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Decompensated Csirrhosis and COVID 19; Report of Two Cases

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ABSTRACT

Coronavirus disease 2019 (COVID-19) has turned to be the primary health concern worldwide and for critical patients in particular. Patients with cirrhosis may experience decompensation, as presented in the current case report. An 82-year-old man with cirrhosis was admitted for hepatorenal syndrome, and hemodialysis was initiated. Due to manifestations of COVID-19 in computed tomography (CT), the therapeutic protocols of coronavirus were initiated, and the patient was successfully rehabilitated by COVID-19 treatment and trice-a-week hemodialysis. The other case was a 59-year-old woman with cirrhosis and hematemesis, elevated creatinine, and progressive loss of consciousness. CT scan was compatible with COVID-19 confirmed by Real-time polymerase chain reaction (RT-PCR). Irresponsiveness to medical therapy led to four courses of hemodialysis. Respiratory distress led to intubation, and eventually, the cardiopulmonary arrest occurred, which led to unsuccessful cardiopulmonary resuscitation. Cirrhosis may be decompensated by COVID-19 and lead to fatal outcomes. Despite all the conventional efforts to help the patients survive, prevention from coronavirus infection remains the mainstay for patients with cirrhosis.

KEYWORDS:
COVID-19; Liver cirrhosis; Hepatorenal syndrome; Hepatic encephalopathy

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INTRODUCTION

At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, China. In February 2020, the World Health Organization designated the disease COVID-19, which stands for coronavirus disease 2019.[1]

The spectrum of symptomatic infection ranges from mild to critical. Most infections are not severe. Among hospitalized patients, the proportion of critical or fatal outcomes is higher. The fatality mostly occurs in patients with advanced age or underlying medical comorbidities. Comorbidities associated with severe illness and mortality include age > 65 years, pre-existing pulmonary disease, diabetes mellitus, chronic kidney diseases, hypertension, cardiovascular diseases, obesity, use of biologic agents (tumor necrosis factor (TNF) inhibitors, interleukin inhibitors, anti-B cell agents), history of

transplantation or other immunosuppressant conditions, and HIV infection.[2,3]

The United States Centers for Disease Control and Prevention (CDC) also includes immunocompromising conditions and liver diseases as potential risk factors for severe illness. In a subset of 355 patients who died because of COVID-19 in Italy, the mean number of pre-existing comorbidities was 2.7, and only three patients had no underlying condition.[3] Particular laboratory features have also been associated with worse outcomes, such as lymphopenia, elevated LDH, elevated inflammatory markers, elevated D-dimer, elevated prothrombin time, elevated troponin, elevated creatine phosphokinase, acute kidney injury, and elevated liver enzymes.[4]

It is unclear whether the alterations in laboratory tests are a reflection of pre-existing liver diseases in patients with more severe courses of COVID-19 or damage occurrence by the virus or is the mirror of a severe inflammatory response with disseminated intravascular coagulation. Perhaps, patients with advanced chronic liver disease are at increased risk of infection due to cirrhosis-associated immune dysfunction.[2]

The current study assesses the effects of COVID-19 on the course of two cirrhotic cases.

Decompensated cirrhosis is defined as an acute deterioration in liver function in a patient with cirrhosis and is characterized by jaundice, ascites, hepatic encephalopathy, hepatorenal syndrome, or variceal hemorrhage.[5]

CASE REPORTS

Case 1

An 82-year-old man with a history of cryptogenic cirrhosis, diabetes, and ischemic heart disease was admitted with a presentation of weakness and fatigue. The diagnosis of cirrhosis had been made for him by the development of ascites within a few months earlier.

A similar condition had occurred for him within the prior month, in which his serum creatinine level was 3.5 mg/dL, and he responded to the routine medication used for hepatorenal syndrome.

Abdominal examinations were unremarkable for peritonitis. Other examinations were not helpful in making a diagnosis for the patient's symptoms. The patient's laboratory data were as follows (Table 1):

Echocardiography revealed a left heart ejection fraction of 55% and pulmonary artery pressure of 25 mmHg. The tapped ascitic fluid was low protein, high serum ascites albumin gradient (SAAG), and negative for spontaneous bacterial peritonitis. Upper gastroesophageal endoscopy was performed in which three F1 varicoses were noted.

The ultrasonographic study of kidneys showed hyperechoic parenchyma.

