

Burkholderia pseudomallei: limb salvage versus major amputation, a dilemma

Key words:

- *Burkholderia pseudomallei*
- Degloving injury
- Melioidosis
- Wound infection

Abstract: Melioidosis, predominantly an infectious disease in the tropical regions of the world, has varying clinical manifestation, such as localised abscess and full blown multiple abscess formation with sepsis. Musculoskeletal infections are usually seen as part of multiorgan involvement. Common manifestation of musculoskeletal melioidosis includes septic arthritis, osteomyelitis, and soft tissue abscesses. In the majority of fatal cases had one or more risk factors, such as diabetes, alcoholism, chronic renal disease, chronic lung disease, and malignancy or immunosuppressive therapy. Prolonged treatment and the need for multiple surgical interventions results in a clinical burden treating this infection. The overall mortality from this infection remains extremely high despite recent advancement in its treatment. We concluded that a high level of suspicion of melioidosis is important for early detection and treatment to reduce morbidity and mortality.

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Melioidosis, also called Whitmore's disease, is an infection caused by *Burkholderia pseudomallei*, which is a Gram-negative saprophyte initially described by Whitmore and Krishnaswami in 1912. Melioidosis



Figure 1. Initial right knee wound posttrauma looks benign, however was severely contaminated

is predominantly an infectious disease in the tropical regions of the world, especially in Southeast Asia and northern Australia (Smith, 2000) with the disease burden of approximately 165,000 new cases annually worldwide with 89,000 mortality annually (Khakhum et al, 2019). The organism causing this infection are often found in contaminated water and soil. The clinical manifestation are variable ranging from localised abscess to full blown multiple abscess and the formation with sepsis. It is associated with high mortality rate (Currie, 2015). We hereby present a rare case of major amputation and mortality caused by post-traumatic infection with melioidosis.

Case presentation

A 43-year-old Malay lady with poorly controlled type 2 diabetes mellitus, presented to our centre after skidding from a motorbike and falling into a paddy field drain. She sustained degloving injury over her right knee (**Figure 1**) with an open comminuted supracondylar right femur fracture with intercondylar split (**Figure 2**).

Upon admission, it was noted that her blood sugar levels were poorly controlled despite

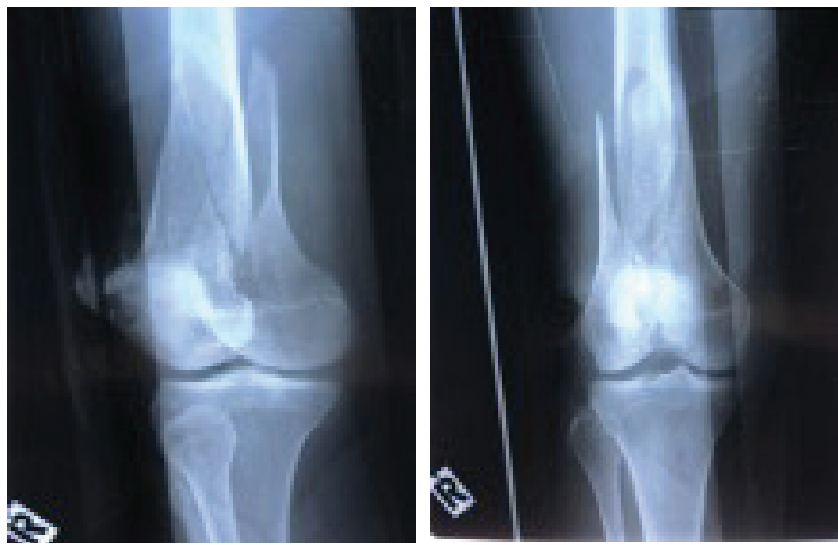


Figure 2. X-ray of right knee on admission.

intravenous insulin sliding scale infusion. Antibiotics were started immediately upon presentation to emergency department. An urgent wound debridement was done and she was put on calcaneal pin traction. She then underwent second look debridement after 48 hours of her first debridement.

Subsequently, an external fixator was applied on her right lower limb. (**Figure 3**) Her wound was managed with povidone-iodine (PVP-I) packed dressing that was changed daily. Her wound condition, however, did not improve even after multiple debridement were performed. The wound was noted to be infected and sloughy on each debridement. There was exudate followed by pus discharge a few days after each debridement.



Figure 3. Wound picture after multiple debridement.

She was initially treated with IV Cefuroxime, Flagyl and Gentamicin in view of contaminated wound over her open fracture site. Her blood and tissue culture showed *Burkholderia pseudomallei* which lead to initiation of IV Ceftazidime. Despite six weeks of intravenous antibiotics based on sensitivity with multiple wound debridement, her wound worsened resulting in right hip disarticulation six weeks post-trauma. Unfortunately, her condition deteriorated further and she succumbed to severe sepsis.

