Non-A Non-B Hepatitis in Parenteral Drug Abusers

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Summary

Nearly nine-tenths of 27 biopsied intravenous drug abusers showed evidence of non-A non-B hepatitis. In between two-thirds and four-fifths non-A non-B infection was the initial viral insult to the liver.

Persons with known HBV infection and viral hepatitis cannot be assumed to suffer from HBV associated liver disease. Vaccination of drug addicts with inactivated HB_sAG will not preclude them from developing chronic liver disease.

There is evidence among haemophiliacs that chronic hepatitis previously assumed to have been attributable to hepatitis B virus (HBV) is more likely to have been due to other, non-A non-B hepatitis viruses.[1] In a recent study on the Delta agent and liver disease we have compared hepatitis B serology and histology in 27 parenteral drug abusers[2] and this has afforded us the opportunity to assess the likelihood of a non-A non-B origin to the hepatitis in these patients. We report this assessment in this paper.

Patients and Methods

Twenty-seven parenteral drug abusers admitted to hospital for liver biopsy during the period January 1st to August 31st 1981 are included in this study. At this time an epidemic of hepatitis B was in progress among drug abusers in Dublin.[3] All patients who were admitted with clinically acute hepatitis were asked the duration of intravenous drug abuse and if they had been jaundiced since or prior to the onset of such abuse.

Patients had the following laboratory investigations performed: Full blood count, platlet count, prothrombin time, serum bilirubin, serum alanine and aspartate transaminases (SCOT, SGPT), alkaline phosphatase, serum proteins and albumin. Serological tests for HBV markers were performed as follows: radioimmunoassay (RIA) for hepatitis B surface antigen (HB_sAg) (Ausria 11, Abbott), immunodiffusion (ID) for anti-HB_s,[4], semi-micro ID for HB_sAg and anti-HB_e; and RIA and enzymeimmunoassay for hepatitis B core antibody (anti-HB_egG) (Corab, Corzyme, Abbott).

Tests for IgM antibody to hepatitis A virus were carried out by RIA (Havab M, Abbott). Patients negative for HB_sAg and by Havab M were also tested for IgM anti-HB_s by RIA.

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HBV serology was taken 10 indicate acute HBV infection if the patient cleared HB_sAg within four months and HB_sAg within two weeks and/or seroconverted to anti-HB_e. If HB_sAg persisted at similar levels for more than six months the patient was defined as being chronically infected with HBV.

Liver biopsies were carried out using a Menghini needle. Histological diagnosis was made in accordance with the criteria suggested by an International Group in 1977.[5]

Where biochemistry was serially repeated and the serum aspartate transaminase (SGPT) fell and rose again by a factor of at least two, or a factor of three if it had previously returned to normal (| 45 i.u./l) a further transaminase peak was deemed to have occurred. Non-A non-B viral infection was assumed to have contributed to the histological findings if tests for hepatitis A were negative, and (a) the histological findings were of chronic hepatitis in the presence of acute HBV serology; or (b) all tests for HBV markers were negative or (c) the histology was of acute hepatitis in the presence of chronic or static HBV serology (IgM anti-HBc negative). Two or more peaks of SGPT were taken as supportive evidence of non-A non-B infection.[6]

A conclusion as to the virus(es) deemed causally related to the histological findings was derived for each patient.

Results

Of the 27 patients 22 were male; their ages ranged from 12 (mean 20.8) to 29 years. The duration of intravenous drug abuse was from six (mean 33.6) to i20 months. Three patients had a history of previous jaundice since the onset of drug abuse; none gave a history of jaundice prior to the onset of abuse. The serological biochemical and initial histological findings and the conclusions concerning the viral origin of the patients' histological hepatitis are shown in the table. Eight patients had a second liver biopsy six or more months after the first and three patients had three liver biopsies at intervals of at least six months. All eleven repeat liver biopsies showed chronic disease, either persistent or active, in agreement with the first biopsy. These results show that non-A non-B virus infection contributed to the hepatitis in 23 (85%) or 24 (89%) of the 27 patients. Furthermore in between 19 (70%) and 22 (81%*) of* the patients non-A non-B infection was the initial viral insult to the liver.

Discussion

The findings in this study are similar to those of Craske who showed that a proportion of hepatitis **in** haemophiliacs was of non-A non-B origin of at least two serotypes[1], the main complication of which was persistently abnormal transaminase levels, a finding common with non-A, non-B post-transfusion hepatitis (PTH).[8] Therefore, it should no longer be assumed that chronic viral hepatitis in the presence of known hepatitis B infection is caused by such infection. This does not exclude a long-term additive effect of HBV infection with non-A non-B which may influence the progression of chronic persistent to chronic active hepatitis, the development of cirrhosis or the ultimate risk of hepatoma. Equally several types of non-A non-B hepatitis may act synergistically.

