



Case report

Characteristic of pancreatic involvement in melioidosis: Case report and literature review

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ARTICLE INFO

Keywords:

Pancreatic

Melioidosis

Burkholderia pseudomallei

Bacterial culture

Case report

ABSTRACT

Background: Intra-abdominal abscesses are a frequent manifestations of melioidosis whereas pancreas is barely affected by this condition. Herein, by delving into the clinical manifestations, diagnostic processes, and the ultimate clinical outcome, we report a case of an unusual presentation of pancreatic melioidosis in a Chinese patient, aiming to shed light on a diagnosis that is not commonly associated with the pancreas.

Case presentation: The patient, a 32-year-old male farmer, suffered from persistent burning pain in his upper abdomen, accompanied by nausea, vomiting, fever and other symptoms, presented to the clinic. His body temperature spiked to 38.5 °C without apparent reason for this fever. A thorough examination, including the blood culture and the imaging examination, led to a diagnosis of pancreatic melioidosis. The patient was promptly treated with intravenous meropenem and ceftazidime. As a consequence, his symptoms eased and discharged in stable condition. The patient continued his treatment with oral trimethoprim-sulfamethoxazole (co-trimoxazole) for three months to control the infection. Following 6 months of regular follow-up, the patient fully recovered.

Conclusions: In tropical regions such as Hainan, it is crucial to consider atypical infection like *B. pseudomallei* in the differential diagnosis, even when they present in atypical locations such as a pancreatic pseudocyst. Detecting pancreatic involvement in melioidosis relies heavily on sensitive bacterial culture and imaging examination. This retrospective study of patients' infection diagnosis aims to shed light on the clinical treatment, and prognosis associated with pancreatic melioidosis, thereby raising awareness about the risk of pancreatic affection in melioidosis cases.

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<https://doi.org/10.1016/j.heliyon.2024.e30299>

Received 28 September 2023; Received in revised form 22 April 2024; Accepted 23 April 2024

Available online 26 April 2024

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1. Introduction

Melioidosis, a disease caused by the bacterium *Burkholderia pseudomallei* (*B. pseudomallei*), poses significant challenges in its diagnosis and control. It is prone to relapse and carries a high mortality rate. Globally, it is estimated to cause approximately 165,000 cases and 89,000 deaths annually [1]. *B. pseudomallei* mainly distributed in tropical and subtropical regions [2]. In China, melioidosis is prevalent in regions such as Hainan, Guangdong, Guangxi, Fujian, Hong Kong, and Taiwan, with Hainan being the epicenter of the epidemic [3]. While melioidosis affects multiple organs, with the lungs and bloodstream being the most commonly infected [4–6], cases involving the pancreas are exceptionally rare. Our literature search identified 11 reported cases of melioidosis with pancreatic involvement, all of which were distributed in Asia [7–12], including five from India [8,10,12], four from Brunei [7] and two from China [9,11] (Table 1).

In an effort to increase the awareness of melioidosis among medical personnel, we summarized the clinical data from a case we treated and from literature-reported patients with pancreatic involvement, aiming to avoid misdiagnosis or missed diagnosis and thus improve the overall standard of clinical diagnosis and treatment for this challenging condition.

2. Case presentation

2.1. Patient information

On October 9, 2022, a 32-year-old male farmer sought treatment in the outpatient department with complaints of “abdominal pain and fever.” The patient had developed a persistent, intensifying burning sensation in the upper abdomen three days earlier, which was progressively worse, accompanied by nausea, vomiting, fever, fatigue, cough, sputum production, dizziness, headache, and shortness of breath. His temperature had risen to 38.5 °C without any apparent cause.

The patient had a medical history of binge eating and alcohol abuse, diabetes mellitus, and chronic pancreatitis for many years. Most notably, in 2020, the patient developed septic shock as a result of a *B. pseudomallei* infection. Then, in 2021, he suffered a recurrence of septic shock, this time due to severe pneumonia and suppurative knee arthritis. Following treatment, he was discharged once his condition improved.

