

# Denture-Associated Oral Microbiome and Periodontal Disease Causing an Anaerobic Pyogenic Liver Abscess in an Immunocompetent Patient: A Case report and Review of the Literature

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## Abstract

Pyogenic liver abscesses (PLA) develop from the spread of infection through the portal circulation, biliary infections or arterial hematogenous seeding in the setting of systemic infections. PLA are often poly-microbial and are uncommonly reported to be due to anaerobic species. We report the case of a previously healthy, immunocompetent 63-year-old man with hepatic abscesses as a result of *Fusobacterium nucleatum* periodontal disease. In addition, a systemic review of the literature is performed. *Fusobacterium* is a very rare cause of PLA in immunocompetent hosts with only a handful of cases reported in the literature. Although anaerobic infections such as *Fusobacterium* most often occur in immunocompromised individuals, clinicians should have a high index of suspicion in immunocompetent patients with periodontal disease or chronic stomatitis.

**Keywords:** Pyogenic; Anaerobe; Liver abscess; *Fusobacterium nucleatum*; Denture; Periodontitis

## Introduction

Pyogenic liver abscesses (PLA) most commonly develop fol-

lowing peritonitis due to intra-abdominal bowel leakage with subsequent spread to the liver through the portal circulation [1] or via direct spread from biliary infections [2, 3]. They may also result from arterial hematogenous seeding in the setting of systemic infections, such as in cases of endocarditis or septic thrombophlebitis [4]. PLA are often poly-microbial and are uncommonly reported to be due to anaerobic species [5, 6]. We report the case of an otherwise healthy immunocompetent patient who developed multiple hepatic abscesses caused by *Fusobacterium nucleatum*. Additionally, we review and summarize the literature on PLA.

## Case Report

A 63-year-old healthy African-American male presented with a 4-day history of food aversion, subjective fevers, chills, chest and abdominal pain. His past medical history was significant for remote history of tobacco and cocaine use and was negative for diabetes mellitus or other medical illnesses. He was not on any prescription or over-the-counter medications. On presentation, he was found to have a fever of 38.3°C, but he was hemodynamically stable. A detailed physical exam was noted for poor dentition but otherwise was unremarkable. Laboratory testing revealed a white cell count of  $22.4 \times 10^9/L$ , aspartate aminotransferase of 93 units/L, alanine aminotransferase of 110 units/L and total bilirubin of 1.2 mg/dL. Contrast computed tomography of the chest, abdomen and pelvis revealed multiple indeterminate hypo-attenuating lesions throughout the liver (Fig. 1). Further imaging with an abdominal sonogram identified multiple complex hypoechoic foci throughout the liver. Magnetic resonance imaging of the abdomen demonstrated multiple cystic lesions with enhancing internal septations and marked diffusion restriction. The largest lesion measured 4.5 cm × 4.1 cm × 3.8 cm (Fig. 2).

Empiric treatment with broad-spectrum antibiotics was initiated on hospitalization day 1 and resulted in immediate resolution of his fever. Successful aspiration from one of the abscess cavities and placement of three drainage catheters in the right hepatic lobe was achieved by interventional radiology. Drainage from the hepatic abscess grew *Fusobacterium nucleatum*, and antibiotics were narrowed based on culture

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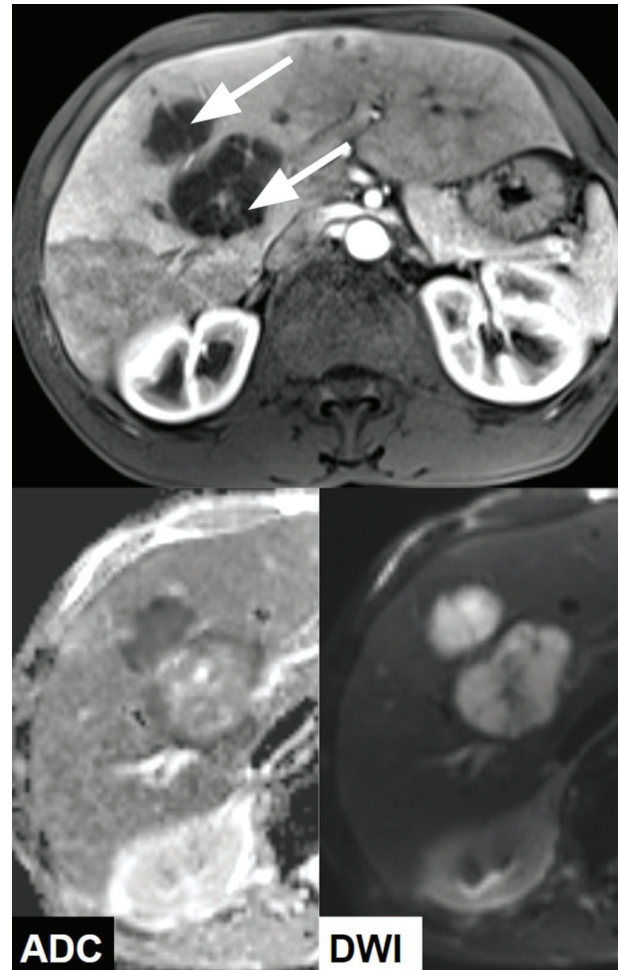
**Figure 1.** CT with contrast showing multiple hypoattenuating lesions in the liver (dashed line).

