Case report

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Pylephlebitis in pediatrics: A diagnostic challenge

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ABSTRACT

Pylephlebitis is defined as suppurative thrombosis of the portal vein as a complication of abdominal infections. In pediatrics, the most frequent etiology is appendicitis, generally of late diagnosis, presenting as sepsis, with a high mortality rate.

Imaging methods are necessary for diagnosis; the most common are the Doppler ultrasound and computed tomography angiography.

Treatment is based on surgery, antibiotic therapy, and anticoagulation. The indication for the latter is controversial, but it may improve prognosis and decrease morbidity and mortality.

Here we describe a clinical case of pylephlebitis secondary to *Escherichia coli* sepsis, which started as acute appendicitis in a pediatric patient who progressed to cavernomatous transformation of the portal vein.

It is important to know the management of this disease because, once the initial symptoms are overcome, it will require close follow-up due to a potential progression to liver failure.

Keywords: *portal vein; thrombophlebitis; appendicitis; pediatrics.*

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INTRODUCTION

Pylephlebitis, or septic portal thrombosis, is defined as suppurative thrombosis of the portal vein or its tributaries as a rare, but serious, complication of abdominal infections. In pediatrics, the most frequent etiology is appendicitis; however, in adult patients, it has been described as a complication of diverticulitis or biliary tract infections.

It was first described in 1846 by Waller and, since then, the first reports described an incidence of approximately 4% in patients with acute appendicitis (Fitz, 1886). Such incidence decreased over the years due to the development of new antibiotic therapies and the early diagnosis of appendicitis, until reaching a current incidence that ranges between 0.3 and 3 cases per 100 000 patients per year.[1,2]

The late diagnosis of these infections favors their torpid course towards peritonitis or sepsis. When a severe infection occurs in anatomical regions whose venous drainage is tributary to the portal vein and its tributaries, endothelial activation secondary to the infection will result in portal vein thrombosis and subsequent portal hypertension. If this condition is not resolved, cavernomatous transformation by sustained portal hypertension may occur and thus cause liver impairment.

The clinical presentation is variable: from asymptomatic, as an incidental finding, to septic shock or liver failure, with a high mortality rate.[3]

The most common symptoms include fever, abdominal pain, nausea, vomiting, and diarrhea.[4] Laboratory findings include leukocytosis and increased acute phase reactants, such as C-reactive protein, erythrocyte sedimentation rate, and procalcitonin.

In the beginning, the course of this condition is usually severe; sepsis has been described in 60% of patients, with a high mortality rate that has reduced from 30–50% to 8.7% in recent years.[2,4]

Once the initial symptoms have resolved, the patient will have symptoms of portal hypertension: splenomegaly, collateral circulation, and ascites, among others. The development of liver abscesses is frequent as a consequence of the dissemination of septic emboli from the portal and/or superior mesenteric vein;[5] lung abscesses[6] and abscesses in the central nervous system have been described less frequently.[7]

The most common etiological agent documented is *E. coli* (20.4%), followed by *Bacteroides* spp. (12.6%), *Streptococcus* spp. (11%), anaerobic microorganisms (9.7%), *Staphilococcus* spp. (5.8%), *Klebsiella* spp. (5.8%), *Clostridium* (4.8%), and *Enterococcus* (4.8%), both in monomicrobial (37.9%) and polymicrobial (24%) cultures.[4]

Diagnosis is based on clinical and laboratory findings, and imaging methods are required. Those most common are Doppler ultrasound and computed tomography angiography because of their availability and usefulness;[8] however, if available at any facility, a magnetic resonance angiography offers greater sensitivity and specificity with low irradiation. The use of phlebography has also been reported, with variable usefulness.[9]

Treatment is based on surgery for the initial condition or suppurative complications resulting from it (abscesses), broad-spectrum antibiotic therapy, and anticoagulation.

Antibiotic therapy is a fundamental pillar of treatment. The recommendation is to cover the most frequent microorganisms, with a minimum duration of 6 weeks.[1] Suggested antibiotic regimens include monotherapy and combination therapy (*Table 1*).[1]

The indication for anticoagulation varies according to each patient's specific characteristics, but it could be beneficial in improving prognosis and reducing morbidity and mortality.

Here we describe a clinical case of pylephlebitis secondary to sepsis due to *E. coli* starting with generalized peritonitis of alleged appendiceal origin in a pediatric patient.

CASE REPORT

This was an 11-year-old, previously healthy boy referred from a different health care center due to septic shock of abdominal source, with *E. coli* bacteremia and diagnostic images compatible with liver abscesses, free peritoneal fluid, and portal thrombosis (*Figure 1*).

The patient's course included the development of anasarca; 3 evacuating paracentesis were performed, and the cytochemical panel results were compatible with bacterial infection. Due to right pleural effusion, a drainage tube was placed for 5 days.

