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Once Universally Fatal: Pylephlebitis

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PRESENTATION

Band-like epigastric pain was the first indication of a potentially deadly disorder for a 56-year-old man. He presented to the emergency department 2 weeks after first developing the pain, which was now accompanied by worsening nausea, diarrhea, chills, anorexia, and dizziness. Before the onset of symptoms, he had been in his usual state of health. His past medical history was significant for hepatitis C, hypertension, diabetes mellitus, alcohol abuse of 6 beers per day, and a 30 pack-year smoking history. The patient, having denied drinking over the previous 2 weeks due to abdominal discomfort, did not report any withdrawal symptoms. He was not taking any medications and had no significant family history.

ASSESSMENT

On physical examination, the patient had a blood pressure of 118/68 mm Hg, a regular heart rate of 80 beats per minute, a respiratory rate of 18 breaths per minute, an oral temperature of 98° F (36.6° C), and an oxygen saturation of 98% on room air. He had mild scleral icterus. An abdominal examination revealed a flat abdomen with normal bowel sounds, tenderness to the epigastrium without rebound, and hepatomegaly, with the liver edge 2 centimeters below the costal margin. Laboratory testing demonstrated a leukocyte count of 16.3 x 10^9 cells/L with neutrophils at 96% and bands at 1%. His platelet count was 158 x 10^9/L. Total bilirubin was measured at 2.1 mg/dL; direct bilirubin, at 1.2 mg/dL. Results from his coagulation profile were within normal ranges, as were levels of creatinine, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, and lipase.

Computed tomography (CT) with contrast of the abdomen and pelvis showed thrombosis of the main portal vein extending into the left portal vein and asymmetric sigmoid colonic wall thickening (Figures 1 and 2). In the absence of systemic inflammatory response syndrome, we could not justify empiric antibiotic treatment until the initial set of blood cultures returned; these grew *Bacteroides uniformis* and *Peptococcus saccharolyticus*.

Given the portal vein thrombosis, combined with the patient's history of alcohol use and probable cirrhosis, a colonoscopy was performed 1 week later to rule out a malignancy that could have spurred thrombosis. This revealed inflammatory thickening of the rectosigmoid junction (Figure 3). The corresponding biopsy showed moderate chronic colitis with chronic hemorrhage, eosinophils, and rare neutrophils consistent with chronic diverticulitis. No granulomas or malignancies were identified.

DIAGNOSIS

Pylephlebitis, a rare and serious complication of intra-abdominal infections, is characterized by suppurative thrombosis of the portal vein or a tributary, fever, abdominal pain, hepatic dysfunction, and bacteremia. It was universally fatal before the availability of antibiotics.[1,2]

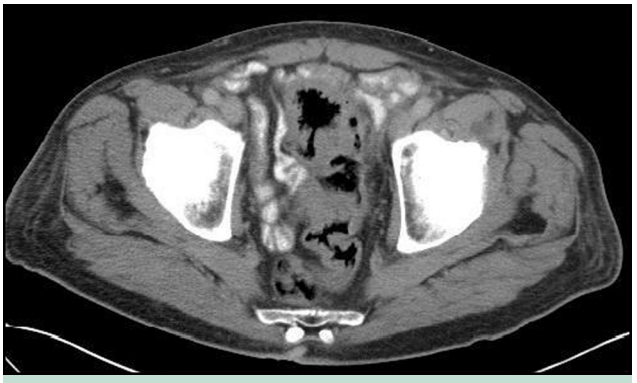

Figure 1 Computed tomography (CT) of the abdomen showed severe sigmoid thickening.

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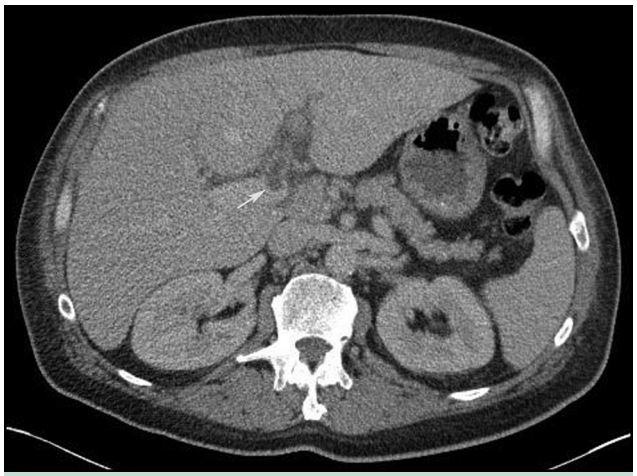

Figure 2 The white arrow on this CT scan of the abdomen indicates a filling defect in the portal vein.

Thrombophlebitis, which begins in the small veins immediately adjacent to the infection, extends into the portal vein.[3] In a review of 100 cases, extraportal extension of thrombosis was most common in the superior mesenteric vein (42%), but, also, it involved the intrahepatic veins (39%) and the splenic vein (12%).[3] Involvement of the mesenteric veins can lead to bowel necrosis and high mortality.[2-4]

As noted, most cases of pylephlebitis present with fever and abdominal pain.[4] Rigors, nausea, and vomiting are less commonly seen.[1,2] Hepatomegaly and jaundice are even more unusual, as they represent a rare subacute course of this illness, as was identified in our patient.[1,2] The most frequently seen laboratory abnormalities are leukocytosis with bandemia and elevations in alkaline phosphatase (3-4 fold) and gamma-glutamyl transferase (5-10 fold).[2,4] As clinical jaundice is an infrequent presenting sign, increases in serum bilirubin (2-6 fold) are rare.[2,4]

