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Short communication

# Fulminant hepatic failure: A rare and devastating manifestation of Coronavirus disease 2019 in an 11-year-old boy



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## ABSTRACT

Although several typical manifestation of novel coronavirus disease 2019 (COVID-19) including respiratory symptoms, weakness, fever, and fatigue have been reported, some rare and novel manifestations have also been observed, particularly in children. We report a pediatric case of fulminant hepatic failure associated with COVID-19. Although the patient was treated for acute fulminant hepatic failure in the context of COVID-19, he died following the progression of the disease to stage 4 hepatic failure with encephalopathy and brain death.

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## 1. Introduction

In December 2019, novel coronavirus disease 2019 (COVID-19) caused by a novel coronavirus, SARS-COV-2, emerged in Wuhan, China, and since then has spread around the world. Although at the start of the outbreak it was thought that children were less likely to be infected with COVID-19, over times the number of reports on pediatric patients increased [1–3]. There are three main categories of SARS-CoV-2 infection including asymptomatic, non-severe symptomatic, as well as severe respiratory and systemic presentations [4], and the incidence of symptomatic infection and critical disease in children is known to be lower than that of adults [3,5]. The typical manifestations of COVID-19 that have been reported include respiratory symptoms, weakness, fever, and fatigue; however, rare and novel manifestations are also seen, particularly in children [6]. In this study, we report a pediatric case with fulminant hepatic failure associated with COVID-19.

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## 2. Case presentation

The patient, an 11-year-old boy, presented to the emergency department for fever, icterus, and abdominal pain that had started 7 days earlier. He had no past medical history of chronic liver disease or of using potentially hepatotoxic drugs or of food poisoning. None of his family members had symptoms of COVID-19 or of hepatic diseases. On admission, he was icteric, dyspneic, and with a decreased level of consciousness. He had been fully alert and responsive 1 week before admission, but severe fatigue, confusional state, and decreased level of consciousness had gradually developed. He had spent 1 month in quarantine owing to the COVID-19 outbreak; however, approximately 10 days before admission, he visited a ranch and a few hours later had fever, chills, and malaise. After 1–2 days, icterus appeared primarily in the eyes and subsequently spread to the rest of the body. There were no complaints of coughing, sneezing, symptoms of upper respiratory tract infection, vomiting, and diarrhea. Unfortunately, due to a lack of resources, he had not been visited by any physician. After 7 days of illness, he was admitted to a general hospital with the primary diagnosis of hepatitis that led to the diagnosis of fulminant hepatic failure after initial evaluation. He was then transferred to our hospital, an Iranian pediatric referral hospital, for liver

**Table 1**  
Laboratory results during 5-day hospital stay.

Parameter	Day in hospital									Normal range
	1	2	2	3	3	4	4	5		
White blood cell count ( $\times 10^9$ cells/L)	20.5	17.41	14.59	15.07	–	7.19	–	20.86	4–10	
Neutrophil count ( $\times 10^9$ cells/L)	66	53.4	66	78	–	84	–	86	2–7	
Lymphocyte count ( $\times 10^9$ /L)	23.5	36.1	22.7	13	–	11.7	–	8.6	0.8–4	
Hemoglobin (g/dL)	11.8	10	7.2	10.4	–	7.8	–	11.5	11–16	
Platelet count ( $\times 10^9$ cells/L)	285	276	256	88	–	65	–	81	150–450	
Alanine aminotransferase (U/L)	1038	–	–	–	–	–	–	–	10–40	
Aspartate aminotransferase (U/L)	1260	–	–	–	–	–	–	–	10–40	
Alkaline phosphatase (U/L)	662	–	–	–	–	–	–	–	180–1200	
Albumin (g/dL)	3.7	–	–	3.6	–	–	–	–	3.5–5.2	
Gamma-glutamyl transferase (IU/L)	30	–	–	–	–	–	–	–	4–50	
Bilirubin total (mg/dL)	19.2	–	–	–	–	–	–	–	0.1–1.2	
Bilirubin direct (mg/dL)	16	–	–	–	–	–	–	–	0.1–0.4	
C-reactive protein (mg/L)	29	–	–	–	–	–	–	–	<6	
Ammonia ( $\mu$ mol/L)	186	230	209	252	235	672	490	–	16–60	
Lactate (mg/dL)	56	39	51	46	70	87	105	–	2–20	
Creatine phosphokinase (U/L)	–	–	–	902	–	–	–	–	24–195	
D-dimers (pg/mL)	–	–	–	<0.2	–	–	–	–	<0.5	
Troponin (ng/mL)	–	–	–	1	–	–	–	–	0–0.3	
Lactate dehydrogenase (U/L)	–	1670	–	–	–	–	–	–	5–746	
Ferritin (ng/mL)	–	2940	–	–	–	–	–	–	30–220	
Fibrinogen (mg/dL)	–	160	–	–	–	–	–	–	150–350	
Prothrombin time (seconds)	29.4	–	–	20.9	–	–	24.1	38.1	11–13.5	
International normalized ratio (INR)	3.8	–	–	2.24	–	–	2.78	5.7		

