Case report

Acute femoral osteomyelitis due to hypermucoviscous Klebsiella pneumoniae

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Abstract

Hypervirulent hypermucoviscous Klebsiella pneumoniae strains have emerged as clinically important pathogens causing invasive infections. K. pneumoniae osteomyelitis is uncommon in adult patients, and may mimic bone tumors on presentation. We report a patient with left rectus femoris muscle abscess and acute osteomyelitis of the left femur due to hypermucoviscous K. pneumoniae with negative blood culture, who was initially thought to have left thigh tumor. The patient’s infection resolved with surgical drainage and debridement and intravenous and antibiotic therapy.

Introduction

Klebsiella pneumoniae is commonly associated with urinary, respiratory, or bile duct infections in humans. It has been reported to cause septic arthritis and osteomyelitis, mostly in children [1], but uncommonly in adults. Hypervirulent hypermucoviscous K. pneumoniae strains have been implicated in invasive infections including bacteremia, liver abscesses, and meningitis [2], but there are few reports of osteomyelitis [2–4]. Of note, most of these cases include patients with positive blood cultures and underlying diseases, such as diabetes [2–4]. Here, we report a case of osteomyelitis caused by hypermucoviscous K. pneumoniae as the primary infection in an adult patient who was initially admitted for the suspicion of a bone tumor.

Case report

A 78-year-old man was presented with pain and swelling of his right thigh with no history of trauma. Magnetic resonance imaging (MRI) of the left thigh revealed inflammation of the right femur (Fig. 1). The left femoral bone tumor was suspected at first, and he was referred to a reference hospital. On admission, two sets of blood cultures were submitted. However, in operation, the left femoral bone grew a mucoid Gram-negative bacillus that was identified as K. pneumoniae by matrix-assisted laser desorption ionization time-of-flight mass spectrometry. The isolate demonstrated a positive string test consisting of a hypermucoviscous K. pneumoniae strain. The pathological diagnosis of the bone specimen was a class II finding, showing only inflammatory cells and no malignant tumor cells. The patient was transferred to our university hospital for treatment.

On examination, the patient was afebrile and had normal vital signs. The physical examination revealed there was swelling and pain at the left femur.

Leukocyte count was 14,920/μL, and the levels of alkaline phosphatase and C-reactive protein were elevated; 1437 U/L and 16.798 mg/dL, respectively. The patient had no known predisposing risk factors (diabetes mellitus, renal disease, malignancy, hepatobiliary disease, and chronic alcoholism) for K. pneumoniae-related community-acquired infection. Intravenous ceftriaxone (2 g every 24 h) was started empirically. Ceftriaxone was replaced by intravenous cefazolin (2 g every 8 h)
the following day when susceptibility results were available (resistant only to ampicillin). The patient’s leukocyte count and C-reactive protein levels decreased; however, the swelling and pain of the left femur did not improve, and fever recurred. [Fig. 2]. Contrast-enhanced computed tomography (CT) of the lesion revealed the formation of an abscess in the right rectus femoris muscle. Surgical drainage and debridement were performed, and a large amount of pus was drained. Hypermucoviscous \textit{K. pneumoniae} was isolated from multiple cultures. Following debridement, the swelling and pain in the left thigh improved, and CT confirmed the resolution of the muscle abscess. The patient was treated with 9 weeks of IV cefazolin and was changed to oral cefalexin (0.5 g every 8 h) on discharge. There was no clinical evidence of recurrence and cefalexin was discontinued after 5 weeks of therapy.

