CASE REPORT

A Fatal Case of Disseminated Melioidosis in a Diabetic Patient: Diagnostic Challenges and Atypical Presentation

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ABSTRACT

In Malaysia, melioidosis is not a notifiable disease but has a high mortality rate, particularly in diabetic patients. Disseminated melioidosis can be fatal, with 16% to 37% of cases presenting with nonspecific symptoms, complicating early diagnosis. Some patients develop abscesses with or without bacteremia. We present a fatal case of disseminated melioidosis in a diabetic patient with vague initial symptoms. Remarkably, she exhibited low septic parameters, including a normal white blood cell count and low C-reactive protein levels, which masked the severity of the infection and delayed appropriate treatment. The absence of early radiological findings and specific laboratory tests further complicated the diagnostic process. This case underscores the necessity for heightened clinical awareness and the advancement of diagnostic tools, particularly in high-risk populations, to facilitate timely interventions and mitigate fatal outcomes.
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Keywords: Disseminated, Melioidosis, *Burkholderia pseudomallei*, Diabetes, Diagnostic challenges

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INTRODUCTION

Melioidosis, caused by the Gram-negative bacterium *Burkholderia pseudomallei*, (*B. pseudomallei*), is an infectious disease prevalent in Southeast Asia, particularly in Malaysia. The disease primarily affects individuals aged 40 to 60 but can occur across all age groups [1]. *B. pseudomallei* is found in soil and water, with human infection occurring through inhalation, skin cuts, or direct contact with contaminated sources [1]. Diagnosing melioidosis is challenging due to its broad spectrum of clinical presentation and the slow growth of the bacterium in cultures[2]. In endemic regions, patients frequently present with pulmonary or soft tissue infections, though the disease can also manifest in atypical forms with severe complications affecting various organs, leading to misdiagnosis [2]. This case report highlights the diagnostic challenges in a fatal case of disseminated melioidosis in a diabetic patient, emphasizing the need for early detection and intervention.

CASE REPORT

A 49-year-old woman with diabetes mellitus and a history of diabetic foot ulcers presented with a shortness of breath (SOB), vomiting, and lethargy over two days, later developing abdominal pain and persistent fever during hospitalization.

Upon admission, she appeared pale but was alert, with vital signs showing tachycardia and mild respiratory distress. Lung auscultation revealed minimal bibasal crepitations. Examination of her diabetic foot ulcer showed clean edges without pus or foul odor. Other systems was unremarkable. Blood tests showed mild hyperglycemia and normal white blood cell count (10.9 x 10^9/L) with a low C-reactive protein level of 13.9 mg/L. ECG findings, including T-wave inversion in leads II and AVF and elevated troponin (2886 ng/L), led to the initial diagnosis of non-ST elevation myocardial infarction (NSTEMI). Chest X-ray suggested fluid overload, further supporting this diagnosis, and she was treated with diuretics and fluid restriction. No antibiotics were initiated due to low septic parameters.

Despite treatment, she developed persistent abdominal pain. An abdominal ultrasound and contrast-enhanced

CT (CECT) scan revealed acalculous cholecystitis (Figure 1), and she was treated with intravenous ceftriaxone and metronidazole. The CECT also showed bilateral pleural effusions, lung collapse, and consolidation. However, her condition continued to deteriorate, leading to the reconsideration of the NSTEMI diagnosis.

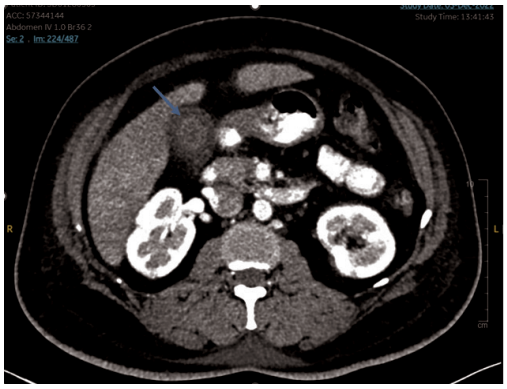

Figure 1: The arrow indicates the location of the edematous gall bladder.

By day 10, she developed septic shock, acute kidney injury, coagulopathy, and transaminitis, requiring intubation. Blood cultures taken earlier confirmed the presence of *B.pseudomallei* (Figure 2) on the second set of cultures, indicating disseminated melioidosis. The isolate was identified using MALDI-TOF(Bruker®) with a score of 2.26 and was resistant to trimethoprim-sulfamethoxazole but sensitive to amoxicillin-clavulanate, ceftazidime, doxycycline, meropenem, and imipenem. Intravenous meropenem was initiated.

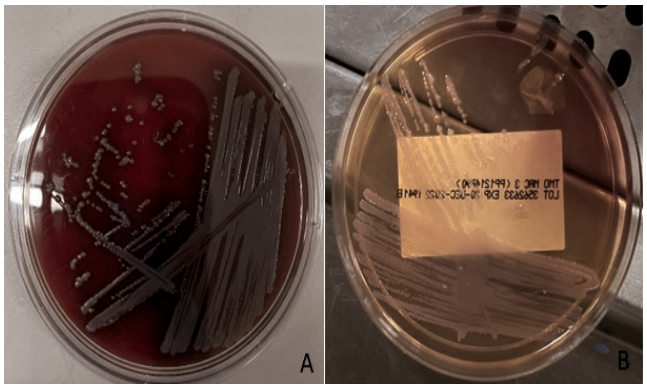

Figure 2: A) pure, 4+ metallic sheen colonies on blood agar. B) pure non lactose fermenter colonies on Mac Conkey agar.

