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REFERENCES

have led to serums chronic atitis, in which an nt in a n retrocrated in patients of termine sympto­mi ng into obtained of these aminoto nor­

non-B hepatitis because their serum samples were consistently negative for the markers of hepatitis B virus infection according to the most sensitive tests available (radioimmunoassays for hepatitis B surface antigen [HBsAg], for antibody to HBsAg, and for antibody to hepatitis B core antigen) and were negative or of constant titer when tested by immune adherence hemagglutination and radioim­munoassay for antibody to hepatitis A virus.

Inocula

Serum was obtained from the patient on March 15, 1973 (16 weeks after the onset of aminotransferase elevations and the day on which the nurse accidentally inoculated herself with a broken capilla­ry pipette contaminated with his semen; Inoculum Ia). Serum was again obtained in February 1978 (5½ years after the onset of aminotransferase elevations; Inoculum Ib) and in October 1978 (six years after the onset of aminotransferase elevations; Inoculum Ic), and plasma was obtained in citrate-phosphate-dextrose in April 1979 (6½ years after the onset of aminotransferase elevations; Inoculum Id). Inoculations of chimpanzees were performed asynchronously over two years. Chimpanzees 922 and 930 were each inoculated intravenously with 1 ml of a 1:10 dilution of Inoculum Ia, as described elsewhere.1 Chimpanzees 960 and 961 were each inocu­lated intravenously with 1 ml of a 1:10 dilution of Inoculum Ib. Chimpanzee 975 was inoculated intravenously with 1 ml of undilu­ted Inoculum Ic, and Chimpanzee 993 with 1 ml of undiluted Inoculum Id.

Chimpanzees

The six inoculated chimpanzees (Pan troglodytes) were born in a breeding colony in the United States (International Center of En­vironmental Safety, Alamogordo, N.M., FDA contract No. 223-77-1004), and at the start of the study they were 14 to 20 months old and weighed from 6 to 9 kg. The care and feeding of these chim­panzees have been described elsewhere.1,4 There was little likeli­hood of prior exposure to hepatitis viruses; the infant chimpanzees, their parents, and their human caretakers were monitored regular­ly for abnormalities of AST and ALT, and for the presence of HBsAg, antibodies to HBsAg, and antibodies to hepatitis B core antigen. None of the chimpanzees except 993 had been inoculated with any other serum; 993 had been inoculated with a 1:1000 dilu­tion of Inoculum Ia 16 weeks previously. This dilution was found to be noninfectious in this chimpanzee and two others.

Figure 1. Data on a Patient with Asymptomatic Chronic Non-A, Non-B, Hepatitis.

Infectivity was detected at times indicated by plus signs and determined through experimental inoculation of chimpanzees with the patient's serum or plasma. AST denotes aspartate aminotransferase, and ALT alanine aminotransferase (normal, <40 IU per liter). Transfusions of 31 units of packed red cells and 43 units of platelets were given during the seven months indicated. Liver biopsy was performed at week indicated (see text).

Figure 2. Data on Nurse Infected with Non-A, Non-B Hepatitis by Accidental Inoculation with Blood from Patient Shown In Figure 1.

ISG denotes inoculation of immune serum globulin, AST aspartate aminotransferase, and ALT alanine aminotransferase (normal, <40 IU per liter). Liver biopsy was performed at week indicated (see text). Bar denotes period during which symptoms were present.
Serologic Studies and Liver Biopsies

Beginning four weeks before inoculation and continuing throughout the study, serum specimens from each of the six chimpanzees were tested weekly for AST and ALT (normal, <40 IU per liter) and for isocitric dehydrogenase. HBsAg and antibodies to HBsAg were tested weekly by means of radioimmunoassay, and antibodies to hepatitis B core antigen by means of complement fixation and radioimmunoassay. We tested selected serum samples for antibodies to hepatitis A virus by immune adherence hemagglutination and radioimmunoassay, for antibody to cytomegalovirus by radioimmunoassay, and for antibodies to Epstein-Barr virus by immunofluorescence. Serial serum samples from these chimpanzees were tested by means of counterimmunoelectrophoresis for an antigen-antibody system previously shown to be associated with non-A, non-B hepatitis. Percutaneous liver biopsies were performed weekly, with anesthesia induced by cyclohexylamine, a drug with no known toxic effects on the liver. Biopsy specimens were stained with hematoxylin and eosin and assessed according to previously reported criteria.\textsuperscript{1,2}

