

Letter to the Editor

A very longstanding inactivity of liver cirrhosis due to HBV/HCV co-infection after spontaneous serum clearance of both viruses

Dear Editor,

Hepatitis B and hepatitis C are the most common cause of chronic liver disease worldwide^{1,2}. Co-infection by the two viruses is not uncommon. In effect, Gaeta et al³ found anti-HCV antibodies in 7% of 837 patients hepatitis B surface antigen positive patients. Cirrhosis was present in 107 of the 709 patients with HBV alone (15.1%) and in 17 of 59 with HCV co-infection (28.8%). Here, we report the case of a patient with dual B and C virus chronic hepatitis, progression to liver cirrhosis, spontaneous clearing of both viruses, no further advancement of the liver functional impairment.

A 28 year-old white man, was admitted to our Unit in 1980 due to HBsAg serum positivity casually discovered some years earlier and mildly elevated serum ALT activity. Three years before coming to our observation he was hospitalized in another hospital where he undertook a liver biopsy, which disclosed the histological images of a so-called "chronic persistent hepatitis". The patient was completely asymptomatic. However, diagnostic laparoscopy with liver biopsy was performed. The liver appeared enlarged, with a surface initially altered by diffuse micronodulation. Ligament teres and parietal peritoneum were very congested. Liver biopsy disclosed the picture of active micronodular cirrhosis. EGDS did not reveal esophageal varices. Patient was discharged without any therapy but with a follow-up program. Patient was again hospitalized in 1993. HBsAg was still positive. Furthermore, HCV-Ab resulted present. Liver enzymes were normal. Serum HBV-DNA (HBV-DNA: 2300 copies/mL) and HCV-RNA (genotype 2; HCV-RNA: 750,000 copies/mL) were both positive. Ultrasonography showed an enlarged liver with diffuse nodularity and increased echogenicity. In the following years the patient has been clinically asymptomatic. Further hospitalization was decided in 1996. HBsAg was negative and HBsAb resulted present. HBV-DNA and HCV-RNA resulted both negative and all laboratory data were in the normal range. Ultrasonography did not show any further modification of the liver and of the other intra-abdominal structures. Patient was referred to our Unit lastly in October 2011. Liver function tests were normal; both HBV-DNA and HCV-RNA were still negative. Ultrasonography and EGDS did not disclose any change as compared to those previously performed. The patient was still completely asymptomatic.

As compared with non-infected patients, HBV/HCV co-infected subjects tend to have more severe liver injury, a higher probability of liver cirrhosis and hepatic decompensation and a higher prevalence of hepatocellular cancer^{4,5}. However, some studies do not support these findings⁶. Actually, accumulating evidence suggest that co-infection by HBV/HCV is heterogeneous with respect to varying states of replication for each virus and profiles of immunity. In most cases HBV/HCV appear to inhibit each other leading to absent or low level replication for HBV or to the absence of HCV-RNA whenever the other virus was actively replicating⁵. Then, clinical outcomes of the co-infection also may be very heterogeneous. To our knowledge a case of HBV/HCV co-infection with an outcome such as that we have described has not been reported in the literature. We don't know when our patient became infected and we cannot establish whether the patient were first infected by HBV or HCV or simultaneously infected. Essentially, we can state that progression of chronic B viral hepatitis to liver cirrhosis was al-

ready established in 1980. At that time HCV was an unknown virus infection. In 1993, we could recognize the presence of HCV infection in the patient in addition to the previously detected HBV infection. In 1998, HBV-DNA and HCV-RNA resulted both negative and liver enzymes appeared normalized. Thirteen years later (2011) HBV and HCV viruses were still not detectable in the serum of the patient. Furthermore, at this time the liver disease did not show any evidence of functional worsening either clinically or by laboratory data. In other words, our report suggests the possibility that longstanding serum disappearance of HBV-DNA and HCV-RNA in a co-infected subject may determine a complete clinical inactivity of the related liver disease despite its progression to liver cirrhosis. With regard to the further progression of established cirrhosis this report shows some analogies between liver disease alcohol-related and liver disease virus related⁷. In both cases the absolute alcohol abstinence or respectively the longstanding absence of serum markers of viral replication may lead to a longstanding complete inactivity of the liver disease.

References

- 1) ITALIAN ASSOCIATION FOR THE STUDY OF THE LIVER; ITALIAN SOCIETY OF INFECTIOUS, TROPICAL DISEASES; ITALIAN SOCIETY FOR THE STUDY OF SEXUALLY TRANSMITTED DISEASES. Practice guidelines for the treatment of hepatitis C: recommendations from an AISF/SIMIT/SIMAST Expert Opinion Meeting. *Digest Liver Dis* 2010; 42: 81-91.
- 2) CAROSI G, RIZZETTO M, ALBERTI A, CARITI G, COLOMBO M, CRAXI A, FILICE G, LEVRERO M, MAZZOTTA F, PASTORE G, PICCININO F, PRATI D, RAIMONDO G, SAGNELLI E, TOTI M, BRUNETTO M, BRUNO R, DI MARCO V, FERRARI C, GAETA GB, LAMPERTICO P, MARZANO A, POLLICINO T, PUOTI M, SANTANTONIO T, SMEDILE A. Treatment of chronic hepatitis B: update of the recommendations from the 2007 Italian Workshop. *Digest Liver Dis* 2011; 43: 259-265.
- 3) GAETA GB, STORNAIUOLO G, PRECONE DF, LOBELLO S, CHIARAMONTE M, STROFFOLINI T, COLUCCI G, RIZZETTO M. Epidemiological and clinical burden of chronic hepatitis B virus/hepatitis C virus infection. A multicenter Italian study. *J Hepatol* 2003; 39: 1036-1041.
- 4) CHU CJ, LEE SD. Hepatitis B virus/hepatitis C virus coinfection: epidemiology, clinical features, viral interactions and treatment. *J Gastroenterol Hepatol* 2008; 23: 512-520.
- 5) GORDON SC, SHERMAN HE. Treatment of HBV/HCV coinfection: releasing the enemy within. *Gastroenterology* 2009; 136: 393-396.
- 6) CHO LY, YANG JJ, KO KP, PARK B, SHIN A, LIM MK, OH JK, PARK S, KIM YJ, SHIN HR, YOO KY, PARK SK. Coinfection of hepatitis B and C viruses and risk of hepatocellular carcinoma: systematic review and meta-analysis. *Int J Cancer* 2011; 128: 176-184.
- 7) MILLS SJ, HARRISON SA. Comparison of the natural history of alcoholic and nonalcoholic fatty liver disease. *Curr Gastroenterol Rep* 2005; 7: 32-36.

A. Rispo, G. Mazzacca
Department of Gastroenterology, School of Medicine, "University "Federico II"
of Naples, Naples (Italy)