and sensitivities. The liver aspirate testing for acid-fast organisms, aerobic and fungal cultures was negative. Stool cultures and examination for ova, parasites, giardia, cryptosporidium, clostridium difficile and entamoeba were all negative. Further infectious disease evaluation was unremarkable, including negative blood and urine cultures, and testing for viral hepatitis and human immunodeficiency virus was negative. Furthermore, tumor markers for alpha-fetoprotein, cancer antigen 19-9 and carcinoembryonic antigen were unremarkable. A trans-thoracic echocardiogram revealed no evidence of valvular vegetations to suggest endocarditis. Furthermore, endoscopic evaluation by colonoscopy revealed two 4 - 8 mm adenomatous polyps in the rectum and mild diverticulosis in the sigmoid colon but without evidence of prior or current inflammation or infection. Finally, a panorex demonstrated multiple missing teeth and lucency around the root of a left mandibular premolar, likely representing a periapical abscess (Fig. 3).

Output from the hepatic drains continued to decrease, and the drains were eventually removed on hospitalization day 14. Affected teeth were extracted prior to discharge, and antibiotics were transitioned to an oral route. He was discharged home after a 4-week hospitalization. At 6 weeks post-hospitalization follow-up, he remained asymptomatic and liver enzymes trended down to normal levels. Clinically significant labs with changes are shown in Table 1. Repeat cross-sectional imaging demonstrated a significant interval decrease in rim enhancement and size of the known liver abscesses, compatible with treatment response (Fig. 4).

## Discussion

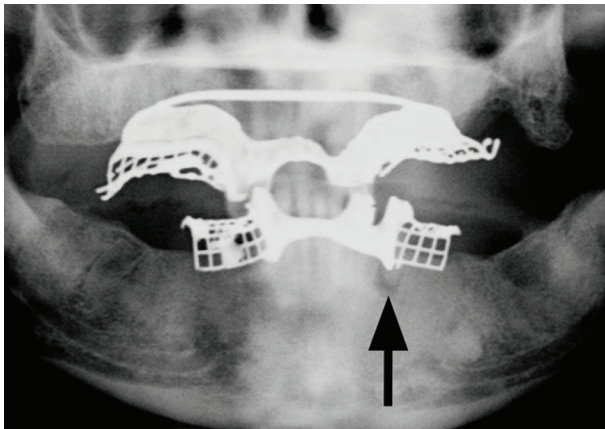
PLA account for nearly 50% of visceral abscess cases in the USA [7]. To date, the largest population-based study on PLA in the USA estimated the annual incidence of PLA at 3.6 cases per 100,000 population, with predominance among men and the elderly [5]. However, there is significant geographic variation globally, as demonstrated by the much higher incidence



**Figure 2.** MRI with contrast demonstrating multiple hepatic cystic lesions with enhancing septa (arrows) and marked diffusion restriction (lesions are hypointense on apparent diffusion coefficient (ADC) and hyperintense on diffusion-weighted imaging (DWI) compatible with abscess).

reported in Taiwan of up to 17.6 per 100,000 individuals [8]. In addition, there is also variation among different disease groups. According to research published by Clinical Infectious Disease (CID) in 2007, individuals with diabetes are at 3.6 times greater risk for PLA [9]. In a retrospective review completed by CID in 2004, out of 79 cases of PLA, 43% of patients had underlying biliary disease [1].