RESULTS

Each of the four samples of the patient's serum or plasma transmitted non-A, non-B hepatitis to the inoculated chimpanzees (Table 1). AST or ALT or both became elevated two to four weeks after inoculation, with peak AST levels of 55 to 306 IU per liter, and peak ALT levels of 92 to 227 IU per liter. Levels of isocitric dehydrogenase paralleled those of AST and ALT (data not shown). Histopathologic changes typical of hepatitis\textsuperscript{3} were seen in weekly liver-biopsy specimens during the period of aminotransferase elevation. None of the six infected chimpanzees acquired HBsAg or antibodies to HBsAg, hepatitis B core antigen, hepatitis A virus, or cytomegalovirus; titers of antibodies to Epstein-Barr virus remained unchanged in all six chimpanzees. Although not all six chimpanzees were inoculated or infected simultaneously, uninfected control chimpanzees were housed in the same facility throughout this study, and none of the controls had elevations in AST or ALT or abnormalities detected on liver biopsy.

An antigen associated with non-A, non-B hepatitis\textsuperscript{4} was detected with counterelectrophoresis in chimpanzees 922, 930, and 993 at the time of AST and ALT elevations and histopathologic changes in liver-biopsy specimens (Table 1), but not in chimpanzees 960, 961, or 975. In all six chimpanzees the development of antibody to the non-A, non-B-hepatitis-associated antigen was detected by means of counterimmunoelectrophoresis.

DISCUSSION

This study documents the persistence of an agent of non-A, non-B hepatitis in the blood of a patient for six years, even at a time when aminotransferase levels had temporarily returned to normal. Earlier studies suggesting the existence of chronic carriers of the non-A, non-B hepatitis agent or agents relied on retrospective analysis of prior episodes of transmission.\textsuperscript{14,15} In this study, the similar incubation periods, the pattern of aminotransferase elevations, the serologic findings of an antigen-antibody system associated with non-A, non-B hepatitis,\textsuperscript{9} and the histopathologic changes observed in biopsy specimens of the liver indicated that the same agent was present in this patient's blood throughout the six-year period.

Of great practical importance is the finding that plasma obtained from this asymptomatic patient, even after his AST and ALT levels had temporarily returned to normal, transmitted non-A, non-B hepatitis, documenting that this agent may persist even when sensitive indicators of liver damage are within the normal range. It has been suggested that elevated levels of AST or ALT may be used to identify blood donors who transmit non-A, non-B hepatitis to recipients of their blood.\textsuperscript{4,22} Other studies have shown that blood from some donors with elevated AST or ALT may not transmit non-A, non-B hepatitis to patients\textsuperscript{23} or to experimentally inoculated chimpanzees\textsuperscript{2} but that 80 per cent of blood donors implicated in transmitting non-A, non-B hepatitis have normal AST or ALT levels when tested retrospectively.\textsuperscript{2} Our study confirms that blood from persons with non-A, non-B hepatitis can be infectious even when AST and ALT levels are normal.

An antigen-antibody system closely associated with non-A, non-B hepatitis and not with other types of hepatitis has been detected in serum by counterimmunoelectrophoresis.\textsuperscript{16} This antigen-antibody system appears to be related to the hepatitis C antigen reported in the serum of some patients with transfusion-associated non-A, non-B hepatitis in Japan.\textsuperscript{16} This antigen was present in the three samples from the patient in this study from whom sufficient serum was available for testing (Inocula Ib, Ic, and Id).\textsuperscript{9} Antibody was present in each of four serum samples obtained during convalescence up to 6.5 years after onset of infection from the nurse who was infected with non-A, non-B hepatitis by accidental inoculation with the blood of this patient;\textsuperscript{17} (Tabor E, Seef L, Gerety R.J. Unpublished data). The antigen-antibody system was detected in all six chimpanzees inoculated with this patient's serum or plasma, including two described previously.\textsuperscript{9} The appearance of the antibody in three
of the chimpanzees (960, 961, and 975) while amino-
transferase levels were elevated suggests that, if
directed to a non-A, non-B hepatitis agent, the anti-
body does not immediately alter the course of the
acute disease. Although many questions remain un-
answered concerning this antigen-antibody system,
detection of the antigen or the antibody in the blood of
the patient, the nurse, and all six inoculated chim-
panzes is further evidence that a single agent was re-
ponsible for all the infections in this study.