**Discussion**

Hypervirulent hypermucoviscous \textit{K. pneumoniae} were reported in Taiwan and Southeast Asia in the mid-1980s and 1990s; however, cases have been reported worldwide in the past two decades [5]. To our knowledge, our patient is the first reported case of hypermucoviscous \textit{K. pneumoniae} osteomyelitis with negative blood cultures (although, the possibility was not ruled out that there was a transient bloodstream infection). Although invasive infections by hypervirulent hypermucoviscous \textit{K. pneumoniae} strains have attracted attention, primary osteomyelitis, which occurs to the bones other than the spine, is rare in adults without specific risk factors such as injection drug use. Osteomyelitis in the adult population is usually exogenous or hematogenous in origin [6] and associated with factors predisposing to \textit{K. pneumoniae} infections [7]. Our patient had no history of trauma and surgical operation, and his medical history suggested no apparent risk factors. Additionally, blood cultures were negative. Our patient’s clinical presentation and course suggest that hypermucoviscous \textit{K. pneumoniae} may cause primary acute osteomyelitis in patients with no risk factors and negative blood cultures, and may be misdiagnosed as bone malignancy. And it is highlighted that biopsy and cultures to establish the diagnosis are needed in the case alike. Huang et al., reported a retrospective case series of osteomyelitis of the femur mimicking malignant tumors, including bone tumors [3]. In this case series, all the hematogenous osteomyelitis cases were monomicrobial, and \textit{K. pneumoniae} was isolated in 60% of the cases (6/10). Table 1 presents an overview of the seven cases of osteomyelitis reported to date that were caused by \textit{K. pneumoniae} and mimicked malignant bone tumors. Blood cultures were positive in all the cases, and most patients had diabetes mellitus. There was only one case without complications. Importantly, while positive blood cultures may lead to the suspicion of osteomyelitis, if the blood cultures are negative, as in our case, osteomyelitis cannot be
diagnosed without biopsy and cultures. Sample collection by needle or surgical biopsy is therefore essential, in cases where bone infection is suspected in addition to bone tumor based on imaging and intraoperative findings. We do not know the capsular serotype of our isolate as typing was not available at our institution. Several virulence factors have been identified in hypervirulent hypemucoviscous K. pneumoniae, including capsular serotypes. Many reports have shown that K1 and K2 serotypes are strongly associated with hyperviscous [8]. There are multiple mechanisms by which K1 and K2 serotypes are highly pathogenic. K1 and K2 strains have a monosaccharide sialic acid on their surfaces, allowing evasion of the host immune cells [9]. Moreover, owing to hyperviscosity, K1 and K2 strains are more resistant than the normal strains to phagocytosis and destruction by macrophages and neutrophils [10]. There are other known determinants of virulence besides K1 and K2 serotypes. The virulence plasmid VPK [11], RmpA (regulator of the mucoid phenotype A gene) [12] and aerobactin (siderophores K. pneumoniae secretes to acquire iron) [11]. Because virulence is determined by these multiple factors, some strains are hypervisculent, but not hypemucoviscous [12]. In order to prove high virulence in these strains, polymerase chain reaction tests are necessary. However, they rarely display resistance to commonly used antimicrobial agents, except for intrinsic resistance to ampicillin due to beta-lactamase [13].

In conclusion, our report demonstrates hyperviscous K. pneumoniae can cause acute femoral osteomyelitis as a primary infection in patients with no known risk factors for infection and with negative blood cultures, and may mimic bone tumor. Therefore, we recommend that cultures of biopsy specimens be performed to facilitate diagnosis, in cases where bone infection is suspected in addition to bone tumor based on imaging or intraoperative findings.

Ethics consent

Written informed consent was obtained from the patient for the publication of this case report.

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Table 1
Clinical features of the seven cases of osteomyelitis caused by Klebsiella pneumoniae.

| Sex   | Age (years) | Underlying condition   | Culture                  | Bone | Blood |
|-------|-------------|------------------------|--------------------------|------|-------|
| Po-Yen et al. (2013) | Male | 57 | None | + | + |
|        | Male | 33 | Drug abuse | + | + |
|        | Female | 54 | Diabetes mellitus | + | + |
|        | Female | 37 | Diabetes mellitus | + | + |
|        | Male | 37 | Diabetes mellitus | + | + |
|        | Male | 13 | Diabetes mellitus | + | + |
| Bonnie et al. (2016) | Male | 60 | None | + | + |

Authorship statement

All persons who meet the authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the writing and revision of the manuscript. Furthermore, each author certifies that this material or similar material has not been and will not be submitted to or published in any other publication before its appearance in IDCases.

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