Given the pleural effusions and respiratory findings, tuberculosis (TB) was considered as differential diagnosis. Sputum samples were sent for GeneXpert and culture for Mycobacterium tuberculosis both yielded negative results. Pleural fluid cultures were also collected, but they were likely contaminated and deemed clinically insignificant. However, no serology or molecular test for *B.pseudomallei* were sent.

Despite intensive care and the escalation of antibiotics, her condition continues to decline. Repeated chest X-rays showed progressive pulmonary infiltrates and unfortunately, she succumbed to septic shock on day 16 of hospitalization.

Table I: Summary of patient's blood investigations

Investigations	On admission	Day 6	Day 10	Day 16	Unit Type	Reference Range
Haemoglobin	11.1	9.5	10.9	9.7	g/dL	12.00-15.00
White cell count	10.94	14.17	20.5	14.07	x109/L	4.00-10.00
Platelet	326	191	128	95	x109/L	150-410
PT	14.4	26.1	29.5	66.3	sec	11.7-15.3
APTT	31.9	38.4	1.3	51.2	sec	26.0-40.0
INR	1.07	1.3	2.25	5.23		
Urea	6.1	14.2	11.1	31.7	mmol/L	2.5-7.2
Sodium	129	130	124	134	mmol/L	136-145
Potassium	6.5	4.4	3.9	5.3	mmol/L	3.5-5.1
Creatinine	89	96	150	335	umol/L	53-97
Albumin	35	30	24	24	g/L	35-50
TB	5.4	21.2	24.9	44.8	umol/L	3.4-20.5
AST	36	408	494	1944	U/L	5-34
ALT	12	293	321	278	U/L	0-55
CRP	13.9	228.3	279		mg/L	0.00-5.00
Trop 1	2886				ng/L	
Blood C&S		No growth	*Burkholderia pseudomallei*			

DISCUSSION

Meliodosis is endemic in Malaysia, and diabetes mellitus (DM) is the most common comorbidity, associated with severe infections [1]. Patients with DM are at increased risk due to impaired immune response, including reduced cytokine expression and phagocyte function. In this case, the diabetic foot ulcer may have served as a potential source of infection, although no direct microbiological evidence confirmed a link to melioidosis. The infection could also have been acquired through inhalation or contact with contaminated soil or water [1].

The patient's misdiagnosis of NSTEMI delayed the initiation of appropriate treatment for meliodosis, allowing the infection to progress. Studies show that untreated melioidosis in diabetic patients can rapidly lead to septic shock and multi-organ failure, especially with additional comorbidities like myocardial ischemia and abdominal infections [3]. Diagnosis was complicated by the slow growth of *B. pseudomallei*, with confirmation only achieved after a second blood

culture, as up to 50% of initial blood cultures for melioidosis can be negative [2]. This highlights the need for timely antibiotic treatment targeted at melioidosis, which is crucial in preventing such fatal complications.

Acalculous cholecystitis a manifestation of melioidosis is rare, with only a few cases reported. Relatively poor blood supply to the gallbladder, compared to organs like the liver or lungs, may explain this rarity [3]. In diabetic patients, melioidosis frequently presents with abscesses in multiple organs, and in this case, the gallbladder may have been involved [3]. Early recognition and surgical intervention could have provided better source control and improved the outcome.

Given the nonspecific presentation of melioidosis, better diagnostic tools are needed, particularly for high-risk individuals like those with diabetes in endemic areas such as Malaysia. Khaejawat et al. (2023) developed a simple diagnostic score based on clinical factors (e.g., diabetes, chronic kidney disease, and environmental exposure) and laboratory findings (e.g., elevated white blood cells, abnormal liver enzymes, high CRP, and positive *Burkholderia pseudomallei* cultures). This score, with high sensitivity and specificity, could have led to earlier consideration of melioidosis and more timely antibiotic treatment in this case [4].

Laboratory confirmation of melioidosis has several challenges. Although culture-based methods are the gold standard, they pose biosafety risks and can take days to produce results. Their sensitivity ranges from 21% to 82% depending on type of sample, and they require containment facilities, which may not be available in all settings [2]. Molecular tests like PCR are faster, but they require advanced infrastructure and are costly [5]. Serological tests, such as IHA and ELISA, are less reliable in acute cases, with sensitivity ranging from 50% to 95%, and often show false positives due to high background antibody rates in endemic areas [2]. Despite these limitations, serology can still be useful when combined with other diagnostic methods, especially for chronic or retrospective cases [2]. Advances in molecular assays or rapid antigen detection could help overcome the limitations of traditional culture-based methods.

Treatment of melioidosis involves an intensive phase followed by a maintenance phase. Guidelines recommend ceftazidime or meropenem for critically ill patients during the intensive phase, typically lasting four weeks, followed by a three-month maintenance phase. In this case, the delayed initiation of appropriate antibiotic therapy due to diagnostic uncertainties likely contributed to the patient's deterioration and eventual death. The atypical presentation of acute abdominal pain may have warranted early surgical consultation and intervention to ensure adequate source control [3].

CONCLUSION

This case underscores the complexity of diagnosing and managing melioidosis, particularly in patients with comorbid conditions and atypical presentations. It highlights the necessity for heightened awareness, advanced diagnostic strategies, and a proactive approach to treatment to improve patient outcomes. Continued research into more sensitive diagnostic tools and effective therapeutic protocols is essential to addressing the challenges posed by this formidable pathogen.

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