The decompensated cirrhosis and hepatorenal syndrome diagnosis was made. The patient did not respond to hydration, and routine treatment with albumin, and octreotide, and midodrine was initiated; however, no response was notified. Therefore, a nephrology consultation was requested. The nephrologist made the diagnosis of end-stage renal disease and ordered hemodialysis. Because of significantly low levels of platelet count, fresh frozen plasma was injected. A surgeon embedded a shaldon for him, and hemodialysis was performed.

A chest computed tomography (CT) was performed (Figure 1), and manifestations compatible with coronavirus infection were detected, confirmed by the positive real-time polymerase-chain-reaction (RT-PCR) test of the novel coronavirus. Therefore, the national treatment protocol for COVID-19 was started, and the patient responded well to the treatment. He achieved an improved general condition and was put on routine thrice-a-week hemodialysis.

Case 2

A 59-year-old woman with a history of cryptogenic cirrhosis was admitted with a chief complaint of hematemesis and new-onset elevated levels of creatinine and electrolyte abnormalities. Her previous creatinine level was 0.8 mg/dL, which turned to 8 mg/dL at the recent admission. Therefore, a nephrology consultant was requested, and four courses of hemodialysis were performed. More laboratory data are presented in table 2.

Due to the legal guardians' unwillingness and the constant hemoglobin level, upper gastroesophageal endoscopy was not performed.

In addition, her ascitic fluid was tapped, and spontaneous bacterial peritonitis was detected. Thus, midodrine, albumin, octreotide, and antibiotic therapy were done.

An RT-PCR for COVID-19 was requested for the

Table 1: The laboratory tests of case 1 at the admission time

FBS (mg/dl)	110	INR	1.6
ESR (s)	14	Alb (g/dl)	3.1
BUN	92	ALP (mg/dl)	2345
Cr (mg/dl)	6.4	ALT (mg/dl)	108
Ca (mg/dl)	8.7	AST (mg/dl)	218
Ph (mg/dl)	5.3	Direct Bil (mg/dl)	0.3
Na (meq/lit)	134	Total Bil (mg/dl)	2
Mg (mg/dl)	2.5		
WBC (*10^3/ml)	16000	Lymph 4.1%	Neut 82.9%
RBC (*10^6/ml)	5.24		
Hb (mg/dl)	9.1	MCV 79.4 (fl)	
Platelets (ml^{-1})	45000		

FBS: fasting blood sugar, ESR: estimated erythrocytic sedimentation, BUN: blood urea nitrogen, Cr: creatinine, Ca: calcium, Ph: phosphorus, Na: sodium, Mg: magnesium, WBC: white blood cell, RBC: red blood cell, Hb: hemoglobin, INR: international normalized ration, Alb: albumin, ALP: alkaline phosphatase, ALT: alkaline aminotransferase, AST: aspartate aminotransferase, Bil: bilirubin, lymph: lymphocyte, Neut: neutrophil, MCV: mean corpuscular volume

Table 2: The laboratory tests of case 2 at the admission time

Cr (mg/dl)	BUN (mg/dl)	K (meq/lit)	INR	AST (mg/dl)	Total Bilirubin (mg/dl)	Direct Bilirubin (mg/dl)	WBC (ml^{-1})	Lymph	Neut	Hb (mg/dl)	Platelets (ml^{-1})
8	103	5.9	1.58	59	6	2.4	22100	7%	86%	8.7	181000

Cr: creatinine, BUN: blood urea nitrogen, K: potassium, INR: international normalized ratio, AST: aspartate aminotransferase, WBC: white blood cells, lymph: lymphocyte, neut: neutrophil, Hb: hemoglobin

patient, and due to the positive results, a chest CT was performed, which represented significant lung involvement compatible with the coronavirus 2019 pattern (Figure 2).

Although all required steps were administered, she lost her consciousness progressively, and the concurrent diagnosis of hepatic encephalopathy, hepatorenal syndrome, and COVID-19 infection was made for her. However, it was unclear whether COVID-19 was responsible for cirrhosis decompensation or it occurred regardless of coronavirus infection.

Because of respiratory distress on the third day of admission, the patient was intubated. Unfortunately, within the 9th day of admission, her general clinical condition worsened, and cardiopulmonary arrest occurred. The patient died following an unsuccessful cardiopulmonary resuscitation.

DISCUSSION

In the current study, two patients with cirrhosis experienced decompensated hepatic function by the incidence of hepatorenal syndrome following COVID-19. The worse condition occurred in case 2, which represented hepatic encephalopathy, and was doomed to die regardless of efforts, including medications and hemodialysis.

Due to the novelty of COVID-19, the information about the short- or long-term impacts of this disease on different organs require extended scientific investigations. Currently, limited data are available linking underlying liver diseases, cirrhosis in particular, with the course of COVID-19.

