CASE REPORT

Chronic Osteomyelitis of the Tibia Caused by *Burkholderia pseudomallei*: A Case Report and Review of Literature

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ABSTRACT

Osteomyelitis accounts for the majority of bone infections with open fractures have higher rates of osteomyelitis in contrast to closed fractures. It is usually seen in open fractures with substantial contamination and soft tissue damage, as well as after internal fixation. Chronic osteomyelitis is recognised by continuance presence of microorganisms, sequestrum, low-level of inflammation and fistulae. The infection can be contained to the bone or spread to the soft tissues, periosteum, and bone marrow. The predominant aetiological agents are *Staphylococcus aureus, Streptococcus species, Enterococcus species, Pseudomonas aeruginosa* and *Enterobacteriaceae*, but rarely due to *Bukholderia pseudomallei*. We report a case of post-traumatic chronic osteomyelitis of tibia due to *Bukholderia pseudomallei*. This case emphasises the significance of considering melioidosis in patients with uncontrolled diabetes mellitus who have undergone surgical intervention and reside in a region where infectious diseases are prevalent.

Keywords: Post-traumatic chronic osteomyelitis, *Burkholderia pseudomallei*, Implant devices, Diabetes mellitus, Tibia

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INTRODUCTION

Bukholderia pseudomallei causing osteomyelitis is rare, yet it is one of the recognised presentations of melioidosis. The diagnosis and treatment of the case post a challenge as the clinical presentation of *Bukholderia pseudomallei* infection is identical with other infectious causes, and long-term treatment involves high costs and results in a loss of productivity. Infection is thought to be initially caused by direct inoculation with contaminated soil, followed by surgical procedures, and accompanied with uncontrolled diabetes mellitus that serves as a significant risk factor. A high index of suspicion towards melioidosis causing chronic osteomyelitis should be considered especially in cases of unresolved infection despite prolonged course of antibiotics.

CASE REPORT

A 30-year-old man with history of non-compliance diabetes mellitus (DM) for three years complained of wound breakdown and pus discharge after requested to be discharged at his own risk a week prior to current admission. The main complaints were associated with three days of fever, minimal pain and swelling of the right lower limb.

He was involved in a road traffic accident (RTA) in early 2015, and suffered an open fracture of the right tibia. Wound debridement was performed, and his right tibia was fixed using an external fixator and plating. Thereafter, conversion into inter-locking nail (ILN) was done in July 2015. He defaulted multiple follow-ups until two years later, when he presented to a different hospital with complaint of pus discharge from the previous wound. The removal of ILN and intramedullary reaming of canal were performed accordingly. Three tissues were collected from different sites of the wound intra-operatively and sent for culture and sensitivity

(C & S). Intravenous (IV) cefuroxime was instituted empirically while waiting for the culture results. The cultures grew *Staphylococcus aureus, Enterococcus faecalis* and mixed growth of more than three types of organism, respectively. The antibiotic was deescalated to cloxacillin and ampicillin. However, on day 4 post-operatively, he requested to be discharged at his own risk. He was an 'amphetamine chaser (shabu)' but denied of abusing other drugs intravenously.

On examination of the current admission, he was conscious without pallor. The vital signs showed that he was febrile with temperature of 38°C, blood pressure of 140/85mmHg, and pulse rate of 88 beats/minute. There were no skin abnormalities noted including injection marks at both upper limbs and elsewhere on the body. Lower limb examination revealed minimal swelling over the anterior aspect of the right lower limb with pus discharging from multiple sinuses at the wound site. There were warmth and mild tenderness associated with the swelling. The range of movement for the knee and ankle were full, with palpable dorsalis pedis and posterior tibialis arteries. The sensation was intact. Review of other systems was unremarkable. A provisional diagnosis of chronic osteomyelitis secondary to infected implant was made based on the history and physical examination.

