GB virus-C (hepatitis G virus) nostalgia

The newly discovered human flavivirus identified as GB virus-C [1] and hepatitis G virus (HGV) [2], presents intriguing challenges in virology, epidemiology, and blood banking. Its clinical relevance for hepatology, however, appears to have been short-lived. Murthy and colleagues in this issue of Kidney International [3] provide additional evidence that the virus is not associated with clinically significant acute or chronic hepatitis. Utilizing an extensive serum bank and clinical database developed for ongoing studies of hepatitis C virus (HCV) in the setting of chronic renal disease, the authors screened 465 patient sera for the presence of GBV-C RNA. In doing so, they identified one of the larger cohorts of GBV-C infected individuals described to date (N = 146), lending strength to their conclusions. GBV-C infection was observed in 29% of patients with end-stage renal disease awaiting renal transplantation, at similar frequencies among those with and without antibody to HCV (35 vs. 29%, respectively). There were no significant differences in history of liver disease, chronic hepatitis, or of elevated ALT between patients with and without GBV-C infection. The authors conclude that GBV-C is not associated with acute or chronic hepatitis, and review the preponderance of evidence that has accumulated over the past few years supporting this position. They certainly are not alone in this viewpoint. In two compelling studies, Alter and colleagues found no association of HGV with community acquired acute hepatitis or post-transfusion hepatitis [4, 5]. Theodore and Lemon were so impressed with the notion of ‘hepatitis virus’ as misnomer that they proposed as an alternative, ‘human orphan flavivirus’ [6]; Pessoa and Wright characterized it as ‘a virus in search of a disease’ [7], and Miyakawa and Mayumi, ‘an accidental tourist’ [8].

As the description ‘orphan flavivirus’ suggests, we simply do not know enough, yet, about the epidemiology and pathogenesis of GBV-C to determine its ultimate clinical significance for humans. There is no question though that it has found a family among the blood-borne viruses that can be transmitted through transfusion [5], intravenous drug abuse [9], and organ transplantation. However, in studies published to date, the clinical significance of such transmission was minimal in the majority, and in those few cases where significant disease was observed, other, unidentified agents may also have been transmitted. As previously alluded [5], this orphan may run, on occasion, with hoodlums. Alternatively, such observations may reflect uncommon outcomes of what are typically clinically silent infections. As with its distant cousin HCV, persistent infection is readily established, but in striking contrast, host development of an antibody response to the GBV-C envelope protein appears to ‘clear’ infection [10]. This observation leads to several considerations. First, to estimate the true prevalence of GBV-C exposure in a population, assays for both RNA and antibody must be performed. In doing so, Gutierrez et al found evidence of GBV-C exposure in 5.5% of volunteer blood donors, 90% of intravenous drug users, and 42 and 43% of patients with chronic and acute nonA-E hepatitis, respectively [10]. Thus, virus infection is even more prevalent than previously suspected, and this suggests that mechanisms of transmission other than blood exposure are also significant. Second, the clinical events occurring simultaneously with seroconversion and clearance of infection are not well characterized. For instance, transient ALT elevation may occur in that setting. Thus, it would be interesting to know for the present and other recent cohort studies, if the addition of anti-E2 antibody screening would alter current conclusions regarding GBV-C and liver disease. The answer will probably once again be ‘no association,’ but until then, the question flickers for another day. Meanwhile, efforts to fully characterize the clinical significance of this virus and its epidemiology will continue.

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REFERENCES


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