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CASE REPORT | LIVER

Fulminant Presentation of Budd-Chiari Syndrome Secondary to COVID-19 Infection

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ABSTRACT

Budd-Chiari syndrome (BCS) is a rare condition characterized by the obstruction of hepatic venous outflow. It is estimated to affect 1 in 100,000 people worldwide. In cases of new BCS, inherited and acquired hypercoagulability states must be evaluated. Coronavirus disease 2019 (COVID-19) can induce a hypercoagulable state because of its extensive inflammatory response, and while it has been reported to cause portal vein thrombosis, it rarely causes BCS. This article presents a case of a 22-year-old man who developed fulminant symptoms and was subsequently diagnosed with BCS and portal vein thrombosis secondary to COVID-19 infection, after ruling out other inherited and acquired causes of BCS. In addition, a literature review is provided to understand the presentation and management of such patients. Although most patients improve with medical management, this article emphasizes the consideration of liver transplant for patients who do not improve.

KEYWORDS: COVID 19; Budd-Chiari Syndrome; portal vein thrombosis; anticoagulation

INTRODUCTION

Budd-Chiari syndrome (BCS) is a rare condition characterized by the blockage of hepatic veins that results in liver congestion. The obstruction can occur because of thrombosis or fibrous effects anywhere along the venous course, ranging from small hepatic vessels to the junction of the inferior vena cava into the right atrium.[1] Coronavirus disease 2019 (COVID-19) infection can trigger a cytokine storm, leading to coagulation abnormalities, such as elevated levels of procoagulant factors like fibrinogen and D-dimer.[2] This article presents a rare case of BCS caused by the hypercoagulable state of COVID-19 and provides a review of the existing literature on all cases of COVID-19-induced BCS.

CASE REPORT

A 22-year-old man with no medical history presented with worsening abdominal distension and tenderness accompanied by flu-like symptoms of fever, chills, and cough for 1 week. He denied alcohol use and illicit drug use including intravenous drugs, and he had never been sexually active. On presentation, he was hemodynamically stable; however, he looked ill. Physical examination revealed scleral icterus and an abdomen that was diffusely tender with a positive fluid wave sign. Laboratory workup revealed white blood cell count 18.2 $\times$ 10^3/mL, platelets 174,000/mL, total bilirubin 6.5 mg/dL, alkaline phosphatase 219 U/L, aspartate aminotransferase 450 U/L, alanine transaminase 488 U/L, D-dimer 774 mg/L, and international normalized ratio 1.62. Polymerase chain reaction testing was positive for COVID-19. Abdominal computed tomography (CT) showed large amounts of abdominal ascites with varices identified in the left upper quadrant and at the gastroesophageal junction (Figure 1). Right upper quadrant ultrasound showed a hyperechoic liver and thrombosis in the left portal vein. Abdominal magnetic resonance imaging (MRI) revealed left lobe hepatomegaly without nodularity and significant thrombosis of the intrahepatic portion of inferior vena cava, hepatic veins, and left portal vein (Figure 2).

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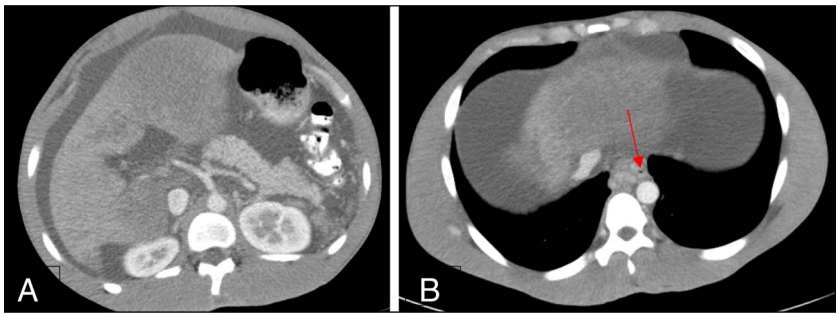

Figure 1. Abdominal computed tomography. (A) Diffuse anasarca and ascites. Also seen is small bowel wall thickening with decreased lumen size—indicative of small bowel congestion related to portal vein and hepatic vein thrombosis. (B) Esophageal varices (red arrow).

