

Melioidosis Acquired by Traveler to Thailand: A Case Report

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Abstract

Background: *Burkholderia pseudomallei* (*B. pseudomallei*) is a gram-negative, saprophytic bacillus found in soil and water, and it is endemic in the tropical and subtropical areas. Melioidosis is a rare infection caused by *B. pseudomallei*, and it occurs only sporadically in travellers returning from disease-endemic areas. Severe clinical disease is seen mostly in patients with alteration of immune status, especially related to diabetes. To our best knowledge, this is the first reported case of melioidosis in a traveller complicated by diabetes in Chongqing, China.

Case presentation: A 55-year-old man with diabetes presented with erosions and ulcers on right leg with purulent discharge and painful sensation for a one-month history. On presentation she had high fever and urinary tract infection, then developed pneumonia, soon after his return from Thailand to China. Cultures from different specimens including blood cultures and urine cultures turned out positive, and then the organisms were finally identified as *B. pseudomallei*, thus the patient's treatment was switched to intravenous meropenem. Subsequently, the patient's urinary tract infection and fever resolved, and after 15 days of receiving meropenem, his general condition improved.

Conclusions: Given the frequency of travel between China and other countries, the existence of imported cases from endemic countries until now is striking, and physicians should be aware of its varied manifestations. In particular, melioidosis should be considered when diabetic patients returning from endemic countries, even without risk factors predisposing to severe disease.

Keywords: Melioidosis; *Burkholderia pseudomallei*; Traveller; Case report

Introduction

Melioidosis is a rare infection caused by *Burkholderia pseudomallei* (*B. pseudomallei*), which with clinical manifestations ranging from skin abscess to overwhelming sepsis and death. *B. pseudomallei* is a gram-negative, saprophytic bacillus found in soil and water, and it is endemic in Southeast Asia, Northern Australia and other tropical regions [1-3]. *B. pseudomallei* is also a major cause of community-acquired septicaemia and pneumonia in adults in the Asia-pacific region, particularly in northeast Thailand [3,4].

In China, the first case of melioidosis was reported in 1990 [5]. Since then several sporadic and epidemic cases had been reported in several tropical provinces, including Hainan, Guangdong, and Guangxi [6,7]. However, the report of melioidosis in Chongqing, China is unknown, here we present a case of melioidosis with prominent tissue necrosis and urinary tract infection in a man in Chongqing.

Case Presentation

In May 2017, a 55-year-old man was admitted to hospital because of erosions and ulcers on right leg with purulent discharge and painful sensation for a one-month history. The erythematous skin changes initially occurred from the anterior tibia and extended up to left leg, which gradually enlarged to erosions and ulcers, and with urinary tract

infection recently. No further complaints were elicited during a systematic enquiry, specifically no chills, night sweats, or weight loss. There was no history of trauma caused by soil or plants. The patient had received a diagnosis of type two diabetes mellitus and he took metformin (500 mg 2 times/d) before admission. He didn't smoke or drink alcohol. He was born in Chongqing, China, and recently had travelled to Thailand on April 2017. One month after arriving home, the patient noted swelling and pain in both legs, with a 15-day history of fever, productive cough with white sputum, then developed a sweating, frequent urination, urgency, dysuria.

On admission to the hospital, his temperature was 38.8°C, a heart rate of 109 beats per minute, a blood pressure level of 142/94 mmHg. Laboratory investigations revealed a leukocyte count of 12.3×10^9 cells/L with markedly elevated 91.0% neutrophils. The C-reactive protein level was greater than 240.4 mg/L. The liver functions stated significantly elevated levels of aspartate aminotransferase (4941.1 U/L, normal range: 15.0-40.0 U/L), alanine aminotransferase (3194.3 U/L, normal range: 9.0-50.0 U/L). The inflammatory markers showed mildly increased procalcitonin (0.93 ng/mL, normal range: 0-0.25 ng/mL). In addition, the glycated haemoglobin A1c blood glucose test result was 11.2%, which is consistent with poorly controlled diabetes, and the results of an HIV test and malaria screen were both negative. Blood and urine were drawn for culturing, and a course of empirical treatment was begun. Subsequently, the aerobic bottles of two sets of blood cultures were positive for gram-negative bacilli, and the same result was also obtained in urine culture. After culturing for 24 h, yielded an oxidase-positive, gram-negative bacillus that grew rapidly

on blood agar as a grey colony with a metallic sheen (Supplementary Figure 1). The organisms were initially identified as *B. pseudomallei* by VITEK-2 Compact GN card (bio number 0003451513500211). The antimicrobial drug therapy was changed to co-amoxiclav, and two days later, when the identification of the organisms was confirmed by 16S rDNA gene sequencing analysis, the patient's treatment was switched to intravenous meropenem. During the 7-day treatment course, the

patient was transferred to the Department of Infectious Disease, the First Affiliated Hospital of Chongqing Medical University for treatment. Subsequently, the patient's urinary tract infection and fever resolved, and after 15 days of receiving meropenem, his general condition improved. Unfortunately, the patient didn't attend his scheduled outpatient appointment after discharge.

