



## Co-infection with Hepatitis B virus (HBV) and Hepatitis C Virus (HCV) may Result in Asymptomatic Carrier Stage: A Case Report

Authors

**Bandana Mehrotra, Ashok Kumar Kapoor, Hari Shyam, Atul Kumar Srivastava, Vasundhara Sharma, Supriya Mehrotra and Rajesh Kumar Srivastava**

### Abstract

A 45-year-old male presented with mild loss of appetite. Serum total bilirubin was 1.2 mg/dl (reference range 0.1 to 1.0 mg/dl). Serum GOT was mildly raised to 56 (reference range 10-35 IU). Serum HBsAg was positive. Serum IgM anti-HCV antibody was also positive. The diagnosis of HBV and HCV co-infection was confirmed by Real-Time PCR. He was diagnosed as a case of asymptomatic HBV and HCV co-infection. Imbalance in the concentration of natural killer cells (NK dim and NK bright) might increase the necrosis of infected hepatocytes. Generation of cytotoxic T lymphocytes might eliminate both HBV and HCV, resulting in cell mediated immunity response and viral clearance.

### Introduction

Both HBV and HCV are hepatotropic viruses with the potential to produce a persistent infection<sup>[1]</sup>. Their life cycles are different because HBV is a DNA virus while HCV is a RNA virus. HBV replicates in nuclei of hepatocytes while HCV replicates in the cytoplasm. During acute viral infection, HBV-specific cytotoxic T lymphocytes (CTL) develop which kill the infected hepatocytes, resulting in viral clearance. During acute hepatitis B infection, HBV replication is controlled by HBV-specific CD8<sup>+</sup> and CD4<sup>+</sup> T-cells and neutralizing antibodies<sup>[1]</sup>. DNA of HBV may integrate with hepatocyte DNA, resulting in persistent source of HBsAg in chronic infection. During inactive stage of HBV infection, anti HBe antibody formation occurs but HBeAg does not circulate. Additionally, SGPT and SGOT levels are normal and blood DNA levels are low (2.1 x

10<sup>3</sup> IU/ml). These individuals are asymptomatic carriers of HBV infection.

Further HCV, infection alone is also often asymptomatic. Moreover, only 10 to 20 % of patients develop symptomatic hepatitis. Blood RNA levels are relatively high (1.3 x 10<sup>7</sup> IU/ml). Both HBV and HCV are non-cytopathic viruses. In HBV and HCV coinfection, cell death may occur following hypersensitivity and /or apoptosis. Rarely, simultaneous infection by HBV and HCV may occur in humans due to similar route of infection<sup>[2]</sup>. Co-infection with HBV and HCV may occur because of intravenous drug intake or blood transfusion. Another route of transmission may be superinfection, i.e. a patient may have chronic infection by HBV. Subsequently, infection by HCV may occur. Clinically, it may result in increased severity of hepatitis and higher incidence of hepatocellular carcinoma<sup>[2]</sup>. Co-infection may result either in

acute fulminant hepatitis or chronic hepatitis<sup>[2]</sup>. Higher incidence of cirrhosis may also develop in patients with dual HBV and HCV infection<sup>[3]</sup>. Spontaneous clearance of single or both the viruses may occur<sup>[3]</sup>. The incidence of co-infection may range between 1 to 15%<sup>[4]</sup>. Further, both HBV and HCV may replicate together *in vitro* in hepatocytes without any interference<sup>[3]</sup>. In an earlier Indian study, 3 of 80 (3.7%) patients with chronic liver disease (CLD) had dual HBV and HCV infection<sup>[2]</sup>. The patients with chronic infection may later progress from chronic hepatitis through cirrhosis to hepatocellular carcinoma<sup>[5]</sup>. In a separate study, 5 of 134 (3.7%) patients on dialysis had HBV and HCV co-infection<sup>[6]</sup>. In another study, 24 of 150 (16%) cases of CLD had dual infection with HBV and HCV<sup>[7]</sup>. Moreover, in a previous study, 50 cases of CLD were investigated; results of the study revealed presence of HBsAg in 26 % cases and 18% patients had anti-HCV antibodies in their sera<sup>[8]</sup>. Herewith, we report a case of CLD with dual infection.

### Case Report

A 45-year-old male presented as a case of anorexia. Serum total bilirubin was 1.2 (range 0.1 to 1.0) mg/dl. Direct bilirubin was 0.75 mg/dl (range 0.02 to 0.025mg/dl). Serum GOT was mildly raised to 56 (reference range 10-35) IU. Serum ALT was 20 (reference range 9-43) IU. Serum total proteins were 8.55gm/dl; serum albumin was 3.56 gm/dl. Serum HbsAg was positive. Serum IgM anti-HCV antibody test was also positive. The viral load of HBV and HCV was quantified by Real-time PCR. The viral load of HCV and HBV were  $1.3 \times 10^7$  and  $2.1 \times 10^3$  IU/mL respectively. He was diagnosed as a case of asymptomatic HBV and HCV co-infection.

### Discussion

Most important feature of hepatitis dual infection was the development of more advanced disease in HBV and HCV infected patients as compared to patients with hepatitis mono-infection. Incidence

of fibrosis as well as of decompensated cirrhosis was also higher in HBV and HCV co-infected patients when compared with mono-infected hepatitis patients<sup>[5]</sup>. Further, potential for reactivation was also relatively higher in patients being treated against hepatitis mono-infection (HBV or HCV) alone<sup>[3]</sup>. Rarely, spontaneous clearance of virus may occur due to development of immune response against both the viruses<sup>[3]</sup>. Another feature of HBV and HCV co-infection was dominance of a hepatitis virus over other virus. The dominant virus replicates actively, resulting in inhibition of replication of a non-dominant virus. Further, co-dominance may also occur which results in near equal replication (NER) of both HBV and HCV. For example, NER of HCV RNA and HBV DNA may occur in co-infected cells as detected by RT-PCR<sup>[9]</sup>. Several mechanisms have been proposed to explain HCV-induced HBV inhibition in humans. First, HCV core protein may bind HBV polymerase, resulting in suppression of HBV. Second, liver-specific microRNA may suppress HBV replication. Third, HCV infection may induce interferon production in hepatocytes which may interfere with entry of HBV in adjacent hepatocytes<sup>[3]</sup>. Several peculiarities of immunopathological response against HCV infection have been observed. For example, HCV-induced CTL response is reactive both against HCV and also against normal hepatocytes, suggesting generation of autoimmune response. Further, role of Th17 and Th8 lymphocytes and of IL 21 has been observed in pathogenesis of HCV infection<sup>[10]</sup>. Th 17 lymphocytes appeared to augment the fibrogenesis. Present patient was first treated with interferon  $\alpha$ /ribavirin to inhibit HCV. Later, the patient was treated with a nucleotide analogue, e.g. lamivudine to control the replication of HBV<sup>[3]</sup>. Reduction in peripheral NK cells was observed in chronic hepatitis C infection.

Two subpopulations of natural killer (NK) cells are known to exist, e.g. NK *bright* and NK *dim*. NK *bright* cells appear to increase inflammation through release of cytokines while NK *dim* are

more cytolytic when compared with NK *bright* cells. Further, imbalance in the concentration of these subpopulations appeared to increase the necrosis of hepatocytes.

### Conclusion

Present case reports a patient with HBV and HCV co-infection. The patient was diagnosed as a case of asymptomatic hepatitis. Both HBV and HCV appeared to co-exist together with active replication of both the hepatotropic viruses. The exact mechanism of co-existence is not clear. However, inhibition of replication of both the viruses may occur due to development of cell mediated immunity resulting in viral clearance.

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