A Case Series of Melioidosis-The Great Imitator in A Mapims Hospital, Melmaruvathur, Tamilnadu, India

Running title: A Case Series of Melioidosis

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Abstract

Background: *Burkholderia pseudomallei* is a saprophytic, aerobic, non-sporing, nonfermenting, facultative intracellular motile gram-negative bacilli found in tropical and subtropical regions. Melioidosis can range from asymptomatic infections to life-threatening illnesses affecting the internal organs, particularly when the host's immunity is compromised. Delayed clinical presentation and a lack of access to critical care resources in high-prevalence areas significantly contribute to this death burden. This disease has a high case fatality rate in endemic areas. The written consent was obtained from the patient after explained them about this study. To increase physician awareness of melioidosis in high-risk patients presenting with diverse clinical symptoms, thereby enhancing diagnostic accuracy and ensuring timely, appropriate treatment.

Case Presentation: Case series: Case 1: 40-year-old male with septic pulmonary emboli; Case 2: 72-year-old female with chronic obstructive pulmonary disease and Type II respiratory failure; Case 3: 25-year-old female with septic arthritis; Case 4: 69years-old male with pneumonia and bacteraemia; Case 5: 54-year-old male with diabetic nephropathy and chronic kidney disease. The appropriate samples were collected from all the cases, and the identification of the isolated organisms and antibiotic susceptibility tests were performed using Vitek 2 automated compact system. The patients were treated with appropriate supportive measures. Among the five cases, three had a better outcome, and two cases had deteriorated.

Conclusion: This case series emphasis that the Clinicians should be aware of the risk of melioidosis, particularly during the rainy season, Diagnostic tests should be enhanced to ensure timely exploration and treatment.

Keyword: *Burkholdria pseudomallei*, Diabetes, Immunocompromised, Sepsis, Pneumonia

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Introduction

Melioidosis, commonly known as Whitmore's disease, is an infectious disease that affects humans as well as animals. This disease is caused by *Burkholderia pseudomallei* (*B. pseudomallei*), a Gram-negative bacillus widespread in contaminated water and soil. [(1)] Melioidosis is most commonly recognized as an acute respiratory illness. *B. pseudomallei* infection can produce a wide spectrum of symptoms, ranging from asymptomatic infection to local abscess, lower respiratory tract infection, and severe illness. [(2)] Melioidosis is a leading cause of life-threatening community-acquired pneumonia and septicaemia in endemic areas, with rates of mortality up to 44%. Pneumonia may be asymptomatic or manifest as a severe necrotizing disease. [(3)] It has been a less suspected, under-diagnosed, and under-reported disease in the Indian subcontinent [7], with around 1,550 of the total 1,700 cases (more than 90%) observed from India in the past 10 years. [(4)] Melioidosis and diabetes mellitus may be correlated since diabetic individuals have a deficiency in their innate immunity, which is combined with poor glycaemic control. Acute cases of melioidosis with diabetes mellitus showed lower cellular adaptive immune response when compared to acute melioidosis cases in non-diabetic patients. [(5)] To our knowledge, this is the first series to describe complete recovery in three of the five cases. The detailed instruction was explained to patient and attender about this study and written consent was obtained from patient. This case series aims to raise physicians' awareness of melioidosis in high-risk patients exhibiting a range of symptoms, thereby improving the likelihood of accurate diagnosis and appropriate treatment.

Case Presentation

Case1:

