of HBs-Ag, anti-HA and antibody to the cytomegalovirus. In addition, the concentration of serum IgM was measured. In HBs-Ag negative sera, anti-HBs and anti-HBc determinations were performed. All tests were coded. The frequency and the age distribution of anti-HA in a control group without hepatitis was established in 380 randomized patients with acute respiratory infections in the Hannover area in 1975. The age-distribution of these patients ranged from six months to 80 years.

Hepatitis B Surface Antigen: Sera were investigated for the presence of HBs-Ag by radioimmuno-assay (Austria II, Abbott Laboratories, Chicago, USA), and counterimmunoelectrophoresis using a human antiserum (Lot. no. 100.06, Immuno AG, Vienna, Austria).

Antibody to Hepatitis B Surface Antigen: The radioimmuno-assay Ausab (Abbott Laboratories, Chicago, USA) was employed for the detection of anti-HBs.

Antibody to Hepatitis B Core Antigen: Anti-HBc was detected by a solid phase radioimmuno blocking assay system (16). Wells of microtiter-plates were coated with HBc-Ag purified from a human liver (16). Sera assayed were assumed to contain anti-HBc if the binding of 125 I labelled human anti-HBc-IgG to the wells was reduced to at least 50%. The standard deviation of radioactive binding in negative samples was about 10%.

Antibody to Hepatitis A Antigen: Anti-HA was also determined by a solid phase radioimmuno assay blocking test (14, 17). Anti-HA titres were expressed as 50% inhibition values. Titres below 1 : 20 were considered negative. Assay conditions were chosen to give 50% inhibition with the chimpanzee reference serum no. 811-501-573 of the National Institutes of Health, National Institute of Arthritis and Infectious Diseases, at a dilution of 1 : 200.

Antibody to Cytomegalovirus: The microtiter complement-fixation technique was used for the detection of antibodies to the cytomegalovirus. The antigen used was obtained from Dr. Krech, St. Gallen, Switzerland.

Immunoglobulin M: The IgM concentrations were measured by radial immuno-diffusion with the use of commercially available antibody agar plates (Behring Werke AG, Marburg, Germany). IgM levels in the serum up to 320 mg/l were regarded as normal.

Results
As shown in Figure 1, a strong association between the prevalence of anti-HA seropositivity and increasing age was observed in patients with HBs-Ag positive viral hepatitis as well as in individuals with acute respiratory infections. In both groups the prevalence of anti-HA increased rapidly after the age of 30 years and exceeded 70% in patients above 50 years. In children and young adults anti-HA was rarely found.

During follow-up seroconversion or an at least four-fold increase in the anti-HA titre was observed in only 14 out of 118 patients with HBs-Ag negative viral hepatitis. Anti-HA was not detectable in sera obtained prior to the onset of clinical symptoms, but low levels of anti-HA were demonstrated in the early acute phase sera (Figure 2). A significant rise in anti-HA titres occurred in patients with both low and elevated initial titres (Figure 2). These ob-