Case Report

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A Case Report on Septic Arthritis caused by *Burkholderia pseudomallei*

Microbiology Section

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ABSTRACT

Melioidosis is an emerging infection in India caused by the environmental saprophyte *Burkholderia pseudomallei*. It is a gram negative, oxidase-positive bacillus that is intrinsically resistant to gentamycin, penicillin, and colistin. Risk factors for this infection include diabetes mellitus, heavy alcohol use, malignancy, chronic lung infection, liver, and kidney conditions. *B. pseudomallei* can lead to variable clinical manifestations, ranging from mild localised abscesses to invasive infections. However, a proper identification system for early detection and speciation is not universally available in all laboratories, and it can be easily misidentified as *Pseudomonas* species due to its unfamiliarity. Consequently, there may be a delay in diagnosis and failure to initiate appropriate and effective treatment, which can worsen the outcome. In this report, the author presents a case of septic arthritis in a 44-year-old diabetic male with clinical symptoms of melioidosis and involvement of multiple organs.

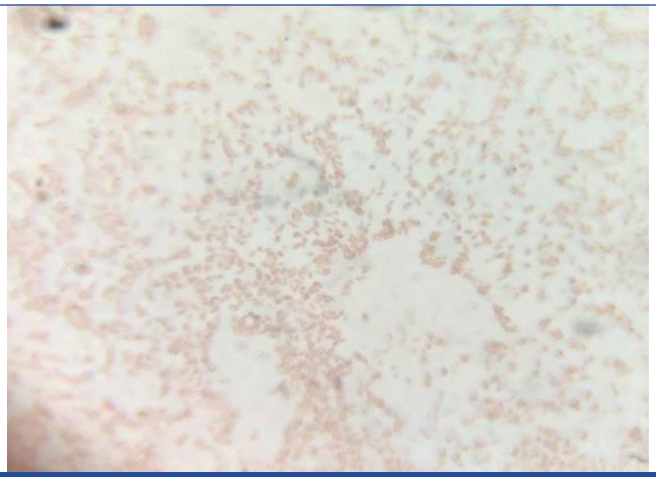
Keywords: Diabetes mellitus, Emerging infection, Melioidosis, Variable manifestations

CASE REPORT

A 44-year-old male patient presented to the referral centre's Emergency Department with complaints of continuous low-grade fever not associated with chills or rigors. He also reported newly developed bilateral painful knee and left ankle swellings, as well as a cough with mucoid expectoration. The patient had previously experienced left elbow pain, which subsided after starting analgesics. He had a two-year history of Type 2 Diabetes Mellitus and was taking medication for it. Additionally, he had a history of heavy alcohol use and worked as a farmer. Earlier, he was admitted to a local hospital in Coimbatore with a 15-day history of continuous low-grade fever and 10-day history of left elbow pain. Laboratory tests revealed an elevated Erythrocyte Sedimentation Rate (ESR) level (>140 mm/hour) and positive Antinuclear Antibodies (ANA) (1:320, nuclear pattern). The patient was started on steroids (inj. efcorlin 100 mg TDS) and hydroxychloroquine (tab. 200 mg BD) for seven days due to suspicion of a mixed connective tissue disorder. Echocardiogram (ECHO) and chest X-ray results were normal. After 48 hours of being asymptomatic, the patient developed high-grade fever accompanied by chills and rigor. He was then prescribed tab. ceftriaxone (1 gm BD) and tab. doxycycline (100 mg BD) and referred to another centre for further management.

Written informed consent was obtained from the patient. On general examination, the patient exhibited fever, pallor, and icterus. Local examination revealed swelling, warmth, and tenderness in both knees and the left ankle. Blood investigations upon admission showed a Haemoglobin (Hb) level of 5.8 g/dL, Total Leucocyte Count (TLC) of 14660/cumm, Erythrocyte Sedimentation Rate (ESR) of 140 mm/hour, and C-Reactive Protein (CRP) of 24 mg/dL. Repeat ANA testing yielded similar positive results, while Line Immunoassay (LIA) was negative. After ruling out other causes for arthritis, septic arthritis was suspected, and empirical antibiotics (inj. cefotaxime 1 gm BD and tab. doxycycline 100 mg BD) were initiated. Blood samples were collected for analysis. The patient underwent arthrotomy for swelling in the left knee joint, and synovial fluid was collected and sent to the laboratory.