The patient was admitted for a fulminant presentation of BCS and portal vein thrombosis (PVT) superimposed with COVID-19 infection without requiring supplemental oxygen. Diagnostic and therapeutic paracentesis revealed a transudative outcome, and treatment with enoxaparin sodium was initiated. During hospitalization, the patient developed hepatic encephalopathy, which was managed with lactulose. Ultimately, the patient was transitioned to warfarin therapy and discharged.

On an outpatient basis, all causes of liver dysfunction were negative, including viral and autoimmune hepatitis panel, antimitochondrial antibody, ceruloplasmin, alpha-1 antitrypsin, and antinuclear antibody. Hypercoagulable workup was unremarkable, which included protein S, protein C, anticardiolipin antibody, antithrombin 3, prothrombin mutation, and factor V Leiden mutation. The patient was ultimately diagnosed with BCS and PVT secondary to COVID-19 infection.

Over the next year, the patient had repeated admissions for decompensated liver cirrhosis. Follow-up MRI of the abdomen showed persistent BCS with new liver nodules, which were subjected to biopsy (Figure 3). The biopsy revealed changes in the liver parenchyma architecture consistent with chronic BCS-induced cirrhosis (Figure 4). The patient also experienced esophageal variceal bleeding, which necessitated discontinuation of anticoagulation therapy. Currently, the patient is being evaluated for liver transplantation.

DISCUSSION

Coagulopathy, a serious complication of COVID-19, has been reported in 49% of critically ill patients and is believed to stem from a heightened inflammatory response and direct activation of the coagulation cascade.[2] Although PVT in the context of COVID-19 has been infrequently documented in the literature, it rarely leads to BCS.[3] We describe a case of both PVT and BCS during the acute phase of COVID-19 infection leading to chronic BCS and cirrhosis.

BCS is associated with a classic triad of symptoms including abdominal pain, ascites, and hepatomegaly, which are present in 60%–80% of patients.[1] Our patient exhibited the fulminant type of BCS, as evidenced by acute abdominal pain, ascites, elevated hepatic enzymes, and hyperbilirubinemia.[4] A similar presentation has been reported in 3 of 4 cases of BCS from COVID-19 (Table 1).[5–7] Interestingly, a prothrombotic state, which can last for months after the acute phase of infection, can be found even when D-dimers are high without severe symptoms. This also suggests a prothrombotic state, which can last for months after the acute phase of the infection.[2]

A Doppler ultrasound of the liver is typically used to diagnose BCS, and it has a sensitivity and specificity of 85% or higher.[8] Although the initial ultrasound in our patient only showed evidence of PVT, an abdominal CT scan was performed to assess vessel patency. However, hepatic vein thrombosis can be falsely positive or indeterminable on CT scans up to 50% of the

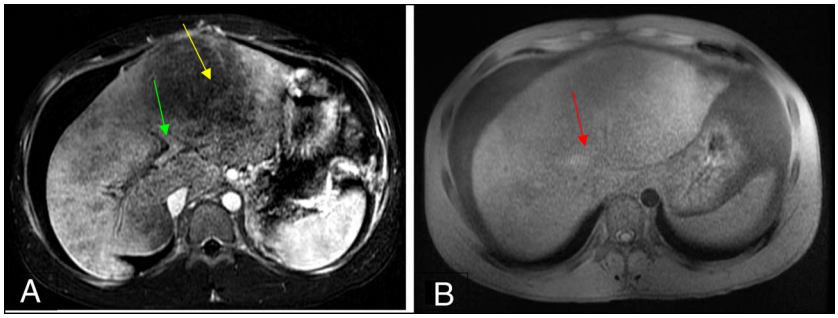

Figure 2. Abdominal magnetic resonance imaging. (A) Nonvisualization of the branches of the left portal vein, indicating thrombosis (green arrow). The main portal vein looks enlarged, most likely acute thrombosis. Also seen is left lobar enlargement—likely from acute congestion (yellow arrow). (B) Hyperintense signal (red arrow) showing hepatic vein thrombosis, without visualization of distal flow.

