

# Pylephlebitis and liver abscess mimicking hepatocellular carcinoma

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**OBJECTIVE:** To characterize the clinical and radiographic findings in patients with pylephlebitis and liver abscess with an emphasis on the findings that help to differentiate this disorder from portal vein occlusion associated with hepatocellular carcinoma.

**METHODS:** We analyzed the clinical findings and radiographic images of four patients with pylephlebitis and liver abscess(es) who had been misdiagnosed as having hepatocellular carcinoma with portal vein thrombosis. Their medical records were reviewed in terms of clinical presentation, physical findings, laboratory data, treatment, and follow up.

**RESULTS:** All patients undergoing color duplex ultrasonography had an echogenic thrombus within an expanded portal vein with negative color-flow findings within the thrombus. Contrast enhanced CT in all the patients demonstrated portal vein thrombosis associated with "liver masses". An intra-abdominal site of infection responsible for the subsequent ascending infection of the portal vein and liver was not identified in any patient on initial CT scan. At presentation, all patients were febrile and three of them had an elevated white blood cell count as well. All patients showed abnormalities of liver function.

**CONCLUSIONS:** Liver abscess(es) associated with pylephlebitis may mimic hepatocellular carcinoma with portal vein thrombosis. Clinical features that help to distinguish the two entities include presence or absence of fever, elevated white blood cell count, elevated alpha-fetoprotein, cirrhosis, and risk factors for hepatocellular carcinoma.

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**Key words:** pylephlebitis; liver abscess; portal vein thrombosis; hepatoma; hepatocellular carcinoma

## Introduction

Septic thrombophlebitis of the portal vein, or pylephlebitis, typically occurs in the setting of suppurative infection located in a region drained by the portal vein, with a precipitating focus of infection found in up to 68% of patients,<sup>[1]</sup> most commonly diverticulitis. In children, appendicitis is the most common etiological factor.<sup>[2]</sup> Other causes

include regional enteritis, ulcerative colitis, omphalitis, necrotizing pancreatitis,<sup>[3]</sup> and foreign body perforation.<sup>[4]</sup> In the pre-antibiotic era, pylephlebitis secondary to appendicitis was the most common cause of liver abscess.<sup>[2]</sup> Liver abscesses are known to present variable radiographic appearances ranging from well circumscribed cavities with enhancing rims and CT attenuation coefficients near that of water to heterogeneous masses indistinguishable from hepatic neoplasms.<sup>[5,6]</sup> When a mixed attenuation liver abscess is associated with pylephlebitis, the radiographic features may be virtually indistinguishable from those of hepatocellular carcinoma (HCC) with portal vein thrombosis. We encountered four such cases misdiagnosed as HCC, with resultant delay in appropriate therapy. The purpose

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of this report was to present the clinical and radiographic findings that might help to distinguish the two entities.

