Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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COVID-19 and Jaundice

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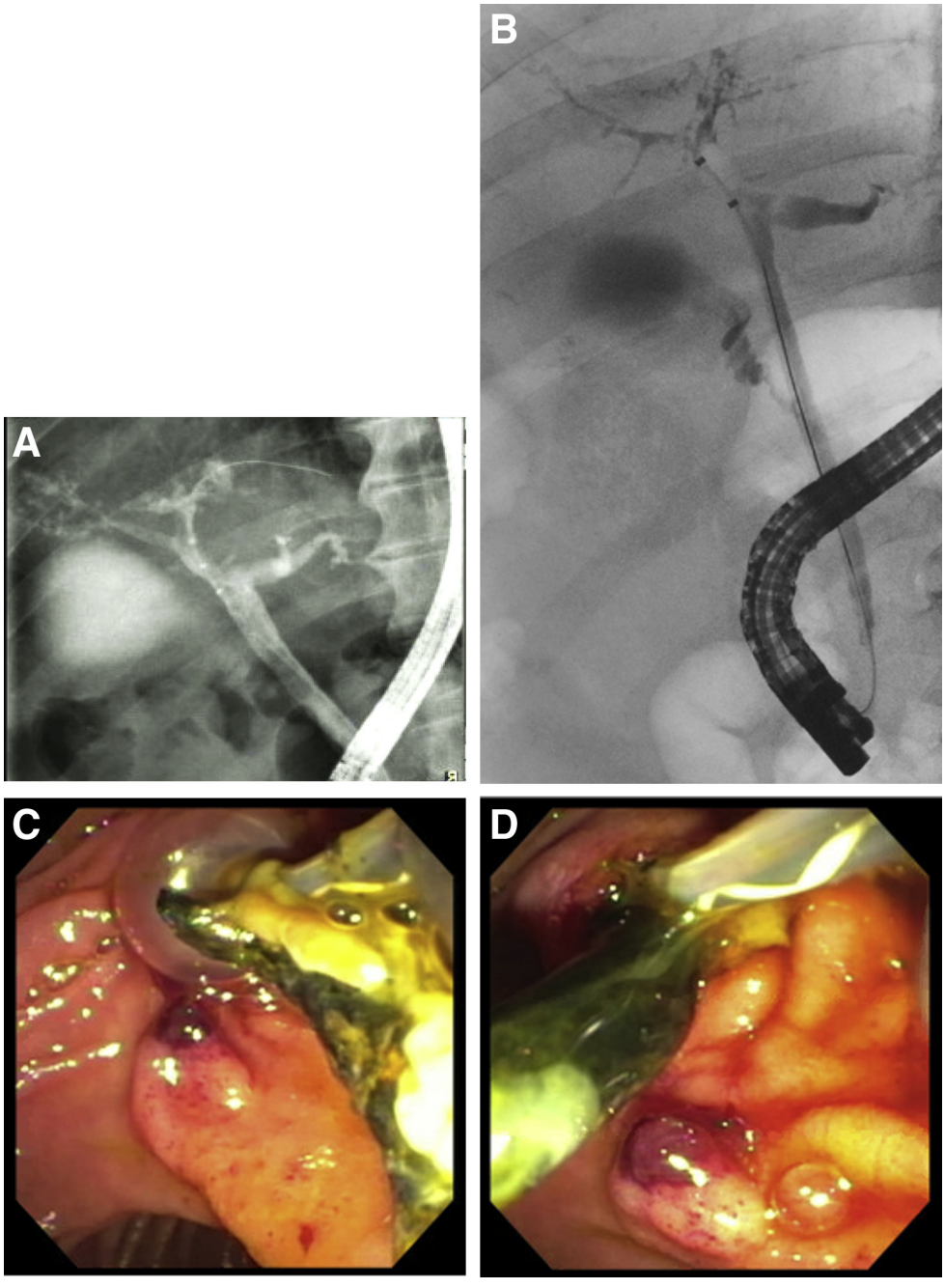

Question: A 63-year-old man presented to his local hospital in March 2020 with symptoms of shortness of breath, weakness, and fevers for 6 days. He had a history of hypertension, obstructive sleep apnea, and diabetes mellitus. He tested positive for severe acute respiratory syndrome coronavirus-2 and was admitted to the hospital for oxygen therapy. He was subsequently intubated for a 2-week period and received therapy for novel coronavirus disease 2019 (COVID-19), including hydroxychloroquine, azithromycin, tocilizumab, and plasma exchange. He was successfully extubated with prolonged weaning of oxygen therapy. His hospital course was complicated by a prolonged intensive care unit stay with culture-negative septic shock requiring vasopressor therapy, bilateral deep venous thromboses (DVTs) treated with inferior vena cava filter owing to large gluteal hematoma formation, and central line–associated candidemia treated with fluconazole.