On 17th september2024, A Forty-year-old male patient presented with complaints of fever, breathlessness for ten days, Grade II to III of New York Heart Association, and Giddiness for three days. He was on irregular medication for diabetes and hypertension. On examination, the patient was fair, conscious, oriented, febrile, and dyspnoeic and his pulse rate was 110 per minute, blood pressure- 100/60mmHg, respiratory rate -24/minute, and temperature-102°C. On systemic examination, cardiovascular systems S1 and S2 were heard, and loud P2 and respiratory system bilateral air entry were present. On Investigation: The electrocardiogram shows sinus tachycardia, the 2D ECHO shows RA RV dilated, and the computed tomography of pulmonary angiography shows pulmonary embolism (Figure: 1). The case was diagnosed as septic pulmonary emboli. The Blood sample was sent for culture and sensitivity shows positive flagged blood culture, The gram stain shows gram-negative bacillus, *B .pseudomallaei* identified by automated Vitek 2 compact sytem (Biomerieux) with AST(Table:1). The treatment was started with Meropenem 1gm IV TDS, ionotropic support, antithrombotic drugs, and other supportive measures. Despite the above treatment, the patient started deteriorating and expired on the 7th day of the treatment.

Case 2:

A seventy-two years old female patient brought to hospital on 4th October 2023 with complaints of acute onset of breathlessness, Grade II -III of New York Heart Association for one week, which was progressive, had fever on and off, not associated with chills and rigor, cough with expectoration with yellowish sputum. She was a known case of chronic obstructive pulmonary disease and diabetes on irregular medication. On examination, the patient was conscious, oriented, obese, and tachypnoeic. Her pulse rate was 103 beats/minute, blood pressure was 130/80mmHg, Respiratory Rate -26/min, Temperature - 100°C. On systemic examination, the Cardiovascular system shows S1, S2 heard, respiratory system bilateral air entry present, bilateral wheeze present, and scattered crepitations were heard. On investigation, chest X-ray CHEST PA- hyperinflated lung fields, multiple opacities feature of consolidation, HRCT-features of consolidation, (Figure:1) this case was diagnosed as COPD & Type II Respiratory

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Failure. The sputum sample was sent for culture and sensitivity. The gram stain shows gram-negative bacillus and the isolated organism was *B. pseudomallaei* by automated Vitek 2 compact sytem (Biomerieux) with AST(Table:1). The treatment was started with Meropenem 1gm IV TDS, non-invasive ventilation support, and other supportive measures. The patient started improving on the fifth day of treatment and the maintenance dose of cotrimoxazole was given for two months.

Case 3:

On 19th October 2023, a twenty-five-year-old female patient presents with a history of swelling over the right knee for the past two weeks. History of road traffic accident two months back she had a patellar fracture which was treated conservatively. She also had native treatment one month back. She had no comorbidities disease in the past. On examination, the patient was conscious, oriented, and febrile. Her Pulse Rate -108bpm; Blood pressure- 100/70mmHg; temperature- 100°F.On systemic examination cardiovascular systems S1, and S2 were heard, and respiratory system- bilateral air entry was present. On local examination, there was an acute local inflammation over the right knee, which was warm, and tender. On investigation count was elevated, X-ray right knee showed soft tissue swelling, edema, and capsular distension. (Figure.1) This case was diagnosed as septic arthritis. An aspirated pus sample was sent for Culture and sensitivity was identified as *B. pseudomallaei* in automated Vitek 2 compact sytem (Biomerieux) with AST(Table:1). The treatment was started with ceftazidime 2g IV two times a day for two weeks and other supportive measures were given. The prognosis of the patient started improving and the maintenance dose of doxycycline was given for 1 month. The patient was recovered from the infection and discharged.

Case 4:

On 25th December 2023, a sixty-nine-year-old male patient came with complaints of cough with expectoration for the past ten days, a History of Breathlessness, and fever for five days. He had a known case of diabetes on regular medication. On examination, the patient was conscious, oriented, and febrile and his pulse rate was 110 beats/minute, Blood pressure - 100/80mmHg, Respiratory rate was 28/minute, and temperature;100.6°F. On systemic examination cardiovascular system S1, S2 heard, Respiratory system – Bilateral air entry, bronchial breath sounds present, right lower crepitation heard. On Investigation: leucocytosis, chest X-ray shows right lower lobe pneumonia consolidation. HRCT shows ground glass opacity, consolidation, and interlobar septal thickening (Figure: 1) and diagnosed as Pneumonia and Bacteremia. A sputum sample was sent for culture sensitivity shows *B. pseudomallaei* in automated Vitek 2 compact sytem(Biomerieux) with AST(Table:1). The treatment was started according to sensitivity Meropenem 1gram IV three times a day and supportive measures were given. The patient started improving after seven days and a maintenance dose of cotrimoxazole was given for two months and recovered from the infection.