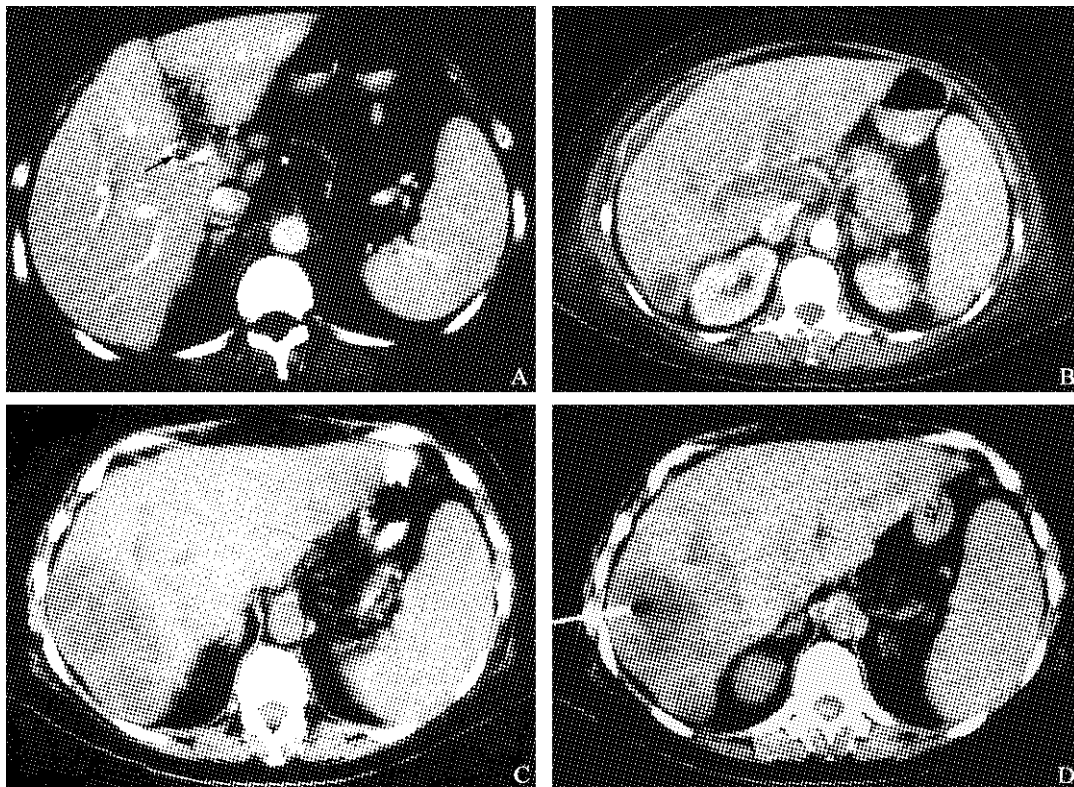
## Methods

Between July of 1995 and September of 1997, four patients were seen at our institution with a presumptive diagnosis of primary hepatic neoplasm associated with portal vein thrombosis, or HCC. The patients (3 women and 1 man) ranged in age from 43 to 73 (mean 54.5 years). They were subsequently shown to have pylephlebitis associated with liver abscess(es) by liver biopsy or drainage, positive blood cultures and virtually complete resolution of clinical and imaging findings in response to appropriate antibiotic therapy. Serial cross-section-

al imaging studies were retrospectively examined in all patients. Medical records were reviewed in term of clinical presentation, physical findings, laboratory data, and results of follow-up GI imaging studies in an attempt to identify a source of infection.

## Results

All patients presented with fever, malaise, and abnormalities of liver function. None of them had clinical or radiographic evidence of cirrhosis, and they were seronegative for hepatitis B and C. Color duplex ultrasound examinations for 3 patients showed an echogenic thrombus in the expanded portal vein and negative color-flow findings in the thrombus. None of the patients demonstrated sonographic findings of cavernous transformation of the portal



**Fig. 1.** 53-year-old woman with pylephlebitis and hepatic abscesses. **A.** Contrast-enhanced CT shows complete left portal vein thrombosis and non-occlusive right portal vein thrombus (arrow). **B.** Follow-up CT scan obtained 4 weeks after **A** shows progression of the thrombosis to involve the right and main portal veins in addition to the left portal vein. There is also a low attenuation lesion in the posterior aspect of the right liver. **C.** Follow-up CT scan 5 weeks after **A** shows interval development of a multiloculated low attenuation lesion in the right liver. **D.** Lesion in the right hepatic lobe was found to be an abscess on CT guided needle aspiration.

vein on their initial examination. In all patients, contrast enhanced CT of the abdomen and pelvis demonstrated portal vein thrombosis and associated "liver masses". In one patient, thrombosis involved only the right portal vein. Hepatic parenchymal abnormalities seen on CT varied from multiple small centimeter and sub-centimeter low-density areas to large, confluent, heterogeneous "masses", which actually represent flow artifacts. In one instance they virtually replaced the right liver. One patient had only sub-centimeter lesions in the lateral segment of the left liver and left portal thrombosis with a non-occlusive thrombus in the right portal vein (Fig. 1A) when she was treated elsewhere. By the time we saw her, the thrombus had extended to involve the main, right and left portal veins, and she had developed large, confluent lesions in the right liver (Figs. 1B, 1C). Needle aspiration of this right-sided lesion (Fig. 1D) yielded gram positive cocci. Initial CT showed nothing indicative of a site of intra-abdominal infection that could be implicated as a source of ascending infection in any of the patients. One patient with no obvious site of ascending infection at presentation was subsequently found to have a "micro-perforation" of a sigmoid diverticulum on a fol-



