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Case report

Sustained virological response after ten days of triple anti-hepatitis C virus (HCV) therapy with telaprevir plus pegylated interferon and ribavirin in an HIV/HCV co-infected cirrhotic woman

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SUMMARY

The introduction of first-generation protease inhibitors for the treatment of chronic hepatitis C in subjects infected with hepatitis C virus (HCV) genotype 1 has significantly improved the sustained virological response (SVR) rate. As liver cirrhosis reduces the probability of achieving SVR, current guidelines discourage response-guided therapy in cirrhotic patients. We report the first case of a cirrhotic woman with chronic HCV and HIV co-infection achieving virological response after an ultra-short course of therapy. A 40-year-old HIV/HCV co-infected woman with compensated liver cirrhosis was treated with anti-HCV triple therapy containing telaprevir plus pegylated interferon and ribavirin. Baseline plasma HCV RNA was 3.6 log IU/ml and transaminases were within the normal range. She harboured IL28B rs12979860 C/C alleles. Ten days after starting therapy, the patient stopped treatment because of mild anorexia and nausea. Virological response was detected at treatment discontinuation and was maintained up to 24 weeks. This case describes an unexpected SVR after a 10-day course of antiviral therapy in a cirrhotic HIV/HCV co-infected woman presenting positive predictive factors for a response (low viral load, IL28B genotype). Nonetheless, there is no evidence to suggest a shorter duration of treatment in this subset of patients.

1. Introduction

Chronic hepatitis C virus (HCV) infection is responsible for significant morbidity and mortality worldwide, by determining liver cirrhosis and subsequent end-stage liver disease and hepatocellular carcinoma. Following the introduction of antiretroviral therapy and the improvement in survival of patients with HIV infection, chronic hepatitis C has assumed growing importance in this population. The recent introduction of first-generation protease inhibitors (PIs) boceprevir and telaprevir in addition to the combination of pegylated interferon (PEG-IFN) and ribavirin has led to a 30% increase in the sustained virological response (SVR) rate in treatment-naive patients infected with HCV genotype 1.[1,2]

Different factors are associated with a better response to treatment, such as HCV genotype, baseline viral load, rapid virological response (RVR), CD4 count, insulin resistance, age, obesity, fibrosis stage, and the host's interleukin-28B (IL28B) genotype.[2] Previous studies have shown that patients with a favourable IL28B genotype achieving RVR obtain similar rates of SVR even with a shorter duration of triple therapy.[3] Nonetheless, little information is available regarding cirrhotic persons living with HIV co-infection.

Clinical trials in the HIV/HCV co-infected population suggest that the safety profile of HCV PIs, especially severity and frequency of adverse events, are similar to those observed in HCV mono-infected subjects,[1] but their use may be complicated by the potential drug–drug interactions with antiretroviral (ARV) drugs.[2] Current data support the use of boceprevir or telaprevir in co-infected patients with high CD4 cell counts not on ARV therapy and in those on selected ARV regimens. For HIV-positive subjects co-infected with HCV genotype 1, current guidelines suggest triple

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therapy with PEG-IFN/ribavirin plus telaprevir for the first 12 weeks of treatment followed by double therapy for 36 weeks in the case of virological response.[2] Nonetheless, the management of triple therapy with telaprevir or boceprevir is particularly challenging in cirrhotic patients, who are more prone to develop adverse events,[4] and requires even more attention in the presence of concomitant HIV infection for the potential drug–drug interactions with ARV and higher incidence of adverse events.[5]

2. Case report

We describe a case of HCV clearance after ultra-short triple therapy with telaprevir plus PEG-IFN/ribavirin in a 40-year-old cirrhotic woman, co-infected with HIV-1 (stage B3 according to the Centers for Disease Control and Prevention (CDC) classification, 1993) and HCV genotype 1c, both diagnosed 19 years ago. Her body mass index was 19.71 kg/m^2. She reported previous intravenous drug abuse, discontinued 10 years before. Liver cirrhosis had been confirmed by liver biopsy 15 years before. Nonetheless, the patient had previously refused antiviral therapy for HCV. After experiencing different ARV regimens (nadir CD4+ count 113 cells/mm^3) mainly because of low tolerability and poor compliance, she had been on stable ARV therapy with a boosted PI-based regimen (tenofovir/emtricitabine plus atazanavir/ritonavir) for 6 years thanks to the low pill burden and once-daily dosing.