Synovial fluid analysis revealed a total cell count (TC) of 30473/cumm, Red Blood Cell (RBC) count of 22000/cumm, sugar level below 10 mg/dL, and protein level of 3.2 gm/dL. Gram staining of all the samples showed irregularly stained gram negative bacilli [Table/Fig-1].



[Table/Fig-1]: Gram stain shows irregularly stained gram negative bacilli under the microscope (100x magnification).

The isolated organism displayed non lactose fermenting moist colonies [Table/Fig-2] on MacConkey agar plates and progressed to dry, wrinkled rough colonies with a cauliflower head appearance by day 7 of incubation at 37°C [Table/Fig-3,4]. It was oxidase positive, capable of hydrolysing bile esculin, reduced nitrate to nitrite, and resistant to Polymyxin B (50 units). Conventional methods indicated

[Table/Fig-2]: Day 2 growth of *Burkholderia pseudomallei* non lactose fermenting colonies with pinkish hue seen on MacConkey agar plate.

that the organism was suspected to be *Burkholderia* species. Further confirmation through Matrix Associated Laser Desorption Ionisation-Time OF Flight (MALDI-TOF) and PCR-based DNA sequencing targeting the 16S rRNA region identified it as *Burkholderia pseudomallei* (Accession number: OR271924).

[Table/Fig-3]: Day 4 growth of *Burkholderia pseudomallei* colonies on a MacConkey agar plate. **[Table/Fig-4]:** Dry, wrinkled, rough colonies with cauliflower head appearance as seen on Day 7 of incubation. (Images from left to right)

Upon identification of *Burkholderia pseudomallei*, the patient was shifted to Inj. Meropenem (1 g) and Cap. Doxycycline (100 mg) for four weeks. Fever spikes began to subside, and the patient received daily wound dressing and regular physiotherapy. He showed symptomatic improvement, became afebrile, and the joint swellings subsided [Table/Fig-5]. Subsequently, he was discharged with Cap. Doxycycline prescribed as maintenance therapy for six months. After four months, the patient was contacted, and it was confirmed that he had fully recovered from his symptoms.

[Table/Fig-5]: Left knee post arthrotomy.

DISCUSSION

Burkholderia pseudomallei shows ubiquitous presence in soil and water, and all occupational groups are susceptible to the disease. It causes melioidosis, also known as Whitmore's disease, named after Captain A. Whitmore, who first isolated this organism. This soil-borne disease is endemic in Southeast Asia and Northern Australia [1]. *B. pseudomallei* is a resilient organism that can survive hostile environmental conditions, including prolonged nutritional deficiency, acidic environments [2], wide temperature ranges (24° to 32°C), and dehydration (soil water content of <10% for up to 70 days) [3]. Infection can be acquired through inhalation, ingestion, or cutaneous inoculation [4].

According to a retrospective analysis study conducted in the Netherlands, around 70% of the patients had one or more risk factors associated with melioidosis, such as diabetes, cystic fibrosis, chronic liver, kidney or lung disease, excessive alcohol consumption, and immunosuppression [5]. In Thailand, between 2012 and 2015, out of 7,126 confirmed cases of melioidosis, the most frequently observed coexisting health conditions were diabetes mellitus (43%), followed by hypertension (15%), and Chronic Kidney Disease (CKD) (11%) [6]. In contrast, a study conducted in India with 189 melioidosis patients, whose infections were verified through culture, showed that individuals with diabetes had a greater risk of musculoskeletal complications (with an odds ratio of 2.14) [7]. Furthermore, it was estimated that having diabetes increased the likelihood of contracting melioidosis by 100-fold [8].

Given his occupation as a farmer and having risk factors such as being diabetic and alcoholic, the patient was at a higher risk of developing *Burkholderia* infection.

The Centres for Disease Control and Prevention (CDC) recommend initial Intravenous (i.v.) therapy of ceftazidime administered every 6-8 hours or meropenem administered every eight hours. Oral treatment should only be substituted when there is evidence of clinical improvement after IV therapy, which consists of trimethoprim-sulfamethoxazole taken every 12 hours or amoxicillin/clavulanic acid (co-amoxiclav) taken every eight hours [9].

