CASE REPORT

Spontaneous clearance of hepatitis C virus during alcoholic hepatitis: the alcohol killed the virus?

Mário Jorge Silva, Filipe Calinas

Gastroenterology Department, Central Lisbon Hospital Centre, Lisboa, Portugal

Correspondence to
Dr Mário Jorge Silva, mariojorgesilva01@gmail.com

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SUMMARY

Spontaneous clearance of hepatitis C virus during chronic infection is uncommon. We report the case of a patient who cleared hepatitis C virus during an episode of presumed alcoholic hepatitis. A brief discussion on the immunological aspects of chronic hepatitis C and the impact of alcohol consumption on it is presented as well.

BACKGROUND

Spontaneous elimination of hepatitis C virus (HCV) is rare in chronic hepatitis C (estimated 0.5%/year/person),[1] especially in advanced stages.[2] To the best of our knowledge, this is the first report of a spontaneous clearance of HCV in chronic hepatitis C during an episode of alcoholic hepatitis.

CASE PRESENTATION

We report the case of a 42-year-old man, referred to our hepatology outpatient clinic in 2002, because of chronic hepatitis C diagnosed 6 years before. He had a history of active excessive alcohol drinking (around 150 g ethanol daily during the past 17 years) and intravenous drug use between 1980 and 1992. Hepatitis C virus viral load was positive, and staging of disease was not accomplished as the patient did not adhere to the visits and was lost to follow-up.

He continued his drinking habits and was admitted 8 years later with a sudden history of asthenia, abdominal pain, jaundice and coluria, with no ascites and no hepatic encephalopathy. He had elevated total bilirubin (10.4 g/dL, 53% direct), slightly prolonged prothrombin time (13.1 s, International Normalised Ratio 1.14), elevated aspartate aminotransferases (AST 367 U/L with AST/alanine transaminase=6) and positive HCV viral load (76 728 UI/mL; 4.9 log 10). Lung and urinary tract infection, as well as superinfection with hepatitis A virus, hepatitis B virus, cytomegalovirus and Epstein-Barr virus, were excluded. Alcoholic hepatitis was presumed, and despite a transient deterioration of liver function (with no further elevation of aminotransferases), no specific therapy was initiated, and evolution was favourable. On discharge, 17 days after admission, HCV genotyping was requested but not performed because viral load was surprisingly undetectable.

OUTCOME AND FOLLOW-UP

Soon after discharge, the patient developed ascites that easily resolved after 3 months of low-dose diuretics. Only after this episode did the patient become abstinent from alcohol. Liver elastography (FibroScan (R)) suggested liver cirrhosis (72kPa), Child-Pugh A, and upper endoscopy revealed small oesophageal varices without red signs. The patient's IL28B polymorphism was rs12979860 (CT) and rs8099917 (TT).

During outpatient follow-up, HCV viral load remained undetectable in four subsequent yearly determinations and aminotransferases normalised. Since being abstinent from alcohol the patient has remained asymptomatic, with no further decompensation of liver cirrhosis and without diuretics.

DISCUSSION

Clearance of HCV in chronic hepatitis C has been associated with several host factors and events. These include favourable IL28B genotype, superinfection with hepatitis viruses (A, B or delta), HIV-coinfection under antiretroviral therapy, withdrawal of immunosuppressive therapy, hepatocellular carcinoma, parturition, gastrectomy and liver transplant.[2–6] However, to our knowledge, association to alcoholic hepatitis has not been described earlier.

Alcohol consumption aggravates hepatitis C by a synergic effect on the progression of liver fibrosis[7] and by modulation of HCV replication. Chronic alcoholism potentiates HCV replication in hepatocyte-derived cell lines expressing CYP2E1, but acute exposure may inhibit HCV replication.[8] There may be a dual effect of alcohol metabolism on HCV replication, where moderate oxidative stress stimulates replication and intense oxidative stress represses it.[8] Chronic alcohol consumption potentially hampers host response to HCV as well, through suppression of HCV core-specific T-cells by induction of Tregs[9] and limitation of dendritic cell function.[10] Alcohol also enhances HCV quasi-species complexity.[8]

Host response to HCV infection depends on T lymphocytes and immunoregulatory cytokines. A T-helper type 1 (Th1) milieu, with IFN-γ expression, is required for host antiviral immune responses, including cytotoxic T-cell generation and natural killer cell activation.[11] In chronic infection, HCV-specific T cells exhibit an exhausted phenotype, with deficient proliferation, infected cell killing and cytokine production.[12] This T-cell dysfunction has been attributed to several mechanisms, including HCV-driven expression of the inhibitory receptor programmed death-1 (PD-1) on virus-specific T cells.[12 13] Interaction with its ligand, PD-L1 (expressed on sinusoidal endothelial cells, Kuppfer cells, stellate cells and type I IFN-exposed hepatocytes) inhibits effector functions and induces T cell apoptosis.[14] HCV-induced proliferation of

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Treg cells may also affect responsiveness of HCV-specific T cells and perpetuate chronic HCV infection.[14]

Alcohol consumption, in parallel to its immunodepressant effects, has been shown to favour Th1 responses in alcoholic cirrhosis, with an intensity of Th1 responses that directly correlates with disease severity.[15]

In conclusion, acute liver injury by alcoholic hepatitis may be another predisposing factor for viral clearance during chronic hepatitis C. In this case, we speculate that the presumed alcoholic hepatitis may have had important effects on the burst of Th1 responses and oxidative stress which caused a non-treatment-induced elimination of HCV in a patient with a favourable rs8099917 IL-28B genotype.

Learning points

- Spontaneous viral clearance is uncommon in chronic hepatitis C.
- Modulation of inflammatory response may lead to clearance of hepatitis C virus.
- Spontaneous elimination of hepatitis C virus may occur during liver injury, including alcoholic hepatitis.

Competing interests None declared.

Patient consent Obtained.

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