Case report

Chronic osteomyelitis caused by *Achromobacter xylosoxidans* following orthopaedic trauma: A case report and review of the literature☆

Sahand Imani[a], Asanka Wijetunga[b,*], Sarah Shumborski[a], Edmund O'Leary[a]

[a] *Department of Orthopaedic Surgery, Hornsby Ku-Ring-Gai Hospital, Sydney, New South Wales, Australia*
[b] *School of Medicine, The University of Sydney, Sydney, New South Wales, Australia*

ABSTRACT

Background: Achromobacter xylosoxidans is an opportunistic environmental aerobe. In cases where *A. xylosoxidans* infects humans, it most commonly manifests as bacteraemia in the immunosuppressed. *A. xylosoxidans* causing chronic osteomyelitis is rare, particularly in the immunocompetent and young.
Case: We present the case of a 23-year-old man with chronic osteomyelitis of the right femur caused by co-infection of *A. xylosoxidans* and *Staphylococcus aureus*. Five years earlier, he had sustained a right femur fracture and was treated with intramedullary fixation at a peripheral hospital in a developing nation. Past medical history was otherwise unremarkable. Management comprised of surgical debridement and culture-directed antibiotic therapy, resulting in clinical cure.
Conclusion: In the context of local trauma and previous surgery, osteomyelitis caused by atypical pathogens must be considered. A multidisciplinary approach commensurate with duration and severity of infection and tailored to the causative organism is paramount.

Introduction

Osteomyelitis is a common musculoskeletal condition associated with significant morbidity and mortality [1–3]. It involves the infection of bone accompanied by inflammation and can result from hematogenous seeding, contiguous spread or direct inoculation following trauma or surgery [4]. Although osteomyelitis can develop in any bone, the vertebral bodies and long bones of the lower extremities are the sites typically affected [5]. Pyogenic organisms are almost exclusively implicated, most frequently *Staphylococcus aureus* [6]. Despite this, culture confirmation remains pertinent to exclude atypical strains and ultimately guide therapy.

The presentation and optimal treatment of osteomyelitis can be variable depending on aetiology. In acute osteomyelitis, onset of symptoms occurs early (<2 weeks) after initial bone infection [7]. It is characterised by inflammatory changes manifesting as dull bone pain, localised swelling, fever and/or erythema. Chronic osteomyelitis (COM) is more insidious, typically evolving over many weeks or months after inoculation [5]. The hallmarks of chronicity are development of sequestrum or involucrum and the presence of a sinus tract [8]. Whilst acute osteomyelitis may be managed with prolonged antibiotic therapy alone, most cases of COM also necessitate surgical debridement.

We report a rare case of femoral COM caused by *Achromobacter xylosoxidans* and *S. aureus* co-infection in a young immunocompetent man. This case highlights the importance of maintaining a high degree of suspicion for osteomyelitis caused by atypical pathogens in settings of previous trauma and surgery. Additionally, given the lack of standardised treatment regimens available for COM, our management can be instructive for fellow clinicians in their future practice. Of note, the patient was informed of (and consented to) de-identified data concerning his case being submitted for publication.

Case report

A 23-year-old man presented to hospital with several months of right thigh swelling and a draining sinus with associated skin changes. There was no history of fever or systemic symptoms. The patient's past medical history was unremarkable. He took no regular medications, was a life-long non-smoker and denied any alcohol or illicit substance use.

Five years prior, the patient suffered a closed midshaft fracture of the right femur following a motorbike accident and was managed with intramedullary fixation at a peripheral hospital in a developing South Asian country. One year post-operatively, the patient developed a surgical site infection. At this point, all hardware was removed, and he was subsequently treated with a two-week course of antibiotics. Records detailing the initial microbe, the antibiotics prescribed and the extent of the revision surgery were unavailable from the overseas institution. The patient then remained asymptomatic for several years and migrated to Australia before experiencing symptoms in his right thigh.