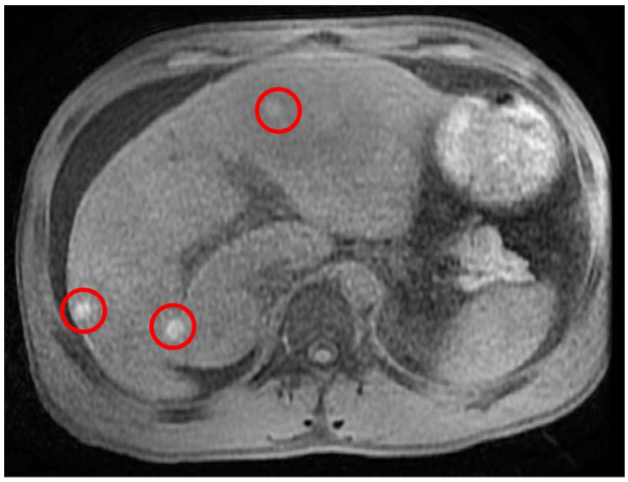

Figure 3. Abdominal magnetic resonance imaging 1 year later. Three new enhancing nodules (red circles) with persistent left lobar congestion.

time.[9] PVT is commonly seen in patients with cirrhosis, malignancy, and hypercoagulable disorders.[10] To explore these potential causes, our patient underwent an MRI, which revealed hepatic vein thrombosis. The patient was also extensively evaluated for hypercoagulable disorders, all of which were negative. Similarly, in 3 other reported cases, thrombophilia workup was conducted before considering the hypercoagulable state of COVID-19 infection as the cause of BCS.[5–7]

Liver biopsy in BCS reveals congestion along with centrilobular fibrosis and hepatocyte loss.[11] However, there is a disconnect between the clinical presentation and histological features, with approximately half of patients with acute BCS showing evidence of chronic damage and fibrosis.[1] Therefore, biopsy alone is not a reliable indicator of BCS duration. Nevertheless, in our patient, the biopsy results, along with identifying the initial event and 1-year follow-up, strongly suggest the development of cirrhosis.

The medical management of BCS involves addressing the underlying cause, controlling portal hypertension, and administering anticoagulation.[12] In 3 reported cases, anticoagulation therapy was successful in resolving symptoms, with one case showing improvement within 1 month of diagnosis.[5,6,13] However, our patient experienced a complicated course, with multiple complications arising from increased portosystemic pressure despite being on anticoagulation. Owing to his high risk of hepatic encephalopathy, transjugular intrahepatic portosystemic shunt was not pursued. Liver transplant is the next management option, required in 10%–20% of patients.[12]

BCS is a rare but life-threatening complication of COVID-19 infection, presenting with fulminant symptoms and demanding immediate diagnosis and treatment. Although the classic triad of symptoms may occur, the histological features may not align with the clinical presentation. Anticoagulation therapy has demonstrated effectiveness in symptom resolution, but in certain circumstances, liver transplantation may be required.

DISCLOSURES

Author contributions: H. Sanekommu: lead writer and coordinated the efforts. S. Taj: obtained images and contributed to

