Massive ascites in a patient with COVID-19 without cirrhosis

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Abstract

Patients with coronavirus disease 2019 (COVID-19) typically present with respiratory distress but there have been reports of gastrointestinal involvement and associated complications. We report the case of a patient with no history of liver disease who presented with typical dyspnea associated with COVID-19 and massive ascites that caused abdominal compartment syndrome. We discuss the hospital course, possible causes, and implications of this presentation.

Keywords: ascites, COVID-19, liver injury, portal hypertension, Sturge–Weber syndrome, sinusoidal obstruction syndrome, hepatic venous outflow tract obstruction
Introduction

Patients with coronavirus disease 2019 (COVID-19) typically present with fever, cough, dyspnea, and myalgias. Many of these cases progress to severe hypoxic respiratory failure, leading to intubation. However, effects on the gastrointestinal system are increasingly recognized. The most commonly reported gastrointestinal symptoms are nausea, vomiting, and diarrhea, but there are also reports of liver injury and portal vein thrombosis caused by a hypercoagulable state. We present the case of a 25-year-old female with no medical history of liver disease who presented with COVID-19 and was found to have massive ascites causing abdominal compartment syndrome.

Case report

A 25-year-old female with a medical history of Sturge–Weber syndrome with associated seizures and nonverbal status presented with dyspnea and 4–5 days of abdominal discomfort and bilateral lower extremity edema. Her mother also noticed decreased oral intake, decreased urine output, and a worsening ability to ambulate. Medications that the patient was taking included stable doses of sodium valproate, levetiracetam, and oxcarbazepine.

On admission, the patient’s physical exam was significant for a firm distended abdomen and +1 pitting edema in her lower extremities; however, her lungs were clear. Rapid and PCR testing revealed she was positive for COVID-19. Laboratory tests revealed elevated levels of aspartate aminotransferase (192 IU/L), alanine aminotransferase (44 IU/L), and gamma-glutamyl transferase (257 IU/L), with a bilirubin level of 0.1 mg/dL. A computed tomography scan of the abdomen revealed abdominal compartment syndrome with tense ascites, a compressed liver with
compressed hepatic veins, intrahepatic inferior vena cava, engorged mesenteric veins, and compressed external iliac vessels (Figure 1).

**Figure 1.** Computed tomography scan of the patient's abdomen showing ascites, a compressed liver, compressed hepatic veins, and an intrahepatic inferior vena cava.

A paracentesis was performed and 2.4 L of clear yellow fluid was removed. Peritoneal studies revealed a transudative fluid consistent with ascites secondary to portal hypertension, with only 1.7 g/dL protein, serum-ascites albumin gradient of >1.1 g/dL, and 2% neutrophils. Cultures were negative for bacterial peritonitis, and cytology results were negative for malignancy. Ultrasonography of the abdomen revealed patent hepatic veins/artery, portal vein, and inferior vena cava.
Three days later, she developed acute hypoxic respiratory failure and was intubated for a total of 9 days and treated with remdesivir for 5 days and dexamethasone for 20 days. Initially, the ascites improved, but later recurred requiring Jackson–Pratt drain insertion for persistent drainage (total of 8 L over 10 days), in addition to bilateral pleural effusions requiring chest tube insertion. The patient was started on diuretics with albumin supplementation.

A liver biopsy (Figure 2) was performed, which demonstrated fragmented, focally nodular (regenerative) liver tissue with marked acute sinusoidal congestion, perivenular hepatocytic atrophy, and focal perivenular hepatocytic loss. A few small foci of lobulitis were present with no steatosis. No significant portal inflammation was present, mild focal bile duct damage was noted, and there was no ductopenia. Portal pressures revealed a hepatic venous pressure gradient (HVPG) of 14 mm Hg, confirming clinically significant portal hypertension. PCR tests for COVID-19 were eventually negative, and the patient was positive for IgG antibodies against SARS-CoV-2 approximately 25 days after admission.

**Figure 2.** Histopathologic images (hematoxylin and eosin stain) of patient’s acute liver injury from liver biopsy showing focal areas of sinusoidal congestion (×10 magnification, left), perivenular
hepatic atrophy and focal perivenular hepatic loss (×10 magnification, middle), and a few small foci of lobulitis (×5 magnification, right).

**Discussion**

The case was discussed on #GITwitter and posted on @GIJournal.

