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Systemic Melioidosis – Two Case Reports of Clinically Misleading Presentations

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Abstract

Melioidosis is a rare and often underrecognized infectious disease caused by the bacterium *Burkholderia pseudomallei*, which is primarily found in Southeast Asia. This disease can lead to severe systemic complications and carries alarmingly high rates of morbidity and mortality. We present two different case reports of melioidosis: one with disseminated melioidosis and the other presenting as pneumonia. Melioidosis can resemble infections like tuberculosis, complicating diagnosis. Sepsis with multiple abscesses can be associated with *Staphylococcal spp.* and *Klebsiella spp.* infection. *Bacillus anthracis* (anthrax), *Francisella tularensis* (tularemia), *Bartonella henselae* (cat scratch disease), and *Yersinia pestis* (plague) can present with similar symptoms. Fungal infections, particularly those caused by *Candida spp.*, can also present with these symptoms. These case reports highlight the difficulties in identifying disseminated melioidosis and the risks of misdiagnosis, which can lead to inadequate patient management. Increased awareness of melioidosis in endemic areas is essential for improving patient outcomes and public health responses.

Keywords: Burkholderia; Pneumonia; Diabetes; Renal abscess; Splenic abscess.

Introduction

Melioidosis, or Whitmore's disease, is a bacterial infection resembling glanders. It is caused by the bacterium *Burkholderia pseudomallei*, a motile, aerobic, non-spore-forming, non-fermenting, facultative intracellular gram-negative bacillus commonly found in soil, surface water, and groundwater. Melioidosis can present as either an acute or chronic infection and may be localized or disseminated throughout the body.^[1]

The disease often resembles other infections, such as tuberculosis, which can make clinical diagnosis challenging. As a result, strong clinical suspicion is essential for achieving an accurate diagnosis. Key risk factors for melioidosis include diabetes, excessive alcohol consumption, chronic kidney disease, and chronic lung disease.^[2]

Bacterial infections such as disseminated Staphylococcal spp. infection, Klebsiella spp. infection, Bacillus anthracis (anthrax), Francisella tularensis (tularemia), Bartonella henselae (cat scratch disease), and Yersinia pestis (plague), along with fungal infections, particularly Candida spp., can present with similar symptoms.

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These two case reports illustrate the challenges in diagnosing melioidosis and underscore the need to raise awareness among physicians, promoting a high level of suspicion for accurate clinical diagnoses. It is crucial to increase clinician awareness through targeted training programs to effectively manage this emerging disease. Proper antibiotic therapy must be administered, including appropriate dosages and durations.

Case Reports

Case 1

A 51-year-old male with diabetes was admitted to the hospital with fever and chills that had persisted for the past 15 to 20 days. He had experienced altered mental status for the last 5 to 6 days and urinary incontinence for one month, for which he had received treatment at a local hospital. Upon admission, the patient presented with a concerning combination of symptoms: fever, rapid and labored breathing, and an elevated heart rate. His extremities felt warm to the touch, yet his blood pressure was alarmingly low, indicating a critical condition. After initiating fluid resuscitation, the patient was started on noradrenaline. He also required 3 liters of supplemental oxygen to ensure adequate respiratory support. A blood culture was taken, and broad-spectrum antibiotics were initiated. Initial laboratory values are presented in Table 1. The patient was diagnosed with septic shock and had a persistent need for vasopressors.

Because tiny nodules and ground-glass opacities were detected on high-resolution computed tomography (HRCT) of the chest (Fig. 1), tuberculosis was considered in the differential diagnosis. A sputum sample for acid-

Table 1. Initial investigations in Case 1					
Laboratory Parameter	Reference	Day 1	Day 3		
Hb (g/dL)	14-18	11	10.4		
TLC (10°/L)	4-11	10.44	9.70		
Platelet (10 ⁹ /L)	1.5-4	135	130		
Urea (mg/dL)	7-20	39.5	54.2		
Creatinine (mg/dL)	0.8-1.3	0.83	0.68		
C-reactive protein (mg/dL)	<1	256.77			
SGOT (U/L)	0-35	132.4/60			
SGPT (U/L)	4-36	60			
Bilirubin (mg/dL)	0.3-1.0	1.29			
Albumin (g/dL)	3.5-5.5	2.70			
HbA1c	<5.7%	7.8%			

fast bacillus testing was sent for analysis, and empirical anti-tubercular medication (isoniazid 300 mg, rifampicin 600 mg, ethambutol 900 mg, pyrazinamide 1500 mg once daily) was initiated alongside antibiotics, specifically piperacillin-tazobactam 4.5 g intravenously (IV) three times daily.

Contrast-enhanced computed tomography (CECT) of the abdomen revealed a right renal abscess and a splenic abscess (Fig. 2). An ultrasound-guided drainage procedure was performed on the abscess, and a pus culture was sent for further analysis.