Case 5:

On 5th January 2024, a fifty-four-year-old male patient came with a fever for the past two weeks, associated with chills and rigors and decreased urine output for one week. He was on irregular medication for diabetes, and hypertension for 15 years. On examination the patient was conscious, oriented, and febrile, mild dehydration was present. His pulse rate was 113 beats per minute with 130/80mmHg blood pressure, and 103°F temperature. On systemic examination cardiovascular systems S1, and S2 were heard, respiratory system bilateral air entry present, abdominal examination colic, suprapubic tenderness was present. Investigation: elevated WBC, urine routine-protein +++, Blood urea-158mg/dL, Serum creatinine-12.1mg/Dl. Ultrasonogram shows multiple simple cysts. The case was diagnosed as diabetic nephropathy and chronic renal failure. A urine sample was sent for culture and sensitivity- *B. pseudomallaei* by automated Vitek 2 compact sytem(Biomerieux with AST(Table:1)). The patient was treated with meropenem 1gram IV three times a day, underwent hemodialysis, and

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supportive measures were given. After five days of treatment, the patient collapsed into cardiac arrest and died.

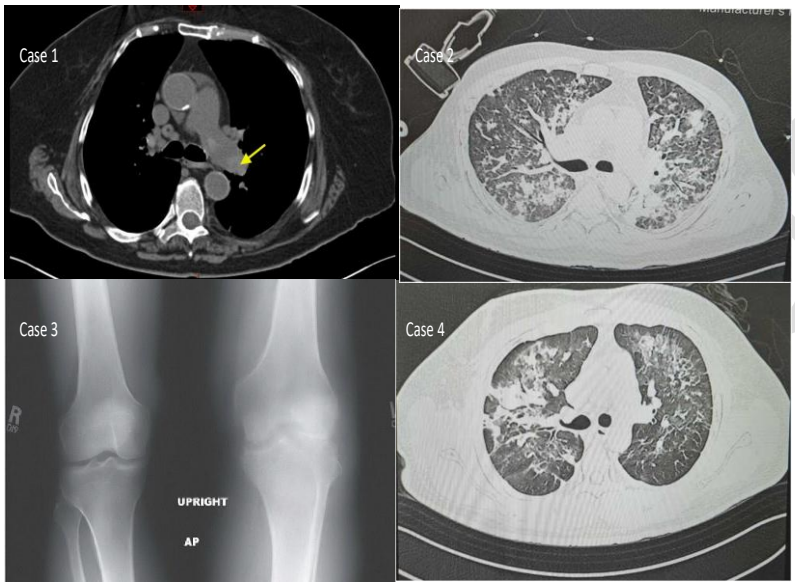


Figure 1. Radiological findings of patients: Case1; Computed Tomography of pulmonary angiography shows pulmonary embolism. Case2; HRCT shows features of consolidation. Case 3; X-ray right knee shows soft tissue swelling, edema, and capsular distension Case 4; HRCT shows ground glass opacity, consolidation, and interlobar septal thickening.

Table 1. Antibiotic sensitivity pattern of isolates

Case	Antibiotic						
	Ceftazidime	Imipenem Meropenem	Clotrimazole	Ciprofloxacin	Gentamicin	Polymyxin B	Tetracycline
1	S	S	R	I	R	R	S
2	S	S	S	R	S	R	S
3	S	S	S	S	S	R	S
4	S	S	R	S	S	R	R
5	S	S	S	R	R	R	R