2.2. Clinical findings

The patient’s temperature was 38.3 °C, pulse 132 beats/min, respiratory rate 20 breaths/min, blood pressure 110/92 mmHg, and weight 40kg. His symptoms acutely appeared, with notable abdominal distension and abdominal tenderness (3+), along with rebound tenderness (3+), especially severe in the upper left abdomen. Laboratory examination showed hemodiastase 972U/L, urinary amylase 1420 U/L, blood glucose 13.36 mol/L, CRP 178.1 mg/L, and procalcitonin 5.44 mg/L.

Ultrasound imaging highlighted the pancreatic head as having diffuse, calcified, and echogenic characteristics (Fig. 1A). Further CT examination showed a clearer picture, showing swelling of the pancreas with flocculent exudate in the surrounding area, suggesting the exacerbation of chronic pancreatitis (Fig. 1B). Additionally, the scan revealed bilateral infectious lesions in the lungs and pleural effusions on both sides (Fig. 1C).

Table 1

Clinical information on 12 cases of melioidosis pancreatic infection.

Case	Gender	Age	Country	Occupation	Risk factors and underlying disease	Presentation
1	male	45	Taiwan/China	construction worker	diabetes mellitus, alcoholic liver cirrhosi	10-day period of fever and cough, in consciousness with 6th and 7th cranial nerve palsy and flaccid paralysis, acute brainstem stroke
2	male	62	Tamil Nadu/India	na ^a	chronic diabetic and hypertension	2-week history of fever and acute onset of abdominal pain for 4 days.
3	male	36	Guangxi/China	fishmonger	diabetes mellitus, 17 years of smoking and drinking history	Fever, chills, weight loss, night sweats, bilateral chest and rib pain
4	male	40	India	na ^a	alcoholism	Fever, abdominal pain
5	male	37	India	na ^a	alcoholism	Abdominal pain, fever
6	female	23	India	na ^a	diabetes mellitus	Abdominal pain, fever, dyspnoea
7	female	32	Brunei	na ^a	Thalassemia, splenectomy	Fever, flank pain, lower back pain, loss of appetite, weight loss
8	male	48	Brunei	na ^a	Diabetes mellitus	Fever, rigor, abdominal pain, loss of appetite, weight loss
9	male	25	Brunei	na ^a	Thalassemia, splenectomy	Fever, rigor, abdominal pain, loss of appetite, weight loss
10	male	27	Brunei	na ^a	Diabetes mellitus	Fever, rigor, bloating, loss of appetite, weight loss
11	male	55	India	farmer	na ^a	Fever, epigastric lump
12	male	32	Hainan/China (this study)	farmer	alcoholism, Diabetes mellitus	Fever, abdominal pain, nausea, vomiting, shortness of breath

^a na: not available.

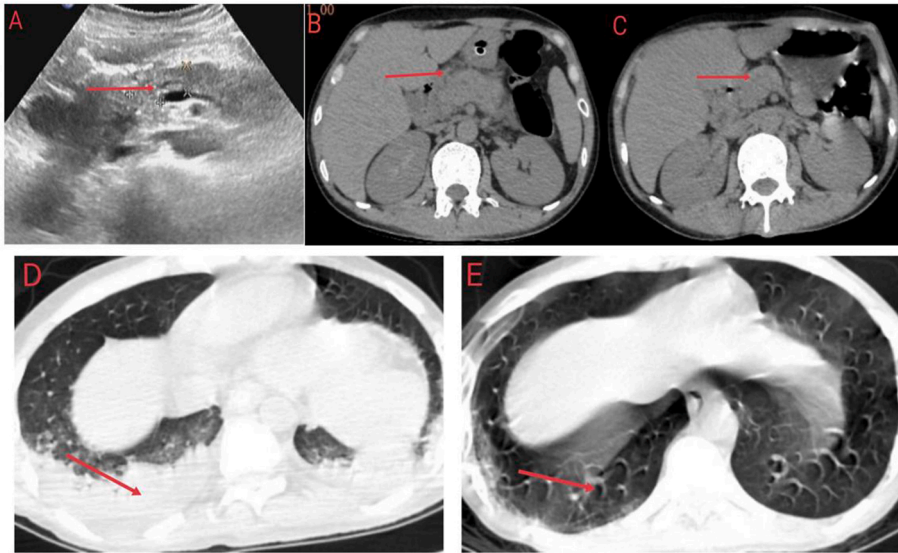


Fig. 1. Imaging findings of our patients.