The blood for C&S was collected and IV vancomycin was commenced. There were abundance of pus exudates and presence of necrotic bones found intraoperatively. Thus, wound debridement and intramedullary reaming of canal was performed, and tissue with pus were sent for C&S. Blood parameters revealed haemoglobin of 12 g/L, leukocytosis of 13 x 10^9 / L and platelet count of 529 x 10^9 / L. The C-reactive protein (CRP) was 17 mg/L (0.01 – 0.5 mg/dL). The imaging was done and findings were in keeping with osteomyelitis, (Figure 1a and 1b). Culture of the tissue demonstrated metallic sheen colonies

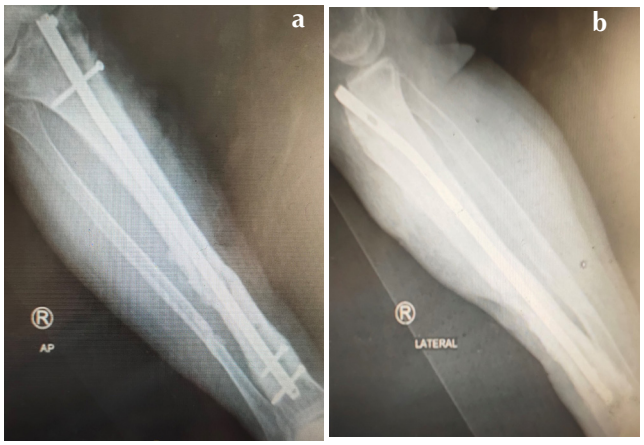

Figure 1: (a) An anterior-posterior view of right tibia and fibula. (b) Lateral view of right tibia and fibula. Both figures showing periosteal reaction along the entire length of tibia with peri-implant lucency. There was callus formation at the distal third of the right tibia and fibula without presence of acute fracture.

that were identified as *Burkholderia pseudomallei* after 48 hours of incubation, with no growth revealed from culture of blood and pus. The isolate was susceptible to trimetophrim-sulfamethoxazole, amoxicillin-clavulanate, ceftazidime, gentamicin, and imipenem. The antibiotic was deescalated to ceftazidime, 2 grams six hourly for six weeks intravenously followed with 12 hourly of oral trimetophrim-sulfamethoxazole, 320-1600mg. He was discharged home six weeks after, with full weight bearing and advice to complete five months of trimetophrim-sulfamethoxazole and comply with metformin. He was well and ambulating without aid during the last follow-up. Repeat imaging (Figure 2a and b) was done and reported as no worsening osteomyelitis.

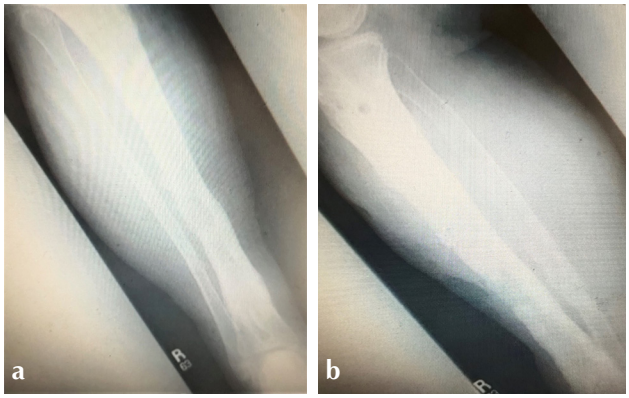

Figure 2: (a) An anterior-posterior view of right tibia and fibula. (b) Lateral view of right tibia and fibula

DISCUSSION

Melioidosis was first described by Whitmore and Krishnaswami in Rangoon, Myanmar, in 1912, caused by soil, Gram – negative, motile bacillus known as *Burkholderia pseudomallei* (1). Melioidosis occurs predominantly in northern Australia, India, and China, with the majority of the cases being from Thailand, Malaysia, Singapore, and northern Australia (2). Our patient suffered an open fracture of the right tibia that potentially provides entry of *B. pseudomallei*. It is a challenge to ascertain the direct relationship of soil exposure causing melioidosis in the above case, as the RTA occurred two years prior to presentation, despite percutaneous inoculation being identified as the principal mode of transmission other than inhalation and ingestion.

