



## Case report

# Acute femoral osteomyelitis due to hypermucoviscous *Klebsiella pneumoniae*



Takayuki Kawamura<sup>a</sup>, Daisuke Ono<sup>a</sup>, Ayako Shirai<sup>b</sup>, Kazuyuki Mimura<sup>b</sup>, Shunpei Iida<sup>c</sup>, Kazuo Saita<sup>c</sup>, Hideaki Oka<sup>b</sup>, Hideaki Ohno<sup>a,\*</sup>

<sup>a</sup> Department of Infectious Disease and Infection Control, Saitama Medical Center, Saitama Medical University, Saitama, Japan

<sup>b</sup> Department of General Internal Medicine, Saitama Medical Center, Saitama Medical University, Saitama, Japan

<sup>c</sup> Department of Orthopaedic Surgery, Saitama Medical Center, Saitama Medical University, Saitama, Japan

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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.

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## 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 grossly appeared infected. The bone biopsy was submitted for microbiological tests (gram stain and culture) and histopathology. Then, the patient was treated with empiric oral levofloxacin (500 mg every 24 h). Blood cultures were negative; left femoral bone drainage 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 / $\mu$ L, 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)

**Abbreviations:** ABX, antibiotics; LVFX, levofloxacin; CEZ, cefazolin; CEX, cefalexin; p.o, per oral; iv, intravenous; BT, blood temperature; CRP, C-reactive protein; WBC, white blood cells; ESR, erythrocyte sedimentation rate

\* Correspondence to: Department of Infectious Disease and Infection Control, Saitama Medical Center, Saitama Medical University, 1981 Kamoda, Kawagoe, Saitama 350-8550, Japan.

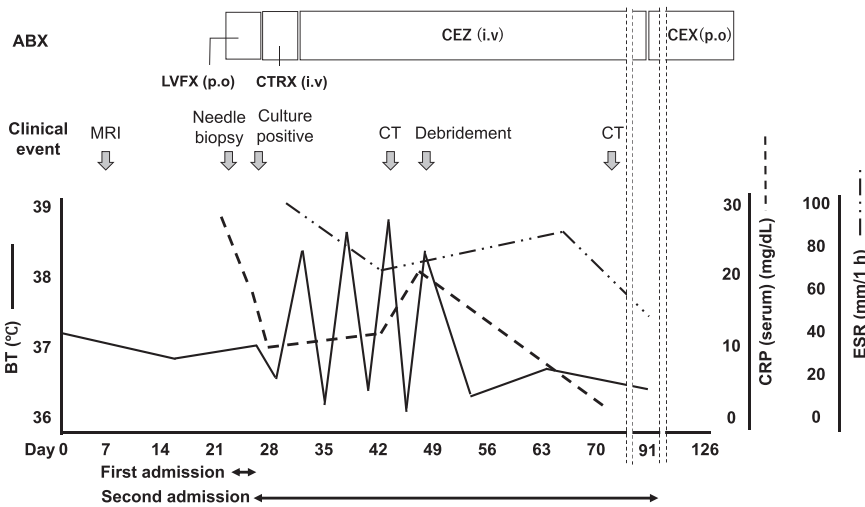
E-mail address: [hohno@saitama-med.ac.jp](mailto:hohno@saitama-med.ac.jp) (H. Ohno).

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**Fig. 1.** Magnetic resonance imaging (MRI) findings. a: T1-weighted MRI image of the right femoral area showing a decreased signal in the right femur, b: T2-weighted MRI image of the right femoral area showing an increased signal in the right femur.



**Fig. 2.** Clinical course of the patient, ABX, antibiotics; BT, blood temperature; CEZ, ceftazolin; CTRX, ceftriaxone; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; i.v., intravenous; LVFX, levofloxacin; p.o., per oral; MRI, magnetic resonance imaging.

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 *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 ceftazolin and was changed to oral cephalixin (0.5 g every 8 h) on discharge. There was no clinical evidence of recurrence and cephalixin was discontinued after 5 weeks of therapy.

**Discussion**

Hypervirulent hypermucoviscous *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 *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 *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 *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 *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 *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 *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

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

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

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 hypermucoviscous *K. pneumoniae*, including capsular serotypes. Many reports have shown that K1 and K2 serotypes are strongly associated with hypervirulence [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 hypermucoviscosity, 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 pLVPK [11], RmpA (regulator of the mucoid phenotype A gene) [12] and aerobactin (siderophore *K. pneumoniae* secretes to acquire iron) [11]. Because virulence is determined by these multiple factors, some strains are hypervirulent, but not hypermucoviscous [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 hypermucoviscous *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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### 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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### Conflict of interest

None.