On hospital day 48, 35 days after vasopressor therapy/hypotension and 34 days after diagnosis of

DVT for which he was not anticoagulated, he was noted to be jaundiced with a total bilirubin of 2.3 mg/dL, alkaline phosphatase of 831 U/L, alanine aminotransferase of 135 U/L, and aspartate aminotransferase of 91 U/L, which had been previously normal throughout his admission. A right upper quadrant ultrasound examination was performed that demonstrated sludge in the gallbladder, no biliary ductal dilation, and patent vasculature. The patient underwent endoscopic retrograde cholangiopancreatography (ERCP), which demonstrated filling defects in the common bile duct as well as an irregular and beaded appearance of the intrahepatic ducts (Figure *A*). A sphincterotomy was performed followed by balloon sweep of the ducts with the removal of "thick stone-like material." A biliary stent was placed; however, the patient's jaundice continued to worsen; 3 weeks later, the bilirubin was 11 mg/dL. A repeat ERCP 151 days after presentation with a limited cholangiogram demonstrated filling defects of the intrahepatic ducts and ductopenia of the right and left intrahepatic ducts with irregularity and beading (Figure *B*). Balloon sweeps were notable for numerous lesions as shown (Figure *C*, *D*).

What was the diagnosis causing the intrahepatic ductal irregularities and filling defects seen on ERCP?

See the *Gastroenterology* web site (www.gastrojournal.org) for more information on submitting your favorite image to Clinical Challenges and Images in GI.

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Conflicts of interest
The authors disclose no conflicts.

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Answer to: Image 1: Sclerosing Cholangitis in Critically Ill Patients and Biliary Cast Syndrome, Likely as Sequelae of COVID-19

This is sclerosing cholangitis in critically ill patients (SC-CIP) and biliary cast syndrome, likely as sequelae of severe acute respiratory syndrome coronavirus-2 infection. COVID-19 has been shown to affect the gastrointestinal system acutely with a variety of symptoms, including nausea, vomiting, diarrhea, and abdominal pain.[1] Furthermore, hepatic involvement in patients with COVID-19 has been observed with biochemical elevations in liver chemistries in 10%–53% of patients and jaundice observed in 5%–18% of patients,[1] which is thought to be multifactorial, owing to hepatic injury resulting from COVID-19–associated sepsis and hypotension and the accompanying cytokine storm, as well as drug-induced liver injury from a variety of medications used to treat COVID-19 infection. Last, microthrombi and microangiopathy is a well-described phenomenon of COVID-19.[2]

Secondary sclerosing cholangitis is characterized by multifocal biliary stricturing and can be due to a variety of causes including infection and ischemic cholangitis.[3] Biliary cast syndrome is characterized by the presence of biliary casts and debris causing biliary obstruction, thought to be due in part to ischemic injury of the biliary tree occurring, for example, in the context of hepatic artery stenosis in patients who have undergone liver transplantation. Biliary casts have been observed in patients with SC-CIP and it is considered a poor prognosticator, often requiring liver transplantation.[3]

Here we postulate that our patient developed SC-CIP and biliary cast syndrome as sequelae of COVID-19. The resultant hypotension and shock from the initial infection likely precipitated biliary ischemia and subsequent sclerosing cholangitis with biliary cast formation. Furthermore, it is plausible that the patient may have developed local microthrombi and microangiopathy, akin to the pulmonary vascular thrombosis and microangiopathy observed in COVID-19 autopsy specimens,[2] resulting in biliary ischemia, especially in a prothrombotic patient who developed bilateral DVTs who could not be anticoagulated. Owing to his persistent hyperbilirubinemia (~9 mg/dL at 6 months from his original injury) and despite technically successful ERCPs and an adequate trial of ursodiol (14 mg/kg), the patient is currently accepted for but pending orthotopic liver transplantation. Gastroenterologists should be aware of these potential long-term sequelae of COVID-19, given the ongoing global pandemic and large number of survivors with prolonged critical illness.

Keywords: SARS-CoV-2; COVID-19; Jaundice; ERCP.

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