



## Concomitant Staphylococcus aureus and Burkholderia pseudomallei infection causing multifocal osteomyelitis a rare presentation of melioidosis in an uncontrolled diabetic host- case series

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### Abstract

**Introduction:** *Melioidosis is a potentially fatal infectious disease caused by a soil transmitted saprophyte Burkholderia pseudomallei, a Gram-negative bacillus with bipolar staining. Melioidosis has expanded its occurrence from the tropics to other parts of the world. It usually causes abscesses in lung, liver, spleen, skeletal muscle and parotids in patient with risk factors such as Diabetes mellitus, heavy alcohol use, smoking, chronic lung and kidney disease, corticosteroid use. This organism is acquired through percutaneous inoculation and inhalation. Melioidosis can present with septicemia, visceral abscesses, cavitary pneumonia and rarely multifocal osteomyelitis.*

**Aims and Objectives:** *Musculoskeletal melioidosis is not common in India even though sporadic cases have been reported mostly involving soft tissues. Objective of this study is early diagnosis and to start appropriate treatment in patient with melioidosis.*

**Material and Method:** *During a period of two years (March 2017 to April 2019), we had seven patients with musculoskeletal melioidosis. All patients presented with multifocal osteomyelitis, recurrent osteomyelitis or septic arthritis cause by concomitant staphylocococcus aureus and burkholderia pseudomallei organism. All patients were diagnosed on the basis of clinical, microbiological and radiological correlation. All patients were treated by surgical debridement followed by a combination of antibiotics; (ceftazidime, amoxy-clavulanic acid and co-trimoxazole and doxycycline) for minimum period of three months to maximum period of six months. All patient were followed up for a period of one year and all patients recovered completely with no recurrences.*

**Result:** *With early diagnosis and appropriate treatment all patient were cured of the infection with no recurrence.*

**Conclusion:** *Diagnosis of Melioidosis missed in many parts of the world due to lack of awareness of this infection and lack of adequate diagnostic techniques. It mimics other disease such as tuberculosis and infections caused by Staphylococcus aureus. Delay in diagnosis or treatment against melioidosis can worsen the outcome. Initial therapy with intravenous antibiotics followed by oral maintenance therapy and appropriate surgical intervention remains vital in the management.*

**Keywords:** *Burkholderia pseudomallei, melioidosis, musculoskeletal infection.*

## Introduction

Melioidosis is an fatal infectious disease, caused by a gram-negative, obligatory, aerobic, non-spore forming bacillus, *Burkholderia pseudomallei* (bipolar staining and is vacuolated and slender and has rounded ends; it is often described as having a “safety pin” appearance). It is oxidase positive. It is a water and soil pathogen. The pathologist Alfred Whitmore and his assistant C. S. Krishnaswami first described melioidosis as a “glanders-like” disease among morphia addicts in Rangoon, Burma, in 1911. *Burkholderia pseudomallei* has off late gained importance as an emerging pathogen in India. It is capable of causing various clinical manifestations like pneumoniae, septicaemia, arthritis, abscess, rare multifocal osteomyelitis and is associated with high morbidity and mortality. Melioidosis, was named from the Greek “melis” (distemper of asses) and “eidos” (resemblance) by Stanton and Fletcher in 1932. In India, most cases have so far been reported from the southern states like Kerela and Tamil Nadu. Isolated cases have also been reported from eastern and northeastern parts of India. Three modes of acquisition, i.e., inhalation, ingestion, and inoculation. Risk factors includes such as Diabetes mellitus, heavy alcohol use, smoking, chronic lung and kidney disease, corticosteroid use, thalassemia, previous trauma, rheumatic heart disease and/or cardiac failure, and surgery. Diabetes mellitus is the most important predisposing risk factor, and it increases the risk of melioidosis by 100-fold. The clinical presentations of bone and joint infections due to *Burkholderia pseudomallei* are indistinguishable from other infectious causes. Melioidosis in bone and joint infection is more common in males. This may be the case because males are exposed to *Burkholderia pseudomallei* while working in the rice paddies and they may be more involved in other outdoor activities. Melioidosis should be considered in the differential diagnosis in patients from the disease endemic area, or who are returning from these areas. Melioidotic bone and joint infections remain uncommon and are usually difficult to differentiate from other causative agents such as *Staphylococcus*, *Streptococcus* and