### References

- [1] Adeyemo AA, Akindele JA, Omokhodion SI. *Klebsiella* septicaemia, osteomyelitis and septic arthritis in neonates in Ibadan, Nigeria. *Ann Trop Paediatr* 1993;13:285–9. <https://doi.org/10.1080/02724936.1993.11747661>
- [2] Prokesch BC, TeKippe M, Kim J, Raj P, TeKippe EM, Greenberg DE. Primary osteomyelitis caused by hypervirulent *Klebsiella pneumoniae*. *Lancet Infect Dis* 2016;16:e190–5. [https://doi.org/10.1016/S1473-3099\(16\)30021-4](https://doi.org/10.1016/S1473-3099(16)30021-4)
- [3] Huang P-Y, Wu P-K, Chen C-F, Lee F-T, Wu H-T, Liu C-L, et al. Osteomyelitis of the femur mimicking bone tumors: a review of 10 cases. *World J Surg Oncol* 2013;11:283. <https://doi.org/10.1186/1477-7819-11-283>
- [4] Khatri A, Kanaparthi NS, Selvaraj BJ, Cho Eunna, El Khoury MY. Primary *Klebsiella pneumoniae* osteomyelitis with bacteremia and sepsis in a patient with cirrhosis. *Case Rep Infect Dis* 2018;2018:3183805. <https://doi.org/10.1155/2018/3183805>
- [5] Shon AS, Bajwa RP, Russo TA. Hypervirulent (hypermucoviscous) *Klebsiella pneumoniae*: a new and dangerous breed. *Virulence* 2013;4:107–18. <https://doi.org/10.4161/viru.22718>
- [6] Lew DP, Waldvogel FA. Osteomyelitis. *Lancet* 2004;364:369–79. [https://doi.org/10.1016/S0140-6736\(04\)16727-5](https://doi.org/10.1016/S0140-6736(04)16727-5)
- [7] Ko W-C, Paterson DL, Sagnimeni AJ, Hansen DS, Von Gottberg A, Mohapatra S, et al. Community-acquired *Klebsiella pneumoniae* bacteremia: global differences in clinical patterns. *Emerg Infect Dis* 2002;8:160–6. <https://doi.org/10.3201/eid0802.010025>
- [8] Paczosa MK, Meccas J. *Klebsiella pneumoniae*: going on the offense with a strong defense. *Microbiol Mol Biol Rev* 2016;80:629–61. <https://doi.org/10.1128/MMBR.00078-15>
- [9] Lee CH, Chang CC, Liu JW, Chen RF, Yang KD. Sialic acid involved in hypermucoviscosity phenotype of *Klebsiella pneumoniae* and associated with resistance to neutrophil phagocytosis. *Virulence* 2014;5:673–9. <https://doi.org/10.4161/viru.32076>
- [10] Zlatkovic N, Aleksić G, Gašić K. Relationships among capsular structure, phagocytosis, and mouse virulence in *Klebsiella pneumoniae*. *Infect Immun* 1995;63:847–52. <https://doi.org/10.1128/IAI.63.3.847-852.1995>
- [11] Hsieh PF, Lin TL, Lee CZ, Tsai SF, Wang JT. Serum-induced iron-acquisition systems and TonB contribute to virulence in *Klebsiella pneumoniae* causing primary pyogenic liver abscess. *J Infect Dis* 2008;197:1717–27. <https://doi.org/10.1086/588383>
- [12] Yu WL, Ko WC, Cheng KC, Lee HC, Ke DS, Lee CC, et al. Association between rmpA and magA genes and clinical syndromes caused by *Klebsiella pneumoniae* in Taiwan. *Clin Infect Dis* 2006;42:1351–8. <https://doi.org/10.1086/503420>
- [13] Zhang Y, Zhao C, Wang Q, Wang X, Chen H, Li H, et al. High prevalence of hypervirulent *Klebsiella pneumoniae* infection in China: geographic distribution, clinical characteristics, and antimicrobial resistance. *Antimicrob Agents Chemother* 2016;60:6115–20. <https://doi.org/10.1128/AAC.01127-16>