Osteomyelitis of a long bone due to *Fusobacterium nucleatum*

in an immunocompetent adult: A case report and literature review

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Abstract

Background

Fusobacterium species are uncommon causes of osteomyelitis. These organisms are normal flora of oral cavity, therefore, they mostly cause osteomyelitis of head and neck. Hematogenous osteomyelitis at distant sites other than head and neck has been rarely reported in pediatric patients or immunocompromised patients. Here, we report the first case of osteomyelitis of a long bone combined with muscle abscess due to Fusobacterium nucleatum in an otherwise healthy adult.

Case presentation

A 59 year-old Asian man was admitted for pain and swelling in the right lower leg which had been persistent for two weeks. Magnetic resonance imaging showed osteomyelitis of right fibula and surrounding muscle abscess of right lower leg. Incision and drainage was done and repetitive tissue cultures grew F. nucleatum. Recurrent periodontitis in this patient was presumed to cause hematogenous seeding of F. nucleatum at a distant site leading to osteomyelitis with muscle abscess. The patient was successfully treated with intravenous ampicillin-sulbactam for 3 weeks and oral amoxicillin-clavulanate for 8 weeks, combined with repeated surgical drainage. He has no evidence of recurrence for 7 months of follow-up.

Conclusions

Clinicians should be aware that F. nucleatum could be the etiologic agent of hematogenous osteomyelitis of long bone in an immunocompetent patient.

Keywords

Fusobacterium nucleatum, Osteomyelitis, Periodontitis
Background

*Fusobacterium species* are gram negative bacilli, nonmotile, nonsporulating, obligate anaerobes from the family of Bacteroidaceae[1]. They have been frequently isolated from a wide variety of clinically significant anaerobic infections that include oral and dental infections, brain abscess, bacteremia, endocarditis and soft tissue infections but occasionally bone and joint infections[2-5]. They are part of normal flora of oral cavity, gastrointestinal, upper respiratory, and female genital tract[6], therefore mostly found in the mouth and to a lesser extent in feces and urogenital tract[7]. Therefore, reported cases of osteomyelitis caused by *Fusobacterium spp.* were mostly in head and neck area associated with chronic periodontitis, odontogenic abscess as contiguous infection. And in hematogenous osteomyelitis pattern, most patients were child and otherwise had predisposing factors that could easily lead to osteomyelitis such as indwelling intravascular catheters, distant foci of infection, intravenous drug abuse, vascular insufficiency, sickle cell disease, traumatic bone injury, open fractures and chronic soft tissue infections[1, 8-12]. From the literature review, there is no report on cases of long bone osteomyelitis by *Fusobacterium spp.* in immunocompetent adults. We describe a case of fibula osteomyelitis combined with muscle abscess caused by *F. nucleatum* in an adult patient with no known predisposing factors.
Case Presentation

A 59-year-old previously healthy man presented with fever, pain and swelling in his right lower leg. About two months before this admission, he had developed pain on his right lower leg. The pain had progressively worsened despite analgesics and his right lower leg had begun to swell. About 2 weeks before this admission, he had been admitted to an outside hospital where he was found to have osteomyelitis of right fibula combined with abscess of adjacent muscles (soleus muscle, tibialis posterior and fibularis longus muscle). He underwent incision and drainage on his right leg. First generation cephalosporin was started empirically. However, repeated cultures from tissues had grown no microorganisms and the leg had been draining pus persistently till transfer to our hospital. For further diagnostic evaluation and treatment, the patient was transferred to our hospital.

His past medical history was negative for diabetes mellitus, arterial hypertension, alcoholism, steroid use and any other systemic infections. And he was 15 pack-year current smoker. He denied history of local trauma, and recreational drug abuse. He recalled recurrent periodontitis for 10 years, and about 3 months before, he had extracted 4 teeth and implanted dentures instead.

On physical examination, the body temperature was 37.1°C, the blood pressure 124/69 mmHg, the pulse 100 beats per minute, and the respiratory rate 18 breaths per minute. Generally, he appeared ill-looking though mental status was alert and oriented. The wound on his right lower leg lateral side was opened in 16cm sized incision and fibula was exposed with sign of inflammation of adjacent muscles and draining pus with foul odor. Laboratory evaluation revealed leukocyte count of 12,980/μL (80% neutrophils), hemoglobin of 9.7 g/dL, platelet count of 385,000/μL, C-reactive protein of 329 mg/L and erythrocyte sedimentation rate of 86 mm/h. Chest radiograph demonstrated no active lung lesion. Computed tomography(CT) of the lower extremities at the outside hospital revealed osteomyelitis of right fibula and muscular abscess along the fibula shaft. Magnetic resonance imaging of the lower extremities (Fig.1), which was taken at our hospital, revealed slightly decreased amount of surrounding abscess but still remaining osteomyelitis of right fibula and no change of periostitis of right proximal tibia compared to CT imaging of outside hospital. Incision and drainage was done at
bedside and tissues were sent for gram stain and culture. Intravenous ampicillin-sulbactam was started as 3g every 6 hours. On hospital day 3, fibula excision was done due to severe osteomyelitis. Findings on microscopic examination of the bone biopsy specimen were consistent with acute osteomyelitis and necrotic tissue with microabscess. Initial tissue culture at our hospital revealed *F. nucleatum* and *Actinomyces meyeri* as the causative organism. Tissue cultures that had been done at the prior hospital was also reported to grow *Fusobacterium spp.* in two out of five specimens. The patient was received repeatedly incision and debridement surgery on hospital day 7 and day 17. Intravenous ampicillin-sulbactam was administered for 3 weeks, then switched to oral amoxicillin-clavulanate 625mg q 8hr for 8 weeks. After 11 weeks of treatment, he was successfully discontinued antibiotics. His leg has been uneventful without recurrence of infection for 7 months of follow up.

