Hepatitis C virus and hepatocellular carcinoma

Dear Editor,

Hepatocellular carcinoma (HCC) is a long-term complication of hepatitis C virus (HCV) infection once the disease has progressed to cirrhosis. Antiviral therapy and, more specifically, the achievement of a sustained viral response through years improve hepatic histology with regression of fibrosis and reduce the risk of HCC (1).

Case report

We present the case of a 72-year-old male patient without previous significant clinical history: no ethylic habit, diabetes mellitus or overweight. As a consequence of hypertransaminase detected in a routine analysis, the patient was diagnosed with HCV genotype 2 in 2000. A liver biopsy showed chronic active hepatitis with grade 3 fibrosis according to Knodell score. In June 2000, the patient started treatment with 3 million units of interferon alpha 2b (IFN) three times a week and 1,000 mg of oral ribavirine daily. After 3 months serum PCR for HCV was negative and viral response was maintained at the end of treatment in June 2001. Subsequently, the patient attended annual follow-up visits and underwent complete biochemical examination including alpha-fetoprotein determination, serum PCR for HCV and abdominal ultrasonography yielding normal or negative results. In August 2008, alpha-fetoprotein level was 156 ng/ml and abdominal ultrasonography showed no lesions in the hepatic parenchyma, no ascites and a permeable portal vein; serum PCR for HCV remained negative.

Two months later, a new biochemical analysis revealed alpha-fetoprotein levels of 404 ng/ml. CT scan and abdominal MRI results revealed a small focal lesion of 15 mm of diameter in the periphery of the segment V of the hepatic vein suggestive of HCC. Thoracic CT scanning and bone gammarraphy did not reveal signs of metastasis and an oral endoscopy did not show signs of portal vein hypertension.

The patient underwent liver resection (atypical hepatectomy-laparoscopic resection of IVb segment), the analysis of the resected sample confirms the diagnosis of hepatocarcinoma without invasion of resection margins or vascular infiltration; the surrounding hepatic parenchyma showing signs of cirrhosis.

Abdominal MRI carried out 9 months after surgery did not show recidive or persistence of the tumor and alpha-fetoprotein level was 1.1 ng/ml.

Discussion

Due to the low incidence of HCC in patients without cirrhosis and to the necessity to establish a prolonged follow-up period to detect the development of cirrhosis and HCC, there are no prospective studies which evaluate the possible effect of antiviral therapy in preventing the risk of HCC in patients with HCV infection without cirrhosis. Data obtained from prospective Japanese studies suggest that IFN therapy in patients without cirrhosis reduces the incidence of HCC. According to one of these studies, which analysed the evolution of 2,890 patients with chronic hepatitis C (CCH), 490 of them not previously treated with IFN, the incidence of HCC after a 4-year-follow-up period in patients treated with IFN was 1.1 vs. 3.1% in untreated patients. The maximum reduction of incidence of HCC was observed in patients who responded favourably to treatment and who suffered advanced fibrosis (F2-F3) at the onset of therapy; it was lower in cirrhotic patients (F4) and unexisting
after 10-year-follow-up in patients with F0-F1 due to the low incidence of HCC in this group (2). The mentioned study has been recently actualized with the calculation of the number of years gained thanks to therapy in relation to age and degree of fibrosis at the onset of therapy. The greatest benefit was observed in young male patients with a fibrosis degree F3 and who responded well to therapy (3). Imai et al. (4) included in their study 419 patients with HCC treated with IFN and other 144 patients without treatment (IFN was not available). After a follow-up period of 4 years, the accumulated incidence of HCC was 6.6% in treated patients vs. 12.2% in the control group (p < 0.004). A further sub-analysis revealed that HCC incidence ranged from 0.9% in patients responding to therapy to 6.1% in patients showing relapse and to 12.8% in patients not responding to therapy and those who did not receive treatment. They concluded, therefore, that the benefit of antiviral therapy in preventing HCC is particularly solid in patients showing a sustained viral response.

The development of HCC after antiviral therapy must only be considered when the period elapsing between the completion of antiviral therapy and the onset of HCC is > 2 yrs. Thus, the risk of suffering microscopic HCC prior to antiviral therapy disappears (5).

All these data show the exceptional character of the case we report here, as our patient developed cirrhosis despite a sustained viral response (1) and the disease progressed to HCC 7 years after such response. This poses the necessity to continue the follow up of patients with HCC even if the virus is eliminated with therapy, in particular if fibrosis degree at baseline biopsy is ≥ 2.

In our opinion, the main risk factor in the case of our patient was the progression of the infection to cirrhosis, despite the achievement of a sustained viral response. Periodic follow up visits have made it possible to detect HCC in a favorable stage and so initiate therapy with the objective to cure the patient (6).

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References