CASE REPORT

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A Case Report on Musculoskeletal Melioidosis

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ABSTRACT

Melioidosis, caused by *Burkholderia pseudomallei*, is an underdiagnosed infection in India with a high case fatality rate if untreated. We report a case of a 59-year-old diabetic male farmer from West Bengal who presented with fever and respiratory distress. Initial empirical therapy with cefoperazone-sulbactam failed to improve his condition. Subsequently, he developed acute pain and swelling in the left shoulder. Imaging revealed osteomyelitis with intraarticular and periarticular abscesses. Surgical debridement and culture studies confirmed *B. pseudomallei*, identified using Ashdown's medium, Gram staining, biochemical tests, and automated Vitek 2 analysis. The organism exhibited resistance to ceftazidime but was susceptible to meropenem and doxycycline. Despite initiation of targeted therapy, the patient took discharge against medical advice, preventing further outcome assessment. This case highlights the challenges of diagnosing melioidosis, particularly in rural settings where it mimics other tropical infections. Early suspicion, appropriate microbiological workup, and prompt initiation of effective antimicrobial therapy are crucial for improved outcomes. Greater clinician awareness and expanded diagnostic capacity are needed to prevent missed diagnoses and reduce mortality in endemic regions.

Keywords: Melioidosis, Burkholderia pseudomallei, Endemic, Diagnosis delay, Clinical microbiology

INTRODUCTION

Melioidosis or 'Whitmore's Disease' is an underdiagnosed and under reported emerging infection in India caused by soil saprophyte *Burkholderia pseudomallei.*[1] It is endemic in Southeast Asia and Northern Australia where it is found in soil and surface water.[2] *Burkholderia pseudomallei* is a Gram-negative, oxidase positive, non-fermenter bacillus which is intrinsically resistant to many antimicrobials e.g., gentamicin, colistin.[3,4] It is transmitted by direct inoculation in the punctured wound, inhalation and ingestion in high-risk individuals e.g., chronic conditions like diabetes, obstructive pulmonary disease, chronic kidney disease and immunocompromised state.[5] The spectrum of clinical illness ranges from local suppurative abscess of joints and viscera to severe systemic diseases like pulmonary infection and sepsis.[6] As the disease often has an indolent course[7], presents with features of other tropical conditions, hence aptly called 'great mimicker', leads to delay in clinical suspicion or diagnosis.[8] In clinical microbiology laboratory it is often misidentified as *Pseudomonas sp*. or other common laboratory contaminants of Gram-negative non fermenter group.[9] Delay in clinical, laboratory diagnosis of melioidosis and initiation of appropriate treatment invariably leads fatal outcome in high-risk individuals.[10] In this case report, we present a case of melioidosis in a 59 years old diabetic male patient.

CASE REPORT

A 59 years old male, farmer by occupation, presented to outpatient department of a rural hospital in Malda district of West Bengal with fever for 10 days duration and

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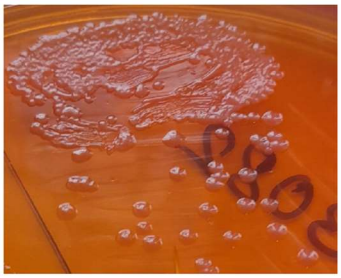
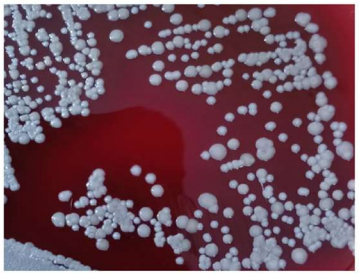
cough with expectoration. He had a history of long-standing type 2 diabetes mellitus which was not controlled by oral medications. Next day he was admitted in a private hospital for sudden onset respiratory distress and high fever. Complete blood count showed low haemoglobin (8.3 gm/dL), total leucocyte count was 9600/cmm and CRP level was elevated (17.72 mg/dL). His chest X-Ray finding was normal and serological tests were negative for dengue, scrub typhus and leptospirosis. Peripheral blood smear and RDT test were negative for malaria. Empirical antibiotic therapy with cefoperazone-sulbactam was started and aggressive control of high blood sugar level was initiated by insulin therapy. Patient continued to have persistent high temperature in the range of 101°C to 103°C. On tenth day of admission patient developed excruciating pain with sudden onset swelling in his left should.