A. Pancreatic ultrasound before treatment: The red arrow indicates diffuse enlargement of the pancreas with blurred margins and thickening of the echogenicity in the head of the pancreas. B. Pancreatic CT before treatment: The red arrow indicates diffuse enlargement of the pancreas with indistinct margins, decreased and uneven density, and irregular linear or strip-shaped opacities around the pancreas. C. Chest CT before treatment: Patchy and dense shadows are visible in both lungs with indistinct borders, bilateral pleural effusions, and prominent lower lobes. D. Pancreatic CT after treatment: The red arrow indicates that the pancreas shrank compared to prior situation, with clear margins and uniform density. E. Chest CT after treatment: Lesions in both lungs significantly decreased.

2.3. Microbiological features of the pathogen

By the third day of the patient's hospitalization, *B. pseudomallei* was detected in blood, sputum, and pancreatic drainage samples (Fig. 2A). Identification of the pathogen was performed by MALDI-TOF MS (RUO database) and confirmed through whole genome sequencing. The genome assemblies of *B. pseudomallei* strain (T165) in this study are available in the figshare (DOI:10.6084/m9.figshare.23902500). After 1 day of cultured on blood agar plates at 37 °C, the colonies were small in size, with a smooth, milk-like and slightly viscous texture. After an additional two days for cultivation, these colonies gradually became pale white, round and opaque (Fig. 2B). Broth microdilution method was employed for antimicrobial susceptibility testing. The isolate was susceptible to amoxicillin-clavulanate, ceftazidime, imipenem, doxycycline and co-trimoxazole, except for intermediate sensitivity to chloramphenicol.

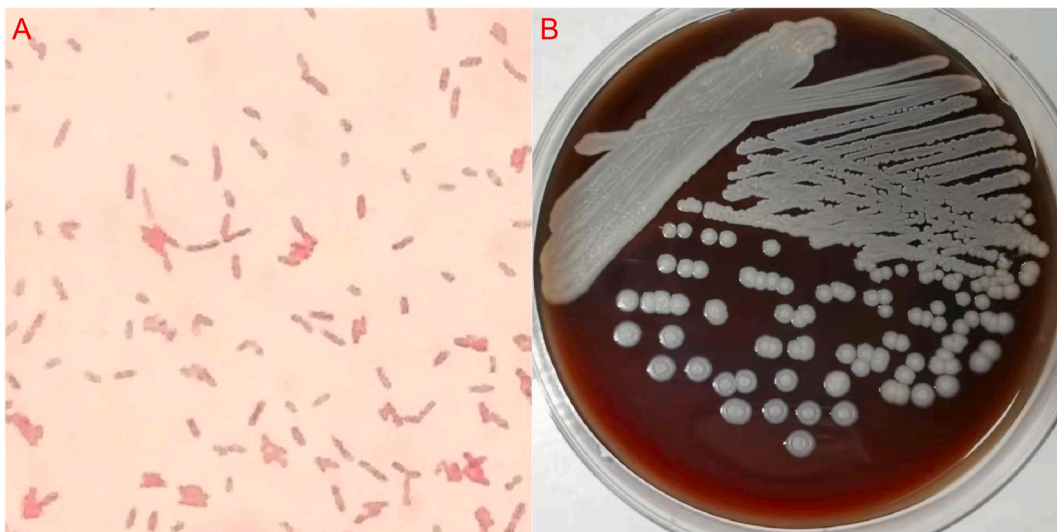


Fig. 2. Morphological characteristic of *B. pseudomallei* and its colony.

A. Gram stained *B. pseudomallei* under the microscope; B. Colonies after two days growth on blood agar.

Table 2
Infection sites, imaging features, therapy and outcomes of pancreas involved melioidosis patients.

