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ORIGINAL ARTICLE

Clinical course of COVID-19 in patients with pre-existing decompensated cirrhosis: initial report from China

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Abstract

Background The clinical characteristics and disease course in COVID-19 patients with pre-existing decompensated cirrhosis has not been described so far.

Methods In this case series, we report three patients with confirmed COVID-19 and pre-existing decompensated cirrhosis from three hospitals in Hubei, the epicenter of the outbreak in China.

Result Patient 1 was a 53-year-old man with hepatitis B virus-related cirrhosis, portal hypertension, and ascites. Though receiving intensive support, he died of irreversible multiple organ dysfunction syndrome 48 days after the onset of the illness. Patient 2 was a 75-year-old woman with a history of schistosomiasis-related cirrhosis, portal hypertension, and ascites. Her family members requested that invasive rescue measures not be undertaken, and she died of acute respiratory distress syndrome 40 days after presenting with COVID-19 infection. Patient 3 was an 87-year-old man with alcohol-related cirrhosis, portal hypertension, and esophageal variceal hemorrhage. He was discharged from the hospital 29 days after illness onset.

Conclusion The case series raise the possibility that decompensated cirrhosis may be a risk factor for a poor outcome in patients with COVID-19.

Keywords COVID-19 · Advanced chronic liver disease · Clinical characteristics

Introduction

The rapidly expanding coronavirus disease 2019 (COVID-19) pandemic has had a major impact on the medical care of many individuals throughout the world [1, 2]. Previous studies have reported that patients with severe COVID-19 disease have abnormal aminotransferase levels, which raise the possibility of significant COVID-19-induced liver injury [3, 4]. This clinical challenge is even prominent in patients with COVID-19 and pre-existing decompensated cirrhosis – in particular, considering their immunocompromised status and worse clinical outcomes than compensated cirrhosis [4, 5]. Acute exacerbation of liver function has been described in decompensated cirrhosis clinical guidelines, although the effects of COVID-19 are not well defined [5, 6]. Since the clinical characteristics and disease course in COVID-19 patients with pre-existing decompensated cirrhosis are incompletely defined, in an effort to better understand this clinical scenario, we herein report three cases of patients with laboratory-confirmed COVID-19 and pre-existing decompensated cirrhosis from three hospitals in Hubei, the epicenter of the outbreak in China.

Case series

A case of COVID-19 was defined as a confirmed positive after one of the following results: (1) demonstration of the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with high-throughput sequencing from nasopharyngeal swab specimens, (2) a positive real-time

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reverse-transcriptase polymerase-chain-reaction assay from nasopharyngeal swab specimens, or (3) the demonstration of SARS-CoV-2 specific IgM and IgG in serum [1–3]. Decompensated cirrhosis was defined as clinically or histologically diagnosed cirrhosis with a history of at least one decompensating event, such as ascites, hepatic encephalopathy, and/or variceal hemorrhage.

Clinical characteristics and laboratory results at admission

Patient 1

A 53-year-old man with hepatitis B virus-related cirrhosis (Child–Pugh class C; Model for End-stage Liver Disease [MELD] score, 15) was diagnosed with decompensated cirrhosis after presenting with ascites previously and has been treated with entecavir. He experienced his first symptoms (fever, cough, sputum, dizziness, and myalgia) on 22 January 2020 after coming back from Wuhan (Hubei, China), and was admitted to the hospital on 25 January 2020 with pneumonia diagnosed by chest CT imaging. The diagnosis of COVID-19 was confirmed on 28 January 2020. Laboratory results on admission showed leukocytosis, lymphopenia and thrombocytopenia, hyperbilirubinemia, hypoproteinemia and prolonged prothrombin time (Table 1). Alanine aminotransferase (ALT), and alkaline phosphatase (ALP) levels were in the normal range; and aspartate transaminase (AST) and gamma-glutamyl transferase (GGT) levels were slightly elevated (Table 1). Chest CT showed bilateral ground-glass opacities, typical of pulmonary COVID-19 infection.

Patient 2

A 75-year-old woman with a 5-year history of cirrhosis (Child–Pugh class C; MELD score, 14) due to schistosomiasis and was diagnosed with decompensated cirrhosis approximately 6 months previously after presenting with ascites. She was admitted to the hospital on 12 March 2020 after 30 days of intermittent fever after coming back from Wuhan (Hubei, China); and was confirmed with COVID-19 on 12 March 2020. Laboratory results at admission revealed leukopenia, lymphopenia and thrombocytopenia (Table 1). In addition, ALT and AST levels were both minimally elevated and GGT and ALP levels were elevated (Table 1). Chest CT scan revealed ground-glass opacities in the left lung, typical of pulmonary COVID-19 infection.