Bone involvement in melioidosis can occur in association with bacteraemia, and interlocking nails, plates, with screws were implanted on him which most probably infected by *B.pseudomallei*. *Bukholderia pseudomallei* forms biofilm on the implanted devices and these can be repeatedly infected. Both necrotic tissue and bone are enriched biofilm-forming substrates with a foreign-body effect that facilitated the colonisation of bacteria (3). The pathogen primarily forms surface colonies, which then develop into an exopolysaccharide matrix that serves as a diffusion barrier (3), thus inhibit antibiotics

to penetrate. These may explained the pathophysiology of *B.pseudomallei* causing chronic osteomyelitis of the tibia and fibula in the presented case. Besides that, for the above patient to develop chronic osteomyelitis, the related process needs to occur repeatedly for significant duration of time.

Previous reports revealed that up to 60% of patients with melioidosis were having pre-existing or newly diagnosed type II DM that shown to have reduced expression of certain cytokines and impaired T-cells which leads to decreased phagocyte activation (4). While, poorly controlled DM as in the above case leads into insulin deficiency that contributes directly to melioidosis. Moreover, drug abuse which would exacerbate patient's immunocompromised state and abstinence of treatment due to defaulted multiple follow-ups are other possibilities that need to be deliberated too in this case. Here, our patient demonstrated a precise relationship between predisposing condition of the host and infected biofilm that attribute to melioidosis in the form of osteomyelitis.

Osteomyelitis is a relatively uncommon melioidosis manifestation, occurring in approximate 4% of cases (2) and any bone can be infected following dissemination of disease elsewhere. Furthermore, depending on the severity of the fracture, osteomyelitis occurred at a rate of 1% to 5% after closed fractures, and 3% to 50% after open fractures (5). With trauma, there is a chance of developing osteomyelitis attributed by severe infection. This made our case susceptible to substantial risk of osteomyelitis as he had a history of open fracture of the right tibia following RTA. The long bones, such as the femur and tibia, are more commonly involved than bones of the upper limb, particularly bones near the knee joint, as demonstrated in this case. Increased vascular supply in the metaphyseal regions of the long bones allows infection to spread to bones and joints.

The manifestation for melioidosis of the bone and joint infections is typically chronic, with a low overall mortality rate. It can be a single or multiple bone or joint involvement, as seen in the past with melioidosis-related musculoskeletal infections. Majority of osteomyelitis around the knee joint associated with septic arthritis (5). This is consistent with contiguous spread of infection. Our case was unique as there was no evidence of septic arthritis or breach of the joint capsule that strongly suggestive of blood dissemination in contrast to contiguous spread.

Despite superficial wounds or fistulae, positive microbiological cultures from bone biopsy around areas of necrosis are needed, as these may contain microorganisms that colonise the wound and lead to false-negative results. To increase the diagnostic yield, several samples should be taken around the infective foci. *Bukholderia pseudomallei* isolation from clinical specimens is the gold standard for melioidosis, and its isolation is interpreted as a significant pathogen.

The cornerstone of osteomyelitis treatment incorporates extensive debridement of infected bone, necrotic tissue, discharge drainage, soft tissue reconstruction and culture-directed antibiotics. The antibiotic of choice for treating melioidosis of the bone includes intravenous ceftazidime or a carbapenem group, followed by at least 12 weeks of oral cotrimoxazole or amoxicillin–clavulanic acid as eradication therapy for deep-seated infection. It is important to complete the therapy, as this may prevent relapse in melioidosis.

CONCLUSION

It is difficult to differentiate *B. pseudomallei* causing osteomyelitis with other causative agents unless proven by culture. Imaging complements culture, thus differentiation from neoplasm and granulomatous disease is possible. Accurate and timely diagnosis of melioidosis remain crucial, hence prompt definitive antimicrobial therapy can be instituted. Our case is rare, yet unique which essentially made melioidosis is one of the differentials in an appropriate clinicoepidemiological setting.

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