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KHUROO MS, SALEEM M, TELI MR & SOFI MA. FAILURE TO DETECT CHRONIC LIVER DISEASE AFTER EPIDEMIC NON-A, NON-B HEPATITIS. LANCET 1980; ii (8185):97-98. PMID: 6105287

FAILURE TO DETECT CHRONIC LIVER DISEASE AFTER EPIDEMIC NON-A, NON-B HEPATITIS

Sir, - A waterborne epidemic of non-A, non-B hepatitis occurred in the Kashmir valley between November, 1978, and April, 1979.[1] From January to March, 1980, the cases recorded during this epidemic were assessed for evidence of chronic liver disease. Four villages in which 102 cases of viral hepatitis had been recorded were surveyed. 4 patients died in the first two weeks of their illness with fulminant hepatic failure. None of the others had since died. One patient was positive for HBsAg, and liver biopsy in this patient 7 months after the infection showed features of chronic active hepatitis and cirrhosis. This patient was excluded from the study. 15 patients were not available for assessment at the time of survey.

The remaining 82 patients were interviewed and given a detailed physical examination. Blood was drawn for estimation of serum bilirubin, serum glutamic pyruvic transaminase (SGPT), and HBsAg. The illness in these patients had lasted from 5 days to 3 months (mean 29 days). The present assessment was done 8 to 17 months after the original illness (mean 14.8 months). None of the patients had persistent jaundice, ascites, or hepatic encephalopathy. 16 (19.5%) had recurrent mild abdominal pain, 11 (13.5%) had lost weight; 8 (9.8%) had anorexia, and 6 occasionally had dark urine. 3 patients had had a second distinct episode of jaundice after recovery from the original illness. 6 patients (7%) had soft palpable hepatomegaly, and in 5 (6 %) the spleen was palpable below the costal margin. Serum bilirubin was below 1 mg/dl in all cases. SGPT levels were within normal limits in 78 cases, in 4 cases SGOT levels were above the upper limit of normal (35, 42, 45, and 50 IU/l). Liver biopsy was not done in any of the cases.

In addition, 30 patients who had had acute viral hepatitis from this epidemic were followed up 2 to 6 months from the onset of their disease by serial liver function tests. In all cases serum bilirubin and serum enzymes returned to normal after a variable interval.

Evidence of chronic liver disease was lacking in most of our patients. Various abdominal complaints and palpable liver and spleen can occur after acute viral hepatitis in the presence of normal liver histology and were seen nearly the same percentage in healthy contacts.[2] None of the patients in the present study had chronic or recurrent jaundice or raised serum bilirubin in one-year follow-up. 4 had raised SGPT levels and could have developed chronic liver disease. However, none had symptoms or abnormal physical findings, and in none was SGPT raised to twice the upper limit of normal. We decided not to do liver biopsies in these cases. Liver functions, especially serum hepatic enzymes, can fluctuate in chronic liver disease,[3] and a single estimation of liver-function tests could have overlooked chronic liver disease in some of our cases. This possibility was excluded, because 30 patients with acute non-A, non-B hepatitis followed prospectively had no residual abnormality of liver function on repeated testing.

Non-A, non-B hepatitis was first described after blood transfusion,[4] and chronic liver disease followed in a high percentage of cases.[3,5,6] We, however, failed to detect chronic liver disease after acute non-parentally transmitted non-A, non-B hepatitis. The reason for this is not clear, but possible explanation are the large amount of viral protein administered during transfusion or, perhaps more importantly, the existence of at least two non-A, non-B viral agents, one of which is more commonly associated with post-transfusion hepatitis as well as an unusual tendency to be associated with the development of chronic liver disease.