Among the various organs that *Burkholderia pseudomallei* affects, bones and joints, when affected, usually recover with a full range of movements and without relapses [10]. Identifying *Burkholderia pseudomallei* from clinical specimens remains the gold standard for diagnosis. Therefore, collecting appropriate specimens for culture is crucial.

The index patient was started on oral ceftriaxone and doxycycline initially, then shifted to IV cefotaxime and oral doxycycline empirically in the referral centre. However, his symptoms did not improve, and he developed complications such as dissemination of septic arthritis, septicaemia, and bronchopneumonia. Once the causative organism was identified as *Burkholderia pseudomallei*, the patient was switched to IV meropenem and oral doxycycline. He responded well to this combination of drugs. Thus, it is important to note that changing to the appropriate medication led to an improvement in the patient's condition.

This case emphasises the need for timely diagnosis and appropriate management, which can contribute to a better prognosis for the patient. It is crucial to quickly identify the condition at an early stage and initiate the appropriate long-term treatment to achieve a cure for the illness [11]. Although musculoskeletal melioidosis is an established entity, it is less commonly reported than other manifestations of melioidosis. Below, a comparison has been tabulated between various studies regarding the characteristics and results of patients with septic arthritis [Table/Fig-6] [12-15].

Author	Place of the study	Year	Clinical picture	Investigations	Co-morbidities	Treatment	Outcome	Profession
Weerasinghe NP et al., [12]	Sri Lanka	2018	Severe painful left hip and swelling with fever for 14 days	TC- 12.4×10^9/L Hb- 9.1 g/dL CRP- 86 mg/dL ESR- 65 mm/hr	Poorly controlled Type 2 Diabetes Mellitus for 11 years Autoimmune Hepatitis for six months on regular medication	i.v. Imipenem and Oral co-trimoxazole for 21 days followed with oral cotrimoxazole 10 week	Recovered	Field officer

Patro S et al., [13]	Odisha, India	2019	Fever for 45 days with left knee joint swelling for three days	Not mentioned	Newly diagnosed diabetes mellitus	i.v. ceftazidime and I.V imipenem for 14 days followed with oral co-trimoxazole for 12 weeks	Recovered	Farmer
Arunpriyandan V et al., [14]	Sri Lanka	2022	Fever with painful joint and swelling of the right knee for 10 days	TC- 18,000/dL Hb- 9 g/dL CRP- 259 mg/dL ESR- 53 mm/hour	Diabetes mellitus for seven years	i.v. ceftazidime for 14 days followed by oral co-trimoxazole for 12 weeks	Recovered	Muddy field worker
Biswajyoti B et al., [15]	Assam, India	2020	Fever with pain and swelling of right ankle joint for 10 days	Hb- 9.8 mg/dL TC- 7.3×10^3/µL ESR- 45 mm/h CRP- 164.2 mg/L	Hypertension for 14 years Diabetes mellitus for seven years	i.v. ceftazidime (1 g) and tazobactam (125 mg) with oral co-trimoxazole twice daily	Succumbed to the infection	Farmer
Present study	Tamil Nadu, India	2023	Continuous low-grade fever and bilateral painful knee and left ankle swelling for 10 days	Hb - 5.8 g/dL, TC- 14660/cumm, ESR-140 mm/hr, CRP- 24 mg/dL	Diabetes mellitus for two years	i.v. Meropenem (1 g) and cap. Doxycycline (100 mg) for four weeks followed by cap. doxycycline for 6 months	Recovered	Farmer

[Table/Fig-6]: Comparison of present study with different studies [12-15].
TC: Total cell count; Hb: Haemoglobin; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate

CONCLUSION(S)

The presented case emphasises the importance of recognising and promptly managing septic arthritis caused by *Burkholderia pseudomallei* to mitigate its potentially devastating consequences on patient health and quality of life. Awareness among physicians, microbiologists, and laboratory technicians is crucial to combat this infection, especially in endemic countries. *Burkholderia pseudomallei* must be kept in mind as a pathogen when treating patients in endemic countries. The long treatment regimen must be followed seriously for clinical improvement of the patient and to avoid relapses.

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