

Liver Abscess Secondary to *Fusobacterium nucleatum* Infection in 15-year-old Male

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Abstract

Pyogenic liver abscess (PLA) is an uncommon condition, which requires early diagnosis and treatment, due to high mortality, morbidity if left untreated. The incidence rate 3.6 per 100,000 populations with overall mortality 0.2 per 100,000 populations in the United States. Predisposing factors for PLA development were immune deficiency, parasitic invasion, genetic disorders (Papillon-Lefevre syndrome, Chronic Granulomatous Disease), abdominal infection [4] and abdominal trauma. The most common cultured bacteria in the last population group were *Streptococcus* species 29.5%, *E.coli* 18.1% and 16.3% polymicrobial.

Here we report a case of PLA secondary due to *Fusobacterium nucleatum* in an otherwise healthy adolescent male with no definitive source of infection (cryptogenic). PLA is very rare and to date there is no case reports published with *Fusobacterium nucleatum* being the causative pathogen in pediatrics (only 13 adult cases have been reported).

Keywords: *Fusobacterium nucleatum*; *Streptococcus*; Papillon-Lefevre syndrome; Chronic granulomatous disease; Abdominal infection; Abdominal trauma

Abbreviations: RUQ: Right Upper Quadrant; PLA: Pyogenic Liver Abscess.

Case Report

15-year-old African-American male with history of asthma, autism spectrum, and obstructive sleep apnea, presenting with 2-week history of illness associated with sore throat, fatigue, RUQ abdominal pain, and jaundice. No recent travel, animal contact, sick contact was reported. Patient had no history of dental infection, caries or history of past maxillo-facial surgery. On admission his hemoglobin was 7.4; AST 64; ALT 67; total bilirubin 1.3; PT 18.2; PTT 30; INR 1.7; eosinophils 0.0; WBC 13.3. Imaging studied revealed hypoechoic abnormality of the liver confirmed to be a multi-loculated complex fluid collection in the right hepatic lobe measuring approximately 13.6 cm x 8.2 cm x 10.1 cm, consistent with a liver abscess (Figure 1).

Meropenem and Vancomycin were initiated. The abscess was aspirated, and two drains were placed by interventional radiology. Aspirate grew *Fusobacterium nucleatum* with negative blood cultures. Antibiotics were then switched to Ertapenem once daily. Intravascular source was ruled out with normal echocardiogram and doppler ultrasound of the neck vessels. Full dental exam was unremarkable. Patient became afebrile after several days, and hospital course was complicated by right sided pleural effusion requiring two thoracentesis, and chest tube placement. He progressively got better over a 30-day period in the hospital. At discharge all drains had been removed and he had significant improvement in the sizes of liver abscess (5.3 cm x 4.9 cm) (Figure 2).

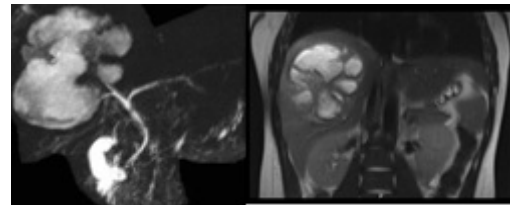


Figure 1: (Day 1) MRI with and without contrast on admission: multi-loculated complex fluid collection in the right hepatic lobe measuring approximately 13.6 cm x 8.2 cm x 10.1 cm.



Figure 2: (Day 36) CT of the same patient on discharge: significant improvement of the lesion, measuring approximately 5.3 cm x 4.9 cm.

Discussion

PLA is a rare condition and with a higher incidence in developing countries.

Prior to technological progress in medicine, up until 1980s, PLA related mortality was as high as 50% [1-7]. Nowadays this number is

low but still significant. Few studies report PLA contributes 2%-14% of mortality rate [5-8] in other countries. The latest studies show that this rate is 0.2 per 100,000 populations in the United States [3]. Prevalence of PLA is higher in adults than in children; males are more affected than females for unknown reasons [1,9]. The right hepatic lobe is being more often affected, most likely due to its being larger and richer vascularization [3].

Etiology

PLA can develop *via* several mechanisms

Dissemination through the portal vein: Any intra-abdominal infection can lead to septic thrombophlebitis which can become a reason of an intra-hepatic solitary or multiple abscesses.

Ascending infection through the biliary tree secondary to biliary tract infection, tumor, strictures.

Hematogenous dissemination: Lemierre's syndrome, septic endocarditis, skin infection (tropical ulcers, fusobacterium infection) can become a reason for dissemination of the infection. One of the studies reported 35% of children with hepatic abscesses had skin infection [10].