transplantation. The laboratory findings are shown in Table 1. At the original hospital the stage of disease progression was 2 and at our center it progressed to stage 3 or 4. Upon admission to our emergency room, the score on the Glasgow Coma Scale (GCS) was 7–8 and he had active gastrointestinal and nasal bleeding. Thus, immediately after arrival, our decision was to intubate the patient and immediately transfer him to the intensive care unit (ICU) where he underwent mechanical ventilation.

Computerized tomography (CT) showed patchy areas of consolidation in both lungs. On chest X-rays (CXR), there was mild bilateral pleural effusion with bilateral paracardiac ground glass opacity and alveolar opacity in the upper zone of left lung (Figs. 1 and 2). A pharyngeal swab sample was collected for COVID-19 real-time reverse transcriptase polymerase chain reaction (RT-PCR) as part of a pretransplantation protocol. Unfortunately, the result of the SARS-CoV-2 RT-PCR was positive, which was very surprising because the SARS-CoV-2 RT-PCR result at the previous hospital was negative.

In addition, to rule out other probable causes of fulminant hepatitis, tests for other viruses including hepatitis A, hepatitis B, herpes virus, Epstein–Barr virus, cytomegalovirus were performed, with all results being negative. Moreover, to rule out metabolic disease, additional tests were run, including amino acid chromatography, organic acid chromatography, and measurement of succinylacetone in urine, all of which yielded negative results.

Treatment for COVID-19 was initiated with hydroxychloroquine and Kaletra, and we also prescribed vancomycin and ceftazidime for other probable bacterial infections. In the ICU, the patient's GCS was 4–5 and decreased further on the following day. Owing to unstable hemodynamics, we added norepinephrine and epinephrine but the patient's condition progressed to hepatorenal syndrome and he underwent dialysis. Unfortunately, after 2–3 days he died in spite of all the medical and supportive measures.

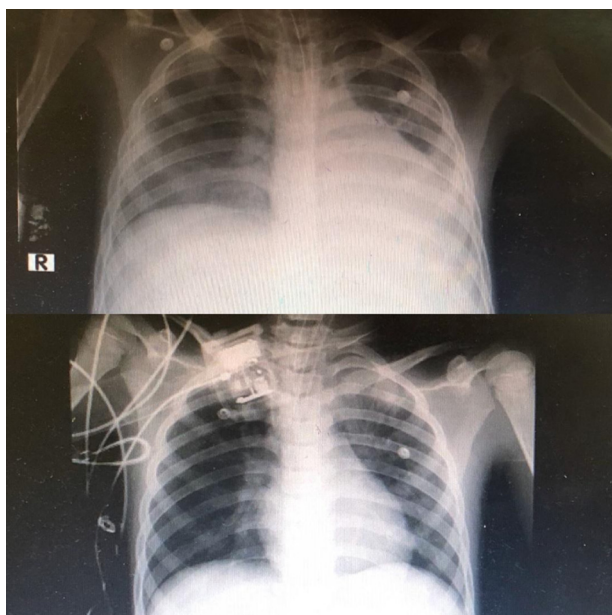
### 3. Discussion

In this study, we report a novel pediatric case of fulminant hepatic failure associated with COVID-19.