@AnandVKulkarni2: Tough case. Looks like acute HVOTO (hepatic venous outflow tract obstruction) or SOS (sinusoidal obstruction syndrome) on history. In the background of Sturge–Weber, it may be vascular involvement of liver, which fits the biopsy. Not sure. Let us know the diagnosis please.

@RohitMehtaniDM: I also feel it could be SOS.

@DrArunKValsan: Looks like sinusoidal obstruction syndrome. COVID can be the precipitant for veno-occlusion. SWS (Sturge–Weber syndrome) could have likely association with NCPH (non-cirrhotic portal hypertension), but here it looks more of a bystander. Any vascular thrombosis? I would give UDCA (ursodeoxycholic acid), diuretic, and anticoagulation. Interesting case.

@theliverdr: The Sturge–Weber syndrome could be the red herring here. Liver involvement in SWS is very rare but could be associated with non-cirrhotic portal hypertension even though it is not yet documented. The acute presentation does not fit with classical NCPH such as focal nodular hyperplasia. The patient has critical COVID-19 and is young. Further details are
missing. For example, a detailed drug history—both prescription as well as alternative medicine use. Drugs that are used for management of clinical complications associated with SWS—such as antiepileptics—any new additions, specifically in the preceding 90 days, should be asked for. There is also emerging evidence of COVID-induced endotheliitis (systemic and organ specific) and direct veno-occlusion-related events reported in literature. COVID-induced pulmonary veno-occlusive disease is well documented. The liver biopsy changes could be a critical COVID variant-induced endotheliitis-related event in the background of SWS, which could predispose to such vascular outcomes. However, I would still rule out other infectious disease and drug-related causes that are associated with sinusoidal obstruction syndrome. I hope the patient will improve and get through this critical phase.

COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, which enters host cells via angiotensin-converting enzyme 2 receptors.⁴ Although these receptors are expressed to some degree in nearly all tissues, they are highly expressed by type 2 alveolar cells of the lungs and cholangiocytes.⁵ Because the virus triggers a cytokine-mediated immune response and inflammation, the liver is a potential pathophysiologic target for the virus.⁴,⁶ There have been several reports of COVID-19 complicated by coagulopathy, resulting in thrombosis of the portal veins.⁶-¹³ Thrombosis from SARS-CoV-2 infection can be triggered by the inflammatory cytokine storm as well as endothelial cell dysfunction and platelet activation, resulting in the generation of thrombin and fibrin but with limited fibrinolysis.¹⁴ Additionally, excessive complement activation favors tissue damage and intravascular thrombosis.¹⁴ The hypercoagulative state generated by multifaceted inflammatory responses to
the virus has been called thromboinflammation, and the hallmark of this is microvascular thrombosis-associated inflammation.\textsuperscript{14}

Because of the potential for thrombosis, we performed abdominal ultrasonography with doppler, which revealed patent vessels. Given the patient’s SARS-CoV-2 positivity and high predisposition for hypercoagulability, anticoagulation was considered. However, it was not initiated until later because early in the hospital course, the nasogastric tube had coffee ground output and there was bleeding in the rectum. The mild sinusoidal dilatation and mild lobular lymphocytic infiltration observed in our case is similar to that observed by Tian et al.\textsuperscript{15} in postmortem liver biopsy samples from four patients with COVID-19. There is also one report of a rare association between Sturge–Weber syndrome and cavernomatous transformation of the portal vein, resulting in portal hypertension that presented with variceal bleeding.\textsuperscript{10}

The prominent finding in this case was the massive ascites. Initially, the ascites improved after remdesivir and dexamethasone were administered for the management of COVID-19. This led us to strongly suspect that the massive ascites was attributable to COVID-19. We sent pleural fluid from our patient for SARS-CoV-2 testing (the peritoneal sample was insufficient). RNA can be detected in ascitic fluid, as first reported by Culver et al.\textsuperscript{16} for a patient with known decompensated liver cirrhosis who presented with severe upper gastrointestinal bleeding. However, the fluid from our patient was negative for the viral RNA. The ascites reoccurred later in the hospital course, and so a liver biopsy was performed. The pathology report indicated that the cause of ascites was extrahepatic, from impairment of either hepatic or portal venous blood flow. Furthermore, the HVPG in our patient was 14 mmHg, consistent with portal hypertension.
Therefore, the patient was treated with diuretics for noncirrhotic portal hypertension and ascites, and an outpatient esophagogastroduodenoscopy was planned to evaluate for varices.

**Conclusion**

We emphasize that clinicians should remain aware of noncirrhotic portal hypertension and ascites as potential sequelae of COVID-19 infection.
References


