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Post Hepatitis C Cirrhosis in Sub-Sahara Kidney Transplant, Treated with Sofosbuvir/Ledipasvir: Report of Case and Review of Literature

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Abstract

Background: Viral hepatitis C is a major public health problem in the world. The advent of direct-acting antivirals has revolutionized the taking in charge and prognosis of patients infected with the hepatitis C virus. The interest of this presentation is to draw attention to the problem of therapeutic care posed by viral hepatitis C in kidney transplant patients in Côte d'Ivoire, a country with limited resources where all direct-acting antivirals are not yet available. **Patient observation**: We report the case of a kidney transplant of 52 years old, chronic bearer of viral hepatitis C virus who after his kidney transplant presented, decompensated active cirrhosis. A treatment based on Sofosbuvir 400 mg/Ledipasvir 90 mg in this patient with genotype 2 for 12 weeks was initiated. A sustained virological response was observed 12 weeks after the end of treatment. **Conclusion**: Direct-acting antivirals offer the possibility of antiviral C treatment without interferon or ribavirin in cirrhotic renal transplant.

Keywords

Côte D'Ivoire, Direct-Acting Antivirals, Kidney Transplantation, Viral Hepatitis C

1. Introduction

Hepatitis C virus (HCV) infection affects more than 200 million people world-

wide and its prevalence is high in patients with end-stage renal disease thus increasing challenges in renal transplant patients infected with HCV. In developed countries around 1.8% to 8% of renal transplant patients are infected with HCV [1]. Despite recent therapeutic advances, the treatment of HCV infection remains a challenge. The arrival of new direct-acting antivirals (DAAs) is a revolution for the treatment of HCV infection and particularly in kidney transplant [2]. In Côte d'Ivoire, a country with limited resources, only a few therapeutic classes of DAAs are available. We report the case of a kidney transplant patient, chronic HCV bearer who presented after his kidney transplant, an array of decompensated cirrhosis in a context of deterioration in general condition and high viral load. The provision of Sofosbuvir/Ledipasvir in Côte d'Ivoire has made it possible to initiate treatment in this patient. All information gathered in this study was processed in accordance with the Code of Ethics. The patient has given his consent regarding this case report.

2. Patient and Observation

A 52-year-old married man residing in Abidjan was hospitalized for general impairment in December 2014. Previously, he has had a kidney transplant since June 2008 from a living donor in New Delhi, India. We do not have a record of his hospitalization for the kidney transplant. His immunosuppressive therapy included Tacrolimus, Mycophenolate Mofetil and steroids. His basic creatinine was between 12 - 14 mg/l. He developed post-transplant diabetes treated with insulin since 2013. The glycated hemoglobin was 13.6%. There were no complications related to diabetes. He had viral hepatitis C since the beginning of hemodialysis. He had never received treatment for viral hepatitis C. We do not have information on viral load before kidney transplant, nor on the evaluation of liver fibrosis at the time of hemodialysis. In the history of the disease, he was hospitalized for an alteration of the general condition, digestive disorders (diarrhea made of pasty stools) and impaired renal function. On physical examination, the patient weighed 62 kg for a height of 173 cm, a body mass index of 20.7 kg/m^2; the temperature was at 37°C and the blood pressure measured at 140/90 mmHg. The patient was asthenic. There was jaundice, ascites of moderate abundance and discreet edema of the lower limbs. There was no hepatic encephalopathy, hepatomegaly, or splenomegaly. He had benefited from symptomatic treatment that had improved his clinical condition with persisting impaired renal function. At a complete blood count, there were a normochromic normocytic anemia with a hemoglobin rate at 10.2 g/dl, white blood cells to 4100/mm^3, platelets at 92,000/mm^3. ALT was 69 IU/L, AST at 196 IU/l, total bilirubin 25.8 mg/l, uremia at 0.38 g/l, creatinine 13.7 mg/l, the rate of prothrombin at 42%. Proteinuria of 24 hours was 0.03 g/24h. The total proteins were measured at 95 g/l; albuminemia at 25.3 g/l, gamma globulins at 17.5 g/l with the presence of a beta-gamma block. The inflammater was at 0.82 (A2-A3 activity), the fibro meter at 0.99, and the cirrhometer at 0.97 (F4 fibrosis). Quantitative HCV-RNA

was at 5,242,045 UI/ml (6.72 log). The patient had a genotype HCV 2a/2c. Alpha fetoprotein was normal (6.39 ng/ml). Retroviral Human Immunodeficiency Virus (HIV) serology was negative. Abdominal ultrasound had found a liver cirrhosis, a para-umbilical right kidney transplant and left kidney failure Stage 3. The liver stiffness by Fibroscan was 61.5 kPa, IQR/med 14% and 100% success rate. The upper gastrointestinal endoscopy had not shown endoscopic signs of portal hypertension. The liver biopsy puncture was not done. The diagnosis of active decompensated viral cirrhosis C in oedemato-ascitic mode was retained with a Child Plugh Turcott B9 score (Ascites: 1; Hepatic encephalopathy: 1; prothrombin: 2; Albumin: 3; Bilirubin: 2). The patient was treated with sofosbuvir 400 mg/lisispavir 90 mg (1 tablet daily) for 12 weeks. Tolerance to anti-HCV therapy was excellent and no side effects were observed. Evolution under treatment of biological, biochemical and virological parameters is shown in Table 1. The patient received treatment based on Sofosbuvir 400 mg/Ledipasvir 90 mg (1 tablet daily) for 12 weeks.