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REFERENCES

1. Alter HI, Purcell RH, Holland PV, Feinstone SM, Morrow AG, Morit-
tage V. Clinical and serological analysis of transfection-associated
4. Alter HI, Purcell RH, Holland PV, Popper H. Transmissible agent in
mission in chimpanzees: a project of the Transfusion-Transmitted
chimpanzees with antihemophilic factor (factor VIII) material: recovery
hepatitis to chimpanzees by factor IX concentrate after fatal complica-
8. Tabor E, April M, Seibl LF, Gerety RJ. Acute non-A, non-B hepatitis:
prolonged presence of the infectious agent in blood. Gastroenterology.
antigen-antibody system in serum associated with human non-A, non-B
2:853-4.
11. Kashi M, Tabor E, Gerety RJ. Antigen-antibody system associated
with non-A, non-B hepatitis detected by indirect immunofluorescence.
12. Hoofnagle JH, Gerety RJ, Tabor E, et al. Transmission of non-A, non-
14. Karmen A. A note on the spectrophotometric assay of glutamico-
34:131-3.
15. Starkel LR, Spencer JA, Wolfsen SK Jr, Williams-Asman HG. Serum
levels of Mr. E, Mr. O, and Mr. N. with particular reference to liver
16. Ling CM, Overy LR. Prevalence of hepatitis B virus antigen as
17. Hollinger FR, Vosdamm D, Dressman GR. Assay of human antigen
and antibody employing double-antibody and solid-phase radioimmu-
noassay techniques and comparison with the passive hemagglutination
18. Hoofnagle JH, Gerety RJ. Barker LF. Antibody to hepatitis B virus
19. Etzioni RH, Ling CM. Radioimmunoassay for anti-core as evidence
20. Miller WJ, Proctor PJ, McAlister WJ, Itohashi OL, Villarroya VM,
Hilleman MR. Specific immune adherence assay for human hepatitis A
antibody: application to diagnostic and epidemiologic investigations.
21. Purcell RH, Wong DC, Moritausy Y, Dienstag JL, Routenberg JA,
Bogg JD. A microtiter solid-phase radioimmunoassay for hepatitis A
22. Smith KO, Goble WD, McCracken AW. Radioimmunoassay tech-
niques for detecting naturally occurring viral antibody in human sera. J
Immunol Methods. 1974; 5:337-44.
23. Harle G, Hamo W. Immunofluorescence in cells derived from Burkitt's
24. Hollinger FR, Alter HI. Summary of workshop B-6: non-A, non-B
hepatitis. In: Vyas GN, Cohen SN, Schmid R, eds. Viral hepatitis. Phi-

LAW-MEDICINE NOTES

Multimillion-Dollar Verdict in Malpractice Case in
Connecticut: A Complex Trial Record

William J. CURRAN, J.D., LL.M., S.M.HvG.

NEW ENGLAND has not been an area where
very large verdicts have been common in medical
malpractice cases. Widespread publicity was
therefore to be expected when the Supreme Court of
Connecticut recently upheld as proper and justified a
jury verdict of $3.6 million.

The defendant was a local general hospital with a
psychiatric ward in which a 23-year-old psychotic pa-
ient harmed herself severely in a seclusion room,
having been unattended for nearly four hours. The
jury had not found negligence against the plaintiff's psy-
chiatrist but returned its verdict only against the hos-
pital. The defendant claimed that the verdict was ob-
viously excessive, being four times as large as any ever
returned in the state, and that "its size alone [was] in-
dicative of prejudice, passion, bias, sympathy and
total misunderstanding of the law and the facts on the
part of the jury." The trial judge had not only denied a motion to set
aside the verdict as excessive but had also remarked
that the evidence would have supported "a substan-
tially higher verdict."

The trial judge's comments were certainly unusual
in the relatively conservative judicial precepts of
Connecticut. Most general discussion of the case will
tend to note only the size of the verdict, not the circum-
stances of the case. As the entire, complex trial record is
examined, however, the full picture of an aggravat-
ed, tragic situation is revealed. The features leading to
a verdict so high can be summarized as follows:

Negligent failure to safeguard a very sick patient; a
blatant effort by the hospital to rewrite, alter, and dis-
guise the patient's record; serious neurologic injury
resulting from the patient's treatment; a 12-year-old
plaintiff with a life expectancy of seven years; and
serious economic loss to the family.

The parties of course disputed the extent of the
hindrances. The plaintiff's expert witnesses in both medical and
economic areas, the use of a 20-minute videotaped motion pic-