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Table 1
Serological, Biochemical and Histological Findings and Conclusions as to Viral Origin of Hepatitis

Patient No.	Initials	Sex	1981 HBV Serology	No. of SGPT Peaks	Histology	Conclusions
1.	C.S.	M	Acute	3	CPH X 3	B on NANB
2.	A.D.	M	Acute	2	CPH X 3	B on NANB
3.	J.A.	F	Acute	Insf.	CPH X 3	B on NANB
4.	D.W.	M	Acute	2	CPH	B on NANB
5.	J.J.	M	Acute	Insf.	Acute	B
6.	M.McC	M	Acute	Insf.	CPH	B on NANB
7.	A.C.	M	Chronic	2	CPH	B _ NANB
8.	J.P.B.	M	+ Insf.	Insf.	CAH	Prob. B
9.	J.T.	M	+ Insf.	Insf.	CAH	B on NANB or NANB on B
10.	D.C.	F	Acute	Insf.	CAH	B on NANB
11.	J.F.	M	Acute	Insf.	CAH	B on NANB
12.	J.D.	F	+ Insf.	Insf.	CPH X 3	B on NANB or NANB on B
13.	E.F.	M	Acute	Insf.	CPH	B on NANB
14.	J.O'C.	M	Acute	2	CPH	B on NANB
15.	B.J.	M	Acute B	2	CPH	B on NANB
16.	J.C.	M	Acute	2	Acute	B on NANB
17.	P.M.	M	Acute	Insf.	CPH	B on NANB
18.	R.F.	M	Acute	Insf.	CPH X 2	B on NANB
19.	M.C.++	M	Acute	Insf.	CPH	B on NANB
20.	G.H.	M	Acute	2	Acute	B
21.	L.M.	F	Acute	2	CPH	B on NANB
22.	M.C.	M	Acute	2	CPH	B on NANB
23.	M.H.	M	Chronic	Insf.	Acute	NANB on B
24.	D.J.	M	+++Anti-HBc	Insf.	CPH	NANB on B
25.	M.O'S.	M	Anti-HBc	Insf.	CPH	NANB on NANB or B
26.	M.McC.	F	Anti-HBc	Insf.	Acute	NANB
27.	M.F.	M	All Neg.	Insf.	CPH	NANB on NANB

+HBsAG positive but only one attendance. ++Also had acute B negative hepatitis in 1979. +++IgM anti-HBC positive in low litre. Insf. = Insufficient data

It has been argued that one cannot distinguish histologically between acute and chronic hepatitis during acute HBV infection.[7] However, it is our experience, both in this study and previously[9,10], that initially diagnosed chronic liver disease remains chronic. We therefore believe that the conclusion that non-A, non-B infection makes a significant contribution to the chronic liver disease found in these parenteral drug abusers is valid.

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Non-A non-B infection preceded HBV infection in between two-thirds and four-Fifths of patients. This can be deduced because in these cases the HBV serology was typically that of acute hepatitis B on histologically established chronic liver disease. However, only three patients had a history of previous overt hepatitis; since non-A non-B PTH is frequently mild or asymptomatic[8], this is perhaps not surprising. We do not believe that the Delta infection which we have previously reported on a high proportion of these patients[2] has contributed to the histology at the present time because the predominant marker was Delta antigenaemia which is found in primary Delta infection concurrent with hepatitis B. Rarely hepatitis B infection has occurred where all HBV serology was negative but HBV markers had been found in the liver by immunefluorescence[11]; we did not test for HBV markers in the liver in this study, but the rarity of this finding suggests that our results cannot account for our one patient (No. 27) of chronic persistent hepatitis with no HBV markers and clinically acute hepatitis. Indeed, this case may well be of acute non-A non-B infection on chronic non-A non-B liver disease of different type. Patient No. 25 may also represent acute non-A non-B on chronic non-A non-B infection. This type of infection does not appear to have been previously described. Except for Delta agent it will not be possible to serologically confirm the existence of underlying non-A non-B chronic liver disease in patients until specific tests for non-A non-B agents become available.

This study suggests that vaccination of drug abusers with inactivated HB_sAG will not prevent the development of chronic liver disease amongst such abusers; vaccines for non-A non-B viruses will also be required. It may, however, slow the progression of such chronic liver disease and lessen the risk of subsequent cirrhosis or hepatoma.

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