On physical examination, the patient was hemodynamically stable and afebrile with a body mass index of 19 kg/m^2 and reported prolonged difficulty gaining weight. He was able to weight bear with minimal pain. His right thigh was swollen, with overlying scaly skin discoloration and a 2 mm draining sinus on the posterolateral aspect of the distal thigh (Fig. 1). The neurovascular status of the limb was intact, with preserved tone, power and range of motion (ROM).

Laboratory investigations indicated a minimally elevated white cell count of 11.5×10^9/L (normal range: $4.0–11.0 \times 10^9$/L). His inflammatory markers were raised with a C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) of 46 mg/L (normal <5 mg/L) and 17 mm/h (normal <12 mm/h), respectively. Electrolytes and liver function tests were within normal range.

A computed tomography (CT) scan was performed, demonstrating a united right femur fracture, an intramuscular collection within the vastus intermedius as well as non-specific bony changes. Further evaluation was undertaken with magnetic resonance imaging (MRI) which revealed radiological findings suggestive of COM of the right femur with extensive intramedullary, cortical and surrounding soft tissue involvement

Fig. 1. Skin changes and draining sinus associated with chronic A. xylosoxidans osteomyelitis of the right femur.

(Fig. 2). A bone scintigraphy scan with technetium-99m and a gallium-67 study confirmed the presence of osteomyelitis confined to the right thigh, whilst excluding other sites of infection not captured by CT and MRI.

Punch biopsy of the skin demonstrated a chronic spongiotic tissue reaction with superimposed lichen simplex chronicus, indicative of long-term dermatitis. Ultrasound-guided aspiration of the sinus was undertaken, and the culture yielded multi-resistant *A. xylosoxidans* (Table 1). Initial sinus tract excision and drainage of the large intramuscular collection were performed with soft tissue and bone samples confirming presence of *A. xylosoxidans* and revealing co-infection with *S. aureus* (Table 1).

One week later, debridement of the medullary canal was performed using a reamer-irrigator-aspirator (RIA) technique. Despite pre-operative antibiotic prophylaxis, during the debridement procedure, the patient developed systemic sepsis. He was subsequently transferred to the Intensive Care Unit (ICU) for post-operative management. Following intravenous fluid resuscitation, transfusion of 2 units of packed red blood cells and vasopressor support with 12 h of intravenous noradrenaline (0.06 g/mL in 5% glucose at 4 mL/hour), haemodynamic stability was restored. In consultation with the Infectious Diseases (ID) Unit at our institution, the patient was commenced on intravenous antibiotic therapy with flucloxacillin (2 g QID) and meropenem (2 g TDS). Blood cultures taken on post-operative day 1 were positive for methicillin-sensitive *S. aureus*, and a repeat sample 48 h later returned a negative result. Throughout the ICU admission, the patient remained alert and oriented, and was respiring spontaneously on room air. After four days of observation in the ICU, he was discharged to the ward following negative blood cultures and a transthoracic echocardiogram excluding infective endocarditis.

Following surgical debridement, the patient was treated with intravenous antibiotics for a period of one month. He was then transitioned to a three-month course of oral flucloxacillin (1000 mg QID) and co-trimoxazole (800/160 mg BD). After one month of oral antibiotics, two months post-debridement, the patient was asymptomatic, weight bearing with no pain, had full ROM in his right hip and knee and maintained intact neurovascular status. The surgical wound healed with no sign of infection, though hyperpigmentation persisted around the wound site. He reported successful ongoing weight gain with no adverse effects from the antibiotic therapy other than intermittent, mild gastrointestinal discomfort which neither impacted upon his appetite nor required medical intervention.

On review six-months from initial presentation, the patient had made a full recovery. The CRP and leukocyte counts were within normal limits, skin changes had resolved and the patient had returned to full function with no reports of pain. At 1-year follow-up, CRP and leukocyte counts again remained within normal limits, and there was no clinical evidence of infection. At this stage, a follow-up plain radiograph of the affected femur showed no residual disease (Fig. 3). The patient was thus discharged from our services.