Elevation in transaminase levels is one of the common findings among patients with coronavirus infection, regardless of the pre-existing hepatic diseases. Most of the studies have represented aminotransferases elevation as a factor related to the severity of coronavirus infection, but not mortality.[3] However, a transient elevation in aminotransferases may be found in other systemic viral infections, as well, a condition that reflects general immune activation or inflammation caused by circulating cytokines without compromising liver function, a phenomenon called "bystander hepatitis".[6] Nevertheless, scientists assume that collateral liver damage from virally induced

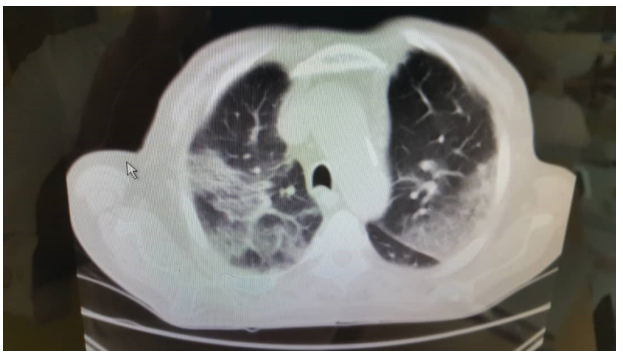

Fig. 1: Chest computed tomogram of case 1 compatible with coronavirus infection.

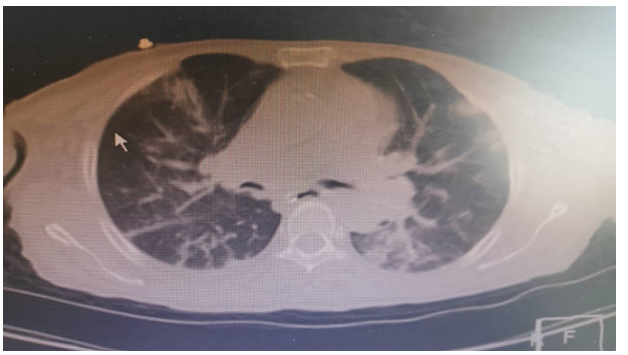

Fig. 2: Chest computed tomogram of the case 2 compatible for coronavirus infection.

cytotoxic T cells and the induction of a dysregulated innate immune response are more responsible for increased aminotransferases than the underlying pre-existing liver dysfunction.[2]

Immune dysfunction is one of the critical points among patients with cirrhosis that predisposes them to diverse infections. Besides, patients with cirrhosis represent poor outcomes after acute respiratory distress syndrome (ARDS), the most significant adverse event due to COVID-19.[7] Although, generally, the outcomes of the patients who require mechanical ventilation because of COVID-19 is poor; worse conditions with a high rate of mortality was noted among intubated cirrhotic patients due to respiratory distress,[8] which occurred in case 2 and despite the medical treatment and hemodialysis, the patient died.

Nathwani and colleagues evaluated 21 cirrhotic patients with COVID-19, among which six patients developed hepatic decompensation during their hospitalization. They represented this rate similar to the pre-COVID published studies. They also reported that despite the longer hospital admission among cirrhotic patients with COVID than those without pre-existing liver diseases, the mortality rate was not different.[9] In response, Garrido and colleagues opposed the previous findings and reported that not only the baseline Child-Turcotte-Pugh (CTP) class but also the incidence of cirrhosis decompensation was a strong predictor of COVID-19 mortality.[10] These findings were confirmed in a multi-center study by Volk and colleagues in the United States 4, 10, 114, 11, 12.[11] Lack of knowledge on the fact that whether the hepatic status of the patients decompensated before COVID-19 or occurred following the infection is the main limitation of this study.

The information about the role of COVID-19 in the development of decompensated cirrhosis and the impacts of cirrhosis decompensation on the coronavirus infection outcomes is limited and requires further evaluations. Nevertheless, due to inadequate knowledge in this regard, prevention from infection remains the mainstay among patients with critical conditions such as cirrhosis.

CONCLUSION

Cirrhosis may be decompensated (hepatorenal syndrome or hepatic encephalopathy) during COVID-19 and may lead to fatal outcomes. Despite all the conventional efforts to help the patients survive, prevention from coronavirus infection remains the mainstay for critical patients such as cirrhotic ones. Also, managing the patients with concurrent decompensation of cirrhosis and COVID-19 has remained unknown.

ETHICAL APPROVAL

There is nothing to be declared.

CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

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