Blood agar plate on Day 1



MacConkey agar plate on Day 1

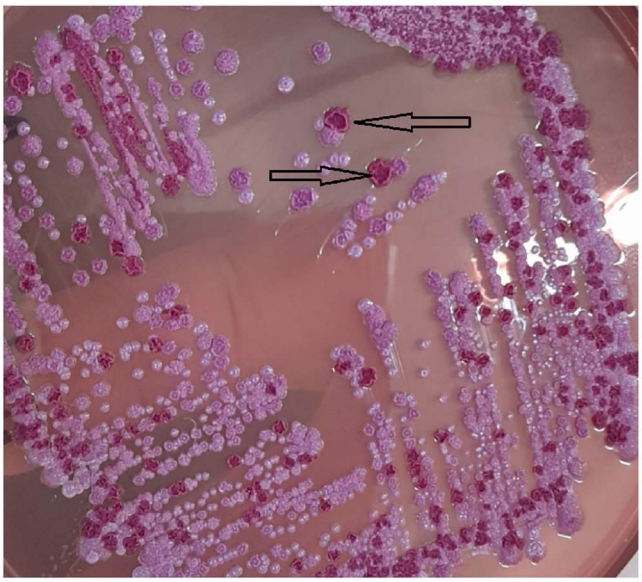


Blood agar plate on Day 2

Ashdown's media on Day 1

Ashdown's media on Day 2

Ashdown's media on Day 3



Ashdown's media after 5 days of incubation showing dry wrinkled colonies (arrow marked) of *Burkholderia pseudomallei*

Image 1 showing colonies of *Burkholderia pseudomallei* on blood agar (day 1 and day 2), MacConkey agar (Day 1) and Ashdown's media on day 1, day 2, day 3 and day 5

Ultrasonography examination of left shoulder revealed "A large ill defined, echogenic, space occupying lesion measuring 48mm x 20mm noticed in the upper arm along the biceps tendon extending up to bicipital groove. Boney irregularity was noted at head and greater tuberosity of humerus". Patient further underwent contrast enhanced MRI examination of left shoulder joint and it showed "Osteomyelitis of humeral head involving intraarticular and periarticular abscess formation". Patient was immediately referred to a teaching hospital in Kolkata for further management.

Upon admission in the teaching hospital patient was subjected to detailed history taking and clinical examination after obtaining written informed consent from patient. Complete blood count showed low haemoglobin count (6.3 gm/dL), neutrophilic leucocytosis (16300/cmm) and high CRP level in blood (148.5 mg/dL). Cefoperazone-sulbactam was continued and levofloxacin was added to antimicrobial therapy. Patient had also received two bags of packed RBC transfusion. Next day patient underwent "incision and drainage of peri humeral abscess through delto-pectoral approach followed by through debridement of infected tissue followed by washing with normal saline and hydrogen peroxide" procedure under general anaesthesia after thorough preoperative evaluation was done and proper consent was taken. Infected tissue materials were sent to microbiology laboratory for Gram-stain, acid fast stain, culture sensitivity and CBNAAT testing.

Day 1

Gram stain of infected tissue showed plenty of pus cells, and Gram negative bi-polar stained bacilli. On the basis of patient history and Gram stain finding sample was inoculated in 5% sheep blood agar, MacConkey agar and in-house prepared Ashdown media. Also, two sets of blood culture from different venepuncture sites were obtained from the patient and put on incubation in BacT/Alert 3D © (from bioMérieux, France) automated blood culture system. Throat swab and urine sample were also put on culture.

Ashdown's media was prepared with trypticase soy agar base and 4% glycerol, 5 mg/L crystal violet, 50 mg/L neutral red and 4 mg/L of gentamicin added to it.[11]

Acid fast staining from the sample showed no acid-fast bacilli.

CBNAAT performed on sample showed absence of *Mycobacterium tuberculosis* in the sample.

Day 2

After 18-24 hours incubation 5% sheep blood agar plate showed non-haemolytic coliform like colonies, MacConkey agar plate showed non-lactose fermenting moist colonies. On Ashdown's media colonies were dry, tiny and purple color.

On subsequent incubation of the 5% sheep blood agar, MacConkey agar and Ashdown's media plates become large, dry and wrinkled which is highly suggestive of *Burkholderia pseudomallei* colonies [see Image 1].