S- Sensitive; I- Intermediate; R- Resistant

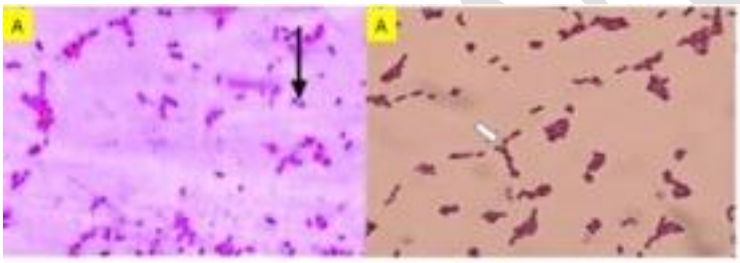
Discussion

Melioidosis, caused by *B. pseudomallei*, is a potentially severe infectious disease that remains underdiagnosed and underreported in regions outside its endemic areas. This under recognition can be attributed to a combination of factors, including a lack of awareness among healthcare professionals, insufficient diagnostic facilities, and the clinical overlap with other diseases that present with similar symptoms. As a result, melioidosis is often misidentified, leading to delayed diagnoses and suboptimal patient outcomes.

One of the key reasons melioidosis is underrecognized is its diverse clinical presentation. It can range from asymptomatic infection to localized abscesses, severe respiratory illness, and even disseminated disease affecting multiple organs.(2) The varied symptoms make it challenging to diagnose without a high level of suspicion, particularly in areas where the disease is not endemic. Moreover, *B. pseudomallei* shares many clinical features with common bacterial infections, particularly those caused by *Pseudomonas* species, which are often

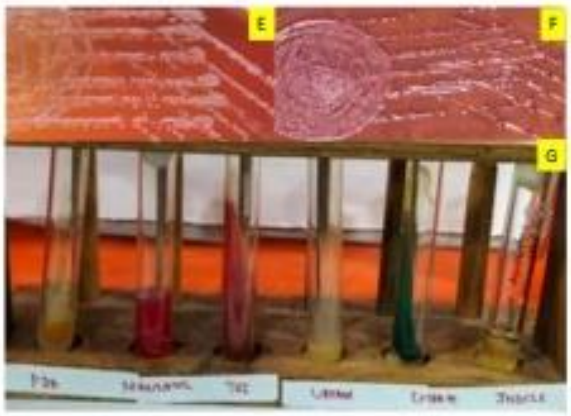
considered environmental contaminants. Consequently, healthcare providers may overlook melioidosis, particularly in cases where the clinical presentation does not immediately point to the disease. In our case series participant received this information in a language they could understand, both verbally and in a written document. Four cases had diabetics comorbidities. Among four, two cases(case2,4) had controlled glycaemic level, other two cases (case 1,5) had uncontrolled glycaemic level. All cases were sensitive to carbapenem, resistant to carbapenem is rare in this organism. Male patients are predominant.

The diagnostic challenges associated with melioidosis are multifaceted. *B. pseudomallei* is a gram-negative, oxidase-positive bacillus that exhibits a characteristic "safety pin" pattern on Gram staining. However, it is often misidentified as other environmental or commensal bacteria, such as *Pseudomonas cepacia*, *B. thailandensis*, or *P. stutzeri*. The organism grows well on standard culture media, the nutrient agar shows grey dry wrinkled colonies, 5% sheep blood agar plate shows nonhemolytic colonies and McConkey agar shows non-lactose fermenting colonies. Catalase positive, oxidase-positive, urease negative, indole and citrate-negative, triple sugar iron shows alkaline /alkaline with no gas, no acid, PDA- Negative. Sugars This organism ferments Arabinose, Arabitol, Dulcitol, Fructose, Galactose, Glucose, Mannose, Sucrose, Ribose, and Trehalose - Posit, and does not ferment Lactose, Maltose, Rhamnose, Tartrate, Xylose, Moller base decarboxylate -Arginine,ornithine-dehydrolysed. [Fig 2 :(A to G)]



A - Gram stain of burkholdria pseudomallei

B- Automated VITEK 2 compact system; C-Sputum sample; D- Blood sample in blood culture bottle