Because the patient was experiencing respiratory distress, a two-dimensional echocardiogram (2D echo) was conducted. The results indicated global hypokinesia and a reduced ejection fraction, likely due to sepsis. The sputum culture tested negative for acid-fast bacilli, while a blood culture revealed the presence of *Burkholderia pseudomallei*. Based on the culture sensitivity results, the patient was treated with meropenem 1 g IV three times daily and ceftazidime 2 g IV three times daily, and the anti-tubercular medications were discontinued. The pus culture was sterile.

Due to the patient's uncontrolled blood sugar levels, he was treated with a combination of regular and long-acting insulin. The requirement for vasopressors was gradually decreased. A follow-up two-dimensional echocardiogram yielded normal findings. The patient received meropenem 1 g IV three times daily and ceftazidime 2 g IV three times daily for 10 days, followed by an additional 7 days of ceftazidime 2 g IV three times daily. Upon discharge, the patient was prescribed oral co-trimoxazole (160 mg trimethoprim and 800 mg sulfamethoxazole) two tablets twice daily for 12 weeks — along with an insulin regimen to manage diabetes. During a follow-up after two months, the patient demonstrated clinical improvement. His blood sugar levels were under control with the insulin regimen, and he was consistently taking co-trimoxazole as advised.

Case 2

A 49-year-old male patient with diabetes was admitted to the hospital due to a cough and sputum production that had lasted for over a month. He also experienced altered sensorium for two days and fever for four days. Notably, he had been hospitalized for pneumonia just one month prior and was a known case of chronic calcific pancreatitis. Upon arrival, he exhibited fever, tachypnea, and tachycardia.

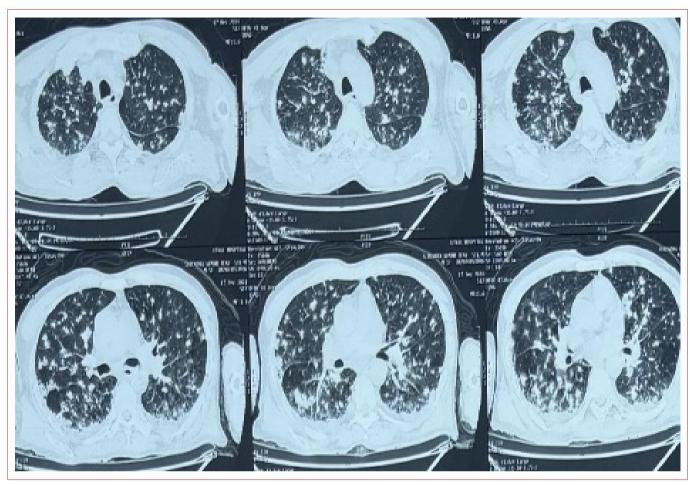


Figure 1. Ground-glass opacity and nodular opacity on high-resolution computed tomography (HRCT) of the chest in Case 1, suggestive of bacterial infection, tuberculosis, or melioidosis.



Figure 2. Contrast-enhanced computed tomography (CT) of the abdomen in Case 1 showing a right kidney abscess and a splenic abscess.

Initial laboratory values are shown in Table 2. Due to the patient's persistent cough, sputum was collected for analysis of acid-fast bacilli, along with Gram staining and culture sensitivity tests. The patient presented with septic shock and required vasopressors. Empirical treatment was initiated with broad-spectrum an-

Table 2. Initial investigations in Case 2				
Laboratory Parameter	Reference	Day 1	Day 3	
Hb (g/dL)	14-18	9.4	9.1	
TLC (10 ⁹ /L)	4-11	22.70	25.80	
Platelet (10 ⁹ /L)	1.5-4	171	165	
Urea (mg/dL)	7-20	56.2	90	
Creatinine (mg/dL)	0.8-1.3	1.20	2.01	
C-reactive protein (mg/dL)	<1	290		
SGOT (U/L)	0-35	62.5		
SGPT (U/L)	4-36	19.8		
Bilirubin (mg/dL)	0.3-1	0.49		
Albumin (g/dL)	3.5-5.5	2.25		
HbA1c	<5.7%	8.5%		

tibiotics, specifically meropenem at a dosage of 1 g IV three times daily. Given the patient's respiratory distress, a two-dimensional echocardiogram was performed, which revealed global hypokinesia and severe left ventricular dysfunction, likely due to sepsis. The patient was diagnosed with pneumonia with consolidation, as demonstrated in Figure 3.

