

Acute Severe Icteric Hepatitis Caused by the Novel Corona virus: A Case Report

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Abstract

- Background** Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) cases are being frequently reported nowadays and the objective of this clinical case report is to highlight its unique presentation as acute icteric sever hepatitis.
- Case report** A 28-year-old female patient presented with 3 days history of fever, abdominal pain, nausea, vomiting and jaundice. Lab investigations revealed positive COVID-19 reverse transcription-polymerase chain reaction test along with picture suggestive of acute severe hepatitis (Aspartate aminotransferase; 2772 U/L (N: <32), Alanine transaminase; 2522 U/L (N: <33), Alkaline phosphatase; 172 U/L (N: 35-104), direct bilirubin 4.2 mg/dl (N: 0-0.3)). The patient was admitted, monitored and started on supportive therapy for 5 days and was discharged well for outpatient follow-up.
- Conclusion** Requesting liver function test for COVID-19 patients who presents with gastrointestinal symptoms is a crucial decision that can guide us with the management of the case since many drugs used in the treatment of the new SARS-CoV-2 infection are hepatotoxic and should therefore be used with caution.
- Keywords** Hepatitis, COVID-19, SARS-CoV-2, COVID-19 hepatitis, icteric hepatitis
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List of abbreviations: aPTT = Activated partial thromboplastin time, ALT = Alanine transaminase, ALP = Alkaline phosphatase, AST = Aspartate aminotransferase, CRP = C-reactive protein, CMV = Cytomegalovirus, ESR = Erythrocyte sedimentation rate, INR = International normalized ratio, PCR = Polymerase chain reaction, PT = Prothrombin time, RT-PCR = Reverse transcription-polymerase chain reaction, SARS-CoV-2 = Severe acute respiratory syndrome coronavirus 2

Introduction

Coronaviruses are large, positive single-stranded RNA viruses with envelope which infect both humans and animals. They were named coronaviruses (Latin: corona = crown) because of their shape as they consist of spherical virions with a core shell and outer projections resembling a solar corona. Four sub-families of coronaviruses exist: alpha-, beta-,

gamma- and delta-coronaviruses. Alpha- and beta-coronaviruses was found to be originated from mammals, particularly from bats while gamma- and delta-viruses originate from birds and pigs. The genome size ranges from 26 kb to 32 kb. Among the different subtypes of coronaviruses that can infect humans, the beta-coronaviruses may cause fatal disease complications, whereas alpha-coronaviruses maybe asymptomatic or cause mild infection. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) belongs to beta-coronaviruses specifically, the B lineage, and is closely related to the SARS-CoV virus ⁽¹⁾. SARS-CoV-2 is 96%

similar at the whole-genome level to the coronavirus found in a bat ⁽²⁾.

SARS-CoV-2 was found to be successfully transmitted from animals to humans in Wuhan, China, in a seafood market. The median incubation period was found to be 3 days (Range was from 0 to 24) ⁽¹⁾. Patients' clinical manifestations included fever, non-productive cough, dyspnea, myalgia, fatigue, normal or decreased leukocyte counts, and radiographic evidence of pneumonia. Organ dysfunction (eg, shock, acute respiratory distress syndrome (ARDS), acute cardiac injury, and acute kidney injury) and death can occur in severe cases ⁽³⁾.

Around 50% of COVID-19 patients presenting to the hospital are reporting digestive symptoms. Rarely, digestive symptoms may occur without any respiratory symptoms. Laboratory tests have shown that patients with digestive symptoms have higher liver tests and prolonged coagulation profile as compared to those without digestive symptoms ⁽⁴⁾. On the initial presentation of COVID-19, the prevalence of abnormal liver function tests is still undetermined. Current approaches to COVID-19 therapies generally fall into two categories: antivirals — which prevent the virus from multiplying — and immune modulators — which help the immune system to fight the virus or stop it from overreacting dangerously. Some potential therapies act in a different way or via multiple mechanisms. In the EU, remdesivir is now licensed for the treatment of COVID-19 in adults and adolescents with pneumonia requiring supplemental oxygen ⁽⁵⁾. This study reports a case of COVID-19 infection presenting solely as acute, icteric hepatitis.