E- Colonies in 5% sheep blood agar; F- Macconkey agar; G-Biochemical reactions

Figure 2. (A to G): Microbiological investigations

Despite these distinctive characteristics, *B. pseudomallei* is frequently overlooked, particularly because its colonies are sometimes mistaken for non-pathogenic environmental organisms. Blood and tissue cultures, which are typically used to diagnose melioidosis, have a relatively low sensitivity, contributing to the initial misdiagnosis in nearly 40% of cases. The limitations of conventional diagnostic techniques, such as low discriminatory power in automated systems like VITEK 2, further complicate accurate identification, especially in regions with limited resources or technical expertise. In addition to diagnostic issues, melioidosis is more common among certain populations, particularly individuals with poorly controlled diabetes and those with chronic kidney disease or immunocompromised states. In the Indian subcontinent, where diabetes is highly prevalent, *B. pseudomallei* infects a significant number of patients with underlying chronic conditions. This highlights the need for heightened awareness in areas with a high burden of diabetes and other risk factors. Indeed, in countries like India, Sri Lanka, and Bangladesh, up to 80% of patients with melioidosis have diabetes. The association between uncontrolled diabetes and melioidosis underscores the importance of maintaining good glycemic control to reduce the risk of infections, particularly in endemic areas.

Treatment of melioidosis is complicated by the organism's resistance to several antibiotics, including penicillin, ampicillin, and the first and second generations of cephalosporins. However, *B. pseudomallei* is generally susceptible to carbapenems, tetracyclines, trimethoprim-sulfamethoxazole, and third-generation cephalosporins. Carbapenems, in particular, remain a cornerstone in the treatment of severe melioidosis, although resistance to these drugs is rare. The increasing availability of more effective diagnostic tests, including molecular techniques and automated systems, has led to earlier detection and treatment, significantly improving patient outcomes. However, a key challenge remains the underdiagnosis of the disease, especially in non-endemic regions where physicians may not routinely consider it in the differential diagnosis.

The prevention of melioidosis is an ongoing challenge, particularly because the organism is commonly found in soil and surface water in endemic regions. Individuals with risk factors such as diabetes, skin lesions, or immunocompromised conditions should avoid contact with contaminated soil and stagnant water. In agricultural settings, wearing boots and protective clothing while working in the fields can reduce the risk of infection. In healthcare settings, stringent infection control measures are essential to prevent laboratory-acquired infections. Plates should be taped shut when incubating. "Sniffing" of plates should not be done because they contain this organism. Healthcare workers handling blood or body fluids should use appropriate personal protective equipment, such as gloves and gowns, and should exercise caution when handling specimens that may contain *B. pseudomallei*.

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The lack of a vaccine for melioidosis further complicates prevention efforts. As the disease remains endemic in regions with high humidity and rainfall, the focus should be on public health strategies aimed at increasing awareness and improving the diagnostic capacity of healthcare facilities. Early detection and prompt treatment, alongside improved surveillance systems, are critical in reducing the burden of melioidosis in endemic regions.

Conclusion

This case series ignites knowledge on melioidosis is an underrecognized infectious disease that presents significant diagnostic and treatment challenges. The disease's diverse clinical manifestations, coupled with the limitations of current diagnostic methods, contribute to its underdiagnosis, particularly in non-endemic areas. Increased awareness among healthcare professionals, enhanced diagnostic capabilities, and better management of underlying risk factors, such as diabetes, are crucial in improving patient outcomes. Public health efforts must focus on increasing awareness, improving diagnostic infrastructure, and implementing preventive measures to mitigate the impact of melioidosis in endemic regions.

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None

Ethical statement

Written informed consent was obtained from the patients.

Conflicts of interest

None

Author contributions

Dr. Arulananthi Venkataraman Arumugam and Dr. Sabarinathan Thiyagarajan and conceived the presented idea. Dr. Arulananthi Venkataraman Arumugam and Dr. Sabarinathan Thiyagarajan and verified the microbiological methods. Dr. Saleem Mohamed Ali encouraged the investigation and supervised the findings of this work. All authors discussed the results and contributed to the preparation of the final manuscript.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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