Case	Pancreatic parts	Abdominal melioidosis	Other sites infection	Imaging	Antibiotic therapy	Other therapy	Duration (days)	Outcome
1	pancreatic tail	urogenic tract	blood, lung, brainstem	CT ^a : Abdominal computed tomography revealed a pancreatic tail abscess.	ceftazidime, meropenem	no	10	died
2	distal body and tail	splenic vein thrombosis	blood	CECT ^b : mildly bulky distal body and tail regions of pancreas with peripancreatic fat streakiness. The retro-pancreatic portion of the splenic vein was distended with non-enhancing intraluminal thrombus and vessel wall enhancement. Prominent venous collaterals were noted in the periportal, peripancreatic, omental, and retroperitoneal locations. Mild splenomegaly was also noted. MRI ^c : abdomen showed a mildly bulky pancreas. The retro-pancreatic portion of the splenic vein showed T2 hyperintense thrombus with restricted diffusion	meropenem co-trimoxazole	subcutaneous enoxaparin for splenic vein thrombosis and glycemic control	14	improved
3	na	liver, spleen	blood, lung	CT ^a : Bilateral upper lung patchy or striped high-density blurry shadows, with small amounts of pleural effusion on both sides. Multiple low-density lesions in the upper part of the right mediastinum, liver, spleen, and pancreas	ceftazidime, imipenem, meropenem Cotrimoxazole	Liver puncture and pus aspiration	15	improved
4	na	no other organ	blood	na ^a	Ceftazidime, Cotrimoxazole	single time aspiration	45	improved
5	na	no other organ	no other sites	na ^a	Meropenem + Cotrimoxazole	percutaneous drainage	30	improved
6	na	no other organ	blood	na ^a	Ceftazidime + Cotrimoxazole	percutaneous drainage	30	improved
7	body of the pancreas	no other organ	blood, psoas	US ^d : none of the patients had a pancreatic abscess detected on US. CT ^a : Axial tomography image showing a large multi-loculated pancreatic abscess (circle) affecting the body of the pancreas	amoxicillin-clavulanic, carbapenem	no	14–56	improved
8	body and tail regions of the pancreas	spleen, liver, splenic vein thrombosis	blood, lung		amoxicillin-clavulanic, doxycycline			improved
9	pancreatic head	liver, ascites	blood					improved
10	tail of the pancreas	liver, spleen, ascites	blood, psoas					died
11	body and tail of pancreas	splenic vein thrombosis	cyst fluid	CECT ^b : a large pseudocyst of size of 20 cm 12 cm × 14 cm in lesser sac. EUS: a well-defined pseudocyst of approximate size 15 10cm with a thick wall seen at body and tail of pancreas with debris content of approximately 10 %.	Meropenem doxycycline	percutaneous drainage	140	improved
12	Diffuse enlargement, Pancreatic head	liver, spleen, ascites	blood, lung	US ^d : thickened echogenicity and calcified plaques in the pancreatic head; CT ^a : Pancreatic swelling with visible flocculent exudation	Meropenem, Cefazidime, Cotrimoxazole	percutaneous drainage	38	improved

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Table 2 (continued)

Case	Pancreatic parts	Abdominal melioidosis	Other sites infection	Imaging	Antibiotic therapy	Other therapy	Duration (days)	Outcome
				around the pancreas, suggesting an acute attack of chronic pancreatitis; Infectious lesions in both lungs and bilateral pleural effusion.				

CT^a: Computed Tomography; CECT^b:contrast-enhanced computed tomography; MRI^c: magnetic resonance imaging; US^d: ultrasound.

^a na: not available.