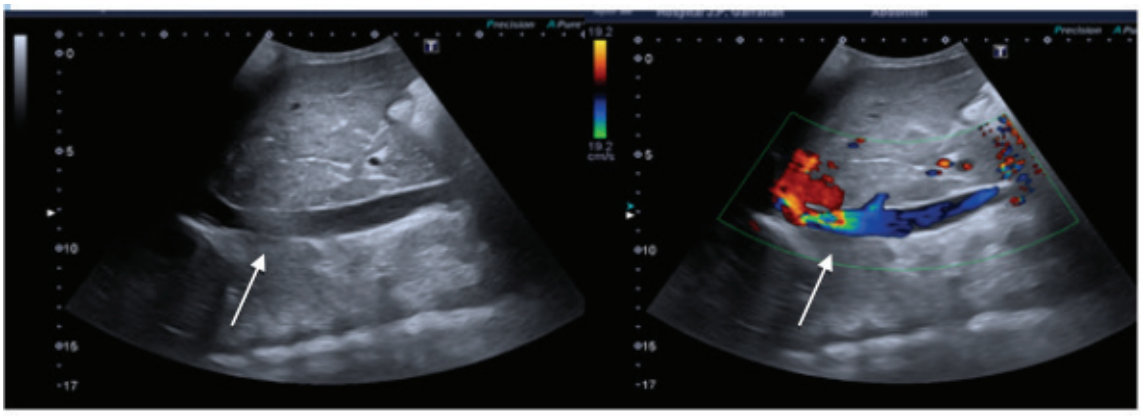
The patient was admitted after 6 weeks with a clinically and hemodynamically stable course, but he was severely malnourished, with palpable hepatomegaly and splenomegaly, without signs of liver failure or portal hypertension.

Antibiotic therapy with piperacillin tazobactam

Table 1. Recommended empiric antibiotic therapies. Options are provided based on monotherapy or combination therapy

MONOTHERAPY
Beta-lactams with beta-lactamase inhibitor
• Ampicillin/sulbactam
• Piperacillin/tazobactam
Carbapenems
• Meropenem
• Imipenem
• Ertapenem
COMBINATION THERAPY
Metronidazole plus one of the following:
Cephalosporins
• Ceftriaxone
• Cefotaxime
Quinolones
• Levofloxacin
• Ciprofloxacin

Figure 1. Color Doppler ultrasound of the liver and porta hepatis



Evidence of thrombus in the portal vein lumen with flow interruption on Doppler ultrasound (right).

was adapted to the sensitivity of the documented microorganism for a total of 8 weeks. Due to suspected pylephlebitis, anticoagulation with subcutaneous enoxaparin was started.

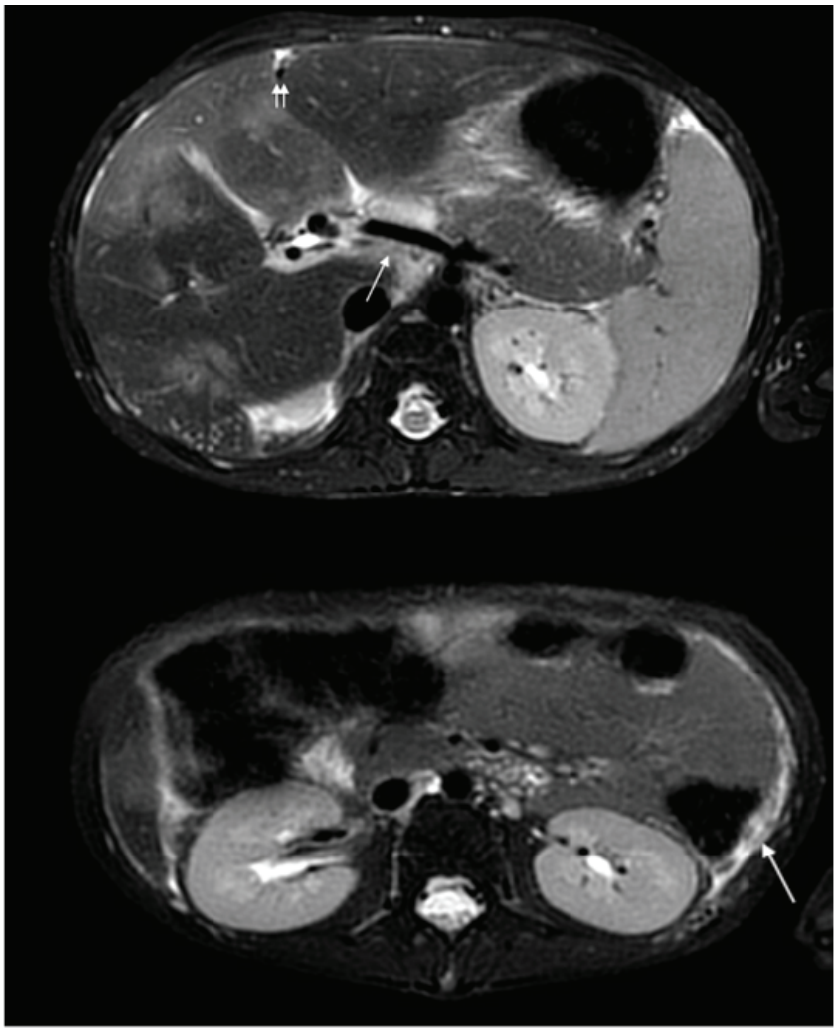
A new magnetic resonance imaging (MRI) was performed 6 weeks after treatment, which showed persistence of thrombosis and signs compatible with cavernomatous transformation and portal hypertension (*Figure 2*). Multiple small liver abscesses were observed, which progressively decreased with antibiotic therapy. Follow-up ultrasounds were performed until the signs of active infection resolved. The patient did not show clinical or laboratory findings that evidenced liver failure throughout his course.