Back in 1936, Andre Lemierre reported an association between oropharyngeal infection and septic thrombophlebitis of internal Jugular vein with septic dissemination of the infection [11]. Subsequently, this clinical manifestation was called by his name: Lemierre's syndrome. As *Fusobacterium* species are part of the normal microflora of oral cavity and oropharynx, it was shown that approximately 81% of Lamierre's syndrome cases were related to these species [12]. Thus, poor oral hygiene, dental infection and caries, as well as maxillo-facial surgeries and procedures increase the risk of hematogenic spread of this infection. In chronic medical conditions and malignancies, this risk is high most likely due to tumor invasion of mucosal layers. However, the most common type of infection with *Fusobacterium* is an otitis media [13], particularly in kids younger than 2 years of age.

In our case, none of the factors described above were reported, and neck vessel image, as well as echocardiography report were unremarkable.

Direct extension: Trauma, post procedural, intra-abdominal abscesses.

Cryptogenic: Despite all the mechanisms described above, up to 66 % of reported PLA cases are cryptogenic [6-8,14].

Factually, one-fifth of PLA cases are the first sign of Chronic Granulomatous Disease [15]. Papillon-Lefevre syndrome, which is an autosomal recessive genetic disorder, characterized by periodontitis and palmoplantar keratoderma, is known by its complication with PLA.

Even though the most common PLA causative microorganisms in adults are *Streptococcus* species (29.5%) and *E.coli* (18.1%); the majority of the PLA cases are multi-microbial [3]. However, in pediatric population, *Staphylococcus aureus* is the most common causative agent (up to 55%) [10,15]. One of the studies conducted in Iran reported 18 cases of PLA in children with different microorganisms and parasites: candidial, amebic and pyogenic. In pyogenic group with 16 patients, *Staphylococcus* was the most common causative organism. Cases of *Klebsiella* and *Enterobacter*

induced PLA were reported as well. *Candida* was an agent in one PLA case and patient deceased from systemic conidial sepsis [16]. The same study reported that 16 out of 18 cases were cryptogenic (with no definitive source of infection) [16].

Prior to 2008, there were only 13 adult and no pediatric cases of PLA reported secondary to anaerobic micro-organism. In the last couple years there are multiple case reports of *Fusobacterium* induced PLA. We present only the most recent of them (Table 1). Possible explanation for this exponential growth of the cases could be the fact that anaerobic species were difficult to isolate in cultures but with improved isolation technique, we are able to identify better now. Our case report is unique, since there was no pediatric PLA case secondary to *Fusobacterium* infection reported.

	Age	Gender	Year of publication
1	59	F	2017
2	88	F	2017
3	51	F	2017
4	66	M	2017
5	57	M	2016

Table 1: Patients with PLA Caused by *Fusobacterium*.

Microbiology

Fusobacterium, is a gram negative, obligate anaerobic, non-spore forming, microorganism of human GI tract, oral cavity in particular. *F. nucleatum* and *F. necrophorum* are two of the most commonly isolated pathogens [17]. It contains adhesions on its membrane (because of lectin) which allow to easily stick to epithelia and teeth surfaces. It releases cytokines and proteases which irritate and inflame tissues, leading to periodontal diseases. The association between *Fusobacterium nucleatum* and chorioamnionitis with preterm labor was found [18]. Even though, the incidence of *Fusobacterium* bacteremia is low (0.55 per 100,000 population per annum) [19], mortality remains significant in developing countries: 47.4 % in Taiwan [20], 4% in Finland [21-26] and 1% in New Zealand [17].

Conclusion

Pyogenic liver abscess is an ominous condition with a high mortality rate if left misdiagnosed or untreated. The incidence of this disease is lower in pediatric population in comparison with adults. The main causative microorganism in adults remains Streptococcal species however staphylococcal PLA is the most common in pediatric population. Anaerobic PLA cases have rarely been reported in adults, with more anaerobic PLA cases published in the last few years. The reason may be industrial progress in medicine and availability to cultivate an anaerobic microorganism, compared to two decades ago.

Fusobacterium nucleatum remains the most common anaerobic microorganism causing PLA in adults. Cryptogenic Pyogenic Liver Abscess should be on the list of differential diagnosis in any child who presents with the same symptoms as our patient.

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Conflict of Interest

All authors have no conflicts of interest to disclose.

Contributors' Statements

Karen Hovsepyan: Dr. Hovsepyan conceptualized, drafted the initial manuscript, reviewed and revised the manuscript, and approved the final manuscript as submitted. Also, agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Deepa Mukundan: Dr. Mukundan contributed to concept of the article, drafted, critically reviewed and revised the manuscript, and approved the final manuscript as submitted. Also, agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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