2.4. Therapeutic intervention

Acute attack of chronic pancreatitis and pulmonary infection was diagnosed on the first day of admission, and the patient was initially treated with intravenous ampicillin-sulbactam (2 g/dose, twice daily) combined with metronidazole (0.5 g/dose, twice daily) to control infection, along with protamine insulin to manage blood glucose levels. Despite these interventions, the patient's condition took a turn for the worse, with continuous thrombocytopenia, chills, intensified fever, and his shortness of breath progressed, ultimately resulting in shock. In response to the patient's deteriorating state, on the second day of admission, he was transferred to the intensive care unit (ICU) for further treatment, where pancreatic intubation was performed for pus-drainage, and a ventilator was placed for assisted breathing. Continuous renal replacement therapy was initiated at the bedside, which aids in clearing inflammatory mediators from the bloodstream. Additionally, the patient received other symptomatic treatments to address his symptoms and stabilize his condition. For infection control, the patient was started on intravenous meropenem (2 g/dose, every 8 hours) for a two-week period. Following the antimicrobial susceptibility results, ceftazidime (1 g/dose, every 6 hours) was subsequently used for an additional three weeks as part of a de-escalation strategy leading up to discharge. The patient also received platelet transfusions. After 38 days in the hospital, the patient felt well with no discomfort. He was discharged in stable condition, with all symptoms resolved and a complete absence of flocculent exudate around the pancreas, as confirmed by CT (Fig. 1D), and the inflammatory foci in the lungs had marked absorption (Fig. 1E). Post-discharge, the patient continued to take oral co-trimoxazole tablets (0.96g/dose, twice daily) for six months to maintain infection control, and insulin to control blood sugar. Six months after discharge, the patient was regularly followed up with, and he had made a full recovery.

3. Discussion

The pancreas is one of the most important digestive organs in the human body [13,14]. While *B. pseudomallei* infections have been documented worldwide, especially in Southeast Asia and Northern Australia, affecting various systems and organs, pancreatic involvement is indeed uncommon. Nevertheless, research conducted by Vui Heng Chong and his colleagues indicated a 6.2 % prevalence of pancreatic involvement, suggesting that it could be underdiagnosed [7]. In light of this, we have scrutinized cases of melioidosis that affect the pancreas to expand the scope of our understanding of this kind of infection and to help to assist in minimizing misdiagnoses in clinical settings.

B. pseudomallei is a gram-negative, short, and rod-shaped bacterium with heavy staining at both ends. It's oxidase and catalase positive, and it is able to thrive at a high temperature of 42 °C. After culturing on blood agar plates at 37 °C for one day, the resulting colonies were small in size, with a smooth, milk-like, and slightly viscous texture. In addition, *B. pseudomallei* produces a peculiar moldy or earthy odor during cultivation, and its biochemical characteristics is marked by its capacity to oxidize glucose, maltose and lactose, reduce nitrate to into ammonia, liquefy gelatin, and test positive for arginine dihydrolase. It is crucial for accurate identification to distinguish these characteristics of *B. pseudomallei* from other bacteria during clinical microbiological testing.

B. pseudomallei infection of the pancreas are exceptionally rare, with only 12 cases, including the one detailed in the present study. The information on the 12 cases of melioidosis with pancreatic infection were shown in Table 1, and a summary of the infection sites, imaging features, therapy and outcomes can be found in Table 2. It has been reported that 58.5 %–84 % of patients with melioidosis are male [15]. Among 12 patients with melioidosis infecting the pancreas, 10 (83.3 %) were male. While the median age for patients with melioidosis was about 50 years [16], the median age for those with pancreatic involvement was 37 years (ranged from 25 to 62 years). However, studies have shown a significant age-dependent increase in pancreatic neutrophil activation and systemic inflammation in mice [17]. Additionally, common comorbidities in the elderly, such as cholecystitis, hyperlipidemia, and diabetes, are known to elevate the risk of pancreatitis. Furthermore, the immune function in older adults is generally weaker, potentially impairing their ability to effectively combat infections and thereby raising the risk of infectious pancreatitis. Therefore, why melioidosis pancreatitis or pancreatic abscess patients were younger than other sites infection warrants further investigation. In the case of the 12 patients examined, all experienced fever, and 9 of them reported abdominal, chest and rib pain. Nausea, loss of appetite and weight loss also happened among half of the patients. Of the 12 patients, only 2 patient had infection isolated to a single site, and the remaining 10 patients had multifocal infections, including 6 with liver infection, 4 with spleen infection, and 4 with lung infection. This suggests that pancreatic infection in melioidosis may be disseminated through the blood stream or have the capacity for distant metastasis.