others. Lack of awareness about the disease, limited laboratory resources to isolate the organism, and confusion with other infectious diseases such as *Mycobacterium tuberculosis*, may lead to the misdiagnosis of melioidosis. Melioidosis is diagnosed on the basis of the clinical and laboratory parameters, and radiology. Prompt administration of appropriate antimicrobial therapy, and achieve better prognostic outcome. Serology may be helpful in cases of culture-negative results, or in the absence of clinical samples from patients with melioidosis. However, the serology results should be interpreted cautiously in endemic areas, where local populations have raised melioidosis antibody levels. Mortality in acute severe melioidosis even with appropriate treatment still remains considerably high, ranging from 30% to 47%. Although not so uncommon in India but early and correct diagnosis and institution of proper antimicrobial therapy is important in order to reduce morbidity and mortality and have a favourable outcome.

## Material and Method

During a period of two years, we had seven patients (All males) with concomitant *staphylococcus aureus* and *burkholderia pseudomallei* organism infection causing melioidosis. All patients were diagnosed on the basis of clinical and laboratory parameters, and radiology. All patients were treated by surgical debridement followed by a combination of antibiotics; (ceftazidime, amoxy-clavulanic acid, co-trimoxazole and doxycycline) for minimum period of three months to maximum period of six months. All patient were followed up for a period of one year and all patients recovered completely with no recurrences.

- 1) **Source:** 7 patients (All male) who attended OPD at Sri Ramachandra Institute of Higher Education and Research (SRIHER), Chennai during the study period of 2 year.
- 2) **Duration of study-** 2 year (March 2017 – April 2019).
- 3) **Number of subjects-** 7 male.

4) **Case:** 48 years, male, farmer by occupation, resident of chennai city, came to OPD at SRIHER, chennai with chief complaint of pain over left elbow followed by bilateral knee and right ankle for past 3 months. Pain was insidious in onset, Sharp and pricking in character. No history of night cries, trauma, weight loss and loss of apatite. Patient was a known case of Uncontrolled Type 2 diabetes mellitus with poor glycemic control. No similar complaint in any of the family member. History was also significant for occupational exposure to soil. His serology was negative for HIV. No history of chronic drug intake in past.

On examination, he was febrile, tachypneic, and tachycardic. He was pale and mildly icteric. Systemic examination was notable for hepatosplenomegaly, and musculoskeletal examination revealed swelling and tenderness over left elbow followed by bilateral knee, and right ankle with restricted left elbow joint and followed by bilateral knee and right ankle joint mobility. Initial evaluation revealed a elevated white cell count (17300 cells/mm<sup>3</sup>, neutrophils 80%), inflammatory markers (erythrocyte sedimentation rate 146 mm, C-reactive protein 89 mg/L) and Elevated serum procalcitonin. Magnetic resonance imaging of left elbow, bilateral knee and right ankle shows multifocal osteomyelitis of left elbow, bilateral knee and right ankle. Patient Initially underwent left elbow arthrotomy. Post operative pus culture shows Stahylococcus aureus infection and treated with appropriate antibiotics for the same. Patient Improved briefly, Patient presented again with recurrence of symptoms after 7 days. Blood culture and echo (TEE, TTE) was done to rule out Infective endocarditis. In view of occupation, uncontrolled diabetes mellitus and non improvement, Melioidosis was suspected. Patient underwent bilateral knee and right ankle arthrotomy. Intraoperatively pus culture, gram stain and culture, Acid fast bacilli stain, Fungal stain and culture, Gene Expert and polymerase chain reaction for melioidosis was sent. Pus culture shows growth of staphylococcus aureus and PCR for melioidosis was positive (All other test were negative) and

diagnosed as a case of melioidosis. Started on Injection ceftazidime 2 gm TDS for 4 weeks followed by Tablet Cotrimoxazole for 6 months. Patient were followed up till 2 year period and showed complete resolution of symptoms with no recurrence.