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THE LANCET, AUGUST 16, 1980 **365-366**

KHARDORI, R. FAILURE TO DETECT CHRONIC LIVER DISEASE AFTER EPIDEMIC NON-A, NON-B HEPATITIS. LANCET 1980; ii (8190):365-366.
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FAILURE TO DETECT CHRONIC LIVER DISEASE AFTER EPIDEMIC NON-A, NON-B HEPATITIS

Sir, -I was appalled to read the report of Dr. Khuroo and his associates (July 12, p. 97) which seems to be based more on imagination than facts. What the authors call non-A, non-B hepatitis is based on exclusion of HBsAg, which does not necessarily even exclude type-B hepatitis. A diagnosis of non-A, non-B hepatitis requires the serological exclusion of: (i) HBsAg, (ii) de-novo appearance of anti-HBs, (iii) seroconversion for anti-hepatitis-A-virus (HAV); and (iv) presence of anti-HAV or anti-HBs early in the acute phase of infection. Apart from these criteria, hepatitis due to Epstein-Barr virus or cytomegalovirus needs to be excluded. If the patients are seen in the early phase HAV can be detected by immune adherence haemagglutination, and it would have been helpful if Khuroo and his associates had done so to determine whether their patients had what looks to me like hepatitis A.

Using alanine aminotransferase (SGPT) as a marker for chronic persistent or chronic active hepatitis is rather crude and also pointless, since the enzyme levels can fluctuate, as was pointed by the authors themselves. Secondly return of serum transaminase levels to normal does not necessarily exclude histologically chronic active hepatitis.[1] Liver biopsy alone is the sole determinant and unfortunately that was not done in the study of Khuroo et al. An antigen-antibody system closely associated with non-A, non-B hepatitis and not with other hepatitis types can now be detected in serum by counterelectrophoresis.[2] This system appears to be related to hepatitis "C" reported in transfusion-associated non-A, non-B hepatitis in Japan.[3] Chronic non-A, non-B hepatitis carrier state has been documented and in a recent study the duration of infectivity extended well beyond 6 years.[4] Lastly Khuroo's suggestion that there may be more than one agent for non-A, non-B hepatitis appears to have been drawn inspiration from Rekela and Redeker's report[5] to the extent that in the closing remarks more or less the same words have been used.

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THE LANCET, OCTOBER 18, 1980 *860-861*

KHUROO MS. CHRONIC LIVER DISEASE AFTER NON-A, NON-B HEPATITIS. LANCET 1980; ii (8199):860-861 PMID: 6105287

CHRONIC LIVER DISEASE AFTER NON-A, NON-B HEPATITIS

Sir, - In our one-year follow-up (July 12) on patients with non-A, non-B (NANB) hepatitis on which detailed epidemiological, clinical, biochemical, pathological, and antigen data are reported elsewhere (*Am J Med* 1980;68:818). NANB hepatitis was diagnosed by serological exclusion of HBsAg (passive haemagglutination), anti-HBc (counter-electrophoresis), and anti-HAV IgM (radioimmunoassay and ELISA) in acute phase sera. At follow-up all patients were tested for HBsAg (CEP0 to exclude the development of hepatitis B in the intervening period. Dr, Khardori's comments (August 16, p. 365) have been written without reference to our Am J Med paper. We did not diagnose NANB hepatitis by exclusion of HBsAg (CEP0 but used very sensitive methods to exclude hepatitis A and B.

Chronic hepatitis has been defined as unexplained persistence of an abnormal transaminase level for more than 20 weeks after acute hepatitis, and only such patients need liver biopsies further to classify chronic hepatitis into chronic persistent and chronic active hepatitis.[1] In our follow-up data, 4 cases showed unexplained persistence of abnormal transaminase levels and could have had chronic hepatitis. As these enzyme levels can fluctuate, serial estimations of SGPT were done in 30 cases to exclude this possibility. 5 cases with normal enzyme levels have had repeat liver biopsies and these showed normal liver histology. With these data we believe that the incidence of chronic hepatitis following non-parenteral NANB is very low and does contrast with the data following post-transfusion NANB hepatitis.[2]

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