Fig. 2. 73-year-old woman with "micro-perforated" sigmoid diverticulum (curved arrow) consistent with focal sigmoid diverticulitis identified on follow-up double contrast barium enema.

low-up air contrast barium enema (Fig. 2), and another patient developed a peri-duodenal inflammatory mass at the site of foreign body perforation that was also discovered later.

At the time of presentation an elevated white blood cell count (WBC) was present in 3 patients, with a mean WBC count of  $14.8/\text{mm}^3$  (range 8.9 to  $21.8/\text{mm}^3$ ). Liver function tests were abnormal in all of the patients, especially the levels of direct bilirubin (range 5.13–73.53  $\mu\text{mol/L}$ , mean 29.07  $\mu\text{mol/L}$ ) and alkaline phosphatase (range 116–666 U/L, mean 372 U/L). None of the patients were coagulopathic, although 3 patients were hy-

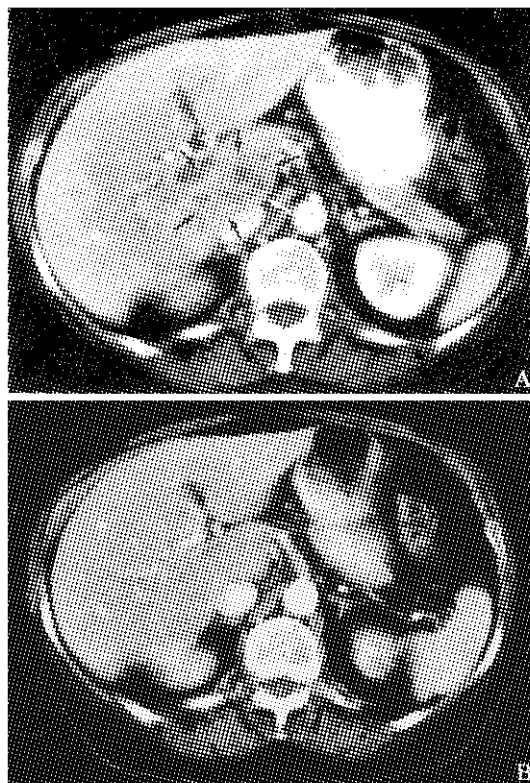


Fig. 3. 73-year-old woman with pylephlebitis and hepatic abscesses. A. Contrast-enhanced CT scan shows multiple low-density lesions in the caudate lobe of the liver (short arrows) and a heterogeneous enhancement pattern throughout most of the liver. Upon fine needle aspiration, these collections were found to be hepatic abscesses. B. Follow-up CT scan at approximately the same level as A obtained 3 weeks later shows interval complete resolution of the hepatic parenchymal abnormalities following treatment.

poalbuminemic.

All patients were treated with intravenous antibiotics and one also received anticoagulation therapy. Two patients underwent image-guided catheter drainage of large hepatic abscesses, and one patient also required surgical drainage and debridement. All patients recovered uneventfully, albeit slowly, with near complete resolution of hepatic parenchymal abnormalities (Figs. 3A and 3B). All four patients progressed to changes of cavernous transformation of the portal vein.