Patient 3

An 87-year-old man with a 7-year history of alcohol-related cirrhosis (Child–Pugh class, B; MELD score, 23) was diagnosed with decompensated cirrhosis approximately 7 years previously after presenting with variceal hemorrhage. He reported a close contact with sick persons several days before he developed cough, white frothy sputum, diarrhea and fever. He was confirmed to have COVID-19 and admitted to the intensive care unit (ICU) on 11 February 2020. Laboratory results on admission showed leukocytosis, lymphopenia and thrombocytopenia, hyperbilirubinemia, hypoproteinemia and prolonged prothrombin time (Table 1). ALT level was normal, while AST and GGT levels were slightly elevated. Chest CT revealed bilateral ground-glass opacities and large bilateral pleural effusions.

Treatment, complications and outcomes

Patients 1 and 2 deteriorated clinically on 2 February 2020 (day 12 from the onset of the illness) and 20 March 2020 (day 38 from the onset of the illness), respectively, and were transferred to the ICU (Table 2). All patients were given antiviral therapy (patient 1: lopinavir plus ritonavir orlly [400 mg/100 mg, BID] combined with inhalation of interferon alfa-2b [500 wu, BID]; patient 2: arbidol orally [200 mg, TID]; patient 3: lopinavir plus ritonavir orally [400 mg/100 mg, BID] combined with arbidol orally [200 mg, TID] and with a switch to inhalation of interferon alfa-2b [500 wu, BID] because of an ongoing increase in bilirubin). In addition, all patients received liver protective drugs (glutathione-based therapy), broad spectrum antibiotics, systemic glucocorticoids, intravenous immunoglobulin therapy and intravenous blood products, such as plasma, albumin and cryoprecipitate. During hospitalization, all developed ascites and patients 1 and 2 developed pleural effusions. Therapeutic paracentesis was performed in all patients, as well as therapeutic thoracentesis in patient 1. Patient 1 and 3 developed melena and were treated with a proton pump inhibitor, somatostatin, and red blood cell transfusion to a target hemoglobin level of 8 mg/dL.

Patient 1 required endotracheal intubation and developed acute kidney injury, requiring continuous renal replacement therapy and extracorporeal membrane oxygenation. He developed progressive acute-on-chronic liver failure, and died of irreversible multiple organ dysfunction syndrome on 10 March 2020 (day 48 from the onset of the illness). Patient 2 and her family members requested that invasive rescue measures not be undertaken, and she died of acute respiratory distress syndrome on 22 March 2020 (day 40 from the onset of the illness). Patient 3 was discharged from the hospital on 11 March 2020 (day 29 from the onset of the illness) after the results of two real-time reverse-transcriptase polymerase-chain-reaction tests (nasopharyngeal swabs) taken 24 h apart were negative for SARS-CoV-2.

Table 1 Clinical, laboratory, and radiographic findings at admission

	Patient 1	Patient 2	Patient 3
Clinical characteristics			
Age (years)	53	75	87
Sex	Male	Female	Male
Exposure history	Travel to Wuhan (Hubei, China)	Travel to Wuhan (Hubei, China)	Contacted with COVID-19 infected patients
Onset symptoms			
Fever	Yes	Yes	Yes
Diarrhea	No	No	Yes
Anorexia	No	No	No
Cough	Yes	No	Yes
Sputum	Yes	No	Yes
Shortness of breath	No	No	No
Sore throat	No	No	No
Dizziness	Yes	No	No
Myalgia	Yes	No	No
Headache	No	No	No
Comorbidities	T2DM	HTN	HTN, CKD
Etiology of cirrhosis	Hepatitis B	Schistosomiasis	Alcoholic liver disease
Interval between onset and admission (days)	3	30	9
Child–Pugh class	C	C	B
MELD score	15	14	23
Laboratory characteristics			
White blood cell ($\times 10^9$/L)	11.39	1	15.68
Neutrophils ($\times 10^9$/L)	10.59	0.7	14.4
Lymphocyte ($\times 10^9$/L)	0.36	0.17	0.74
Platelet ($\times 10^9$/L)	77	28	74
ALT (U/L)	26	44	19
AST (U/L)	42	103	41
GGT (U/L)	61	125	51
ALP (U/L)	62	148	NA
Total bilirubin (μmol/L)	40.4	22.2	62.5
Direct bilirubin (μmol/L)	12	15.3	38.1
Albumin (g/L)	21.19	23.4	24.2
Lactate dehydrogenase (U/L)	22	409	326
Blood urea nitrogen (mmol/L)	11.5	9.3	14.35
Serum creatinine (μmol/L)	66.2	98.2	192
APTT (s)	28.2	55.5	48.3
Prothrombin time (s)	17.2	17.7	17.4
International normalized ratio	1.59	1.59	1.44
D-dimer (μg/L)	0.66	18.05	2.1
C-reactive protein (mg/L)	1.95	25.87	86.97
Procalcitonin (ng/mL)	0.6	0.1	2.01
Chest CT evidence of pneumonia			
Typical signs of viral infection	Yes	Yes	Yes

