Fusobacterium nucleatum: A cause of subacute liver abscesses with extensive fibrosis crossing the diaphragm, mimicking actinomycosis

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Abstract

Introduction *Fusobacterium nucleatum* is a Gram-negative, obligate anaerobic bacterium which predominantly resides within the oral cavity and causes acute abscesses and venous thrombosis, primarily in the head and neck region, but could have unique clinical presentations in different anatomical regions of the body.

Case report We present a case of subacute liver abscesses extending to the lung. The histopathological examination showed extensive necrosis and fibrosis. The chronic course, extensive fibrosis and extension across the anatomic barriers were suggestive of actinomycosis. Two sets of blood cultures grew *Fusobacterium nucleatum*, only 16S rRNA analysis of the liver tissue and pleural fluid revealed *F. nucleatum* DNA without other organisms. The clinical and pathological features of our case illustrate that *F. nucleatum* may mimic actinomycosis.

Conclusions This case illustrates that *F. nucleatum* should be considered in patients with subacute infections with extensive fibrosis that crosses anatomic barriers, mimicking actinomycosis.

Keywords Liver abscess, fibrosis, *Fusobacterium nucleatum*, actinomycosis.

Introduction

Fusobacterium nucleatum is part of the oropharyngeal and gastrointestinal flora.¹ It causes a variety of infections including liver abscesses, either mono-bacterial or as co-infection with other pathogens. Usually, infections due to *F. nucleatum* as well as most other anaerobes cause acute exudative infiltrates and tissue necrosis. In

comparison, *Actinomyces* organisms are characterized by a chronic course and extensive fibrosis, often mimicking malignancy.² We describe a case of liver abscesses with indolent presentation, extensive fibrosis and extension across the diaphragm. Blood culture and 16S rRNA analysis of liver tissue plus pleural fluid revealed *F. nucleatum* only. The chronic course, extensive fibrosis and extension across anatomic barriers, mimicking actinomycosis, has not been previously reported in *F. nucleatum* liver abscesses.

Case report

A 69-year-old female with a remote history of thyroid cancer presented to her primary care physician with right upper quadrant and right lower chest pain that radiated to the back, difficulty breathing and infrequent dry cough for 2 weeks duration. Her chest X-ray was normal. Laboratory tests showed white blood cells (16,000/cmm), hemoglobin (12.6 g/dL), platelets (443,000/cmm), alkaline phosphatase (194 U/L). She was given a 5 days course of azithromycin 500 mg orally daily for presumed bronchitis. After 3 weeks the symptoms worsened. Computed tomography showed multiple liver cystic lesions and right sided pleural effusion/infiltrates. She was thought to have

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cystic malignancy and pneumonia (Figure 1). Her pain became pleuritic with intermittent chills, night sweats and dry cough. She presented to the emergency room. Physical examination revealed normal temperature, diminished breathing sounds on the right lung base and distended and tender abdomen. Her laboratory tests showed white blood cells (28,600 /cmm), hemoglobin (8.4 g/dL), platelets (778,000/cmm), alkaline phosphatase (336 U/L). Repeated imaging at the time of admission showed that the lesions had enlarged. The blood culture was drawn, and she was started on ampicillin/sulbactam 3000 mg IV every 6 hours, empirically for presumed aspiration pneumonia. Ultrasound guided thoracentesis one day after admission revealed exudative effusion with negative Gram stain and cultures.

Figure 1. Computed tomography of the abdomen showing multiple liver cysts, extending to the diaphragm with pleural effusion and right lower lung infiltrates (arrows)

The following day, computed tomography guided core liver biopsy revealed acute inflammation, necrosis and extensive fibrosis without evidence of malignancy (Figure 2). Liver biopsy specimens Gram stain, acid-fast and silver stains and cultures were negative. Five days later, however, 2 sets of blood cultures drawn on admission revealed *F. nucleatum*. She was suspected of having a mixed infection with *Actinomyces* species based on the pathological findings. However, 16s rRNA analysis of liver tissue and pleural fluid revealed *F. nucleatum* DNA without other organisms.

Figure 2. Hematoxylin and eosin stain of core liver biopsy showing extensive fibrosis

Treatment was changed 6 days later at the time of discharge to ertapenem IV 1000 mg IV every 24 hours for 25 more days and then switched to metronidazole 500 mg orally three times a day for three more months. She continued to improve, one month after discharging home, repeat laboratory tests showed white blood cells (6,200 /cmm), hemoglobin (15 g/dL), platelets (373,000 /cmm), alkaline phosphatase (67 U/L) and imaging showed progressive resolution of abscesses. On follow up visit 6 months after treatment she remained well without any symptoms.

Discussion

Subacute infection with extensive necrosis and fibrosis that crosses anatomic barriers is characteristic of actinomycosis.^{3,5} *Fusobacterium nucleatum*, an obligate anaerobic filamentous Gram-negative rod, is known to cause abscesses and venous thrombosis but has not been reported to cause extensive fibrosis mimicking actinomycosis.^{6,15} *Fusobacterium* species are indigenous to the oral cavity and the gastrointestinal tract flora.^{16,17} They are considered commensal but have been associated with mono-bacterial and mixed infections. The pathogenesis is suspected to be a hematogenous seeding from an upper respiratory tract or a gastrointestinal focus. The histopathology usually reveals acute inflammation, necrosis with abscess formation and rarely, thrombophlebitis. In comparison, actinomycosis is characterized by chronic presentation, acute and chronic inflammatory infiltrates and extensive fibrosis, mimicking malignancy.^{3,5} It often causes sinus formation and crosses anatomic barriers with or without sulfur granule formation.

Our patient developed several cystic liver lesions with right lower lung infiltrates and pleural effusions. Initially, she was suspected of having cystic liver neoplasm with right lower lung pneumonia and empyema or an atypical granulomatous infection including mycobacteria or fungi. Parasitic causes like echinococcosis and/or amebic liver abscesses were less likely based on the clinical presentation and in the absence of risk factors such as travel or residence in endemic areas. Malignancy and granulomas, however, were not detected in the liver tissues. Blood cultures revealed *Fusobacterium nucleatum*, but we suspected mixed infection with *Actinomyces* species based on the histopathological findings. Molecular analysis, however, revealed *F. nucleatum* DNA without any other organism. Liver tissue and pleural fluid cultures were negative, probably because of antibiotic therapy.

The treatment of *F. nucleatum* infections is based on susceptibility to β -lactams/ β -lactamase-inhibitors and metronidazole whereas *Actinomyces* species are resistant to metronidazole. Duration of antibacterial treatment for actinomycosis is

generally prolonged whereas the length of therapy of *F. nucleatum* infections is not clear. We elected to continue therapy for 4 months with combination of parenteral and oral antibiotics until resolution of the liver abscesses was documented.

Conclusions

This case illustrates that *F. nucleatum* should be considered in patients with subacute infection with extensive fibrosis that crosses anatomic barriers, mimicking actinomycosis.

Consent: The authors obtained written consent from the patient for publication of this case report and the accompanying images.

Authors' contributions statement: BH and RK were involved in the diagnosis of the case and writing the manuscript. AH and DS provided pathology slide image and interpretation. AA provided the images and interpretation. All authors revised and approved the final version of the manuscript.

Conflicts of interest: All authors – none to declare.

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