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LETTER TO THE EDITOR

Evidence of HCV recovery after therapy of hepatitis C virus infection by direct acting antivirals

Introduction

Hepatitis C virus (HCV) infection is among one of the most important causes of chronic liver disease worldwide (71 million patients chronically infected according to the recent WHO re-evaluation of hepatitis epidemiology) resulting in an increased morbidity and mortality related to hepatic (cirrhosis and hepatocellular carcinoma) and extrahepatic manifestations [1]. Interferon-including regimens have been proved to allow a complete virologic recovery in patients having achieved a sustained virologic response (SVR). This recovery is defined by undetectability of HCV RNA in the serum by a sensitive assay (lower limit of detection $\leq$ 15 IU/mL) 12 weeks and/or 24 weeks after treatment completion and in parallel by undetectability of HCV RNA in the peripheral blood mononuclear cells and in the liver [2]: this complete recovery is permitted by the absence of reservoir or putative genomic integration by opposition with human immune deficiency virus or hepatitis B virus infection. The management of patients with HCV-related liver disease has been considerably improved over the past two decades thanks to a better understanding of the pathophysiology of the disease, and because of developments in diagnostic procedures and improvements in therapy and prevention. The infection is cured in more than 95% of patients who are treated by oral direct acting antivirals (DAAs) [3] but the reality of a complete virologic recovery remains debatable since liver biopsies to exclude occult liver infection are no longer performed.

We report a case from our ''real-life'' practice giving the first evidence that DAAs combination results indeed in virologic recovery.

A 61-year-old man was diagnosed as infected by HCV-genotype 1a at a time of putative living donation of kidney to his daughter (31-years-old with end-stage kidney disease related to focal and segmental glomerulosclerosis and requiring hemodialysis since February 2016). The pre-transplantation evaluation confirmed that she was negative for HCV antibodies. The donor had an asymptomatic Child A score 5 cirrhosis (prothrombin rate 100%, total bilirubin 7 μmol/L, albumine 48 g/L, platelets count 215,000/mm^3) with a liver stiffness values by fibroscan of 16.8 kPa (IQR 4.5 and TDR 100%) and a fibrotest fibrosis score of 0.78. The patient did not undergo an upper endoscopy for esophageal varices screening according to the Baveno VI recommendations (fibroscan < 20 kPa and platelets count > 150,000/mm^3).

A combination by sofosbuvir and ledipasvir was administered for 12 weeks since the baseline viral load was 6.47 log and was well-tolerated. HCV RNA was undetectable at week 4 and 12 (end of therapy) and 24 weeks after the end of treatment evidencing a SVR which allowed the kidney donation on February 2016.

Given a donor-recipient ABO mismatch, a strong immunosuppression protocol was given including pre-transplantation desimmunisation with plasmatic exchanges and rituximab and post-transplant immune suppression by tacrolimus 7 mg $\times$ 2/d, mycophenolate 750 mg $\times$ 2/d and 20 mg/d of prednisone. She was discharged at day 21 with a creatinine value of 81 μmol/L.

At 6 months post-transplantation, both the patient and his daughter (who remained anti-HCV antibodies-negative) were HCV RNA-negative by using sensitive assays (COBAS 6800 HCV Test, threshold < 15 UI/mL) evidencing that the so-called SVR was associated with a complete recovery, allowing organ transplantation without HCV transmission.

To our knowledge, this is the first case that reports a living organ donation from a HCV-infected donor who achieved SVR with a DAA regimen suggesting that DAA-associated SVR corresponds, like after interferon-including regimen, to a complete virologic recovery. Even if DAAs are highly efficient and well-tolerated after renal transplantation [4], it is likely easier to treat living organ donors before transplantation than organ recipients after transplantation as suggested by the KDIGO recommendations [5].

Disclosure of interest

L. Parlati, L. Sirmai, M.-A. Dupuy, D. Glotz declare that they have no competing interest.

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