## Discussion

Although pylephlebitis was uniformly fatal in the pre-antibiotic era, the morbidity and mortality are still thought to be high. Saxena et al<sup>[7]</sup> reported a mortality of 70% in an outcome review from 1996 and Plemmons et al<sup>[11]</sup> a mortality of 32% in a review of 18 patients from 1995. In contrast, Lim et al<sup>[6]</sup> reported no mortality in 7 patients seen at their institution. Plemmons and Saxena found a significant association between the presence of "severe sepsis" and subsequent death in the cases reviewed, although it should be noted that 5 patients with severe sepsis reviewed by Plemmons were also included in the review by Saxena. Although all of the patients discussed by Lim et al<sup>[6]</sup> had either a pyogenic liver abscess or systemic bacteremia, no mention was made of the presence of severe sepsis, and it is likely that these patients were diagnosed earlier in their disease process.

Given the high mortality associated with advanced pylephlebitis, early diagnosis is essential and is often facilitated by the utilization of imaging modalities such as CT, MR and color Doppler ultrasonography. Characteristic CT findings of pylephlebitis include the presence of gas (early) or thrombus (later) within the portal vein, associated with an infectious or inflammatory intra-abdominal focus (i. e. diverticulitis, appendicitis) responsible for pylephlebitis. If treatment is delayed, diminished portal vein blood flow may lead to low attenuation lesions within the liver that may liquify, resulting in hepatic abscess(es).<sup>[8]</sup> These individual findings can be seen in several other pathologic

conditions not associated with pylephlebitis, thus it is essential that radiographic findings be utilized in conjunction with clinical features in arriving at a diagnosis. Findings on color Doppler ultrasonography include identification of echogenic thrombus within the lumen of the portal vein, with lack of flow by color Doppler. Later, cavernous transformation of the portal vein with collateral formation may develop.<sup>[9]</sup> Magnetic resonance imaging has also been shown to be a valuable tool for imaging this disease process. Portal vein thrombus less than 5 weeks old appears hyperintense on both T1 and T2 weighted images, while older thrombus is hyperintense only on T2 weighted images.<sup>[10]</sup> In addition, on gadolinium enhanced scans the portal vein thrombus does not enhance in pylephlebitis, as would be the case with tumor thrombus. Liver abscesses tend to have more surrounding edema on the T2 weighted sequences than would be expected with HCC.

While the availability of sophisticated cross-sectional imaging studies such as CT, MR and color duplex ultrasound makes earlier diagnosis possible, it is this ability to image that may lead to error in diagnosis. Patients may be imaged at a stage in their disease where the clinical picture is evolving, making them more vulnerable to an errant diagnosis based on imaging findings alone. It is also possible that, given the liberal use of oral antibiotics by some practitioners, patients may be incompletely treated early in the disease process, leading to a clinical form fruste of the disease, again making them more vulnerable to an error in diagnosis based on later imaging findings.

The diagnosis of pylephlebitis can be challenging because the clinical signs and symptoms may be nonspecific, and the individual radiographic features described above are not pathognomonic. Seen at only one point in time, the imaging findings in pylephlebitis with hepatic abscess may be very similar to portal vein occlusion related to tumor in-growth from HCC. The fact that no causative intra-abdominal process was identified on the initial CT in any of our patients, combined with imaging findings frequently seen in HCC with portal vein occlusion, predisposed to the initial error in diagnosis. When serial scans are available and

very rapid progression of the imaging findings is noted, with extension of portal vein thrombus, enlargement of liver lesions, and/or development of new lesions over a brief interval (Figs. 1A, 1B and 1C), one should favor a diagnosis of infection. In addition, the absence of "flow" within the portal vein thrombus, as demonstrated by color duplex ultrasound or gadolinium enhanced MRI, is more characteristic of "bland thrombus" rather than tumor thrombus and, again, would favor the diagnosis of infection. The most important clinical features helping to differentiate the two entities are the relatively acute onset of illness, the presence of fever, although perhaps low grade, and an elevated WBC. The absence of risk factors for the development of HCC, including being seronegative for hepatitis B and C without imaging findings of cirrhosis and having a normal serum alpha-fetoprotein, would also argue against a diagnosis of HCC.

Knowledge of the characteristic clinical and radiographic features of pylephlebitis may lead to earlier diagnosis and treatment, potentially decreasing the high morbidity that has been reported in the literature.

### Competing interest

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

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