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Molecular Analysis and Ex Vivo Infectivity of Seronegative Occult Hepatitis C Virus: A Study in Single Haemodialysis Centre

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Abstract

Background: In occult hepatitis C virus infection (OCI), hepatitis C virus ribonucleic acid (HCV RNA) is detectable in peripheral blood mononuclear cells (PBMCs) but is not evident in serum or plasma. Understanding of OCI in patients with seronegative anti-HCV antibodies is limited. Methods: In this study, six HCV isolates from haemodialysis (HD) patients with seronegative OCI were identified by molecular assays and phylogenetic analysis. The virus infectivity was assessed ex vivo using a primary naïve PBMC culture system. HCV isolates obtained from the PBMCs of 10 patients with chronic HCV infection (CCI) were characterised concurrently and used as positive controls in the cell culture. Results: Sequence analysis of the 5' untranslated region (UTR) and non-structural 5B (NS5B) region revealed that HCV genotype 3 was the most prevalent virus type in both the OCI and CCI groups. One of the occult HCV isolates was identified as a mixed type. The mean viral load (log₁₀ RNA copies/10⁶ cells) in the PBMC samples of the OCI group (M = 3.4, SD = 0.7) was lower than that of the CCI group (M = 4.6, SD = 1.7). Upon culture, de novo OCI-HCV replicates were detected in five out of six naïve PBMC cultures. Analysis of the replicates showed a single guanine addition in the domain III of 5'-UTR but the overall molecular structure was retained. Conclusion: Seronegative OCI is an active form of infection that replicates at a low level in PBMCs. Seronegative OCI may share the same route of transmission as CCI. The retained viral competency may have an implication for its persistence. © 2024, Penerbit Universiti Sains Malaysia. All rights reserved.

Author Keywords

genotype; hepatitis C virus; patients; PBMCs; sequence analysis

Index Keywords

alanine aminotransferase, antiviral agent, aspartate aminotransferase, creatinine, hemoglobin; adult, Article, bacterium culture, bacterium identification, bacterium isolation, cell culture, chemical structure, clinical article, clinical feature, cross-sectional study, DNA extraction, DNA sequence, ex vivo study, female, gene amplification, gene sequence, hemodialysis, Hepatitis C virus, human, male, molecular genetics, multilocus sequence typing, peripheral blood mononuclear cell, phylogeny, real time reverse transcription polymerase chain reaction, sensitivity and specificity, sequence analysis, virus detection, virus infectivity

Chemicals/CAS

alanine aminotransferase, 9000-86-6, 9014-30-6; aspartate aminotransferase, 9000-97-9; creatinine, 19230-81-0, 60-27-5; hemoglobin, 9008-02-0

Tradenames

GoTaq

Manufacturers

IBM, United States; Promega, United States

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