Figure 1. Enhanced magnetic resonance imaging of right lower leg showing a fibula enhancement and adjacent muscular abscess. (fat saturated contrast enhanced T1W1)
Discussion

Anaerobes have been regarded as uncommon causes of osteomyelitis because these organisms were difficult to isolate from infectious sites due to their fastidious nature. However, due to development of methods detecting anaerobes, reports of anaerobic osteomyelitis have been increasing; up to 39% of osteomyelitis were associated with anaerobic infections in a study[13]. Anaerobic osteomyelitis has been usually reported in patients with complicated bone fractures or underlying chronic disease, commonly as non-hematogenous disease. The predominant anaerobes causing osteomyelitis are *Bacteroides*, *Peptostreptococcus, Fusobacterium*, and *Clostridium* spp. and *Propionibacterium acnes*[13, 14].

*Fusobacterium* spp. are commonly found in periodontal disease and produces tissue irritants such as butyric acid, proteases and cytokines. They have strong adhesive properties due to the presence of lectins, and these outer-membrane proteins mediate adhesion to epithelia and tooth surfaces, and coagglutination with other suspected pathogens[7].

*Fusobacterium* spp, which are members of the oral normal flora, were most frequently isolated from cranial or facial infections[14]. The species most commonly isolated is *F. necrophorum* [3, 10, 11] and cases of *F. nucleatum* are relatively rare[1, 13]. Table 1 shows cases of osteomyelitis which have been reported in the medical literature caused by *Fusobacterium* spp. other than head and neck site. As it shows, most of the cases are of children and patients with predisposing factors for anaerobic hematogenous osteomyelitis. To our knowledge, our patient is the first case of long bone osteomyelitis caused by *F. nucleatum* in a immunocompetent adult. Many patients with anaerobic osteomyelitis have an anaerobic infection elsewhere in the body that is the source of the organisms involved in osteomyelitis. And osteomyelitis of long bones is generally due to hematogenic spread, trauma, or the presence of a prosthetic device[14]. Our patient had no specific infection source except recurrent history of periodontitis. Patients with periodontal disease are predisposed to systemic infection due to anaerobic bacteria such as *Fusobacterium* spp. There are few case reports of long bone osteomyelitis following oral infection[15]. In our patient also, his poor dentition may cause *F. nucleatum*
bacteremia and cause hematogenous osteomyelitis of lower leg and abscess of adjacent muscle.

Management of osteomyelitis includes symptomatic therapy, immobilization for some patients, adequate drainage of purulent material, and antibiotic therapy consisting of parenteral administration of antibiotics for at least 4-8 weeks and in some cases even longer[16]. *Furobacterium spp.* are commonly sensitive to the usual anti-anaerobic antibacterial agents including penicillin G, clindamycin, metronidazole, chloramphenicol, imipenem, and cefoxitin[11]. But there is evidence of emerging resistance in some *Fusobacterium spp.* isolates to penicillins, carbapenems, and clindamycin[16, 17]. The first description of a β-lactamase in *Fusobacterium spp.* was reported in 1985, and this was shown primarily to be a penicillinase with little activity against cephalosporins[18]. After that, several studies have been reported of β-lactamase production of *Fusobacterium spp.* Fatal sepsis due to a β-lactamase-producing strain occurred in an immunocompromised patient[19].

Proportion of penicillin resistance of *Fusobacterium spp.* are 0-22.7% in studies which were done from 1999 to 2011[20-26]. And proportion of resistance of β-lactam-β-lactamase inhibitors are much lower (0-7%)[20-26]. There were regional differences between penicillin resistance, but resistance of β-lactam-β-lactamase inhibitors were relatively similarly low in different regions[27]. And recently, as *Bacteroides* became more resistant to carbapenem, carbapenem resistance of *Fusobacterium spp.* was also reported in a study from Taiwan, 4% of *Fusobacteria* isolates were “nonsusceptible” to imipenem and 8% to meropenem[20]. Our patient was successfully treated with β-lactam-β-lactamase inhibitors. Duration of antibiotics therapy is debated, but prolonged duration of high-dose β-lactam therapy is recommended because of the endovascular nature of the infection. Surgical debridement is crucial given the tendency toward abscess formation[11].
Conclusion

We report the first case of osteomyelitis by *F. nucleatum* in an adult patient with no definite risk factors for hematogenous osteomyelitis in whom recurrent periodontitis might have been a probable source of bacteremia. Efforts to isolate anaerobic pathogens should be made in patients with characteristics of anaerobic infections, such as large abscesses.
Consent

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Series Editor of this journal.

Competing interests

The authors declare that they have no competing interests.

Authors’ contributions

Lee MJ took care of the patient and drafted and revised the manuscript. Ha YE reviewed the manuscript. Lee YJ, Park HY and Lee JH have been involved in patient clinical care and contributed to the draft of the manuscript. Sung KS performed the surgical support in the patient clinical care. Kang CI, Chung DR, Song JH and Peck KR contributed in coordinating the manuscript and to the draft of the manuscript. All authors have read the manuscript and approved its final version.
References


Additional files provided with this submission:

Additional file 1: Table_1_Fusobacterim.docx, 21K
http://www.biomedcentral.com/imedia/1286847901701947/supp1.docx