Although there have been a significantly smaller number of reported cases of COVID-19 in the pediatric population compared with the adults, the number of infected children has seen a moderate increase [2,7]. Children with COVID-19 infection may be asymptomatic or have fever, dry cough, and fatigue with a few upper respiratory symptoms including nasal congestion and runny nose; other patients might show gastrointestinal symptoms including abdominal discomfort, nausea, vomiting, abdominal pain, and diarrhea [2,8,9]. In addition to the typical manifestation, rare and novel symptoms have also been seen, particularly in children such as our patient. Fulminant hepatic failure is considered the fourth main cause of liver transplantation in children, preceded by extrahepatic cholestatic liver diseases, intrahepatic cholestasis, and metabolic diseases followed by primary liver tumor and cystic fibrosis [10]. Acute liver failure is a life-threatening condition with sudden onset of liver injury, decreased liver function, hepatic encephalopathy, and coagulopathy in patients without preexisting liver disease. However, etiologic factors might change depending on geographic variation, age, and socioeconomic status. Viral agents and drugs mostly cause acute liver failure, but sometimes no etiologic factor can be found. However, viral infections are the most common reasons [7]. Because of the unusual manifestation of COVID-19 in children, it should be ruled out as the cause of acute liver failure. The incidence of hepatic abnormalities significantly increases after infection with SARS-CoV-2 and during the course of the disease [11]. Elevated liver biochemistry profiles may reflect a direct virus-induced cytopathic effect and/or immune damage from the provoked inflammatory response [12]. In addition, SARS-CoV-2 infection might induce rhabdomyolysis with an initial increase in creatinine kinase level [13]. Increasing evidence has demonstrated the frequent incidence of liver injury in COVID-19, especially in patients with multiple organ injury. Liver injury itself often manifests as transient elevation in serum aminotransferases. However, acute liver failure and intrahepatic cholestasis have been reported [14]. Liver damage in patients with coronavirus infections might be directly caused by the viral infection of liver cells. Patients with severe COVID-19 seem to have higher rates of liver dysfunction [15]. Hepatic dysfunction in severe COVID-19 is accompanied by a greater activation of the coagulative and



**Fig. 1.** Computed tomography (CT) scan showing patchy areas of consolidation in both lungs. Mediastinal lymph node is mildly prominent.



**Fig. 2.** Chest X-ray (CXR) showing bilateral paracardiac ground glass opacity with alveolar opacity in upper zone of left lung and right paracardiac region with mild bilateral pleural effusion.

fibrinolytic pathways, relatively lower platelet counts, rising neutrophil counts and neutrophil-to-lymphocyte ratios, and high ferritin levels [16].

In fulminant hepatic failure, hepatic transplantation is the only therapy that has been proven to improve survival in the majority of patients, despite specific therapeutic options for distinct orthotopic etiologies. The result is determined by complications such as severe coagulopathy, infection, renal dysfunction, or increased intracranial pressure. The decision regarding transplantation depends on the probability of spontaneous hepatic recovery, which can be determined by multiple factors. The most important variables for predicting the need for transplantation during fulminant hepatic failure include the degree of encephalopathy, the age of the patient, and the underlying cause of hepatic failure [17]. Owing to the acute fulminant hepatic failure in our patient, the only treatment option was liver transplantation; however, because of the progressive course of the disease and its rapid progression to stage 4 with encephalopathy and brain death, he died.

#### 4. Conclusion

In conclusion, in patients with fulminant hepatic failure, especially in cases with symptoms including fever, respiratory distress, and diarrhea, we should rule out COVID-19 infection as the underlying cause. The need for emergency liver transplantation



in fulminant hepatic failure due to COVID-19 and the indications for transplantation should be further evaluated.

#### Disclosure of interest

The authors declare that they have no competing interest.

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