International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 09, Issue 09, September 2024,
https://doi.org/10.23958/ijirms/vol09-i09/1962

Case Report

An Unclear Relationship Between Idiopathic Non-Cirrhotic Portal Hypertension, Pyogenic Liver Abscess, Or Portal Vein Thrombosis

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Received 24 August 2024; Accepted 10 September 2024; Published 14 September 2024

Abstract

Background: Pyogenic liver abscess (PLA) remains rare in the United States (US). Data shows that Klebsiella pneumoniae is becoming the leading bacterial cause of PLA. Causes of bacterial seeding in the liver include biliary tract pathology, portal vein bacteriemia, systemic bacteremia, penetrating wounds, or liver surgery. We describe a case of cryptogenic Klebsiella pneumoniae PLA, associated with an incidental finding of idiopathic non-cirrhotic portal hypertension (INCPH). ***Case presentation:*** A 55-year-old female, with no past medical history, presented with 7 days of nocturnal fever, dry cough, mild back pain, and jaundice. On admission, she was febrile, tachycardic, and jaundiced. The abdomen was soft, non-tender and Murphy's sign was negative. Laboratory workup revealed normocytic anemia, leukocytosis with neutrophilia, and evidence of cholestasis. Imaging with liver ultrasound (US), Computer Tomography (CT), and Magnetic Resonance Imaging (MRI) showed a heterogeneous cystic mass in the left hepatic lobe, heterogeneous hepatic parenchyma, and a large stone in the fundus of the gallbladder without evidence of cholecystitis, along with signs of portal hypertension (PHTN). CT-guided drainage showed purulent fluid. The patient was treated with antibiotics. Klebsiella was isolated in both blood and pus cultures. Further workup for liver disease was inconclusive. A liver biopsy showed evidence of non-cirrhotic portal fibrosis (NCPF). ***Conclusions:*** The incidental discovery of PHTN in patients with underlying liver disease should prompt a full diagnostic workup. Diagnosis of INCPH requires clinical signs of PHTN, patent portal veins on imaging, exclusion of cirrhosis on liver biopsy, and exclusion of chronic liver disease that might cause either cirrhosis or NCPF. The management of INCPH, regardless of the cause, involves reducing the portal pressure.

Keywords: ***Pyogenic liver abscess; Klebsiella pneumoniae; Portal hypertension; Idiopathic non-cirrhotic portal hypertension; Non-cirrhotic portal fibrosis; Case report.***

Introduction

Pyogenic liver abscess (PLA) remains rare in the United States (US) [1]. Recent data shows that Klebsiella pneumoniae is becoming the most common bacteria in PLA both in the US and internationally [2]. Mechanisms of bacterial seeding in the liver include biliary tract pathology, portal vein bacteriemia, systemic bacteremia, penetrating wounds, or liver surgery [3]. We describe a case of cryptogenic Klebsiella pneumoniae PLA, associated with an incidental imaging finding of portal hypertension (PHTN), secondary to non-cirrhotic portal fibrosis (NCPF).

Case Presentation

A 55-year-old Hispanic female presented with nocturnal fever, dry cough, mild back pain, and jaundice for 7 days. She stated that she had dark yellow urine and solid brown feces. Her symptoms were associated with loss of appetite, decreased oral intake, and subjective weight loss for the past few weeks. She denied chills, abdominal pain, nausea, vomiting, diarrhea, hematochezia, melena, dysuria, increased frequency in micturition, headaches, chest pain, shortness of breath, and palpitations.

One week prior, our patient had presented at another hospital facility with similar symptoms. She was tested and found positive for SARS-COV-2 PCR at the time. She was discharged on antibiotics, for unclear reasons, and acetaminophen. She had no known past medical history and did not take any medications. Her family history was unremarkable. She denied smoking, alcohol, or illicit drug use. She stated she had no prior unprotected sexual encounter. She moved to the United States (U.S.) 18 years prior to her presentation, from Mexico. Before her last admission, she had not seen a physician since her arrival in the U.S., because of her undocumented status and the lack of health insurance.

On admission, the patient had a temperature of 39.4°C (102.9°F), a blood pressure of 104/69 mmHg, a heart rate of 125 beats per minute, a respiratory rate of 18 breaths per minute, and an oxygen saturation of 99% on room air. On physical examination, the patient was lying in bed, breathing comfortably. Scleral icterus was present, with dry oral mucosa. Cardiac auscultation revealed a regular tachycardia, normal S1 and S2 with no audible murmurs. Lungs were clear to auscultation with no crackles or wheeze. The abdomen was soft, and non-distended, with normal bowel sounds in all quadrants, without palpable fluid or organomegaly. No lower extremity edema was appreciated. There was no spinal or paraspinal tenderness.

