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Combination Therapy of Simeprevir and Sofosbuvir in Recurrent HCV Genotype 4 After Liver Retransplantation: Case Report

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Conflict of interest: None declared

Patient: Male, 50
Final Diagnosis: Recurrent hepatitis C
Symptoms: —
Medication: —
Clinical Procedure: Anti hepatitis C therapy
Specialty: Gastroenterology and Hepatology

Objective: Unusual clinical course

Background: The treatment of hepatitis C virus (HCV) infection is evolving rapidly. Many studies have been completed during the last 2 years, with more studies still in progress. The management of recurring HCV infection following liver organ transplantation remains very challenging, especially for HCV genotype 4 (GT-4). More research is needed in this area.





Case Report: We report on a patient with a recurring HCV infection and fibrosing cholestatic hepatitis following liver retransplantation, who was successfully treated with a combination therapy of simeprevir and sofosbuvir without interferon/ribavirin. As far as we know, this is the first reported case of this kind.

Conclusions: This information may be of importance and inform future management of patients with recurrent HCV infections following liver transplantation.

MeSH Keywords: Antiviral Agents • Hepatitis C, Chronic • Liver Transplantation

Abbreviations: HCV – hepatitis C; GT-4 – genotype 4; FCH – fibrosing cholestatic hepatitis; SVR –sustained viral response

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/896810>

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Background

End-stage liver disease associated with HCV infection is a common indication for liver transplantation and accounts for up to 40% of all liver transplantations [1]. An uncommon and challenging difficulty associated with recurrent HCV infection following liver transplantation is fibrosing cholestatic hepatitis (FCH), which can cause earlier graft loss, death, or both [2].

There are several HCV genotypes with subtypes and treatment strategies tend to differ depending on the genotype [3].

HCV GT-4 is very common in Africa and the Middle Eastern region, where it is responsible for more than 80% of all HCV infections. It is the cause of approximately 35 million cases of chronic HCV infections worldwide [4,5]

A recent meta-analyses found sustained virological response (SVR) rates in HCV GT-4 infected patients range from 28% to 71%, however, most studies were small and had dissimilar study designs [6].

As mentioned by Riad et al., "HCV GT-4 demonstrated little treatment response rates and differences when compared to other genotypes. However, the reasons' underlying these discrepancies remains uncertain due to the limited number of studies on HCV GT-4" [7].

Case Report

We describe a patient with a history of HCV GT-4 infection with liver cirrhosis and FCH. The 47-year-old man was a null responder to two initial treatments with ribavirin and peg-interferon- α -2a. After careful evaluation for a liver transplant, he received a living donor transplant of his younger brother's right liver lobe.

Two years after the initial transplantation, the patient met the criteria for liver retransplantation, as the patient had a recurrence of HCV infection and FCH, reducing his health-related quality of life. The multidisciplinary transplantation board decided to list him again as a potential recipient for a whole graft transplant. The retransplantation was uneventful; and tacrolimus was administrated at a low daily dose.

Four years after retransplantation, a recurrent HCV infection was diagnosed. The patient's liver enzymes were elevated with GGT concentrations reaching a peak at 1500 U/ml. Histological examination showed inflammation grade 2 and fibrosis stage 2.

We decided to use a dual therapy for three months, combining simeprevir and sofosbuvir and excluding interferon and ribavirin. After one month of treatment, a rapid virological response

was achieved, meaning that at week 4 of treatment HCV RNA was undetectable in the patient's serum. An end-of-treatment viral response was observed after 12 weeks of treatment, with SVR maintained one year after treatment.

Discussion

There have been several studies highlighting the safety and the efficacy of anti-HCV therapies that are interferon-free, though not for cases of HCV GT-4.

Tanaka et al. reported the safe administration of 24-week antiviral therapy using daclatasvir and asunaprevir in a case with HCV recurrence after liver transplantation and an additional HIV infection [8].

Similarly, Leroy et al. concluded that therapy with sofosbuvir combined with ribavirin or daclatasvir helps improve the clinical condition of patients with recurring HCV infection and FCH after liver transplantation, and often leads to a SVR at 12 weeks [9].

Good viral responses with little effect on blood levels of immunosuppressant therapy were demonstrated in the cases reported by Kawaoka et al., who used therapy with daclatasvir and asunaprevir for recurrent HCV infection after liver transplantation [10].

The phase II COSMOS study [11] used a combination of simeprevir and sofosbuvir with or without ribavirin in both previously treated and untreated patients with chronic HCV GT-1 infections. The SVR within 12 weeks was 96% and 93% in the prior null responder groups treated with ribavirin or without ribavirin, respectively. It is important to note that this study involved HCV genotype 1 versus genotype 4.

Moreno et al. published a study of HCV GT-4 patients titled "Efficacy and safety of simeprevir with PegIFN/ribavirin in naïve or experienced patients infected with chronic HCV genotype 4" [12]. This phase III open-label, single-arm study reported an evaluated efficacy and safety of simeprevir with peginterferon- α -2a/ribavirin in patients with chronic HCV GT-4 infection. This study confirmed the safety and efficacy of simeprevir with ribavirin/peginterferon- α -2a in treatment-naïve or previously treated patients with chronic HCV GT-4 infection was comparable with previous reports of treatment of HCV GT-1 infection.

Molina et al. indicated that sofosbuvir and ribavirin provided high rates of SVR after three months of treatment in previously treated and untreated patients co-infected with HIV and HCV GT-1, -2, -3 and -4. Thus suggesting that interferon-free combination regimens make sofosbuvir plus ribavirin a useful treatment option for this patient population [13].

Ruane et al. suggested that the use of sofosbuvir plus ribavirin over 24 weeks is an efficacious and well-tolerated treatment in HCV GT-4 infected patients [14].

Razek et al. posit that interferon-free HCV therapy combinations administered for 12 weeks or less will soon become the optimal therapy, with the potential for cure [15].

Antiviral therapy after liver transplantation is a complex matter because of possible side effects and inferior efficacy in patients that are liver transplant recipients as well as due to drug interactions with immunosuppression. Indeed, fibrosis progression will accelerate under immunosuppression therapy [16].

FCH is a rare and challenging post liver transplantation complication due to HCV relapse. HIV infected patients with FCH have an inferior prognosis.

Borentain et al. reported the successful treatment of patients infected with HCV GT-4 and HIV using ribavirin and sofosbuvir. Four weeks after treatment, they observed HCV relapse related symptoms, normalization of liver biochemistry, and substantial decline in HCV load [17].

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These studies suggest that HCV infection can be treated without interferon, and these new regimens are safe, have excellent efficacy, and minimal adverse events.

In summary, we present a case report of a patient with recurring HCV GT-4 infection after liver retransplantation, who showed a rapid SVR and a normalization of liver enzymes after having been efficaciously treated with a combined dual therapy of simeprevir and sofosbuvir without the use of ribavirin or peg-interferon- α -2a.

Conclusions

Interferon/ribavirin free dual therapy with sofosbuvir and simeprevir might be a useful and safe approach for the therapy of HCV GT-4 infections in general and potentially for recurrent HCV GT-4 infections after liver transplantation.

Statement

The authors declare no conflict of Interest.

The authors certify that they have no financial support.