The most common clinical presentation of PLA includes fever, chills, malaise and right upper abdominal pain. The patient in our case presented with shortness of breath and chest pain, which may be attributed to diaphragmatic irritation from liver enlargement. Physical examination findings often include right upper quadrant abdominal tenderness, jaundice and hepatomegaly. In our case, the patient's physical exam was relatively benign with exception of fever and poor dentition. With PLA, common laboratory abnormalities include (in order of prevalence): hypoalbuminemia, elevated  $\gamma$ -glutamyltransferase, elevated alkaline phosphatase level and leukocytosis [6, 10], all of which were observed in our case (Table 2). Approximately half of patients will have elevated aspartate and alanine ami-



**Figure 3.** Panorex demonstrating multiple missing teeth with lucency around the root of a left mandibular premolar (arrow), likely representing a periapical abscess.

nottransferases, elevated total bilirubin levels, normocytic anemia and hyponatremia [6]. Blood cultures are only positive in 30-60% of cases, but organisms are isolated from the majority (70-80%) of abscess aspirates [6, 11].

Meddings et al conducted a study reviewing nearly 18,000 cases of PLA in the USA and found that the most commonly recorded bacterial infections were due to *Streptococcus species* (29.5%) and *Escherichia coli* (18.1%) [5]. In contrast, anaerobic species were uncommon (8.6%), but were likely underreported because of their difficulty to culture. Kaplan et al conducted a population-based surveillance study in the Calgary Health Region and determined that 49% of PLA infections were polymicrobial. The most commonly identified organisms were *Streptococcus milleri* group (44%), *Klebsiella species* (27%) and anaerobes (20%). The anaerobes included *Clostridium perfringens* (4%), *Bacteroides species* (4%), *Pep-*to*streptococcus species* (3%), *Fusobacterium necrophorum* (3%), *Actinomyces species* (1%), *Prevotella species* (1%), *Lactobacillus* (1%) and *Veillonella* (1%) [7]. Amebic abscesses account for the minority of hepatic abscesses in the United States but should be considered in patients with recent travel to an endemic area. Interestingly, in Asian populations, *Klebsiella pneumoniae* has been identified as the most common cause of PLA [1, 12].

Percutaneous drainage, along with targeted antimicrobial therapy, is the mainstay of treatment. Implications for surgi-

**Table 1.** Laboratory Data: Hospitalization Days 1, 28 and 64

Test (normal range)	Day 1	Day 28	Day 64
WBC (3.5 × 10 <sup>3</sup> - 10.5 × 10 <sup>3</sup> /μL)	28.5	7.6	5.4
Albumin (3.4 - 5 g/dL)	2.7	2.9	3.2
ALT (0 - 55 units/L)	117	29	17
AST (5 - 34 units/L)	88	28	20
ALP (40 - 150 units/L)	179	182	87
Total bilirubin (0.2 - 1.2 mg/dL)	1.6	0.4	0.4

WBC, white blood cell; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase.



**Figure 4.** CT with contrast showing interval decrease in rim enhancing fluid collections at 10 weeks (dashed line).

cal drainage include abscess rupture, incomplete percutaneous drainage, multi-loculated abscesses and inadequate clinical response 4 - 7 days after percutaneous drainage. Recommended antibiotic treatment includes parenteral therapy for 2 - 3 weeks followed by oral therapy for 2 - 6 weeks or until clinical, laboratory and radiographic studies show resolution of the abscess [13]. The overall mortality rate associated with PLA has improved significantly since 1980, from greater than 50% to 10% in developed countries. Independent risk factors for mortality include the need for open surgical drainage, the presence of anaerobic infection, bacteremia or septicemia, and comorbidities such as advanced age, cirrhosis, chronic renal failure and malignancy [5].

The periodontium, also called alveolodental membrane or periodental membrane, is the tissue that surrounds and supports the teeth in the maxillary and mandibular bones, including the gingiva, cementum, periodontal ligament, and alveolar and supporting bone [14]. Periodontitis is defined as inflammation of the periodontium caused by bacteria that infect the roots of the teeth and surrounding gum crevices, producing bleeding, pus formation, and gradual loss of bone and tissue that support the teeth [15]. Dentures are an artificial replacement of one or several of the teeth (partial denture) or all of the teeth (full denture) of either or both jaws [16]. Recent developments in the field of microbiology have isolated the main microorganisms involved in the etiology of periodontitis. These are mainly Gram-negative species including: *Aggregatibacter actinomycetemcomitans*, *Tannerella forsythia*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Campylobacter rectus*, *Treponema denticola* and *Fusobacterium nucleatum*. Virulence factors produced by these microorganisms have been identified, and their role in periodontal destruction is well established [17].

