

CASE REPORTS

A Multiple Choice Answer?

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Disclosure: None of the authors have any conflicts of interest associated with the work presented in this manuscript. Authorship: All authors had access to the data and played a role in writing this manuscript. Originality: The work represented in this manuscript is original, and the submission is not under review by any other publication.

KEYWORDS: abscess, fusobacterium, liver, pyogenic.

A 49-year-old man with a history of hypertension presented to our hospital with a 2-week history of sharp pain in the right upper abdomen and right lower chest radiating to the back. The patient reported a few days of fevers, chills, drenching night sweats, shortness of breath, malaise, and fatigue. He denied recent travel. Vital signs were temperature 38.4°C, blood pressure 119/74 mmHg, heart rate 95 beats/minutes, respiratory rate 16 breaths/minutes, and oxygen saturation 96% on 5 L nasal cannula. Physical examination revealed poor dentition, right upper abdominal quadrant tenderness, and dullness to percussion over the right lung base.

Initial labs showed white blood count (WBC) 22,540/mm³, alkaline phosphatase 280 units/L, bilirubin 1.1 mg/dL, aspartate aminotransferase (AST) 28 units/L, alanine aminotransferase (ALT) 33 units/L. Blood cultures were negative. An human immunodeficiency virus (HIV)1/HIV2 antibody screen was negative. Computed tomography (CT) of the chest demonstrated a large cystic lesion in the diaphragmatic dome of the liver with multiple lesions in the right lobe of the liver. Elevation of the right hemidiaphragm and moderate right pleural effusion were noted. CT abdomen showed multiple areas of fluid collection within the liver suspicious for liver abscesses (see Figure 1). Multiple gallstones were seen within gallbladder with a large stone in the region of the gallbladder neck vs. cystic duct without evidence of extrahepatic biliary dilatation. There was mild distention of the appendix with minimal soft tissue stranding.

The patient underwent ultrasound-guided drainage of the largest liver abscess. Cultures from the aspiration grew *Fusobacterium nucleatum*. The patient's stool studies for ova and parasites were negative. The patient was started on piperacillin/tazobactam and metronidazole, then switched to ertapenem. A hepatobiliary iminodiacetic acid (HIDA) scan confirmed cholecystitis, and the patient underwent open cholecystectomy. Pathology on the gallbladder returned as chronic cholecystitis with cholelithiasis. A full dental examination revealed possible periapical abscesses of teeth #12 and #30 and stringent daily oral hygiene was recommended. Tooth extraction was initially recommended but ultimately postponed. Plans were made for dental follow-up.

With continued antibiotic treatment, the patient's fevers resolved and leukocytosis improved. A follow-up CT abdomen/pelvis obtained on hospital day 10 showed a reduction in size of the multiple liver abscesses. There was also increased prominence of the appendix with mild stranding. The patient was taken for appendectomy. Pathology was consistent with acute appendicitis with focal fat necrosis. The patient was ultimately discharged with the plan being to continue ertapenem until radiographic resolution of all the abscesses was demonstrated.

Discussion

Pyogenic liver abscesses are infrequently encountered in the western population, but when present, result in significant morbidity and mortality.¹ Mortality rates range from 6% to 31%, decreased from 100% mortality in the preantibiotic era.¹ The leading cause of pyogenic liver abscesses has been in the past ascribed to ruptured appendicitis.² However, biliary tract pathology is now the leading cause, accounting for 43% to 60% of cases.² In addition, hematogenous seeding of infection from the oral cavity has been recognized in the literature as a potential source of infection in the development of pyogenic liver abscesses.²

The empiric treatment of pyogenic liver abscesses is intravenous broad-spectrum antibiotics, most commonly metronidazole in combination with quinolones, aminoglycosides, third generation cephalosporins, carbapenems, piperacillin/tazobactam, ampicillin-sulbactam, or amoxicillin/clavulanate.¹ The optimal treatment course is controversial but suggested to include 2 weeks to 3 weeks of intravenous antibiotics followed by at least 3 weeks to 4 weeks of oral antibiotics.¹