Discussion

Melioidosis is caused by *Burkholderia pseudomallei*, which is a motile aerobic, non-spore forming Gram-negative bacilli. It is an opportunistic organism (Mahfouz et al, 2006) living in natural environment especially in stagnant water and rice paddies. Subhadrabandhu et al, 1995; Suputtamongkol et al, 1999).

This disease is known to be transmitted via direct contact with contaminated soil or water. Other mode of transmission includes inhalation/ aspiration which causes melioidosis pneumonia (Puthuchery et al 1992; How et al, 2006; Inglis et al, 2006; Chen et al, 2015). The clinical manifestation of melioidosis is broad. Patient may have an asymptomatic infection with delayed conversion to clinical evident infection, a localised soft tissue infection, pneumonia or even septic shock with multiple abscesses.(Puthuchery et al 1992; How et al, 2006; Inglis et al, 2006)

An underlying diabetes mellitus (Suputtamongkol et al, 1999; Pagalavan et al, 2005) as well as a severely contaminated wound involving paddy field post-trauma were among her risk factors to this opportunistic infection. Suputtamongkol et al, concluded that among diabetic patients, rice farmers had 3 to 9 times higher risk of developing melioidosis than non-diabetic and non-rice farmers. This shows synergistic effect between an impaired host immunity with the exposure to *Burkholderia pseudomallei* as risk factors for melioidosis. (Suputtamongkol et al, 1999).

Multiple studies have also shown that diabetes mellitus is the most common underlying condition associated with melioidosis infection and more likely to develop severe infection as compared with non-diabetic patients (Suputtamongkol et al, 1999; Currie, 2000; Simpson et al 2003; Pagalavan, 2005; Mahfouz et al, 2006; Chen et al, 2015; Kronsteiner et al, 2019). This is likely due to diabetes mellitus causes impair

neutrophil functions which includes chemotaxis, adhesion and phagocytosis (Marhoffer et al, 1992; Simpson et al, 2003; Pandey et al, 2010; Wiersinga et al, 2018). Other risk factors including chronic renal disease, chronic lung disease and thalassemia has been associated with higher mortality (Currie, 2015)

In our local setting, Tang et al reported that there was a total of 46 confirmed cases between 2013 to 2017. Out of which, 46% required ICU admission with an overall mortality of 52%. High incidence of melioidosis may be due to the exposure to contaminated soil and water as high number of population are engaged in agricultural activities (Ahmad et al, 2009). However, only 28.9 % of our patients were given antibiotic for melioidosis on admission.

A high level of suspicion is important in detection of *Burkholderia pseudomallei* infection. Melioidosis should be considered as an important differential diagnosis in patient who has history of contact to contaminated soil or water or recent travel history to endemic area, especially in those patients who are immunocompromised (Puthuchery et al, 1992) Melioidosis remains to be greatly under-diagnosed and there is need for greater awareness which enable early detection and treatment to overcome the high mortality rates (Subhadrabandhu et al, 1995; Chen et al, 2015). Early identification and treatment with specific antibiotic may reduce the risk of morbidity and mortality in patients with *Burkholderia pseudomallei* infection.

Treatment of musculoskeletal melioidosis involves appropriate intravenous antibiotic and early surgical intervention that includes wound debridement, arthrotomy washout, decompression, external or internal fixation and antibiotic bead placement (Pattamaspong et al, 2011; Gouse et al, 2017; Pandey et al, 2010). Ceftazidime powder in calcium hydroxyapatite block may improve the outcome of patient with melioidosis osteomyelitis as *Burkholderia pseudomallei* often shows resistance to gentamicin (Ng et al, 2006). Patients with musculoskeletal melioidosis may require repeated surgical intervention (Pattamaspong et al, 2011; Gouse et al, 2017; Pandey et al, 2010). Patients who have recovered from melioidosis require long term oral antibiotic for maintenance as there is risk of relapse and recurrence (Dance, 2014). Hence, course of treatment for melioidosis is time consuming and cost intensive.

Conclusion

This case study presents a rare case of post-traumatic *Burkholderia* spp. infection causing hip

disarticulation and mortality in a young patient with the risk factor of diabetes mellitus and exposure to contaminated water. To conclude, a high level of suspicion of this fatal organism is important for early detection, and it should lead to more aggressive management including early debridement and a lower threshold for major amputation, eventuating in a lower risk of morbidity and mortality. **WAS**

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