Discussion

Several features from our case are noteworthy. Firstly, *A. xylosoxidans* is an aerobic gram-negative rod commonly found in contaminated water and soil [9]. It is an opportunistic pathogen with innate resistance to many hospital disinfectants and is thus often associated with nosocomial infections [10,11]. Most reported cases of *A. xylosoxidans* infection present as primary bacteraemia in comorbid or immunocompromised hosts, usually those with haematological malignancies [12]. Hence, our case of a young
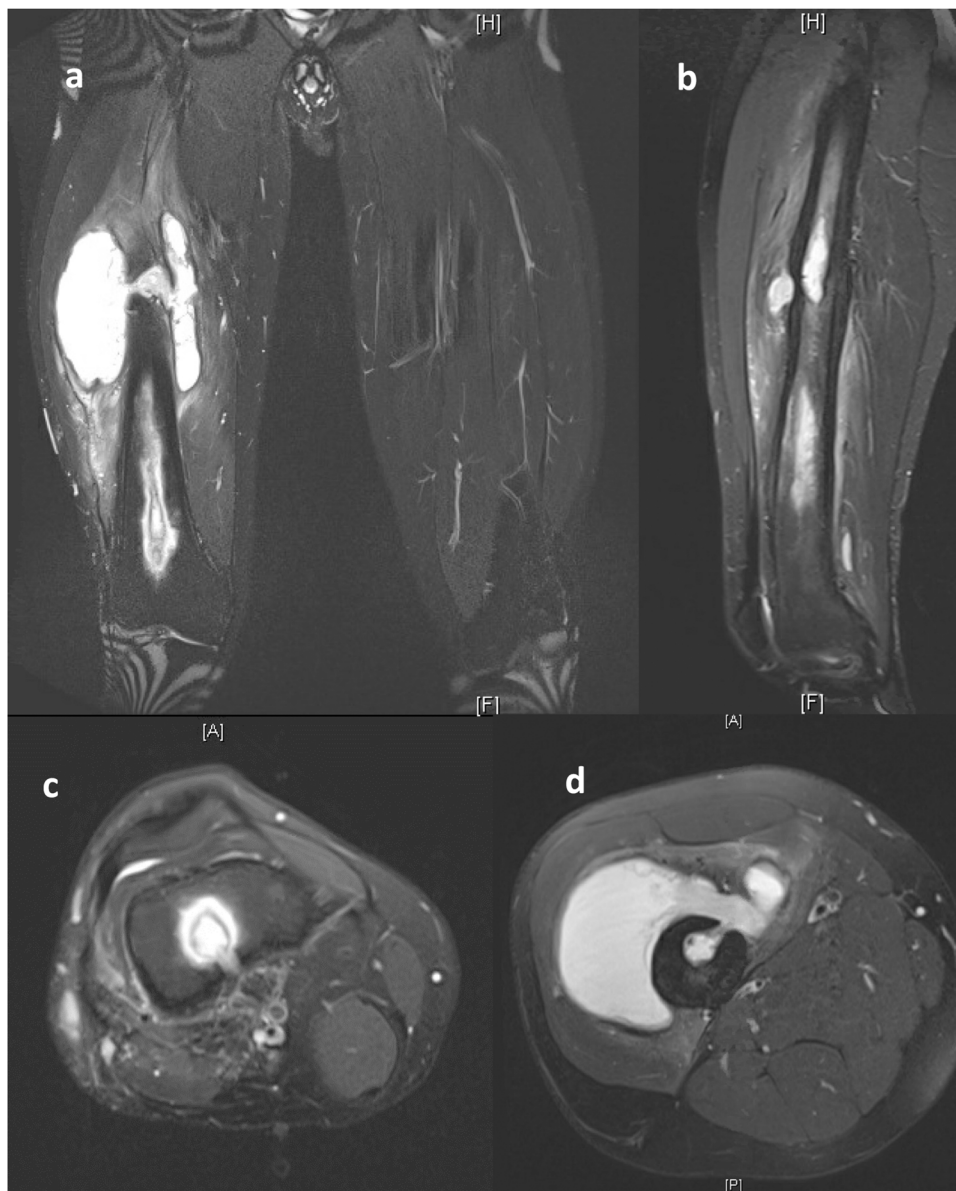
Fig. 2. Pre-operative fat-suppressed T2 magnetic resonance images. a) Coronal image of bilateral thighs demonstrating medial and lateral thigh collections, an inferior intramedullary collection and myositis of the vastus intermedius muscle. b) Sagittal image of the right thigh demonstrating superior and inferior intramedullary collections. c) Axial image of the right thigh demonstrating a posteromedial draining sinus tract. d) Axial image of the right thigh demonstrating an anteromedial draining sinus tract and medial and lateral thigh collections.