Case presentation

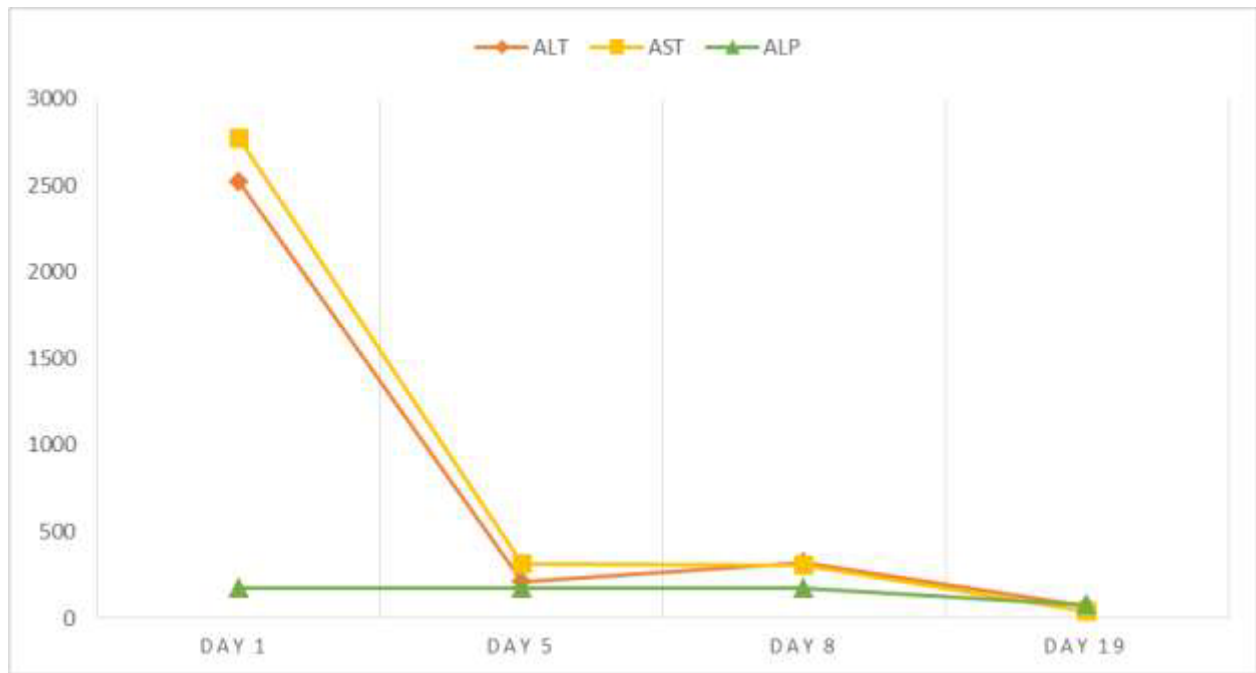
A 28-year-old healthcare worker female with negative past medical history presented to our emergency department complaining of nausea, vomiting, epigastric pain, dark urine, pale stool, and jaundice for 3 days. Further questioning

revealed that these symptoms were preceded by fever, which lasted for 3 days and was relieved by Paracetamol with no respiratory symptoms.

At the time of presentation, her temperature was 36.8, there was epigastric tenderness and jaundice. There was no hepatomegaly or splenomegaly. Her chest examination and x-ray were normal.

