Review Article

HEPATITIS G VIRUS; STRUCTURE, EPIDEMIOLOGY AND CLINICAL SIGNIFICANCE

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ABSTRACT

Hepatitis G virus is a new member of hepatotropic virus belonging to the family of Flaviviridae. Its genome consists of 2900 amino acids. This new virus which has been identified two years ago is a positive stranded RNA virus and causes both acute and chronic hepatic disease. The structure, epidemiology and clinical importance of hepatitis G virus will be discussed in this article.

Key Word: Hepatitis G virus

INTRODUCTION

Until now five hepatitis viruses namely A-E have been described. After the discovery of hepatitis B virus surface antigen during the 70's, hepatitis A virus has been described. Cases lacking the markers for either virus were named non-A, non-B hepatitis. It has been claimed at many studies that, the causative agent of non-A, non-B hepatitis is not a single agent. In fact, in 1989 hepatitis C virus has been cloned, and subsequent studies have revealed that 90 percent of transfusion-related hepatitis are due to hepatitis C virus (1). One year later Reyes et al. have succeeded to clone hepatitis E virus and described it as the causative agent of enteric non-A, non-B hepatitis (2). Despite all these, still we have some clues suggesting the existence of probable non-A,B,C,D,E hepatitis agent besides the formerly discovered agents of hepatitis.

Epidemiologic studies of cryptogenic hepatitis cases, in which none of the agents have been isolated, point to the existence of other viruses with probable parenteral transmission. Retrospective analysis of the stored serum of a surgeon from Chicago, who had hepatitis in 1967 has failed to reveal any known hepatitis agent. After inoculation of the surgeon's serum to the tamarins, two different viruses in the tamarin serum have been isolated and named GB virus - A and GB - virus B (3). Subsequently it has been shown that GBV-A virus is widespread amongst animals but, does not cause hepatitis but GBV-B, on the other hand, can be transmitted and a cause of hepatitis in the animals. Same studies revealed that none of the these agents cause hepatitis in humans (4). Later on, another virus has been isolated in the serum of a South-African person and called as GBV-C, which also causes hepatitis in humans (5). Similar to these studies done at Abbott laboratories, "Genlabs" laboratories in January 1995 reported a new blood-borne hepatitis agent and called hepatitis G virus (6). It has been shown that these two viruses namely HGV and GBV-C which were described by two different centers have a quite similar molecular structure and belong to the family of Flaviviridae.

EPIDEMIOLOGY OF HEPATITIS G VIRUS

It is known that HGV like HCV is transmitted by blood and products. Thus, hemophiliacs, IV drug addicts, hemodialysis patients and polytransfused patients carry a higher risk for HGV infection (7). Seroprevalence of HGV in healthy blood donors is about 2 percent and varies according to the community in which studies have been done (8,9). Vertical transmission is possible. Feucht et al. have found that, 3 children of 9 mothers infected with HGV had HGV-RNA positivity in their sera (10). According to the same study, vertical transmission of HGV is relatively easier than that of HIV and HCV. The identification of HGV-RNA in semen also supports the sexual transmission of HGV (11).

Another risk for HGV infection is hemodialysis. 3.1 percent of 519 chronic hemodialysis patients were found to harbour the virus, while a similar group of healthy blood donors had only 0.9% of HGV-RNA seroposivity rate (12).

STRUCTURE OF THE HGV GENOME

HGV is a positive single stranded RNA virus and its genome is made up of 2900 amino acids. This genome consists of helicase motifs, 2 protease motifs and RNA dependant RNA polymerase motifs (Fig 1). Analytic studies showed that HGV and GBV-C have 95 percent similarity at the amino acid level and 80 percent homology at the nucleotide level (13). However, the homology between HGV and GBV-A, GBV-B and HCV is quite limited being only 26% among HGV and HCV. These results reveal that HGV and GBV-C are the different isolates of the same virus but GBV-A, GBV-B and HCV are completely different viruses.