According to a study of 84 patients hospitalized with pyogenic liver abscesses of which 70 cases were cultured, the most typical organisms isolated from liver abscesses are *Streptococcus* spp. (40.5%), *Escherichia coli* (27.4%), *Klebsiella* spp. (14.3%), and anaerobic organisms (17.9%).¹ The anaerobic Gram-negative bacterium *Fusobacterium nucleatum*, known to play a role in periodontal disease, is an uncommon cause of liver abscesses: a review of the literature revealed only 14 cases of liver abscesses caused by *Fusobacterium nucleatum*, five cases of which occurred in



FIGURE 1. CT image of the abdomen showing multiple areas of fluid collection within the F1 liver, suspicious for liver abscesses. Abbreviation: CT, computed tomography.

patients with known immunodeficiency, and a retrospective study of 70 cases of liver abscesses revealed only 2 cases linked to this bacterium.^{1,2} Though accounting for a minority of cases of pyogenic liver abscesses, it is commonly cited as a cause of liver abscesses resulting from spread of infection from the oral cavity. Four case reports have implicated severe dental disease or recent dental work in the development of pyogenic liver abscesses involving *Fusobacterium nucleatum*.² For example, a literature search revealed a case report of a patient with a liver abscess due to *Fusobacterium nucleatum* resulting from hematogenous spread of infection from the oral cavity.²

Although *Fusobacterium* has rarely been reported in biliary culture from patients with cholangitis or gangrenous cholecystitis,³ this organism has been identified as a causative organism in appendicitis. In two separate studies of 41 children with appendicitis and 30 patients older than 12 years with gangrenous or perforated appendicitis, *Fusobacterium nucleatum* or *Fusobacterium* spp. were isolated in 44% and 33% of cases, respectively.^{4,5} Nevertheless, the

mechanism of appendicitis causing liver abscesses is thought to be by direct spread via the peritoneum after perforation.² Thus, despite the isolation of this bacterium from appendectomy specimens, appendicitis is less likely the source of infection in this patient given that there is no evidence that appendiceal perforation occurred in this case.

Our patient was found to have dental abscesses, cholecystitis requiring cholecystectomy, and appendicitis requiring appendectomy—all of which, to varying degrees, were plausible sources of infection by virtue of their known role in the development of pyogenic liver abscesses. Although periodontal disease was the likely source of *Fusobacterium nucleatum* infection, we could not exclude the leading causes of pyogenic liver abscesses, appendicitis and/or biliary tract disease. As a result, the patient underwent 2 surgeries and was counseled to maintain good oral hygiene in order to eliminate all persisting sources of infection.

This was an unusual case in which the question “What is the source of infection?” appears to have had multiple correct answers. We theorize that leaving any 1 of the 3 possible sources of infection in place could have led to treatment failure. This patient is a humbling reminder that not every clinical problem will have one clear solution. In such cases, all possible underlying conditions need to be managed appropriately to achieve the desired outcome.

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References

1. Ruiz-Hernandez JJ, Leon-Mazorra M, Conde-Martel A, Marchena-Gomez J, Hemmersbach-Miller M, Betancor-Leon P. Pyogenic liver abscesses: mortality-related factors. *Eur J Gastroenterol Hepatol.* 2007;19:853–858.
2. Kajiya T, Uemura T, Kajiya M, et al. Pyogenic liver abscess related to dental disease in an immunocompetent host. *Intern Med.* 2008;47:675–678.
3. Marne C, Pallares R, Martin R, Sitges-Serra A. Gangrenous cholecystitis and acute cholangitis associated with anaerobic bacteria in bile. *Eur J Clin Microbiol.* 1986;5:35–39.
4. Rautio MM, Saxen H, Siitonen A, Nikku R, Jousimies-Somer H. Bacteriology of histopathologically defined appendicitis in children. *Ped Infect Dis J.* 2000;19:1078–1083.
5. Bennion RS, Baron EJ, Thompson JE Jr, et al. The bacteriology of gangrenous and perforated appendicitis—revisited. *Ann Surg.* 1990;211:165–171.