Table 1
Antibiotic susceptibilities for each bacterium.

	Acromobacter xylosoxidans	*Staphylcoccus aureus*
Sensitive	Meropenem	Dicloxacillin
	Co-trimoxazole	Flucloxacillin
		Cefalexin
		Cefalothin
		Cefazolin
		Clindamycin
Resistant	Ceftazidime	Penicillin G
	Piperacillin	Ampicillin
	Gentamicin	Amoxycillin
	Ciprofloxacin	

Note: Bacteria isolated from intra-operative bone and deep tissue specimens.

Fig. 3. Antero-posterior plain radiograph of the right femur 12 months post-operatively showing bony remodelling and cortical thickening.

immunocompetent man with primary *A. xylosoxidans* osteomyelitis is a unique presentation.

To the best of our knowledge, only eight previous cases of *A. xylosoxidans* osteomyelitis have been reported in the literature (Table 2) [13–19]. Amongst six of these, either a penetrating trauma, puncture wound and/or surgery preceded the occurrence of osteomyelitis. Given that our patient's initial femur fracture was a closed injury, we suspect that inoculation with *A. xylosoxidans* was then likely hospital acquired, during operative fixation of the

fracture. This suggests that a history of previous trauma and/or surgery may be considered as a risk factor for atypical osteomyelitis, whilst emphasising the importance of infection control practices in hospital settings [20].

A. xylosoxidans is known to be resistant to a broad range of antibiotics. This is attributed to the genus's ability to encode for apparatus such as aminoglycoside-modifying enzymes, β-lactamases as well as active efflux pumps [21,22]. Historically, one of the few agents to which *A. xylosoxidans* has been most susceptible to is piperacillin-tazobactam [23,24]. However, our isolate was resistant, indicating the growing threat that this bacterium poses. Additionally, in this patient, co-infection with *S. aureus* which required additional antibiotic cover only became apparent with bone cultures, suggesting that aspirate and sinus tract samples may not be sufficient for identifying all pathogens in COM.

Although clinical practice may vary between institutions, establishing a multidisciplinary team is encouraged in managing the complexities of COM [25]. Seeking input from radiologists and combining imaging modalities allow for precise localisation and characterisation of the infection. Similarly, attempts should be made to identify the causative pathogen and its susceptibilities prior to extensive debridement, under guidance of the ID team. In this way, targeted antibiotics can be commenced prior to surgical manipulation of the infection, reducing the risk of bacteraemia [25]. Yet, as was observed in our patient, systemic sepsis may still develop and hence forewarning the ICU is sound practice.

Finally, at present, there is a lack of consensus guidelines to inform the optimum management of COM [26]. Considering the recurrence rates for COM can range between 30–50% at 12-months [27], the combination of RIA debridement and four-month duration of targeted antibiotics proved to be highly effective for our patient. In recent years, the RIA method has become increasingly recognised for its efficacy and safety in the management of COM, whilst evidence in favour of longer durations (≥8 weeks) of antibiotic therapy is now emerging [28,29]. Awaiting new insights, it may be reasonable for fellow clinicians to utilise a similar management approach to ours in their future practice and modify it according to their own clinical context.

Table 2
Summary of previously reported cases of osteomyelitis caused by *Acromobacter xylosoxidans*.

