CASE REPORT

Pyogenic Liver Abscess and Gastrointestinal Lemierre Syndrome due to *Fusobacterium nucleatum*

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Abstract

Pyogenic liver abscess (PLA) affects men disproportionately to women and is occurring with increasing incidence. The mortality associated with PLA nears 15% in the Western world. PLA constitutes a significant number of total liver abscesses and can rarely be caused by the gram-negative bacilli, *Fusobacterium*. Virulent strains of *Fusobacterium* have been described as a rare cause of thrombophlebitis and metastatic abscesses. *Fusobacterium necrophorum* is specifically implicated in the development of Lemierre syndrome (LS) which comprises periodontal abscess and internal jugular vein thrombosis. Similar infection involving intra-abdominal abscess and abdominal vessel thrombosis suggests a gastrointestinal (GI) variant of LS. We describe a case of liver abscesses and hepatic vein septic thrombosis due to *Fusobacterium nucleatum* in a healthy adult male patient without significant risk factors.

Keywords: *Fusobacterium nucleatum*, pyogenic liver abscess, Lemierre syndrome, septic thrombosis, hepatic vein thrombosis

INTRODUCTION

PLA accounts for approximately 13% of all intra-abdominal abscesses, with the majority occurring in the right lobe. Propensity for the right lobe is thought to be due to its larger size and more robust blood supply as compared to other liver segments[1]. PLA is most commonly caused by bacterial infection. Although uncommon in North America, it is known to cause significant morbidity and mortality[2,3]. *Fusobacterium nucleatum* is a rare cause of PLA. It has also been implicated in LS, which involves the progression of a tonsillar abscess to internal jugular vein septic thrombosis, though *F. necrophorum* is the most commonly identified pathogen[4,5]. The similarities between classic LS and a comparable liver infection, where liver abscess progresses to hepatic vessel septic thrombosis, has led some to consider this a GI variant of the syndrome. Rare case reports have shown a relationship between *Fusobacterium nucleatum* and this GI variant of LS involving hepatic abscess and occasional hepatic vessel thrombosis[5,6,7].

According to a review from 2016, *F. nucleatum* had been implicated in less than a dozen case reports of GI-variant LS involving portal vein thrombosis, and hepatic vein thrombosis was considered an even greater rarity[5]. The following details a case of PLA and hepatic vein thrombosis caused by *Fusobacterium nucleatum* in a young, immunocompetent patient.

CASE PRESENTATION

A 27-year-old previously healthy Caucasian male initially presented to the emergency department (ED) with the chief concern of daily high-grade fever and right sided, pleuritic chest pain for four days. Chest pain was persistent, and the fever was responsive to ibuprofen and acetaminophen.

The patient was a former smoker for seven years but had quit one year prior to presentation. He consumed alcohol socially and denied intravenous (IV) drug use. The patient had traveled to Las Vegas one month prior to presentation but denied ever traveling outside of the United States. No pet or animal exposures were reported. He was in a monogamous sexual relationship with a female for the last seven years and denied a history of same sex intercourse. The patient had never been incarcerated or homeless. He denied past medical or surgical history, and his medications included only ibuprofen and acetaminophen as needed for his ongoing illness.

Upon initial presentation, physical exam revealed only tachycardia with a heart rate of 120 beats per minute. Electrocardiogram showed sinus tachycardia. Complete blood count (CBC) revealed mild leukocytosis with left shift. Chest x-ray (CXR) was negative. Computed tomography (CT) of the chest revealed minimal bibasilar atelectasis without filling defects, pneumothorax, pleural effusion, consolidation, or lymphadenopathy. Atypical presentation of a viral syndrome was considered the most likely diagnosis, and he was given IV fluids and ketorolac with improvement in his symptoms. The patient was discharged home and instructed to return to the ED upon worsening of symptoms.

He returned to the ED several weeks later and reported persistent fever with night sweats and chills as well as occasional headaches, fever and dry cough. He stated that his chest pain had gradually changed into right upper quadrant (RUQ) pain with a constant dull ache.