She was included in an Early Access Program (EAP) using telaprevir (750 mg three times daily) + PEG-IFN alfa-2a (180 μg/week) + weight-based ribavirin (1000 mg/day). Her baseline CD4+ cell count was 309 cells/mm^3 (32.5%) with plasma HIV-RNA <37 copies/ml. At baseline, liver stiffness was 20.9 KPa and indirect biochemical markers of liver fibrosis APRI (aspartate aminotransferase to platelet ratio index) and FIB-4 were 0.67 and 1.74, respectively. An abdominal ultrasound showed mild hepatomegaly with irregular margins and surface, and patchy parenchyma in the absence of focal lesions, while no splenomegaly or other signs of portal hypertension were recorded. No oesophageal varices were observed endoscopically. Child–Turcotte–Pugh stage was A6. She harboured IL28B rs12979860 C/C alleles.

At baseline, HCV-RNA was 3.6 log IU/ml (Abbott Real-Time HCV Assay; detection limit <1.1 log IU/ml) and transaminases and creatinine were within the normal range. The white blood cell count was 3.2×10^9/l, haemoglobin 13.2 g/dl, and platelet count 116×10^9/l. The only adverse events experienced by the patient were mild anorexia and nausea. Ten days after starting therapy, the patient voluntarily interrupted PEG-IFN, ribavirin, and telaprevir, maintaining ARV therapy.

At treatment discontinuation, liver enzymes were normal and HCV-RNA <12 IU/ml. This undetectable HCV was maintained up to 24 weeks post-treatment. Indirect fibrosis biomarkers and liver stiffness showed a significant improvement from baseline to 24 weeks after treatment completion (Table 1).

Table 1
Plasma HCV-RNA and liver fibrosis over time

	HCV-RNA, log IU/ml	FIB-4	APRI	Liver stiffness, KPa
Baseline	3.6	1.79	0.67	20.0
End of treatment	<1.1	4.50	1.56	
Week 12 post-treatment	<1.1	1.37	0.41	
Week 24 post-treatment	<1.1	1.10	0.32	12.0

HCV-RNA, HCV plasma load; APRI, aspartate aminotransferase to platelet ratio index.

3. Discussion

We report a case of HCV clearance after only 10 days of triple antiviral treatment. This observation shows the high virological efficacy of first-generation PIs, leading to very early undetectable HCV-RNA in this HIV co-infected cirrhotic woman with favourable predictors for a virological response. SVR after this ultra-short therapy also improved liver fibrosis, apparently reversing biochemical and 'elastometric' cirrhosis. Nonetheless, regular monitoring of liver disease and screening for its complications remains essential in this subject.

Our patient presented a key factor associated with a poor response to antiviral therapy, i.e., liver cirrhosis, together with other factors associated with a favourable response to treatment, i.e., IL28B genotype CC, the absence of insulin resistance or metabolic syndrome, and a low baseline viral load. The latter in particular may represent the key factor explaining the HCV clearance.[2]

Current guidelines do not consider the use of response-guided therapy in the setting of liver cirrhosis and HIV infection,[2] even though this could be attractive since a significantly higher incidence of adverse events has been observed in HIV-infected[5] and in cirrhotic subjects.[4] Nonetheless, our observation represents a single case of an unexpectedly positive response to an ultra-short treatment schedule in a patient with many factors that positively affected the probability of achieving a virological response. Treatment shortening, even with response-guided therapy, is not advisable in cirrhotic patients, since the advanced liver fibrosis and the reduced liver function are major obstacles to this goal, and the achievement of SVR in this subset of patients represents a major prognostic goal. Even though an adequate characterization of host and viral factors associated with the response to antiviral therapy would help clinicians to predict the maintenance of virological response after premature treatment discontinuation for adverse events, which is frequently observed in this group of patients, this evaluation must not be carried out to select candidates who would benefit from a shorter duration of treatment. Both baseline and on-treatment factors associated with virological response should be evaluated and combined to assess the overall probability of a response to treatment.

To conclude, this single observation must not lead to the consideration of a shorter treatment duration in cirrhotic patients, who deserve to receive the best treatment regimen in order to achieve SVR and improve their prognosis. Rigorous clinical studies in cirrhotic patients with favourable predictors of a virological response are needed to evaluate the efficacy and safety of shorter treatment regimens.

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Ethical approval: Written informed consent was obtained from the patient for participation in the Early Access Programme.

Conflict of interest: HH, EM, MM, LDT, GM, CU, SB, and AL declare no financial or personal relationships with other people or organizations that could inappropriately have influenced (biased) their work.

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