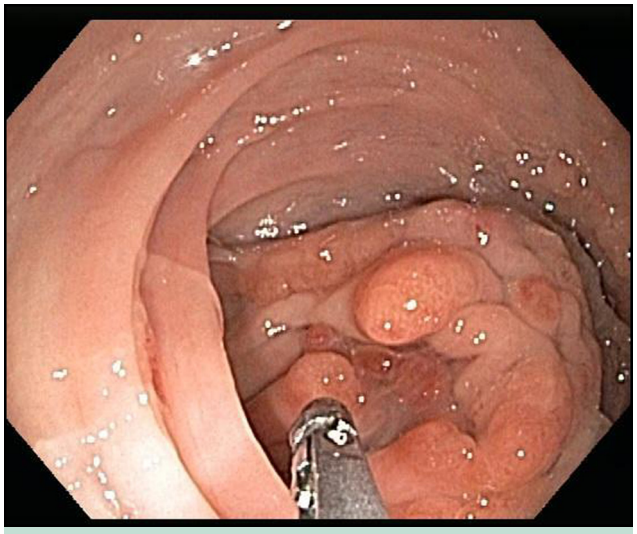

Figure 3 The rectosigmoid colon was visualized during colonoscopy.

The source of pylephlebitis is most commonly appendicitis or diverticulitis, though it can occur also as a complication of ascending cholangitis, septic choledocholithiasis, inflammatory bowel disease, pancreatitis, or gastrointestinal perforations from cancer or trauma.[1,2] Multiple organisms are isolated from blood cultures in 23-88% of patients.[1,3,4] Isolates are usually normal bowel flora, such as *Bacteroides fragilis* and *Escherichia coli*. *Aeromonas hydrophila*, *Streptococcus* and *Staphylococcus* species, *Proteus mirabilis*, *Klebsiella pneumoniae*, *Clostridium* species, yeasts, *Citrobacter* species, and rarely, *Enterococcus* species have been described as well.[3,4]

Diagnosis requires a known abdominal source of infection and imaging that identifies the portal vein thrombus.[5,7-9] CT with oral and intravenous (IV) contrast is the imaging modality of choice, as it can identify the intraabdominal source and the portal vein thrombosis.[2,5,7] A limited ultrasound with Doppler of the liver can identify flow abnormalities but is more useful for assessing progression or resolution of the thrombus.[2,5] Magnetic resonance imaging also is of use in differentiating acute from chronic thrombosis.[9]

The incidence of this disease is difficult to estimate, but it has appeared to increase over the last 15-20 years.[1,5,7] A retrospective study of 141 patients with portal vein thrombosis identified pylephlebitis in only 7% of patients diagnosed before 1990 but 56% after 1994.[10] This may be attributed to advances in readily-available imaging modalities.[1,5,7]

MANAGEMENT

Antibiotics are the mainstay of treatment for pylephlebitis.[1] Agents of choice include metronidazole with a third-generation cephalosporin or a fluoroquinolone, or monotherapy with an extended-spectrum penicillin or a carbapenem.[1,2,6] Therapy should last 4-6 weeks; parenteral antibiotics are administered for the first 1-3 weeks until clinical improvement is noted, and then oral antibiotics are used for the duration of the treatment period.[1,2] Oral metronidazole and a fluoroquinolone are standard choices.[1,2,6]

While surgical intervention is not usually indicated, it may be necessary if the precipitating abdominal focus requires open surgical treatment or drain placement.[8,11] In select critically-ill patients who have failed other approaches, another treatment option is percutaneous drainage of the focus in the portal vein under radiologic guidance.[11]

The use of anticoagulation in the management of pylephlebitis is controversial, and to date, there have been no randomized controlled trials to investigate its efficacy.[1,3,4,6] In uncomplicated cases, anticoagulation is not likely to become the standard of care, as the thrombosis tends not to be occlusive.[1] Yet, anticoagulation might be useful in mesenteric vein thrombosis, in patients with hypercoagulable states, or when *Bacteroides* species are the causative pathogens.[1,3,10,12] *Bacteroides* species have been

demonstrated to promote fibrin clotting and to produce transient anticardiolipin antibodies and factors that break down heparin.[1,12] The use of heparin in the acute setting can prevent worsening ischemia in pylephlebitis and reduce the incidence of bowel infarction from 30-40% to 3-5%.[4]

Initially, the patient was treated with IV piperacillin-tazobactam and a heparin drip. Abdominal pain and leukocytosis quickly subsided, and his blood cultures cleared the following day. Due to his generally mild and uncomplicated clinical course, he continued piperacillin-tazobactam for 1 week and was then discharged with instructions to complete a 3-week regimen of oral ciprofloxacin and metronidazole. In addition, because *B. uniformis* was identified, we chose to prescribe warfarin for 6 months. No consensus exists on the optimal length of time to administer anticoagulation in patients with pylephlebitis, so we based our decision on the recommended duration of anticoagulation in patients with provoked deep venous thrombosis. We cannot be certain if anticoagulation reduced the severity of our patient's illness, but given his etiology, it might have reduced the risk for further complications.

On outpatient follow-up at 2 and 6 weeks and at 3 and 6 months, the patient remained asymptomatic. During this time, results from his liver function panel normalized. Because the patient was clinically stable, no further imaging was carried out to assess for recanalization of the portal vein.

We recommend that the diagnosis of pylephlebitis be considered in any patient presenting with an infectious focus in the abdomen and evidence of portal vein thrombosis on abdominal CT. Treatment is comprised of broad-spectrum antibiotic therapy, along with consideration of anticoagulation and surgical intervention in selected patients. This disease, once universally fatal, now carries an estimated mortality of 11-32%.[1-3]

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