Gram stain from colonies showed Gram negative bi-polar stained bacilli [see Image 2] which were also motile, tube catalase and oxidase test positive. Clinician was informed about the possibility of Melioidosis and asked to start meropenem empirically. Both conventional and automated identification were put.

Throat swab culture after 24 hours incubation showed growth of non-pathogenic organisms and aerobic culture of urine showed no growth.

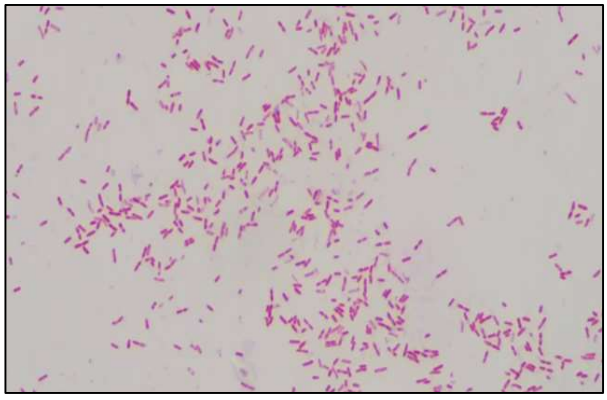


Image 2 showing Gram stain from Ashdown's media showing Gram negative bacilli showing bi-polar staining (safety pin appearance)

Day 3

Conventional identification showed the isolate utilized citrate as sole source of carbon and amino acid arginine dihydrolysed. Automated identification by Vitek 2 Compact © (from bioMérieux, France) showed isolate as *Burkholderia pseudomallei* with 97% confidence.

Three discs diffusion screening test was done by preparing 0.5 McFarland standard colony suspension from 48 hours grown colonies ➔ lawn culture done on Mueller Hinton agar plate ➔ antibiotic discs of colistin (10µg), gentamicin (10µg) and amoxicillin clavulanic acid (20/10µg) put on the dried Mueller Hinton agar plate within 15 minutes of lawn culture, maintaining at least 24mm distance between discs. Zone diameter was interpreted based on interpretive standards for *Pseudomonas aeruginosa* and Enterobacteriaceae according to Clinical and Laboratory Standards Institute (CLSI) recommendations. [12,13]

Antimicrobial susceptibility testing was done by disc diffusion method following The European Committee on Antimicrobial Susceptibility Testing (EUCAST) guideline, 2023[14] using antibiotic discs of meropenem (10µg), ceftazidime (10µg), co-trimoxazole (1.25/23.75µg) and doxycycline (30µg) on Mueller Hinton agar.

Isolate in duplicate nutrient agar slant was sent to Center for Emerging and Tropical Disease (CETD), Kasturba Medical College, Manipal following WHO Guidelines for Cat B samples transport for confirmation.

Day 4

Three discs screening test showed the isolate was susceptible to amoxicillin and clavulanic acid and resistant to both colistin and gentamicin [see Table 1 & Image 3].

Table 1: Three discs screening test of *Burkholderia pseudomallei*

Antimicrobial agent	Disk potency (µg)	Interpretation
Colistin	10	Resistant
Gentamicin	10	Resistant
Amoxicillin-Clavulanic Acid	1.25/23.75	Sensitive

Table 2 showing antimicrobial susceptibility test result of *Burkholderia pseudomallei*

Antimicrobial agent	Disk potency (µg)	Interpretation
Meropenem	10	Sensitive
Ceftazidime	10	Resistant
Co-trimoxazole	1.25/23.75	Intermediate*
Doxycycline	30	Sensitive

Note: *Intermediate = Susceptible, increased exposure. A microorganism is categorized as "Susceptible, Increased exposure" when there is a high likelihood of therapeutic success because exposure to the agent is increased by adjusting the dosing regimen or by its concentration at the site of infection

Antimicrobial susceptibility test showed isolate were susceptible to meropenem and doxycycline, intermediate susceptible to co-trimoxazole and resistant to ceftazidime [see Table 2 and Image 4]. Clinician was asked to continue meropenem therapy and to add doxycycline in the treatment regime.

Day 6

All the blood culture showed no growth after 5 days of incubation at 37°C.

Day 7

Clinician informed the microbiology laboratory that patient took discharge against medical advice upon cessation of fever and mild improvement of his clinical condition. Further communication with patient and his relatives could not be done hence outcome of the patient could not be assessed further.