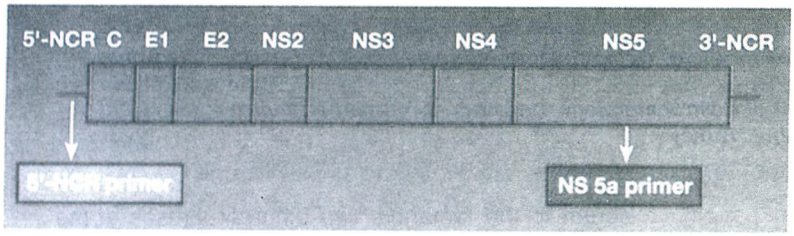

Fig. 1 : Structure of the HGV genome and localization of primers

DIAGNOSIS OF HGV INFECTION

Hepatitis G virus infection can be recognized by nucleic acid technology. RT-PCR is the most sensitive test for its diagnosis. In this technology, HGV-RNA is extracted from serum or plasma and complimentory DNA is obtained after reverse transcription. Primers from the non-coding region and the NS 5 region of HGV are utilized for a single round amplification using a modified PCR technology (14).

RT-PCR test used in the diagnosis of HGV is more sensitive and specific than the ELISA technique. But, since RT-PCR is time consuming, troublesome and expensive especially for the donor screening, we need more practical and sensitive tests alternative to RT-PCR. Presence of Anti-E2 antibody derived from the serum of patients who recovered from HGV infection is a marker for past infection and is identified with ELISA technique (15). It is inevitable that we need more tests with the same sensitivity using ELISA technique for diagnosis and studies related to this subject are still continuing.

CLINICAL SIGNIFICANCE OF HEPATITIS G

The clinical picture of HGV infection and its course have not been completely understood, yet. Since sensitive and practical techniques for the diagnosis of HGV have not been found until now. Available data support the fact that HGV infection is not rare in the community, and causes both acute and chronic hepatitis. HGV, more commonly causes persistent viremia without a serious clanical outcome. Most of the cases have normal physical findings, transaminase levels are within normal limits and usually an asymtomatic carrier state is observed. When the data concerning the transfusion or transplantation acquired, HGV hepatitis patients with good follow-up have been investigated. It has been shown that after 2-4 weeks of incubation, a moderate ALT elevation lasting 6-8 weeks was present. In these patients ALT elevation usually abates after 12-14 weeks and rarely persists longer (16).

Dual infection of HGV either with HBV or HCV is common especially in high risk groups. The contributon of HGV to the hepatic injury in these patients is minimal (17,18). In other words, accompanying HGV infection does not worsen the histologic picture. Besides, interferon treatment causes diminution or disappearance of HGV-RNA and its withdrawal causes there the reappearence of the virus (19).

HGV plays a role in the etiology of fulminant hepatitis. A study regarding fulminant hepatitis showed 3 HGV-RNA positivity in 6 patients (20). The HGV hepatitis cases in this study shared quite similar clinical and biochemical characteristics with HCV.

HGV also plays a role in the etiology of posttransfusion hepatitis. Three of 12 posttransfusion hepatitis patients with unknown etiology who had been followed up by "National Institute of Health", had HGV-RNA positive sera (4). The incubation periods, the clinical findings and biochemical results of these patients were quite similar to those of HCV infection but their progression chronicity was less common.

The role of HGV in the etiology of hepatocellular carcinoma is controversial. Four out of 34 (12%) HCC patients were found HGV-RNA positive in the study of Perez et al. Since these patients also had HBV or HCV in addition to HGV, the role of the latter is not

clear. In 85 cases with HCC and without coinfection with other viruses, there were 7 patients (8%) with HGV seropositivity (21,22). Briefly more studies are needed on this matter.

HGV plays a role in the etiology of community acquired hepatitis. HGV like HCV plays a role in the etiology of posttransfusion hepatitis, fulminant hepatitis and community acquired hepatitis. A study documented that 38 non-A, non-E hepatitis cases had 5 HGV patients (23). Despite all these, many points related to HGV is still unknown. Whether it has genotypes, extra hepatic involvement and its relation to the autoimmune hepatitis, hepatocellular cancer and its replication location still need to be investigated.

In conclusion, HGV is transmitted by blood and blood products, causes acute and chronic hepatitis and plays a role in the etiology of fulminant and posttransfusion hepatitis. There are evidences concerning its vertical and sexual transmission. Its relation to hepatocellular carcinoma, autoimmune hepatitis and fatty liver needs further investigations and its treatment is not clear yet. We need further broad spectrum studies to resolve all these.

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