Single Case

A Novel Culprit in a Patient with Budd-Chiari Syndrome

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Keywords

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Abstract

Budd-Chiari syndrome (BCS) is an uncommon illness that is characterized by obstruction of hepatic venous outflow. Patients typically present with nausea, vomiting, and abdominal pain, which can further progress into signs associated with liver failure, including jaundice, encephalopathy, and coagulopathy. The most common causes of BCS include pathologies that induce portal vein thrombosis, such as myeloproliferative disorders, malignancy, and acquired hypercoagulable states. In this case report, a patient who presented with abdominal pain and distention is diagnosed with BCS caused by an unusual etiology. He was found to have significant eosinophilia, prompting additional evaluation for parasitic infections. Using stool diagnostics/studies, he was found to have *Dientamoeba fragilis* trophozoites. The patient was treated with enoxaparin, warfarin, and metronidazole with a resolution of his symptoms. This case outlines a novel cause of BCS as well as the proposed mechanism of *Dientamoeba fragilis* induction of BCS.

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Introduction

Budd-Chiari syndrome (BCS) is an uncommon illness that affects an estimated 0.4–0.8 patients per million and is characterized by obstruction of hepatic venous outflow from the hepatic venules to the junction of inferior vena cava (IVC) and right atrium [1]. Patients with this disease present similarly to those with hepatic disease, with primary complaints of nausea, vomiting, and abdominal pain, which eventually can progress to include ascites, jaundice, hepatomegaly, encephalopathy, and coagulopathy. The severity and speed at which these symptoms progress further divide BCS into acute, subacute, and chronic. The rarity of the condition often delays diagnosis until life-threatening symptoms become apparent. Hypercoagulable states are the primary cause of BCS, usually seen in patients with a history

of myeloproliferative disorders, malignancy, and acquired hypercoagulable states [1]. Otherwise, BCS is caused by extravascular obstruction. Here, a patient is presented with symptoms of BCS with an unusual cause.

Case Report

A 49-year-old male with no past medical history presents to his primary care physician with the chief complaint of nausea, vomiting, and abdominal pain for 2 months. He has also noticed increased abdominal, lower extremity, and scrotal distention, resulting in difficulty wearing clothes that previously fit him 2 months prior. The patient also complains of dull, crampy, diffuse abdominal pain, and weight loss from 210 pounds to 190 pounds (10% of total body weight). Travel history was notable for a family visit to Bangladesh 7 months prior to presentation. Outpatient CT of the abdomen and pelvis with intravenous contrast demonstrated chronic thrombosis of the left renal vein which extended into the IVC, intrahepatic IVC and hepatic vein compression, thrombosis of the peripheral, middle, and right hepatic veins, and evidence of portal hypertension. These findings were concerning for BCS, and thus, the patient was directly admitted to the hospital medicine service for further evaluation and management.

Upon admission, the patient was noted to be hemodynamically stable, with a blood pressure of 126/87, pulse of 82, respiratory rate of 19, temperature of 99.0°F, and oxygen saturation of 96% on room air, pertinent physical exam findings included a distended abdomen with normal-appearing skin, a positive fluid wave with shifting dullness, and tenderness to palpation in the right upper quadrant. No hepatosplenomegaly was appreciated on palpation. The patient's lower extremities were noted to have pitting edema to the middle thighs bilaterally. The scrotum was found to be edematous as well, measuring about 30 cm in circumference. Initial laboratory values revealed an aspartate transaminase of 71 U/L, alanine transaminase of 88 U/L, alkaline phosphatase of 360 U/L, total bilirubin of 1.4 mg/dL, total protein of 7.2 g/L, albumin of 2.6 g/L, prothrombin time of 15.6 s, partial thromboplastin time of 33 s, and international normalized ratio of 1.2. Interestingly, patient was also noted to have a white blood cell count of 12,680 cells/mm³, platelet count of 63,000 platelets/μL, and absolute eosinophil count of 5,360 cells/μL. Further laboratory evaluation demonstrated negative values for hepatitis A, hepatitis B, and hepatitis C as well as no clear risk factors for the development of hypercoagulable states. Abdominal ultrasound revealed coarsened liver echotexture with no discrete mass. The main portal vein demonstrated a bidirectional waveform suggesting high resistance. Minimal flow was identified within the left portal vein, while the middle and right portal vein demonstrated normal-appearing flow. Left and right hepatic veins demonstrated a pulsatile waveform. A moderate amount of ascites surrounds the liver. Given findings consistent with hepatic vein thrombosis, therapeutic dose enoxaparin was initiated at 1 mg/kg twice daily. Ultrasound elastography demonstrated a medial liver stiffness of 15.6 kPa with an IQR/Med of 15.7, indicating a markedly elevated fibrosis score of F4. Paracentesis demonstrated 3.5L of red, cloudy peritoneal fluid with significant for a white blood cell count of 1,821 cells/mL, 89% of which were eosinophils, albumin of 1.3 g/dL, and protein of 3.1 g/dL, resulting in a serum ascites albumin gradient suggesting portal hypertension.