Due to respiratory distress, the patient was intubated, and his requirement for vasopressors increased. A sputum culture identified the presence of *Burkholderia pseudomallei*. Based on culture sensitivity, the patient was treated with meropenem 1 g IV three times daily and ceftazidime 2 g IV three times daily. Unfortunately, the patient's condition gradually deteriorated, with increasing

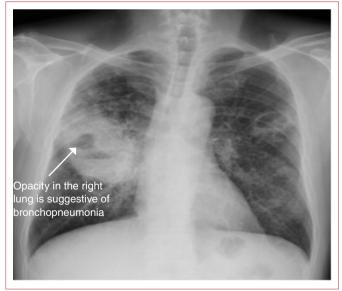


Figure 3. Chest radiograph (X-ray) of Case 2 showing inhomogeneous opacity in the right lung.

Comparison	Case 1	Case 2
Age	51	49
Comorbidities	Diabetes	Diabetes, chronic calcific pancreatitis
Clinical signs	Fever, altered sensorium, urinary incontinence	Cough and sputum production, altered sensorium, fever
Interventions	Antibiotics, USG-guided drainage of renal abscess	Antibiotics, mechanical ventilation
Outcome	Survived	Death

vasopressor requirements, the development of superadded infections, worsening pneumonia, and ultimately multiorgan dysfunction leading to death.

Table 3 presents a comparative overview of various factors, including age, comorbidities, clinical signs, interventions, and outcomes.

Discussion

Melioidosis is an infectious disease caused by *Burkholderia pseudomallei*, found in the rhizosphere and groundwater of tropical and subtropical regions, affecting both humans and animals. Traditionally endemic to Southeast Asia and Australia, its presence is expanding to the Americas, Madagascar, Mauritius, India, and parts of South Asia. In India, cases primarily arise from coastal states such as Karnataka, Kerala, Tamil Nadu, Puducherry, and Odisha. Factors such as a rising diabetic population, climate change, high population densities, and intensive agriculture may increase incidence rates and recognition of this infection in new areas. [4]

The mortality rate for acute melioidosis can be as high as 90%, typically ranging from 20% to 50% globally, particularly in regions with limited healthcare resources. Factors influencing outcomes include timely clinical assessment, early diagnosis, appropriate antibiotic use, and effective management of comorbidities, which are critical for both adults and children. Data from Thailand identify independent risk factors for death and treatment failure, such as bacteremia, respiratory and renal failure, and age over 50, with similar findings reported in Australia. There are also significant challenges in diagnosing melioidosis in India and South Asia due to difficulties in clinical recognition and limited laboratory testing capacity.^[5]

A systematic review of melioidosis shows mortality rates ranging from 10% to 50%, influenced by early treatment and overall health. Mortality rates, while historically high, have decreased due to improved treatments. Early antibiotic intervention, especially with carbapenems or ceftazidime, significantly lowers these rates. Factors such as septic shock, bacteremia, and underlying conditions (e.g., diabetes, kidney disease) increase the risk of death. Regional variations in mortality are evident, with higher rates in low- and middle-income countries. Treatment generally includes an intensive phase with intravenous antibiotics, followed by an oral eradication phase.

This pathogen affects various parts of the body, including the lungs, liver, and kidneys. Studies show that systemic melioidosis has a high mortality rate, estimated between 30% and 50%.^[7] Melioidosis poses challenges due to diagnosis difficulties, a lack of effective treatments, and high comorbidity rates. Recent research has improved our understanding of its epidemiology, pathogenesis, and treatment, but many questions remain. Localized melioidosis generally has a good prognosis but can progress to systemic spread if untreated.^[8]

Melioidosis can present with a wide range of clinical manifestations, from isolated cutaneous lesions to systemic involvement, fulminant sepsis, and potentially death.^[2] Disseminated infections can manifest as pneumonia, abscesses in the liver, spleen, kidneys, prostate, skin, and subcutaneous tissue, as well as septic arthritis, osteomyelitis, and meningoencephalitis.^[9]

Given the nonspecific and diverse clinical manifestations of melioidosis, it is crucial to consider this disease in individuals who present with fever, abscesses in internal organs, and underlying risk factors. The presence of both renal and splenic abscesses can provide an initial indication for diagnosis.

Burkholderia pseudomallei is often misidentified. [4] Melioidosis is frequently misdiagnosed due to its diverse and nonspecific clinical symptoms, which can mimic other common illnesses such as tuberculosis, pneumonia, and sepsis. It can present with symptoms like fever, cough, chest pain, headache, and muscle aches, similar to other respiratory and systemic infections. Its clinical presentation may resemble tuberculosis, pneumonia, infective endocarditis, and sepsis, complicating diagnosis based on symptoms alone. [10] Melioidosis can affect multiple organs, including the lungs, liver, spleen, prostate, joints, bones, and brain, further complicating diagnosis. In our

first case, misdiagnosis led to the initiation of antitubercular therapy, but it was later confirmed as disseminated melioidosis after the culture sensitivity report. In the second case, a delayed diagnosis required intubation, and the patient ultimately passed away due to a superadded infection. Case one involved septic shock from disseminated melioidosis, while case two was initially diagnosed as pneumonia before complications arose.