Anticoagulation was adjusted and completed over 6 months, with no evidence of recanalization. Pro-coagulant conditions, such as antiphospholipid syndrome and paroxysmal nocturnal hemoglobinuria, were ruled out.

A complete immunological panel test was performed, which included determination of immunoglobulins, HIV serology, expanded lymphocyte populations, and dihydrorhodamine, all of which were normal, thus ruling out immune compromise.

The patient had a good clinical course, recovered his nutritional status and normal liver function. He continues receiving follow-up by the Departments of Clinical Pediatrics, Hepatology, and Hematology.

Figure 2. Magnetic resonance imaging of the abdomen with contrast



Top: The arrow indicates the region of the porta hepatis, where dilated hepatic artery and absence of visualization of the portal vein are observed. Small collateral vessels are observed in its place. The double arrow identifies the patent umbilical vein as an indirect sign of portal hypertension.
Bottom: The arrow indicates dilated posterior parietal veins as an indirect sign of portal hypertension.

DISCUSSION

The case reported here serves as evidence of one of the most severe courses of a highly frequent clinical condition, such as acute appendicitis.

One of the most important aspects that is worth highlighting is diagnostic delay, which allows the condition to progress to a serious infection. In this case, the delay was 6 weeks; Yoon et al., reported an average delay in the diagnosis of appendicitis of 1–6 weeks and attributed this to an atypical presentation.[10]

Although the microorganism was isolated in our patient, it should be noted that blood cultures are positive in 62% of patients with pylephlebitis,[4] which is not mandatory for diagnosis. In addition, it is essential to consider the culture of anaerobic bacteria due to the frequency of their isolation, which is often not included in routine cultures.

While the most common symptoms and laboratory findings may correspond to the initial infection, they may also be attributable to these overlapping with pylephlebitis itself, especially in those patients with liver abscesses, such as the case of this report.

The challenge in this clinical case was to determine whether the liver abscesses were the cause or the result of portal thrombosis. The fact that the patient did not have a related medical history and that his liver parenchyma was

otherwise healthy, as per the images, and that he did not have any predisposing condition, ruled out the possibility that his condition had originated from the liver. This, together with the cytochemical findings of the paracentesis, reinforces the hypothesis that the condition had started with acute appendicitis, whose late diagnosis favored the progression to generalized peritonitis and the subsequent pylephlebitis.

The patient progressed to thrombosis and, subsequently, portal hypertension, which led to cavernomatous transformation. Although liver function was preserved at that time, if venous recanalization was not achieved, the patient could have progressed to liver failure.

In the most recent systematic reviews, the most frequent finding is extrahepatic portal vein thrombosis (57%), although thrombosis of the superior mesenteric vein or the right branch of the portal vein has also been described.[4]

The indication for anticoagulation is controversial. However, it is administered to more than 97% of patients, which significantly increases the chances of resolution.[11] Despite this, the number of patients who do not achieve recanalization is still high. In any case, given that few complications associated with anticoagulation have been reported, it is increasingly used in view of the possibility of partial or total resolution of thrombosis. It is administered for an average of 4 months; low molecular weight heparin and warfarin are preferred.[4]

Surgery is indicated for the treatment of the generalized peritonitis that originated the thrombophlebitis or for the drainage of suppurative complications, such as abdominal collections, liver abscesses, among others.[12]

A long-term follow-up of chronic portal hypertension is of utmost importance because it may lead to liver failure, which may require liver transplantation as its most unfavorable outcome. For this reason, it is important for pediatricians to be aware of this condition, because an early diagnosis will offer the possibility of preventing irreversible complications. ■

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