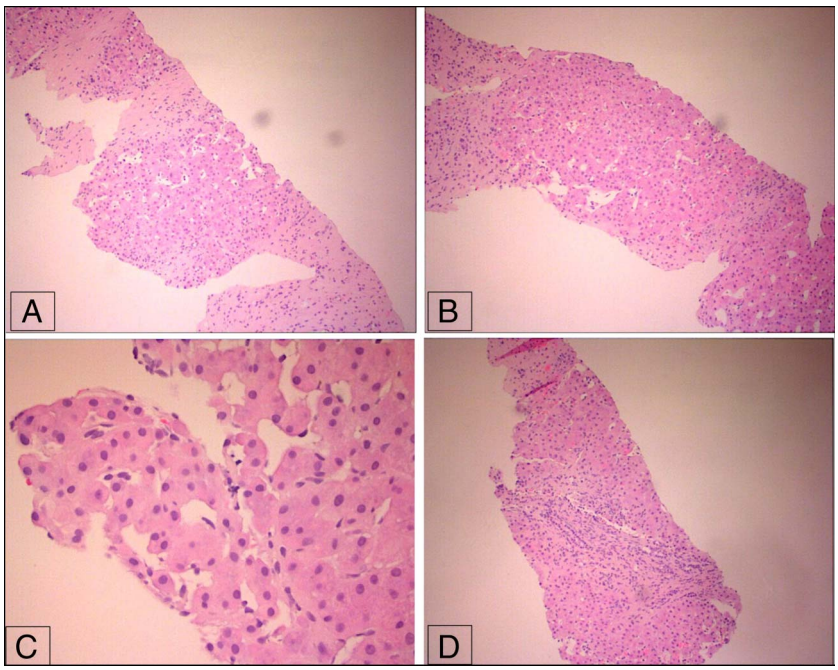

Figure 4. Liver biopsy showing evidence of stage 4 Budd-Chiari syndrome-induced cirrhosis. (A) Liver parenchyma architecture is distorted and showing broad bridging fibrous septa surrounding nodules. (B and C) Periseptal sinusoids are dilated. (B) Mild ductular reaction and cholestatic hepatocytes.

Table 1. Characteristics and summarization of the 4 known cases of COVID-19-induced BCS

Paper	Age	Sex	Medical history	Clinical type of BCS	Clinical presentation	Time of onset	Workup	Management of thrombosis	Follow-up
Hassan et al[5]	48	Female	HTN	Fulminant	Abdominal pain/ distension, ascites, and hepatomegaly	3 d	Negative thrombophilia screen test	LMWH initially, with transition to oral warfarin	1 mo: Asymptomatic
Lecca Espinoza et al[6]	50	Female	Asthma	Fulminant	Right upper quadrant abdominal pain, nausea, vomiting, jaundice, and fever	Abdominal pain—6 d Fever/ jaundice—2 d	Thrombophilia workup—low levels of anticardiolipin IgM	Oral rivaroxaban	3 mo: MRI showed resolution of thrombosis and undetectable anticardiolipin IgM levels
Rozenshteyn et al[13]	50	Male	Alcoholic cirrhosis	Unsure—time line not given	Altered mental status, jaundice, and ascites	Not mentioned	Not mentioned	Anticoagulation—specifics not mentioned	Not mentioned
Margaria et al[7]	62	Female	Nephrolithiasis, obesity, and HTN	Fulminant	Bilateral leg swelling, pruritus, shortness of breath, and jaundice	1 wk after hospitalization for COVID-19-related pneumonia	Echocardiogram was unremarkable; hepatitis panel was negative	Thoracocentesis for hepatic hydrothorax secondary to BCS	Symptoms improved

BCS, Budd-Chiari syndrome; COVID-19, coronavirus disease 2019; HTN, hypertension; IgM, immunoglobulin M; LMWH, low molecular weight heparin; MRI, magnetic resonance imaging.

case presentation. C. Kilada: contributed to introduction and table. J. Ravilla: reviewed and edited the paper and contributed to discussion. C. Ramirez: edited the paper for style. PE Gonzalez: edited the paper for style and obtained pathology slides. S. Imburgio: contributed to case presentation and table. A. Johal: conducted literature review and contributed to editing and formatting the paper. X. Sun: lead pathologist who interpreted the pathology slides. PN Shah: lead radiologist who helped interpret the images. M. Hossain: coordinated and lead the group and edited the paper. H. Sanekommu is the article guarantor.

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