Two years after the end of the treatment, the patient presents a good general condition; the viral load of HCV is always negative (HCV RNA <15 UI/ML), the liver tests are normal (AST at 42 UI/L, ALT at 40 UI/L Rate of prothrombin at 72%.

3. Discussion

3.1. Epidemiology

Chronic infection with HVC is the most common cause of liver diseases after

Table 1. Evolution under treatment of clinical and biological parameters.

Parameters	Week 0	Week 4	Week 8	Week 12	SVR* 12
General condition					
asthenia	Yes	Yes	No	No	No
nausea	Yes	No	No	No	No
ascite	Yes	Yes	No	No	No
headache	No	No	No	No	No
HCV RNA (UI/ml)	5,242,045	<15	<15	<15	<15
HCV RNA (Log)	6.72	<1.2	<1.2	<1.2	<1.2
Platelets (/mm^3)	92,000	80,000	82,000	96,000	120,000
White Blood Cell (/mm^3)	4100	5000	48,000	4800	4400
Neutrophil (/mm^3)	767	2575	1709	1800	1399
Hemoglobin (g/dl)	10.2	10.9	9.5	10.2	11
AST (UI/l)	196	46	43	44	45
ALT (UI/l)	69	28	29	28	44
Creatinin (mg/l)	13.7	15.6	14	13.9	15.6
Rate of prothrombin (%)	42	67	53	54	70

*Sustained virologic response 12 weeks off therapy.

kidney transplantation [3]. The main risk factors for HCV infection in kidney transplant recipient are: dialysis duration and dialysis mode; this is the case of our patient who had contracted HCV probably at his extra-renal cleansing. The risk is higher in hemodialysis than peritoneal dialysis and center hemodialysis than that of home hemodialysis [3].

3.2. HCV Viral Load and Liver Fibrosis

We do not have values of HCV viral load and information on liver fibrosis before kidney transplant, but probably he would have had relatively lower hepatic fibrosis and viral load for transplant, compared to viral load and fibrosis after kidney transplant. In the literature, it has been shown a significant increase in HCV viremia a year after the introduction of immunosuppressive treatment with Mycophenolate mofetil [4]. Corticosteroids are also responsible for an increase in viral replication and more rapid progression to cirrhosis in immuno-competent subject [5]. After kidney transplant, there is a rise in serum concentration of HCV RNA which is probably due to the decrease of the immune response under immunosuppressive therapy, and for the establishment of a new balance between the production of virions and their clearance [3] [6] [7] [8].

3.3. Influence of HCV on the Renal Graft Survival

In our case, we observed normal kidney function and an absence of proteinuria six years after kidney transplant. Hestin *et al.* [9] showed that the presence of anti-HCV antibodies before kidney transplantation was predictive of the appearance of proteinuria after transplantation and graft survival of patients infected with HCV and proteinuric is less than that of non-proteinuria patients. Cosio *et al.* [10] reported that HCV-infected kidney transplants have a high prevalence of acute or chronic vascular rejection in the first six months after transplantation, resulting in decreased graft survival. Conversely, other authors have reported a lower rate of acute rejection in kidney transplant patients with HCV compared to kidney transplant patients not infected with HCV [11]. This reduction in graft survival seems to be due to the appearance of glomerular diseases attributable to the virus [11]. Recently, it has been shown that in HCV + kidney transplant patients with de novo glomerular diseases, the occurrence of these glomerular was not related to either an increase in the serum HCV RNA concentration after transplantation, nor to an effect describes the virus on kidney cells, but rather to a change in the immune response [7].

3.4. Combination Sofosbuvir/Ledipasvir and HCV Genotype 2

There are no major studies evaluating the combination Sofosbuvir/Ledipasvir in HCV infected patients with HCV genotype 2 and Ledipasvir has a low activity on HCV genotype [12]. The combination Sofosbuvir/Ledipasvir was approved by the European Association for the Study of Liver (EASL) for the treatment of HCV genotype 1, 4, 5, and 6 [13]. Therapeutic options for treating patients in-

fected with HCV genotype 2 are based on the combination Sofosbuvir/Ribavirin or Sofosbuvir/Daclatasvir [13]. Given the recognized side effects of ribavirin such as anemia [14] and the unavailability of DAAs such as Daclatasvir in Côte d'Ivoire at the time of treatment of our patient, the only treatment option based on DAAs without interferon or ribavirin in this infected HCV kidney transplant recipient genotype 2 was Sofosbuvir/Ledipasvir; which justified its use in our patient. The rapid virological response was observed at initiation of treatment as well as the sustained virological response at 12 weeks after the end of treatment. We did not find in the literature a study evaluating the combination sofosbuvir/ledipasvir in kidney transplant patients infected with HCV genotype 2. However a rapid virologic response was observed in 22 of 25 patients (88%) in the series Kamar *et al.* [15]; they also found that at the end of treatment, HCV RNA was undetectable in all patients. 4 to 12 weeks after therapy with DAAs, all patients had a sustained virologic response and normalization of transaminases. Tolerance to anti-HCV therapy was excellent and no adverse effects were observed. They therefore concluded that the DAAs are effective and safe for treating HCV infection after kidney transplantation.

4. Conclusion

Hepatitis C in the kidney transplant is common. Here we report the efficacy of the Sofosbuvir/Ledipasvir combination in a genotype 2 positive HCV patient. This is the first case diagnosed in black francophone Africa. The evolution was favorable with a sustained viral response 12 weeks after the end of treatment. The hope of accessible treatment and affordable is therefore possible in black Africa for HCV positive hemodialysis patients as well as HCV positive kidney transplant patients.

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