Case	Age (years)	Sex	Site	Comorbidities	Co-infection	Treatment	Recovery	Follow-up (months)
Current case	23	Male	Femur	None	*S. aureus*	Antibiotics and debridement	Complete	12
Pamuk et al. 2015 [13]	15	Female	Talus, Navicular, Cuneiform	None	None	Antibiotics	Complete	1
Shinha et al. 2015 [14]	39	Male	Hallux	Diabetes mellitus	None	Antibiotics and amputation	Complete	6
Ozer et al. 2012 [15]	55	Male	Calcaneus	Foot drop, Squamous cell carcinoma	*E. faecium*	Antibiotics	Complete	6
Stark 2007 [16]	61	Male	Fibula	Good's Syndrome	None	*N/A*	Deceased	*N/A*
Walsh et al. 1993 [17]	55	Female	Sternum	Rheumatic heart disease, Mitral valve replacement	None	Antibiotics and debridement	Complete	1
Walsh et al. 1993 [17]	65	Male	Sternum	Coronary artery disease	None	Antibiotics and debridement	*N/A*	*N/A*
Hoddy et al. 1991 [18]	11	Male	Metatarsal	None	None	Antibiotics and debridement	Complete	2.5
Dubey et al. 1988 [19]	13	Female	Tibia	*N/A*	*E. agglomerans*	Antibiotics	Complete	*N/A*

Note: *S. aureus* - Staphylcoccus aureus; *E. faecium*- Enterococcus faecium; *E. agglomerans*- Enterobacter agglomerans, N/A - not available/not reported.

Conclusion

Osteomyelitis caused by *A. xylosoxidans* is highly unusual and should be excluded in instances of drug-resistant COM and in patients with a history of trauma and/or surgery. This case emphasises the complexity of musculoskeletal infections and the multidisciplinary approach that is necessary for their effective management in the absence of standardised best-practice guidelines.

Author statement

SI and AW performed the literature search and prepared the manuscript. SS and EO critically reviewed the content and revised the manuscript. All authors were involved in the patient's care.

References

[1] Kremers HM, Nwojo ME, Ransom JE, Wood-Wentz CM, Melton LJ, Huddleston PM. Trends in the epidemiology of osteomyelitis: a population-based study, 1969 to 2009. J Bone Joint Surg Am 2015;97(10):837–45.

[2] Tice AD, Hoaglund PA, Shoultz DA. Risk factors and treatment outcomes in osteomyelitis. J Antimicrob Chemother 2003;51(5):1261–8.

[3] Huang CC, Tsai KT, Weng SF, Lin HJ, Huang HS, Wang JJ, et al. Chronic osteomyelitis increases long-term mortality risk in the elderly: a nationwide population-based cohort study. BMC Geriatr 2016;16(72):1–7.

[4] Lazzarini L, Mader JT, Calhoun JH. Osteomyelitis in long bones. J Bone Joint Surg Am 2014;86(10):2305–18.

[5] Sia IG, Berbari EF. Infection and musculoskeletal conditions: osteomyelitis. Best Pract Res Clin Rheumatol 2006;20(6):1065–81.

[6] Kavanagh N, Ryan EJ, Widaa A, Sexton G, Fennell J, O'Rourke S, et al. Staphylococcal osteomyelitis: disease progression, treatment challenges, and future directions. Clin Microbiol Rev 2018;31(2):e00084–17.

[7] Hatzenbuehler J, Pulling TJ. Diagnosis and management of osteomyelitis. Am Fam Physician 2011;84(9):1027–33.

[8] Lee YJ, Sadigh S, Mankad K, Kapse N, Rajeswaran G. The imaging of osteomyelitis. Quant Imaging Med Surg 2016;6(2):184–98.

[9] Igra-Siegman Y, Chmel H, Cobbs C. Clinical and laboratory characteristics of Achromobacter xylosoxidans infection. J Clin Microbiol 1980;11(2):141–5.

[10] Marion-Sanchez K, Olive C, Platon MG, Cesarine M, Derancourt C, Pailla K. Achromobacter xylosoxidans in hospital environments: still waters run deep!. Trans R Soc Trop Med Hyg 2020;114(6):470–2.

[11] Pereira RH, Leão RS, Carvalho-Assef AP, Albano RM, Rodrigues ERA, Firmida MC, et al. Patterns of virulence factor expression and antimicrobial resistance in Achromobacter xylosoxidans and Achromobacter ruhlandii isolates from patients with cystic fibrosis. Epidemiol Infect 2017;145(3):600–6.