Laboratory workup is detailed in Table 1. A Complete Blood Count (CBC) revealed normocytic anemia and mild leukocytosis with neutrophil predominance. Liver Function Tests (LFT) showed cholestasis; albumin was low and the prothrombin time was elevated at 18.7s. Basic Metabolic Panel showed hyponatremia with normal potassium and renal function. Blood cultures were drawn. Urinalysis showed positive bilirubin, increased urobilinogen (1 mg/dL), and positive ketones.

A chest radiograph did not show any focal lung disease. A right upper quadrant ultrasound (US) showed a 5.8 cm heterogeneous cystic mass in the segment IV of the liver with dilated bile ducts within the mass (raising the suspicion of cholangiocarcinoma or a liver abscess), heterogeneous hepatic parenchyma (suspicious of hepatocellular disease or fatty changes), a large stone in the fundus of the gallbladder, without wall thickening, pericholecystic fluid, or biliary duct dilation. A CT abdomen and pelvis with contrast showed a 6.2 x 5.8 cm heterogeneous hypoattenuation, without biliary dilatation (**Figure 1-A**). An abdominal MRI showed enhancing internal septa and walls, more in favor of hepatic abscess or hydatid cyst (**Figure 1-B**). Additional findings on both the CT and MRI included a cavernous transformation of the portal vein, an enlarged spleen with homogeneous enhancement, paraesophageal varices, and a spleno-renal shunt indicating PHTN (**Figure 1**).

Alpha-fetoprotein (AFP) and Carcinogenic Antigen 19-9 (CA-19-9) were within normal range. Serologies for Entamoeba Histolytica and Echinococcus Granulosus were negative. CT-guided drainage of the liver abscess performed on day 4, brought a pink purulent fluid (**Figure 2-A**). Cultures and sensitivities from the pus and the blood isolated Klebsiella pneumoniae, sensitive to ceftriaxone and ciprofloxacin. A colonoscopy was performed to rule out colorectal cancer or diverticulosis as potential causes of portal bacteremia resulting in PLA. However, the colorectal mucosa was intact. Further diagnostic workup for liver disease was inconclusive, including viral hepatitis serology, iron studies, and autoimmune workup (**Table 1**). Schistosoma antibodies were also negative. It was decided to perform a CT-guided liver biopsy to evaluate the etiology of the liver disease. An upper endoscopy to screen for varices found one column of large (>5mm) varices in the lower third of the esophagus which were banded successfully (**Figure 3**). Our main differentials were: 1- liver abscess leading to portal vein thrombosis (PVT) and INCPH 2- pylephlebitis of unknown source complicated by PVT and liver abscess. However, the lack of reported past medical illness by the patient, prior medical records, and prior imaging renders the diagnosis uncertain.

The patient was treated with intravenous (IV) fluids and piperacillin-tazobactam for broad-spectrum antibiotic coverage of the liver abscess. On day 6 (day 2 post-drainage), she became afebrile. The antibiotic regimen was changed to IV ceftriaxone based on culture sensitivities with a plan to complete two weeks of parenteral antibiotherapy. Initial abscess drainage output was 20-30 mL, which decreased to less than 5 mL daily. The drain was removed on day 14 of hospital admission. Improvement in both inflammatory and cholestatic laboratory parameters was noted. The patient completed 14 days of parenteral antibiotics. On discharge, she was transitioned to oral ciprofloxacin 750 mg every 12 hours to complete a 4-week course. A repeat endoscopy to follow up on the resolution of varices was scheduled on discharge. The liver histology revealed evidence of non-cirrhotic portal fibrosis (NCPF) (**Figure 4**). The patient was then referred to the gastroenterology clinic but was lost to follow-up.