Most of the patients were evaluated for inflammatory markers such as CRP, ESR and PCT, but because none of these symptoms were specific, the diagnosis primarily relied on imaging examination and bacterial culture. *B. pseudomallei* is inherently resistant to most

antimicrobial agents, including penicillin, ampicillin, first- and second-generation cephalosporins, the aminoglycosides such as gentamicin, tobramycin, and streptomycin, and polymyxin [18]. The current standard treatment for melioidosis involves an initial intensive therapy with ceftazidime or meropenem, followed by an eradication phase with co-trimoxazole [19]. All reported patients with pancreatic melioidosis of the pancreas were treated with guideline-listed medications. Despite this, two patients died after receiving combination antimicrobial therapy.

Computer tomography (CT), magnetic resonance imaging (MRI), and ultrasound (US) were the imaging modalities employed to diagnose pancreatic melioidosis. For specific infectious parts of the pancreas, among the seven patients with detailed data available, both the body and tail of the pancreas were affected in three patients, only the tail was involved in two patients, only the body as affected in one patient, only head involved in one patient. In our case, we observed diffuse enlargement of the entire pancreas, with thickened echo at the head. The results suggested that the pancreatic tail could be the most susceptible to *B. pseudomallei* infection.

4. Conclusions

This study highlighted a rare case of pancreatic involvement in melioidosis within a patient from a tropical region of China. Despite being an atypical site for melioidosis, the case emphasizes the necessity for healthcare providers to suspect *B. pseudomallei* as a potential pathogen when encountering younger patients with pancreatic pseudocysts or abscesses, especially in endemic regions such as Hainan. Appropriate use of bacterial culture and imaging examinations was crucial in diagnosing this atypical presentation of melioidosis. The successful treatment and subsequent recovery of the patient illustrate the potential for favorable outcomes with prompt diagnosis and appropriate management.

5. Limitations

As with all case reports, this study presents several limitations inherent in general. One major limitation is its $n = 1$ scenario, which makes it challenging to draw broader conclusions or to establish robust evidence for clinical practice. The findings are specific to this individual patient and thus may not represent the broader spectrum of pancreatic melioidosis or other manifestations of the disease. Additionally, the diagnosis and treatment protocols followed may not be universally accepted or available in all clinical settings. Finally, the retrospective design of the review limits the control over variables that could influence outcomes, such as the timing of diagnosis and treatment initiation, and it does not allow for the establishment of a cause-and-effect relationship. Further studies with larger sample sizes and prospective designs are required to gain a more comprehensive understanding of the characteristics, optimal diagnostic methods, and treatment protocols for pancreatic involvement in melioidosis.

Ethics approval and consent to participate

Ethical approval No.: Med-Eth-Re[2019]75.

The project, Clinical analysis and molecular epidemiological characteristics of human melioidosis in Hainan Province, directed by Hua Wu from our hospital - was reviewed by the Medical Ethics Committee of Hainan General Hospital. This project conformed to the relevant laws and regulations, and was approved for implementation. All local, national or international guidelines and legislation were adhered to in the production of this study.

Written informed consent for the publication of all his data and images was obtained from the patient in the study.

Funding disclosure

This study was supported by Hainan Provincial Natural Science Foundation of China (821MS130, 820QN271), Hainan Province Science and Technology Special Fund (Grant No. ZDYF2022SHFZ050), and Hainan Province Clinical Medical Center. The funding bodies had no role in the design of the study or collection, analysis, processing or interpretation of data or in writing the manuscript.

Data availability statement

We confirm that all supporting data for this study have been provided in the figshare (DOI:10.6084/m9.figshare.23902500), ensuring the transparency and reproducibility of our research. In this manner, we commit to offering our research findings in an open format to the scientific community, facilitating further study and validation.

CRedit authorship contribution statement

Wu Yuanxing: Methodology, Conceptualization. **Liu Lin:** Writing – review & editing, Writing – original draft, Methodology, Data curation, Conceptualization. **Wu Yujiao:** Writing – original draft, Methodology, Data curation, Conceptualization. **Wu Hua:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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