**Figure 1:** X-ray Right foot AP view



**Figure 2:** X-ray left elbow AP and Lateral view



**Figure 3:** X-ray bilateral knee Ap and lateral



**Figure 4:** 1 year follow up, Right knee, Left knee and Left elbow



**Figure 5:** 1 year follow up Right ankle

### Result

With early diagnosis and appropriate treatment all patient were cured of the infection with no recurrence.

### Discussion

Melioidosis, caused by soil and water bacterium *B. pseudomallei*, is endemic to the tropical regions. Recent studies have reported an increase in the cases of melioidosis diagnosed from India, owing to improved microbiological diagnostic techniques and polymerase chain reaction (PCR)-based diagnostics. Identified risk factors include poorly controlled diabetes mellitus, harmful consumption of ethanol, malignancy, and chronic immunosuppression. A high clinical suspicion and adequate microbiological facilities are necessary to make a diagnosis of melioidosis. Multifocal osteomyelitis is a rare presentation of melioidosis. Previously reported cases have been acute in their presentation, with a mean duration of symptoms of less than 2 weeks. This suggests that a multifocal presentation usually follows bacteremia and subsequent inoculation of multiple sites. Our patient presented with symptoms for 3 months with multifocal osteomyelitis. In India, quite a number of cases were reported though many are still underreported due to its protean manifestations. Diabetes mellitus has been found to be one of the most frequent predisposing factors. Human infection occurs through inhalation or direct inoculation on damaged skin. Our patient was exposed to soil, contaminated water and paddy fields which could be the source of infection. Vidyalaxmi et al. found a correlation of 76% of diabetes with Melioidosis. Melioidosis is a systemic manifestation with pulmonary involvement as the commonest manifestation. It is also associated with liver and spleen. Bone involvement has been reported in 16% cases by Chiranjay et al. The drug of choice is Ceftazidime in systemic melioidosis. The clinical presentation is quite variable. It can mimic conditions from acute or chronic forms of infection to various rheumatoid disorders. 4 Patient had initial presentation of chronic granulomatous osteomyelitis due to

melioidosis, which remains indistinguishable from tuberculosis or staphylococcal abscess except by microbiological culture. One should always consider melioidosis as a differential diagnosis with atypical presentations especially if patient is from endemic area. One patient presented initially with polyarthralgia-like symptom whose serology was similar to typhoid. Later, he presented with multifocal osteomyelitis in elbow, knee and foot. All of them were diabetic. Blood culture is usually negative. Even though various indirect hemagglutination tests are reported, we have no experience in using it for diagnosis. All our patients had full recovery. Till now, there has been no relapse in any of our patients. However, 10% relapse even after 20 weeks of treatment is reported. However, relapse rate increases to 30% if duration of treatment is less than eight weeks. We realize that distribution and frequency of musculoskeletal melioidosis is probably greatly underestimated. It is quite difficult to prevent it in rice producing areas and probably this is why it is more common in southern India. The longer duration of treatment and the cost of antibiotic therapy are important issues. Awareness of this infection, with all its forms of presentation will help early detection, isolation of the organism and disease management.

### Conclusion

Diagnosis of Melioidosis missed in many parts of the world due to lack of awareness of this infection and lack of adequate diagnostic techniques. It mimics other disease such as tuberculosis and infections caused by *Staphylococcus aureus*. A high index of suspicion of melioidosis is required to make the diagnosis. Delay in diagnosis or treatment against melioidosis can worsen the outcome. Initial therapy with intravenous antibiotics followed by oral maintenance therapy and appropriate surgical intervention remains vital in the management. Those patients with deep-seated or complicated infections require intravenous antibiotics for 4–8 weeks, followed by oral antibiotics for a minimum of 12 weeks. Ceftazidime is usually the intravenous antibiotic of choice, which is followed by oral

therapy such as cotrimoxazole. Some countries are now using outpatient antimicrobial therapy for their clinically stable patients. Unfortunately no vaccine has yet been developed for this disease, which makes the awareness and understanding of melioidotic bone and joint infections, and the need for timely diagnosis and treatment, all the more relevant to microbiologists today. With increasing awareness and better diagnostic facilities, probably musculoskeletal melioidosis will be increasingly diagnosed in future

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