Table 1: Laboratory workup performed in our patients

Laboratory test	Results (Normal ranges)
Complete Blood Count (CBC)	Hemoglobin 10.6 g/dL (12.0 - 16.0 g/dL) MCV 89.4 fL (80.0 - 99.9 fL) Leukocytes 12910 cells/uL (4.80 - 10.8 cells/uL) Neutrophils 86.8 % (44.0 - 77.0 %)
Liver Function Tests (LFT)	AST 35 (≤ 32 U/L) ALT 49 (≤ 33 U/L) ALP 301 (35 - 105 U/L) Total bilirubin 3.04 (0.20 - 1.20 mg/dL) Direct bilirubin 1.90 (0.00 - 0.30 mg/dL) Albumin 3.3 g/dL (3.5- 5.2 g/dL)
Basic metabolic panel	BUN 10.0 mg/dL (6.0 - 23.0 mg/dL) Creatinine 0.70 (0.50 - 0.90 mg/dL) Sodium 126 mmol/L (136 - 145 mmol/L) Potassium 3.7 mmol/L (3.5 - 5.1 mmol/L)
Lipid panel	Total cholesterol 91 mg/dL (≤ 200 mg/dL) HDL cholesterol 19 mg/dL (≥ 50 mg/dL) LDL cholesterol 53 mg/dL (≤ 129 mg/dL) Triglycerides 94 mg/dL (≤ 150 mg/dL)

Iron studies	Iron 26 ug/dL (30-160 ug/dL) TIBC 171 ug/dL (220-430 ug/dL) Ferritin 243 ng/dL (15/150 ng/mL)
Bacterial cultures	Blood culture: Growth Klebsiella pneumoniae Abscess fluid culture: Growth Klebsiella pneumoniae
Viral hepatitis panel	Hepatitis B surface antigen (HBsAg) non reactive Hepatitis B surface antibody (HBsAb) non reactive Hepatitis C virus (HCV) antibody non reactive
Liver parasites serology	Schistosoma antibodies IgG negative Entamoeba histolytica serology negative Echinococcus antibodies IgG negative
Autoimmune workup	Antinuclear antibodies negative Anti-smooth muscle antibodies weakly positive 1:20 Anti-LKM antibodies negative < 20.1 Antimitochondrial antibodies negative <1:20 Anti neutrophil cytoplasmic antibodies negative
Tumor markers	Alpha fetoprotein (AFP) negative Carcinogenic Antigen 19-9 (CA-19-9) negative

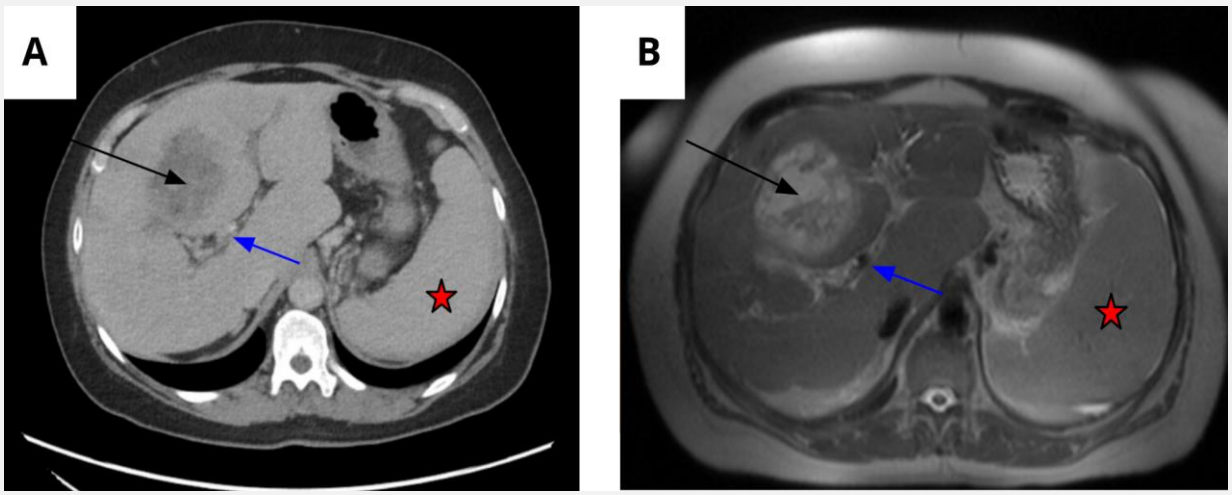

Figure 1: Heterogeneous cystic liver mass in the segment IV of the liver measuring 6.2 x 5.8 cm on Computed Tomography (**A, Black arrow**), and Magnetic Resonance Imaging with enhancing internal septa, and enhancing walls (**B, Black arrow**). Additional findings of portal hypertension included a cavernous transformation of the portal vein (**Blue arrow**), splenomegaly (**Red star**) and spleno-renal shunt