T2DM type 2 diabetes mellitus, *HTN* hypertension, *CKD* chronic kidney disease, *MELD score* Model for end-stage liver disease score, *ALT* alanine aminotransferase, *AST* aspartate transaminase, *GGT* γ-glutamyl transpeptidase, *ALP* alkaline Phosphatase, *APTT* activated partial thromboplastin time

Table 2 Treatment, complications, and outcomes

	Patient 1	Patient 2	Patient 3
Treatment			
ICU admission	Yes	Yes	Yes
Antiviral treatment	Yes	Yes	Yes
Antibiotic treatment	Yes	Yes	Yes
Glucocorticoids	Yes	Yes	Yes
Intravenous immunoglobulin	Yes	Yes	Yes
Oxygen therapy	Yes	Yes	Yes
Noninvasive ventilation	No	Yes	Yes
Invasive mechanical ventilation	Yes	No	No
CRRT	Yes	No	No
ECMO	Yes	No	No
Complications during hospitalization			
Bacterial pneumonia	Yes	No	Yes
Fungal pneumonia	Yes	No	No
Pleural effusion	Yes	Yes	Yes
Ascites	Yes	Yes	Yes
Melaena	Yes	No	Yes
Acute on chronic liver failure	Yes	No	No
Acute kidney injury	Yes	No	No
Shock	Yes	No	Yes
ARDS	Yes	Yes	No
Outcomes	Death	Death	Cure
Length of stay, days	45	10	29

ICU intensive care unit, *CRRT* continuous renal replacement therapy, *ECMO* extracorporeal membrane oxygenation, *ARDS* acute respiratory distress syndrome

Discussion

Given that cirrhosis is one of the leading causes of death and illness globally [7], understanding how SARS-CoV-2 infection influences the clinical course in this setting is important. In this study, we report for the first time the clinical characteristics of three COVID-19 patients with pre-existing decompensated cirrhosis. Two patients with Child–Pugh C class disease died, while the patient with Child–Pugh Class B did not. Furthermore, the patient with the highest MELD score survived, while the ones with lower MELD scores did not. This raises the possibility that clinical decompensating events may be more important in predicting outcome of patients with COVID-19 and pre-existing cirrhosis.

COVID-19 patients with pre-existing decompensated cirrhosis seem to have a higher complication and mortality rate than those with COVID-19 alone [1–3]. In this study, all patients were admitted to the ICU and two of them died during hospitalization. A possible explanation for this might be the poorer immune function in patents with decompensated cirrhosis, since immunodeficiency is more prominent as the disease progresses [8]. Our data were consistent with previous work suggesting that patients with acute respiratory distress syndrome and cirrhosis, regardless of the disease stage, had worse outcomes than patients with acute respiratory distress syndrome without cirrhosis [9].

We were surprised by the outcome of patient 3, who was considerably older than the other patients reported. However, he may have had better liver function than patients 1 and 2, given his lower Child–Pugh class and international normalized ratio. On the other hand, he had chronic kidney disease, which could be another risk factor for an adverse outcome of COVID-19. We recommend that for COVID-19 patients with pre-existing decompensated cirrhosis, while following the management principles of COVID-19, adequate nutritional support and proactive treatment to prevent decompensating events of liver cirrhosis are important.

We recognize that this study is limited by the small sample size. However, the death of 2 patients is notable. We expect that further studies with larger samples (COVID-Cirrhosis-CHESS, NCT04329559) will shed light on the clinical course of COVID-19 in patients with pre-existing cirrhosis.

In conclusion, we report here on the clinical course of COVID-19 patients with pre-existing decompensated cirrhosis. The data suggest that in patients with COVID-19, decompensated cirrhosis might be considered as a risk factor for a poor outcome.

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Compliance with ethical standards

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