Case Report

COVID-19 in a patient with pre-existing liver disease

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ABSTRACT

Although Coronavirus Disease 2019 (COVID-19), the clinical disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is characterized by respiratory symptoms predominantly, the liver is the main actor in the progression of the disease. Liver involvement exhibits various clinical manifestations from asymptomatic elevations of liver function test to severe hepatic decompensation. In cases of underlying liver failure, the clinical presentation may become more dramatic and requires priority in the management. Treatment of these patients is troublesome due to the potential hepatotoxicity of agents used for the COVID-19. Data on COVID-19 patients having pre-existing liver failure conflicts, and whether these patients are more susceptible to the infection remain unclear. However, in patients with advanced chronic liver failure, the virus can critically compromise survival and result in negative consequences. Here, we present the critical management of a COVID-19 patient having pre-existing cirrhosis and review the current issues.

Keywords: Acute-on-chronic liver failure, cirrhosis, COVID-19, cryptogenic.

The tropism of the novel Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) to angiotensin-converting enzyme-2 (ACE-2) receptors is well established and the presence of ACE-2 receptors on hepatic endothelial cells and cholangiocytes predisposes to hepatic effect.[1] Immune-mediated damage, ischemic hepatitis secondary systemic inflammatory response, drug-induced liver injury, and direct virus-induced cytopathic effect due to virus replication within infected hepatocytes are also potential mechanisms for the development of hepatic failure. The proportion of Coronavirus Disease 2019 (COVID-19) patients who had a pre-existing liver disease was reported to range from 2 to 11%.[2] According to the most recent Centers for Disease Control and Prevention (CDC) update (February 8, 2021), people with chronic liver disease, including Hepatitis B and C, have a high susceptibility to COVID-19 infection.[3]

Despite conflicting data on the prevalence and severity of COVID-19 in liver injury due to the heterogeneity of study populations, a recent multi-center study indicated that hospitalization and mortality were particularly high in patients with underlying liver disease, especially in cirrhotic patients.[4] In this report, we presented the critical care management of a COVID-19 patient with pre-existing cirrhosis.

CASE REPORT

A 45-year-old male patient with a history of cryptogenic cirrhosis was admitted to the emergency service with a sudden alteration in consciousness and respiratory insufficiency. On clinical examination, there were moderate ascites (Grade 2), hepatic encephalopathy (Grade 2), and tachypnea with a respiratory rate of 32 per minute. Laboratory testing revealed elevated levels of C-reactive protein (62.7 mg/L), slightly elevated total bilirubin (1.93 g/dL), increased blood ammonium (111.1 µg/dL), creatine (2.01 mg/dL), blood urea (91 mg/dL), lactate (2 mmol/L), interleukin-6 (187.1 pg/mL) and D-dimer (>4,400 µg/L). The whole blood count was as follows; hemoglobin 5.8 g/dL, hematocrit 19.7%, leucocyte count 11,300/uL, and platelet

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Figure 1. Thorax computed tomography shows the centrilobular ground-glass opacities on the left and interlobular septal thickening on the right lower lobe.

count 201,000 u/L. The international normalized ratio (INR) was 1.59. His Child-Pugh and Model for End-Stage Liver Disease (MELD) scores were 9 (B; severe functional disturbance) and 21, respectively. The thorax computed tomography was compatible with COVID-19 pneumonia (Figure 1). His nasopharyngeal swab was positive for SARS-CoV-2 real-time polymerase chain reaction, so he was transferred to the COVID-19 pandemic intensive care unit (ICU). He was started on wide-spectrum antibiotics, favipiravir, methylprednisolone, gastrointestinal prophylaxis, and enteral laxative agents. A high-flow system was used to administer oxygen. However, on the third day, his clinical condition gradually deteriorated and he required invasive mechanical ventilator support with a high fraction of inspired oxygen. There was a stepwise increase in the liver function tests and coagulation parameters were impaired. The patient required repeated transfusions of fresh frozen plasma, erythrocyte suspension, and human albumin. Hemodynamic instability continued despite the incremental dose of inotropic infusion. Nevertheless, he died on the 11th day of his admission due to multiorgan failure refractory to the aggressive treatment. A written informed consent was obtained from the patient.