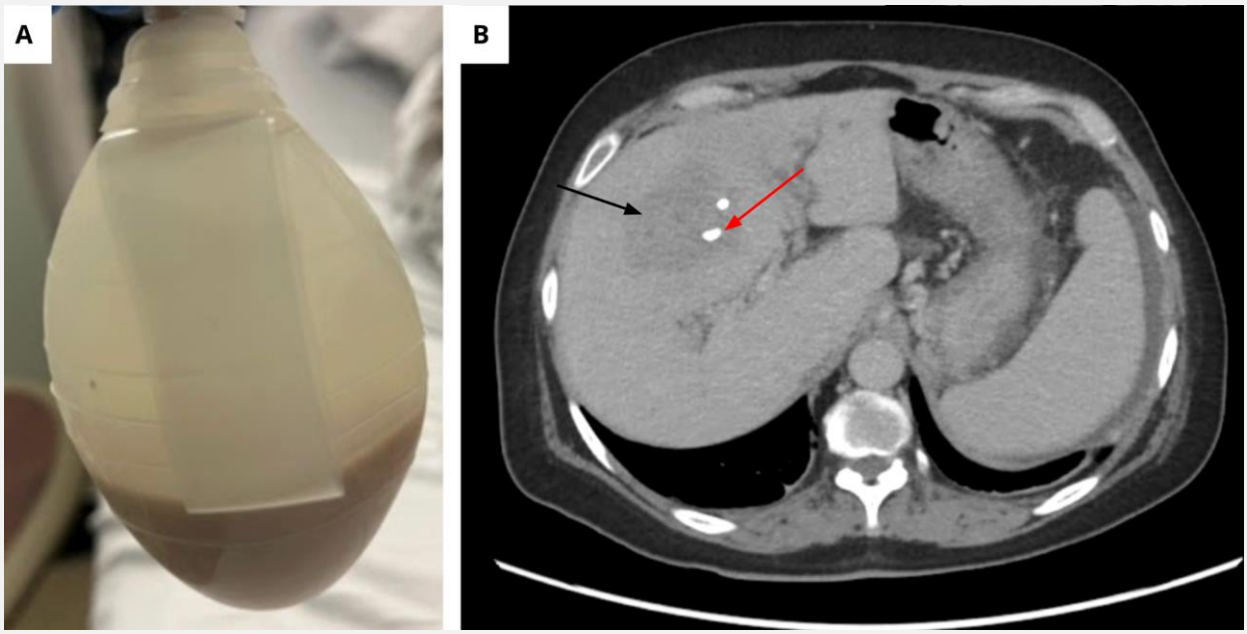

Figure 2: Pink-chocolate purulent fluid drained from Klebsiella pneumoniae liver abscess (A), and post-drainage CT scan showing resolution of the liver abscess (**B, Black arrow**) with the drain in place (**B, Red arrow**)

