

# A Case of Severe Acute Respiratory Syndrome Coronavirus 2 Treatment With Remdesivir in a Hepatitis C-Coinfected Patient Resulting in Temporary Viral Control and Posttreatment Flare

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We report a case of a man with chronic hepatitis C infection treated with remdesivir for COVID-19, resulting in lowered HCV viral load, followed by a rebound after its discontinuation. Concomitant treatment with tocilizumab possibly caused loss of anti-HBs.

**Keywords.** anti-HBs; COVID-19; hepatitis B; hepatitis C; remdesivir.

The coronavirus disease 2019 (COVID-19) pandemic has united the world in a race to understand its pathology to develop effective treatments. Although it typically presents with respiratory symptoms, gastrointestinal manifestations and liver injury are frequently reported [1]. Liver injury is mostly attributed to immune-mediated damage as a result of severe inflammatory response; however, direct cytotoxicity has not been completely excluded [2]. Drug-induced hepatotoxicity is another major contributor; the administration of antivirals such as lopinavir/ritonavir and remdesivir as well as other potentially hepatotoxic medications must be carefully weighted and adequately monitored, particularly in patients with pre-existing hepatic disease such as chronic viral hepatitis [3]. In addition, reactivation of hepatitis B virus (HBV) in patients with COVID-19 has been described, particularly in patients treated with immunosuppressants, possibly contributing to hepatic damage [4, 5].

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We present the case of a 47-year-old male with chronic hepatitis C virus (HCV) and past exposure to hepatitis B who developed severe COVID-19 pneumonia. Administration of remdesivir resulted in a temporary lowering of HCV viral load, followed by a significant rebound after its discontinuation with a hepatitis flare. A loss of anti-HBs titer was also noted, probably related to the administration of tocilizumab. This report aims to emphasize the need for adequate monitoring of liver parameters and viral load as well as serology in patients with chronic hepatitis, especially during the administration of known hepatotoxic drugs, immunosuppressants, and antivirals with potential anti-HBV or HCV activity.

## CASE REPORT

A 47-year-old male presented to the emergency department on June 28, 2020 complaining of a 2-week feeling of myalgia and malaise, followed by dry cough and increasing dyspnea over the previous 72 hours. The patient was morbidly obese, with current alcohol and benzodiazepine abuse as well as a past history of intravenous drug consumption and tobacco use. In 2014, he had been diagnosed with chronic HCV infection but had abandoned follow-up; medical records at the time also revealed previous HBV infection (negative HBs antigen, positive antibodies for HBs and HBc). His usual medication consisted of escitalopram 5 mg and clobazam 10 mg once daily. Physical examination on admittance revealed fever (39.3°C) and tachypnea with inability to complete a full sentence. His peripheral oxygen saturation was 91%, with an arterial pO<sub>2</sub> of 59.9 mmHg. Relevant laboratory findings included elevated inflammatory markers such as C-reactive protein (9.1 mg/dL), ferritin (1569 ng/mL), and interleukin (IL)-6 (57.1 pg/mL), as well as creatinine kinase (812 U/L) and lactate dehydrogenase (457 U/L), with thrombocytopenia (74 × 10<sup>9</sup> cells/L). There was no relevant change in leukocyte count, transaminase, or bilirubin levels. The presence of hepatitis C antibodies as well as anti-HBs and anti-HBc was confirmed. Hepatitis C virus viral load was 15 700 UI/mL (log<sub>10</sub> 4.20).

A severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR) test (nasopharyngeal swab) was found to be positive. Thoracic computed tomography scan revealed extensive bilateral, predominantly peripheral ground-glass opacities, typical of COVID-19 pneumonia.