Associated symptoms included malaise, poor appetite, and a five-pound unintentional weight loss. Physical examination revealed tachycardia with a heart rate 119 beats per minute, fever of 101 degrees Fahrenheit, and mild RUQ tenderness. The remainder of his examination was normal including the oral cavity. Laboratory evaluation revealed leukocytosis with white blood cell count of 21,400 cells/mm^3 with 86% neutrophils, anemia with hemoglobin 10.6 g/dL and hematocrit 31%, thrombocytosis with 697 platelets per mcL, elevated erythrocyte sedimentation rate of 75, mild transaminitis with alanine aminotransferase of 57 IU/L and aspartate transaminase of 54 IU/L, elevated alkaline phosphatase of 281 IU/L, and a normal total bilirubin of 0.4 mg/dL.

Based on his clinical presentation, a repeat CXR was performed and revealed right lower lung atelectasis and a small right-sided pleural effusion. The patient was started on IV ceftriaxone and azithromycin with concern for community acquired pneumonia. Chest CT revealed no acute findings of infection in the lungs. However, multiple hypodense lesions with irregular borders were noted in the right hepatic lobe. The largest and most superior of these measured approximately 3.3 x 3.0 cm. The remainder of the visualized portions of the upper abdomen were unremarkable.

Magnetic resonance imaging (MRI) of the abdomen revealed four cystic lesions consistent with abscesses in the right hepatic lobe (Figure 1). The lesions demonstrated enhancement of a somewhat thickened rim with no enhancement of the central lesions. The largest cystic lesion measured 6.4 x 5.6 x 5.2 cm. A thrombus was noted within the right hepatic vein, completely occluding the vessel, as well as a filling defect in the middle hepatic vein which remained patent. No significant intrahepatic or extrahepatic ductal dilation was noted.

Hepatitis testing, HIV serology, and blood cultures were all negative, as was hypercoagulability workup. A CT-guided percutaneous biopsy and drainage of the liver lesions was performed. The fluid aspirated was purulent, and three drains were left in place after the procedure. Culture revealed *Fusobacterium nucleatum* isolated from three of four abscess fluid cultures.

Once culture results were available, the patient was switched to IV piperacillin/tazobactam and started on anticoagulation. He improved clinically with resolution of fever and leukocytosis and the drains were eventually removed. He was discharged with six weeks of oral amoxicillin/clavulanic acid as well as warfarin with close follow-up and imaging.

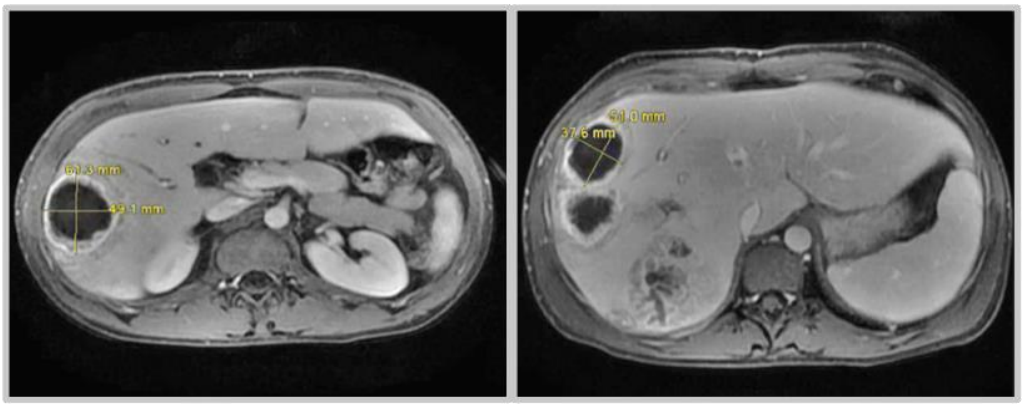

Figure 1. MRI of the abdomen showing pyogenic right-sided liver abscesses with rim enhancement.

DISCUSSION

The pathogenesis of liver abscesses is broad and includes infection after ischemic episodes, bacterial translocation via the portal vein, septic emboli, hematogenous spread from distant sites of infection, post-traumatic or post-surgical infection, parasitic exposure, malignancy, and foreign bodies[3]. Infectious liver abscesses can be separated into two primary groupings based on the type of pathogen involved – pyogenic and amebic. Amebic liver abscesses result primarily from infection with *Entamoeba histolytica*, which can occur if mature cysts are ingested via contaminated food or water[8]. The majority of PLA are the result of bacterial infection with positive cultures identifying a pathogen more than 90 percent of the time[9]. The differential diagnosis for PLA may include other infections such as hepatosplenic candidiasis, bacillary peliosis hepatis, and extrapulmonary tuberculosis, among others[10].