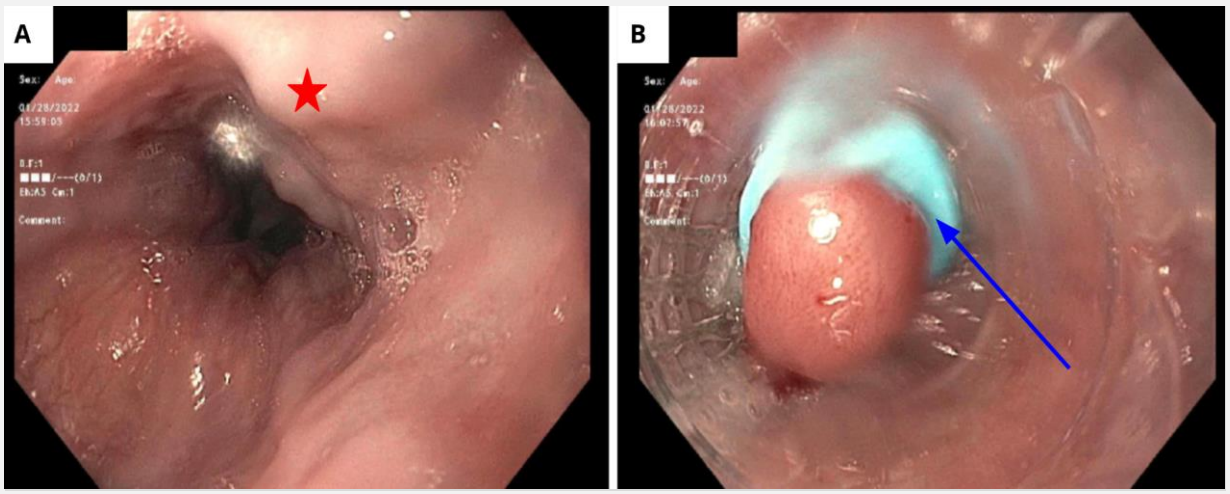

Figure 3: One column of non-bleeding large (>5cm) varices in the lower third of the esophagus (**A, Red star**), without stigmata of recent bleeding. Two bands were successfully placed with complete eradication (**B, Blue arrow**).

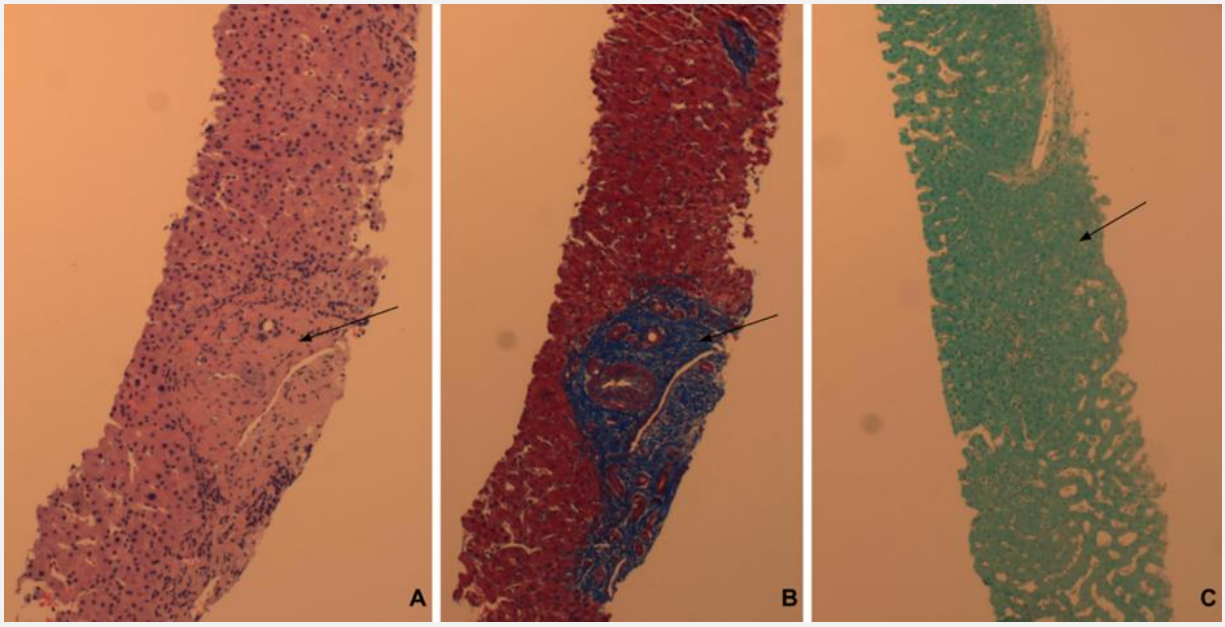

Figure 4: Normal liver parenchyma with a few chronic inflammatory cells within portal tracts on hematoxylin-eosin stain (**A, Black arrow**), with mild portal fibrosis on trichrome stain (**B, Black arrow**), and normal reticulin pattern of hepatic plates on reticulin stain (**C, Black arrow**) indicating the absence of liver fibrosis (original magnification X100)

Discussion

Pyogenic liver abscesses remain rare in the U.S. The incidence ranges from 2.3 to 3.6 cases per 100,000 people, and the mortality is from 6 to 10% in North America [1,4]. Recent data shows that Klebsiella pneumoniae is becoming the most common bacteria in PLA [2]. Bacterial seeding occurs most commonly through biliary tract pathology (cholangitis, cholecystitis, biliary strictures, gallstones, malignancy, and congenital anomalies), but can also be secondary to portal vein bacteriemia (bowel leakage, peritonitis), hepatic artery bacteremia, or penetrating wounds or liver surgery [3]. Our patient had systemic bacteremia, asymptomatic gallstones, and a negative colonoscopy.