Day 9

Report from CETD confirmed the isolate as *Burkholderia pseudomallei* as both antigen detection by monoclonal antibody based latex agglutination for *Burkholderia pseudomallei* and polymerase chain reaction (PCR) assay targeting T3SS1 gene were positive.

Image 3 showing three discs diffusion screening test for *Burkholderia pseudomallei*, isolate was resistant to colistin and gentamicin but susceptible to amoxicillin-clavulanic acid

Image 4 showing antimicrobial susceptibility testing of *Burkholderia pseudomallei* against meropenem, ceftazidime, co-trimoxazole and doxycycline by Kirby-Bauer disc diffusion method following EUCAST guidelines 2023

DISCUSSION

Ubiquitous presence of *Burkholderia pseudomallei* in soil particularly in agricultural fields makes the occupations associated with farming susceptible to it.[15] It enters the host by either direct inoculation if there is any breach in skin or upon rainfall, aerosolization of soil bacteria oc-

curs which enters host by inhalation.[5,16] In India most of the cases were reported along the coastal regions of Karnataka, Kerala, and Tamil Nadu.[17] In India there is a large population of type 2 diabetes mellitus patients and most of the people from rural areas are engaged farming activities, both these conditions make a large proportion of population vulnerable to melioidosis. But due to similar clinical manifestations of other tropical diseases, lack of awareness among clinicians and lack of infrastructure in laboratory confirmation of melioidosis, it is difficult to assess the correct magnitude melioidosis in India.[18]

In our patient, two risk factors e.g., farming activity and presence of long-standing uncontrolled diabetes mellitus made him highly vulnerable to melioidosis. Studies showed that presence of diabetes increases chance of melioidosis by 100 times more than non-diabetic.[19] From clinical history it was evident that he was suffering from musculoskeletal abscess due to melioidosis. Studies showed that musculoskeletal complications are more common in diabetics.[20]

Though studied showed that sometimes melioidosis takes an indolent course of infection but in our patient, there was rapid course of illness and deterioration of his conditions in the peripheral hospital where he was initially getting his treatments.

The Centers for Disease Control and Prevention recommends using ceftazidime or meropenem by intravenous route and co-trimoxazole or amoxicillin-clavulanic acid or doxycycline by oral route as intensive phase therapy for 2 – 8 weeks followed by above mentioned oral medications for 3 to 6 months as eradication therapy.[5] Our patient despite receiving cefoperazone-sulbactam from early phase of his illness continued to deteriorate till meropenem and doxycycline started based on laboratory reports. But due to patient's decision to take discharge against medical advice at the early phase of intensive therapy despite extensive counselling about the disease and its poor outcome without targeted antimicrobial therapy, it was hard to assess outcome of his illness.

This case highlighted the need of awareness of possible *Burkholderia pseudomallei* infection when history and clinical pictures are suggestive of melioidosis among clinicians in peripheral hospitals. Appropriate sample processing should be done employing correct diagnostic techniques for early and correct diagnosis of melioidosis which will eventually help clinicians to initiate early and appropriate antimicrobial therapy thus reducing morbidity and mortality in melioidosis cases as mortality in untreated melioidosis is very high (40%).[21]

In this case we have used in house prepared Ashdown's media for isolation of *Burkholderia pseudomallei* from clinical samples. As it is selective media for *Burkholderia pseudomallei,* and based on suggestive Gram stain finding, catalase and oxidase test report, a presumptive identification had been done on day 2 of sample processing and this ultimately helped clinician to start appropriate antimicrobial therapy from that day.

CONCLUSION

Musculoskeletal melioidosis requires prompt diagnosis, early and appropriate antimicrobial therapy to prevent progression of disease to visceral abscess and septic shock which ultimately leads to fatal outcome. In endemic areas like our country awareness among physicians, microbiologists, and laboratory technicians is essential for early diagnosis and successful treatment of melioidosis. Capacity building for molecular confirmation of melioidosis is required in more centres across India as India has a large susceptible population and perfect environment for *Burkholderia pseudomallei* infection.

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Author Contribution: SK: Contributed to data collection and analysis. **SD**: Focused on data analysis and interpretation. **TM**: Involved in data collection. **SGB**: Contributed to all study stages, including conception, design, data collection, analysis, and manuscript preparation.

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