The incidence of PLA in the United States according to the Nationwide Inpatient Sample between 1994 and 2005 was 3.6 per 100,000 population[11]. A study reviewing

cases of PLA in Minnesota between 1980 and 2014 demonstrated an increasing incidence of the disease, hypothesizing that increased hepatobiliary interventions and multidrug resistant organisms were to blame[12]. The most common causal organisms are *Streptococcus* species and *E. coli*, as well as *Klebsiella*, *Proteus*, *Staphylococcus* and polymicrobial infections involving anaerobes[1,9]. General risk factors for liver abscess, including malignancy, dialysis, and advanced age, occur at a lower frequency in *Fusobacterium* infection. This was demonstrated in a review of Fusobacterial PLA, with the majority of cases occurring in immunocompetent young to middle-aged adults. These patients lacked the general risk factors outlined above but instead had other potential risk factors for hematogenous spread including periodontal disease or recent pharyngitis[13]. A retrospective analysis of PLA in Taiwan demonstrated an age range of 19 to 89 years with mean age of 57.6, indicating an increased risk for PLA in adults versus children[14]. The clinical manifestations of the disease can be broad, but fever and RUQ abdominal pain are seen in the majority of patients[10].

The *Fusobacterium* genus consists of at least 13 facultatively anaerobic gram-negative bacilli, with *F. nucleatum* and *F. necrophorum* being the type species of the group. They are often found as a component of normal GI, genital, and oral flora[4,15]. However, if isolated, these organisms should be treated as pathogenic. Infections caused by Fusobacteriaceae are known to affect multiple body systems including the head, neck, GI tract, and the female genitourinary system, and infections can range from mild to severe[16]. Despite this, *Fusobacterium* species are rarely isolated in clinical practice and are an extremely rare cause of PLA[6]. *F. necrophorum* has been associated with LS, which presents with history of recent oropharyngeal infection and internal jugular vein thrombosis[4]. According to the reviewed literature, *Fusobacterium necrophorum* contributes to less than 1% of bacteremia cases caused by non-spore-forming anaerobes, highlighting its rare isolation in human disease in general[17]. There have also been cases linking *Fusobacterium* to hepatic abscess and portal vein or, more rarely, hepatic vein thrombosis, lending to the recognition of a GI variant of LS.

The ability of pathogenic *Fusobacterium* species to produce thrombophlebitis and metastatic abscesses is well-described[17]. Studies have demonstrated their ability to activate the intrinsic pathway of coagulation via the human Hageman factor (factor XII)[18], cause platelet aggregation[19], and display hemagglutination activity on human erythrocytes[20]. Virulence factors of *F. nucleatum* allow for host immune-modulation and survival in unfavorable conditions[21].

Treatment of PLA due to *Fusobacterium nucleatum* with antimicrobial therapy in conjunction with drainage of identified abscesses is generally favorable[6]. *Fusobacterium* species are usually susceptible to amoxicillin, clindamycin, and metronidazole, with variable sensitivity to second and third generation cephalosporins[13,22]. If beta-lactams are chosen, beta-lactam plus beta lactamase inhibitors are preferred due to rising incidence of beta lactamase production[22,23,24]. The duration of antibiotic treatment is typically 4-6 weeks, depending upon resolution of abscesses, specifically in patients with multiple abscesses[9]. However, prolonged antimicrobial therapy may be indicated in patients with risk factors for treatment failure including, but not limited to, older age, septic shock at presentation, and anemia[13]. Thrombus resistance to antimicrobial penetration in the GI variant of LS may delay treatment response. Therefore,

a prolonged antimicrobial regimen is often necessary[25].

The role of anticoagulation in the treatment of LS remains unclear, and therefore, use of anticoagulant therapy in treating the GI variant is similarly based on the discretion of the provider. Studies have indicated no significant differences between groups who receive prophylactic or therapeutic anticoagulation therapy and those who do not[26]. However, other studies have demonstrated a high occurrence of new thromboembolic complications and recurrent LS even in hospitalized patients[27], and anticoagulation remains an important part of treatment for many clinicians[26].

In summary, Fusobacterial PLA and associated GI-variant LS are rarely diagnosed, and index of suspicion for septic thrombosis should remain high in these cases. Treatment is multimodal including appropriate antimicrobial therapy, drainage of abscesses, and the consideration of anticoagulation.

Notes

Potential conflicts of interest: The author reports no conflicts of interest in this work.

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