*Fusobacterium* is an anaerobic, Gram-negative, invasive, adherent, non-motile, non-spore forming, pro-inflammatory, spindle-shaped rod. *Fusobacterium nucleatum* and *Fusobacterium necrophorum* are the most common species of *Fusobacterium* responsible for human infection. *Fusobacterium nucleatum* is indigenous to the human oral flora and plays a

**Table 2.** Case Reports of Immunocompetent Patients With Pyogenic Liver Abscess Caused by *Fusobacterium*

Age (years old) Sex	Presentation	Imaging	Associated infection	Organisms	Treatment	Prognosis
Crippin et al 1992 [3]	69 M 3-week history of fever and malaise	CT	Dental disease, molar abscess	<i>Fusobacterium nucleatum</i>	Percutaneous drainage and IV antibiotics for unknown duration. Dental surgery following hospitalization	No recurrence in 72 months of follow-up
Memain et al 2001 [21]	24 F 3 months of diarrhea and fevers	US & CT	Tonsil infection, sepsis	<i>Fusobacterium nucleatum</i>	Metronidazole and fluoroquinolone for 4 weeks. Tonsillectomy was performed without any histological abnormality	Rapid improvement with antibiotics treatment and intensive care. Follow-up course unknown
Kajiya et al 2008 [22]	59 M Fever, chills, malaise	US & CT	Dental caries, poor dental hygiene	<i>Fusobacterium nucleatum</i>	Impipenem/cilastatin, due to sensitivities changed to clindamycin (unknown durations). Patient refused percutaneous drainage	Full resolution of abscess on CT and US after 1 month
Fatakhov et al 2013 [23]	30 M Several days of fevers, chills, malaise, nausea, vomiting, diarrhea	US & CT	None	<i>Fusobacterium necrophorum</i>	Percutaneous drainage. Metronidazole and piperacillin/tazobactam for 8 days, narrowed to levofloxacin and metronidazole until abscess resolved on imaging (2 weeks post-drainage)	Abscess was resolved on CT at 2 weeks after drain insertion
Nagpal et al 2015 [24]	69 F 2-month history of vague RUQ pain, fevers and chills	US & CT	Severe chronic periodontitis Diverticulitis	<i>Fusobacterium nucleatum</i>	Percutaneous drainage. Vancomycin (stopped after 3 days) and meropenem, later changed to ertapenem for total of 2 weeks. Discharged on oral penicillin for 4 weeks	Full resolution on repeat CT at 4 months post-discharge
Ahmed et al 2015 [2]	21 M 2 weeks of RUQ pain, fevers, chills, weight loss, fatigue, diarrhea	CT	Recent routine dental cleaning. Complicated by sepsis, empyema, abdominal and pelvic abscesses	<i>Fusobacterium nucleatum</i>	Empiric vancomycin and piperacillin/tazobactam for unknown duration, treated with IV ertapenem for 8 weeks. Percutaneous drainage of PLA. Required VATS procedure for trapped lung. Drainage of abdominal and pelvic abscesses	Resolution of abscesses on CT after 9 weeks of treatment

RUQ: right upper quadrant; US: ultrasound; CT: computed tomography; IV: intravenous; PLA: pyogenic liver abscess; VATS: video-assisted thoracoscopic surgery.

major role in periodontal disease [18]. This anaerobe has also been associated with many other infections, including peritonsillar abscesses and appendicitis [2]. Interestingly, a study conducted by Genome Research in 2012 showed a highly significant prevalence of *Fusobacterium nucleatum* in human colorectal tumor specimens [19]. However, only six cases of mono-microbial liver abscesses have been reported to be due to *Fusobacterium* in immunocompetent hosts (Table 2). These cases were published between 1977 and 2015. Out of the six cases, five were linked to periodontal disease; in one of the cases, a source of the infection was never discovered. In their research, Shi et al also found a significant increase in the bacterial load of *Fusobacterium nucleatum* in patients who wear dentures, especially those who develop stomatitis [20]. In our patient, given the right hepatic lobe distribution, bacteremic spread of infection originating from a dental source was likely, given the identified organism and the patient's history of tooth abscess.

### Conclusions

*Fusobacterium* is a rare cause of PLA in immunocompetent individuals and is commonly associated with periodontitis, as observed in this case. As demonstrated by Table 2, other case reports have also shown a correlation between anaerobic PLA with *Fusobacterium* and dental disease in otherwise healthy individuals. Our patient likely acquired this invasive strain of *Fusobacterium* from his dental abscess which was identified and treated during his hospitalization, in the setting of chronic denture use. Thus, chronic denture use should be considered as a possible contributing factor for infection in similar cases, and may have been overlooked in previous case reports.

### Conflict of Interest

No potential conflicts of interest.

### Financial Support

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