DISCUSSION

Our case presented that the management of acute-on-chronic liver failure was a clinical challenge and associated with poor prognosis

in COVID-19 infection. Acute impairment of liver function secondary to superimposed liver involvement by infection was the most likely reason for sudden hepatic encephalopathy and resulted in multiorgan failure. According to a multinational cohort study, baseline liver disease was a main determinant of outcome during COVID-19 infection. This study found that mortality among cirrhotic patients was 32% compared with 8% in those without. During co-existing COVID-19 infection, the Child-Pugh classification was a good outcome predictor in patients with cirrhosis.[5,6] A retrospective multicenter study (COVID-Cirrhosis-CHESS study group) was conducted in 16 hospitals in China, and the findings demonstrate that the cause of death in 21 COVID-19 patients with preexisting cirrhosis was mostly due to respiratory failure rather than a deterioration of liver function. However, in China, the main cirrhosis etiology was chronic Hepatitis B virus; thus, the authors emphasized that this result could not be generalized to all geographic regions.[6] Another case series from Italy demonstrated that 26% of those cirrhotic patients presented with Model for End-Stage Liver Disease (MELD) Score ≥15. Thirty-day mortality was 34%; however, respiratory failure (71%) was the leading cause of death. Study results showed that patients with cirrhosis have a poor outcome.[7] Liver injury during COVID-19 infection manifests with the mild or moderate alteration of transaminase levels, mostly in hepatocellular characteristics.[2] An autopsy of a patient with COVID-19 revealed the microvesicular steatosis and mild inflammatory infiltrates accompanied by T cell overaction. This result considered that the liver injury in COVID-19 was likely immune-mediated rather than a direct cytopathic effect of the virus.[8] The activation of an immune-mediated pathway predisposes the increased risks in critical patients, including end-stage liver failure and liver transplant recipients.[9] As a result, the European Association for the Study of the Liver (EASL) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) recommended postponing elective procedures and routine tests in these patients during the pandemic. Meanwhile, emergency medical care must be conducted under appropriate measures for the prevention of COVID-19 exposure.[10] Innovative technologies such as telemedicine

and remote monitoring were introduced for the standard health care of these patients during the pandemic.[11] Global Liver Institute created a medical update data source named "COVID-19 Response Program for Liver Patients" to inform the patients with pre-existing liver disease.[12]

Many drugs used to treat COVID-19 have hepatotoxic effects. During pharmacological management of COVID-19, treatment must focus on both inhibiting the inflammatory process and promoting recovery, as well as protecting liver functions. In cirrhosis, symptomatic treatment with acetaminophen and avoidance of non-steroidal anti-inflammatory drugs is recommended. Cautious use of antiviral agents in patients with decompensated liver disease and drug–drug interactions in post-liver transplant patients have to be considered.[8] Hydroxychloroquine is a frequently used antimalarial agent that inhibits glycosylation of cell receptors and prevents viral entry into cells. The use of this drug in immunocompromised patients requires special attention, and interactions with immunosuppressive drugs must be taken into account. Tocilizumab is a monoclonal interleukin (IL)-6 receptor antagonist. Liver function tests must be assessed before initiating the treatment, and the drug must be avoided if serum aminotransferase levels are greater than 1.5 times the upper normal limit.[13] Healthcare providers are advised to use the "HEP Drug Interactions" website of the University of Liverpool for interactions between patients' pre-existing treatments and drugs used to treat COVID-19.[14] Recently, the American Association for the Study of Liver Disease released an expert panel consensus statement including the clinical practice advice for hepatology and liver transplant professionals.[15]

In conclusion, given that the majority of patients with cirrhosis have hepatic decompensation, an acute liver injury in these patients may progress more severe and fatal. However, existing data is not strong enough to suggest the aggravation of liver failure is directly related to SARS-CoV-2 infection itself. Further research on patients with pre-existing liver diseases may reveal the histopathological pattern of this virus on the damaged liver in the near future.

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