Given persistent eosinophilia, parasitic workup was initiated, including schistosomiasis serology and stool ova and parasite screen. Both tests were completed with negative results. Given persistent eosinophilia and concern for false-negative results, a second stool ova and parasite screen was completed. As results were pending, the patient was in stable condition for discharge, at which point he was initiated on a 7-day course of empiric albendazole 400

mg twice a day for presumed parasitic infection and a prescription for warfarin 5 mg to be taken on a daily basis. Stool ova and parasite screen ultimately demonstrated *Dientamoeba fragilis* trophozoites. The patient's primary care physician was notified of the result, at which point the patient was initiated on a 10-day course of metronidazole 500 mg twice a day. Upon completion of the metronidazole therapy, the patient had significant improvement in abdominal pain and distention. At the 1-month follow-up appointment, laboratory evaluation revealed an aspartate transaminase of 29 U/L, alanine transaminase of 32 U/L, platelet count of 341,000 platelets/ μ L, white blood cell count of 6,100 cells/ mm^3 , and absolute eosinophil count of 210 cells/ μ L. Repeat abdominal ultrasound demonstrated normal portal vein blood flow, no discrete hepatic mass, and no vascular congestion, demonstrating resolution in the patient's hepatic congestion.

Discussion

Dientamoeba fragilis is a flagellate that is closely related to trichomonads. Infections with this parasite are found worldwide, making it difficult to use travel history alone as an indication for testing. To date, no specific products have been consistently seen to harbor the parasite. While the complete life cycle is not fully understood, trophozoites are typically found in the lumen of the colon, where they multiply by binary fission and are shed into the stool [2]. Transmission is suspected to be via the fecal-oral route. The most common symptoms of this infection include diarrhea, abdominal pain, weight loss, nausea, and fatigue. Real-time PCR is the best diagnostic test for *Dientamoeba fragilis* regarding sensitivity and specificity; however, triple feces test is the next best investigation, as the parasite is not always found in every stool specimen [3]. Treatments of this infection include metronidazole, tetracyclines, and carbarsone [4].

BCS is a rare condition in which the etiology is unknown in approximately 20% of all cases [5]. The most common identifiable cause of BCS is a hypercoagulable state. In this case, the patient was found to have a parasitic etiology of BCS. While there are rare cases of parasitic infections causing BCS, the authors cannot find another case that involves *Dientamoeba fragilis* as the causative species. The most common of the rare parasitic infections having been reported to cause BCS include amebiasis, aspergillosis, and echinococcosis [6].

The mechanism of thrombosis in patients with a parasitic infection is varied. If the parasite is large enough, it has been reported that the parasite itself can cause an occlusion in the vessel it has invaded, as seen in one such case of a patient with pulmonary artery occlusion secondary to *Ascaris lumbricoides* infection [7]. Another mechanism involves hydatid cyst formation, which can subsequently cause BCS by mass effect [8]. This mechanism has been documented in patients with *Echinococcus multilocularis* infection [9]. A final mechanism of thrombosis in those with parasitic infections is peripheral blood eosinophilia, a normal response seen in patients with parasitic infections. Eosinophils have various crystalloid granules named major basic protein, eosinophilic cationic protein, and eosinophil peroxidase [10]. These proteins are known to induce a hypercoagulable state by depressing fibrinolysis, inhibiting heparin-sulfate and exogenous heparin binding to antithrombin (resulting in unhindered factor X activation and thrombin generation), stimulating platelets to release PF4 (again inhibiting heparin binding to antithrombin), inhibiting PC activation (leading to loss of the inhibitory effect of aPC on factor V and factor VIII), and stimulating endothelial cellular exposure of tissue factor (activating factor X) [11]. Eosinophils have also been demonstrated to express tissue factor, which can ultimately activate the coagulation pathway via factor VII and X [12]. In regards to the presented patient's physical exam, lab, and imaging findings, it is more likely that peripheral blood eosinophilia induced by *Dientamoeba fragilis* is the cause of BCS in this case.

Treatment of patients with BCS typically includes anticoagulation if thrombosis is present and therapy for the underlying cause. In the patient presented, his treatment regimen included anticoagulation with enoxaparin and warfarin, as well as antimicrobial therapy with metronidazole. Ultimately, the patient had resolution in his symptoms. With adequate anticoagulation and treatment of the underlying cause, it is possible for patients to recover normal hepatic function, even after initial signs of chronic liver failure are apparent. This case exemplifies that when there is high clinical suspicion for parasitic infection in a patient with BCS, such as travel to endemic areas and eosinophilia, it is imperative to investigate further to obtain the proper diagnosis.

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There are no nonauthor contributors in this case report.

Statement of Ethics

The subject of the above case report has provided their written informed consent to publication of the case. This study protocol was reviewed and the need for approval was waived by the Institutional Review Board at the Baton Rouge General.

Conflict of Interest Statements

The authors have no conflicts of interest to declare.

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Author Contributions

Jeremy Polman, DO: Dr. Polman is the primary author of this manuscript. He had direct interaction with the patient's medical records and interpreted all information relevant to the case. He personally collected all information required for the manuscript completion. Jeremy Polman has approved the final version of the manuscript.

Sainandan Reddy, MD: Dr. Reddy was directly involved in the patient's care. He gathered information necessary for creation of the manuscript. He helped research specific information from various medical journals during research and reference creation. Sainandan Reddy has approved the final version of the manuscript.

Aaron C. Williams, MD: Dr. Williams was directly involved in the patient's care. He gathered information necessary for creation of the manuscript. He helped research specific information from various medical journals during research and reference creation. Aaron Williams has approved the final version of the manuscript.

Aaron DeWitt, MD: Dr. DeWitt is the academic chair of scholarly activities at the Baton Rouge General Internal Medicine residency program. He assisted in the editing of the manuscript, directed research toward specific articles, and helped organize the manuscript in a logical manner. Aaron DeWitt has approved the final version of the manuscript.

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