[12] Aisenberg G, Rolston KV, Safdar A. Bacteremia caused by Achromobacter and Alcaligenes species in 46 patients with cancer (1989-2003). Cancer 2004;101 (9):2134–40.

[13] Pamuk G, Aygun D, Barut K, Kasapcopur O. Achromobacter causing a thrombophlebitis and osteomyelitis combination: a rare cause. BMJ Case Rep 2015 bcr2015210718.

[14] Shinha T, Oguagha IC. Osteomyelitis caused by Achromobacter xylosoxidans. IDCases 2015;2(1):11–2.

[15] Ozer K, Kankaya Y, Baris R, Bektas CI, Kocer U. Calcaneal osteomyelitis due to Achromobacter xylosoxidans: a case report. J Infect Chemother 2012;18 (6):915–8.

[16] Stark Jj. Alcaligenes xylosoxidans osteomyelitis without trauma in a patient with Good's syndrome. Eur J Intern Med 2007;18(5):447.

[17] Walsh RD, Klein NC, Cunha BA. Achromobacter xylosoxidans osteomyelitis. Clin Infect Dis 1993;16(1):176–8.

[18] Hoddy DM, Barton LL. Puncture wound-induced Achromobacter xylosoxidans osteomyelitis of the foot. Am J Dis Child 1991;145(6):599–600.

[19] Dubey L, Krasinski K, Hernanz-Schulman M. Osteomyelitis secondary to trauma or infected contiguous soft tissue. Pediatr Infect Dis J 1988;7:26–34.

[20] Gomez-Cerezo J, Suárez I, Ríos JJ, Peña P, De Miguel MG, De Jose M, et al. Achromobacter xylosoxidans bacteremia: a 10-year analysis of 54 cases. Eur J Clin Microbiol Infect Dis 2003;22(6):360–3.

[21] Hu Y, Zhu Y, Ma Y, Liu F, Lu N, Yang X, et al. Genomic insights into intrinsic and acquired drug resistance mechanisms in Achromobacter xylosoxidans. Antimicrob Agents Chemother 2015;59(2):1152–61.

[22] Doi Y, Poirel L, Paterson DL, Nordmann P. Characterization of a naturally occurring class D β-lactamase from Achromobacter xylosoxidans. Antimicrob Agents Chemother 2008;52(6):1952–6.

[23] Amoureux L, Bador J, Verrier T, Mjahed H, De Curraize C, Neuwirth C. Achromobacter xylosoxidans is the predominant Achromobacter species isolated from diverse non-respiratory samples. Epidemiol Infect 2016;144 (16):3527–30.

[24] Wittmann J, Dreiseikelmann B, Rohde C, Rohde M, Sikorski J. Isolation and characterization of numerous novel phages targeting diverse strains of the ubiquitous and opportunistic pathogen Achromobacter xylosoxidans. PLoS One 2014;9(1)e86935.

[25] Lima ALL, Oliveira PR, Carvalho VC, Cimerman S, Savio E. Recommendations for the treatment of osteomyelitis. Braz J Infect Dis 2014;18(5):526–34.

[26] Marais LC, Ferreira N, Aldous C, Le Roux TLB. The management of chronic osteomyelitis: part II-principles of post-infective reconstruction and antibiotic therapy. SA Orthop J. 2014;13(3):32–9.

[27] Tice AD, Hoaglund PA, Shoultz DA. Outcomes of osteomyelitis among patients treated with outpatient parenteral antimicrobial therapy. Am J Med 2003;114 (9):723–8.

[28] Tosounidis TH, Calori GM, Giannoudis PV. The use of Reamer–irrigator–aspirator in the management of long bone osteomyelitis: an update. Eur J Trauma Emerg Surg 2016;42(4):417–23.

[29] Park KH, Cho OH, Lee JH, Park JS, Ryu KN, Park SY, et al. Optimal duration of antibiotic therapy in patients with hematogenous vertebral osteomyelitis at low risk and high risk of recurrence. Clin Infect Dis 2016;62(10):1262–9.