The laboratory results showed the following: COVID-19 polymerase chain reaction (PCR) test was positive, white blood cell count $3.22 \times 10^3/\mu\text{L}$ (N: 4.0-10.0), lymphocyte count $1.22 \times 10^3/\mu\text{L}$ (N: 1.0-3.0), aspartate aminotransferase (AST) 2772 U/L (N: <32), alanine transaminase (ALT) 2522 U/L (N: <33), alkaline phosphatase (ALP) 172 U/L (N: 35-104), albumin 4.2 g/dL (N: 3.5-5.2), total bilirubin 4.3 mg/dL (N: up to 1.2), direct bilirubin 4.2 mg/dL (N: 0-0.3), indirect bilirubin 0.1 mg/dL (N: 0-0.8), D-dimer 1.4 mg/L (N: <0.5), international normalized ratio (INR) 1.16 (N: 1-1.2), prothrombin time (PT) 14.5 s (N: 11-15), activated partial thromboplastin time (aPTT) 33.2 s (N: 25-37), erythrocyte sedimentation rate (ESR) 22 mm/1st hr (N: 0-20), C-reactive protein (CRP) 9.8 mg/L (N: <5.00), urea 23 mg/dL (N: 17-49), creatinine 0.5 mg/dL (N: 0.5-0.9). Screening for virology including: hepatitis viruses (A, B, C and E), Herpes virus, Cytomegalovirus (CMV), Human immunodeficiency virus (HIV) and Epstein-barr virus (EBV) were negative. Tests for autoimmune diseases and Wilson's disease came back negative as well. Abdominal ultrasound with Doppler study showed non-specific findings suggestive of acute hepatitis with normal vasculature.

Patient was admitted for 5 days and was given intravenous fluid 500 ml *4, Odanstron amp. 8 mg *3, Metoclopramide amp. 10 mg *3, Esomeprazole vial 40 mg *1. On the fourth day of admission, oral feeding started as the symptoms and lab results showed improvement (figure 1). On the following day the patient was discharged to out-patient clinic for follow up.



ALT = Alanine transaminase, AST = Aspartate aminotransferase, ALP = Alkaline phosphatase

Figure 1. Liver function test during the disease course

Discussion

In a study done in Hubei, China, 204 patients with COVID-19 were taken where most of them presented with fever or respiratory symptoms. About 18.6% presented with a gastrointestinal symptom like abdominal pain, vomiting and diarrhea. In six cases, there were gastrointestinal symptoms without any respiratory symptoms⁽⁴⁾. In our report, the patient presented with gastrointestinal symptoms without the involvement of other systems.

Investigations showed that the cause of gastrointestinal symptoms in our case were due to acute severe hepatitis caused by the SARS-CoV-2. This was supported by the documented positive COVID-19 RT-PCR test and the exclusion of other causes of acute severe hepatitis.

In a case report, a 59-year-old woman with a medical history of well-controlled human immunodeficiency virus (CD4 499 and viral load undetectable), hypertension, hyperlipidemia, Graves' disease, and a left facial paralysis secondary to previous actinomyces infection, presented with acute, non-icteric hepatitis. Her laboratory results were as follow: serum bilirubin 0.6 mg/dL (N: up to 1.2), AST 1230 IU/L

(N: <50), ALT 697 IU/L (N: <50), alkaline phosphatase 141 IU/L (N: <125)⁽⁶⁾, whereas our patient had no significant past medical history and laboratory results revealed higher bilirubin, ALT, AST and ALP.

In the previous study, the patient received hydroxychloroquine 200 mg twice a day for 5 days. She got well and was discharged home after 8 days from hospital admission⁽⁶⁾, while our patient received supportive treatment only and was discharged well after 5 days of admission.

The proposed mechanisms of liver injury caused by SARS-CoV-2 is thought to be either due to the angiotensin-converting enzyme 2 (ACE2) mediated hepatic injury, the destruction caused by cytokine storm or drug induced liver injury. Since our patient did not receive any medication except for low dose of Paracetamol tablet (total of 1.5 g/day for 3 days) and there was no evidence of cytokine storm, the main culprit of liver injury in our patient is the cytopathic effect of COVID-19 virus mediated by ACE2 receptors found in the liver and bile ducts.

In conclusion, it is important to recognize acute severe icteric hepatitis as a presentation of SARS-CoV-2 infection even in the absence of

respiratory symptoms and liver function test should be done especially in patients presenting with gastrointestinal symptoms. Since many of the drugs that are used in the treatment course of COVID-19 can exacerbate liver injury, it is of great importance to exclude hepatitis due to SARS-CoV-2 before commencing them.

Author contribution

Both authors contributed to the data collection, patient's follow-up and to the writing of the manuscript.

Conflict of interest

There are no conflicts of interest.

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