The patient was admitted to an isolation ward where, as per hospital protocol concerning COVID-19 patients presenting with respiratory insufficiency, he was medicated with lopinavir/ritonavir (LOP/r) awaiting remdesivir availability, as well as tocilizumab (80 mg, administered once on the second day of hospitalization). He did not receive any plasma or intravenous

immunoglobulin. The patient's respiratory condition continued to decline over the following 4 days, with increased oxygen dependence (maximum fraction of inspired oxygen [FiO<sub>2</sub>] 60%) and need for intermittent proning. After 6 days, LOP/r was discontinued and the patient was started on remdesivir (200-mg loading dose followed once-daily 100 mg for 5 days). During hospital stay, liver parameters were monitored, and HCV viral load repeated after 4 days of remdesivir was found to be significantly decreased (23 UI/mL, log<sub>10</sub> 1.37). A small rebound was noted 2 days after remdesivir suspension (463 UI/mL, log<sub>10</sub> 2.67). No significant change in transaminase levels was noted until 30 days after hospital admission, with aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels rising to 215 U/L and to 370 U/L, respectively, and HCV viral load of 280 000 UI/mL (log<sub>10</sub> 5.45). At this point, HBV immunologic status was re-evaluated, and the patient was found to have lost anti-HBs, with no detectable viral deoxyribonucleic acid (DNA); hepatitis B surface antigen was not measured at the time. Transaminase levels spontaneously decreased to basal levels over the following 14 days, the patient remained asymptomatic and was discharged after 2 negative SARS-CoV-2 PCR tests, to be followed-up in Hepatology consultation. Upon re-evaluation 3 months later, the patient presented with an asymptomatic elevation in transaminase levels (AST 114 U/L, ALT 160 U/L) along with thrombocytopenia (platelet count 82 × 10<sup>9</sup>/L), with no change in coagulation parameters or albumin level. Additional investigation revealed that HCV viral load had further risen to 2 130 000 UI/mL (log<sub>10</sub> 6.33); a transient elastogram was performed, with a fibrosis score of 33.9 kPa, and no esophageal varices were present on endoscopy. Genotyping indicated the presence of type 3a, and testing for the presence of mutation resistances was not performed at the time. The patient was referred for treatment of HCV infection with direct-acting antivirals.

#### Patient Consent

Informed consent was obtained from the patient for publication of this case report.

#### DISCUSSION

Over the course of the SARS-CoV-2 pandemic, many antiviral and immunomodulatory therapies have been proposed. The full impact of these agents in patients with pre-existing hepatic disorders such as chronic viral hepatitis still remains to be evaluated.

Remdesivir is a broad-spectrum antiviral whose ability to delay chain termination by inhibiting ribonucleic acid (RNA)-dependent RNA polymerase confers activity against several RNA viruses including coronaviruses, ebola, and HCV [6, 7]. Recently published evidence of shortening the time to recovery [8] has added remdesivir to the anti-COVID-19 arsenal in many institutions. Due to limited worldwide experience with

this drug, its effects on patients with chronic hepatitis C are virtually unknown; however, remdesivir's mechanism of action is similar to other direct-acting antivirals such as sofosbuvir, rendering it a plausible hepatitis C inhibitor. In this case, remdesivir likely resulted in the significant decrease in HCV viral load, followed by a rebound rise after its withdrawal. It remains to be seen whether this exposure might have selected for any mutation conferring resistance to other direct-acting antivirals.

Concerning hepatitis B, a few reports of HBV reactivation in COVID-19 patients [5, 9] have confirmed the need to closely monitor HBV serology as well as viral load and hepatic enzymology, especially in patients subjected to immunosuppressive treatments [10]. The effects of tocilizumab, an IL-6 antagonist, on patients with hepatitis B exposure have not yet been completely clarified; although infrequent, there are published reports of significant reduction and even loss of anti-HBs titers [11] after tocilizumab administration.

#### CONCLUSIONS

In conclusion, treatment of SARS-CoV-2 in patients with chronic viral hepatitis requires close monitoring but does not necessarily preclude the use of antivirals such as remdesivir or immunosuppressors; further studies are needed to evaluate long-term effects, including the acquisition of cross-mutations to other direct-acting HCV antivirals. It is unfortunate that testing for resistance mutations is not widely available, although it must be considered in patients with risk factors such as exposure to antivirals with HCV activity and is mandatory in case of treatment failure.

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