There are no specific clinical or radiological features that definitively point to melioidosis, making it difficult to differentiate from other illnesses. *B. pseudomallei* can be mistaken for other bacteria such as *Pseudomonas* spp. in microbiology laboratories, particularly in areas where melioidosis is not endemic or in inexperienced laboratories. Blood cultures, a common diagnostic method, may have low sensitivity and may not always isolate the bacteria, leading to missed diagnoses.^[11]

While serological and molecular methods have been evaluated, culture remains the gold standard for diagnosis, and slow growth on standard media can delay identification. Limited awareness of melioidosis among clinicians and laboratory staff contributes to misdiagnosis and underreporting.

Early suspicion of melioidosis, a bacterial infection caused by *Burkholderia pseudomallei*, is crucial due to its potential for severe illness and varied presentation. Red flags include prolonged fever, especially in individuals with risk factors such as diabetes, chronic kidney disease, or occupational exposure to soil and water. Cough, chest pain, and respiratory distress mimicking pneumonia are also important indicators. Localized skin infections, abscesses, and neurological symptoms such as disorientation or seizures should also raise concern.

The diagnosis of melioidosis relies on culturing *Burkholderia pseudomallei*, which grows well under standard conditions but cannot be confirmed with traditional methods. In laboratories without automated systems, it can be preliminarily identified by its gram-negative, oxidase-positive, motile bacilli, bipolar staining pattern, and distinct wrinkled colonies with a metallic sheen after extended incubation. [12]

Barman et al.^[13] documented a case in which melioidosis went undiagnosed for two months. Clinical diagnosis is particularly challenging, especially since the disease can mimic other infections such as tuberculosis, which is prevalent in resource-limited countries like India. Ad-

ditionally, melioidosis can resemble pyogenic abscesses and other tropical illnesses, leading to severe septicemia and multiorgan dysfunction syndrome.

Vidyalakshmi et al.^[14] identified a 76% correlation between diabetes and melioidosis. Diabetes mellitus is a significant risk factor, and the rising incidence of diabetes is believed to contribute to the increasing prevalence of melioidosis. In both of our cases, diabetes was a common risk factor.

The antibiotic treatment of melioidosis involves an initial intensive therapy that includes either ceftazidime or meropenem. This is followed by eradication therapy using trimethoprim-sulfamethoxazole or amoxicillinclavulanic acid. The duration of treatment varies depending on the severity of the disease and the extent of organ involvement. Eradication therapy should be administered for a minimum of three months.[15] It is recommended to extend the initial intensive phase of treatment to four weeks if specific complicating factors are present, such as multilobar pneumonia, positive blood cultures, or admission to the ICU. In this case, our patient received 17 days of intensive-phase treatment with 15 mg/kg of trimethoprim IV, followed by three months of eradication therapy with co-trimoxazole (trimethoprim 160 mg and sulfamethoxazole 800 mg), two tablets twice daily.

Due to the high mortality rate and variable antibiotic sensitivity, a strong clinical suspicion is vital for accurate diagnosis, especially since symptoms are nonspecific and resemble other diseases. This is particularly important for patients with risk factors such as diabetes, chronic alcohol use, kidney or lung disease, immunosuppression, and travel to endemic areas. Young patients with multisystem disease or abscesses should also be evaluated for melioidosis. Microbiological confirmation is necessary for diagnosis, even if patients initially respond to antibiotics, to justify prolonged treatment and address potential side effects, highlighting the challenge of antimicrobial stewardship.

Limitation

In the first case, the patient exhibited fever with chills and altered mental status. In contrast, the second case involved a patient who presented with a cough accompanied by sputum production. This indicates a lack of generalizability between the two cases. Additionally, the second patient had a history of chronic calcific pancreatitis, which resulted in an immunocompromised state. This condition ultimately led to a secondary infection alongside pulmonary melioidosis and contributed to the patient's death.

Conclusion

These case reports emphasize the importance of raising awareness among physicians and fostering a high level of suspicion for accurate clinical diagnosis. It is essential to enhance clinician awareness through targeted training programs to manage this emerging disease. Administering the correct antibiotic therapy—using appropriate dosages and durations—along with ensuring patient adherence to a prolonged treatment course and conducting regular clinical follow-ups will help ensure a cure for laboratory-confirmed cases of melioidosis.

Clinical Significance

- Melioidosis often resembles other infections, such as tuberculosis, as well as other bacterial and fungal infections, which can make clinical diagnosis challenging.
- These case reports illustrate the challenges in diagnosing disseminated melioidosis, highlighting the risk of misdiagnosis and the potential for improper management of affected patients.
- The results highlight the necessity for greater awareness of melioidosis in differential diagnoses, especially in endemic areas. This understanding can lead to better patient outcomes and strengthen public health responses.

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