Incidental findings of PHTN on abdominal imaging should prompt physicians to review the history and perform a full diagnostic workup to rule out liver cirrhosis and schistosomiasis, the two most common causes of PHTN [5]. Following an inconclusive workup for both cirrhosis and schistosomiasis in our patient, a liver biopsy was indicated, and the diagnosis of NCPF was made on histology. Diagnosis of INCPH requires clinical signs of PHTN (ascites, esophageal &/or gastric varices, splenomegaly/ hypersplenism, porto-venous collaterals), along with patent portal veins on imaging (doppler US or CT), exclusion of cirrhosis on liver biopsy, and exclusion of chronic liver disease that might result in cirrhosis (Hepatitis B &/or C, non-alcoholic steatohepatitis, hemochromatosis, Wilson's disease, primary biliary cirrhosis) or NCPF (Congenital liver fibrosis, sarcoidosis, schistosomiasis) [6]. Based on the diagnostic criteria, our patient was diagnosed with INCPH.

INCPH is thought to be secondary to chronic infections, medication or toxic exposure, genetic disorders, thrombophilia, and immunological disorders [6]. It is often misdiagnosed as liver cirrhosis. A higher incidence of portal vein thrombosis (PVT) has been documented in patients with INCPH than in patients with liver cirrhosis [7,8]. The relationship between INCPH and PVT remains incompletely characterized. Intrahepatic PVT was incriminated as a prominent pathophysiological factor in the development of INCPH [8], with the hypothesis that PVT and INCPH are different presentations of the same disorder [8]. Moreover, PVT and INCPH share similar histological features [8].

In this patient with PLA, along with signs of INCPH and PVT, it is unclear which disease process preceded, as cases of PLA leading to PVT (a cause of INCPH) [9], and pylephlebitis complicated by liver PVT and PLA [10] have both been described in the literature. Furthermore, It is unclear if an isolated 5.8x6.2cm liver abscess could result in a significant enough inflammatory response to lead to INCPH. Therefore, given the absence of medication or toxic exposure, genetic disorders, thrombophilia, or known immunological disorder in our patient, we suspect that the INCPH was secondary to the underlying bacteremia from unclear etiology. The lack of past medical records and imaging renders the diagnosis uncertain.

Our patient was managed with prophylactic endoscopic variceal ligation. The focus of INCPH treatment revolves around the management of PHTN. A repeat endoscopy is required every 2-3 weeks until variceal eradication is confirmed, and follow-up should be carried out every 6 months [11].

Long-term complications of INCPH include PVT (46%), and the development of liver failure (21%), with a possible causal relation between them [8]. The prognosis is poor for patients with concurrent INCPH and PVT [8]. Therefore, anticoagulation has been proposed by several authors as a means to prevent disease progression [7,8], however, given the risk of variceal bleeding present in these patients, larger trials are necessary to establish clear guidelines regarding anticoagulation in this patient population.

Conclusion

The incidental discovery of PHTN in patients with underlying liver disease should prompt a full diagnostic workup to rule out liver cirrhosis. The relationship between PLA, PVT, and INCPH remains unclear in the literature, and further studies should help establish this association. The management of INCPH involves reducing the portal pressure to prevent variceal bleeding and death.

Abbreviations

AFP: Alpha-fetoprotein

CA 19-9: Carcinogenic Antigen 19-9

INCPH: Idiopathic non-cirrhotic portal hypertension

NCPF: Non-cirrhotic portal fibrosis

PHTN: Portal hypertension

PLA: Pyogenic liver abscess

LFTs: Liver Function Tests

PVT: Portal vein thrombosis

Ethics approval and consent to participate

Informed consent was obtained for this case report. Patient data is deidentified, therefore, exempt from institutional board review (IRB) approval

Conflict of interest statement

The authors declare no conflict of interest

Informed consent

Informed consent was obtained for this case report

Data availability

All data underlying the results are available as part of the article and no additional source data are required

Funding Statement

None

Authors contributions

Y.K, D.M, A.P., S.A. contributed to patient care, chart review, drafting the case report, and approval of the final version; M.A.J, S. D. K. contributed to drafting the case report, and approval of the final version; A.Y., H.A. contributed to chart review, drafting the case report, and approval of the final version.

Acknowledgments

This case was previously presented as a poster presentation in the ACG 2022 Annual Meeting (C0596).

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