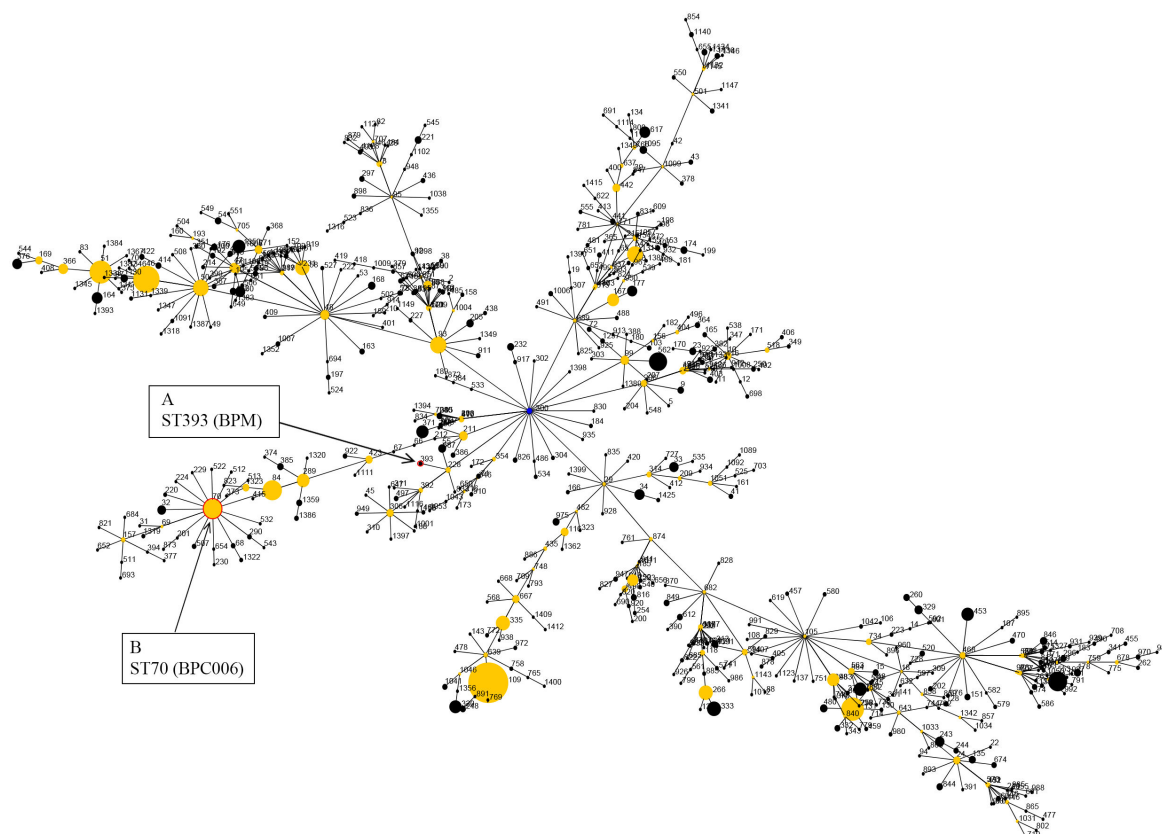


Figure 1: The e BURST diagram displaying relatedness of the ST393 isolate (A) and other sequence types of the historical *B. pseudomallei* strain collection in the MLST database. The e BURST analysis showed it was more closely related to ST393 from Thailand, not related to ST70 (B) from Chinese origin.

Since VITEK-2 Compact (GN Card) (bioMérieux, France) is prone to produce false positive or false negative results [7], 16S rDNA gene sequencing analysis is required to confirm the identification of *B. pseudomallei*. And then the isolates were sent to a biosafety level two plus Mycobacteriology Laboratory for further analysis. Moreover, PCR amplification, we used the two primers F (5'-GATCATGGCTCAGATTGAAC-3') and R (5'-CTACGGTTACCTGTTACGA-3') that could specifically detect the *B. pseudomallei* isolates [8,9], produced the predicted 1397bp band for *B. pseudomallei* isolates (Supplementary Figure 2). The PCR product was sequenced by BGI (Beijing, China). The isolate showed a 99% similar to *B. pseudomallei* (GenBank accession nos. CP004379.1 and CP004380.1). Based on these data, we concluded that this infection case was caused by *B. pseudomallei*.

Melioidosis is rare in most parts of China, there were only 0-3 cases reported annually, and most of them occurred in travellers returning from disease-endemic regions [8,9]. In this case, we cannot be certain

that whether this melioidosis acquired by the traveller to Thailand, the disease-endemic country in the Asia-pacific region. To our best knowledge, no documented cases of melioidosis acquired in Chongqing had been reported, so the multilocus sequence typing (MLST) was used to study the molecular epidemiology of *B. pseudomallei*, and the MLST was performed by using PCR amplification conditions and primers as previously described [10], generated an allelic profile (Supplementary Figure 2) that was compared with those of strains of *B. pseudomallei*, *B. thailandensis*, and Mallei stored in the database (<http://bpseudomallei.mlst.net>). The result showed that the novel sequence type (ST) was identified as ST393 (BPM), which is a strain of Thailand origin. However, it had previously been reported that the *B. pseudomallei* ST70 (BPC006) was the predominantly isolate of Chinese origin, which was considered as China's standard strain [11]. And an evolutionary analysis of ST393 with burst analysis software (<http://eburst.mlst.net>) suggested that it was not related to ST70 (BPC006) (Figure 1).

Discussion

Clinical diagnosis of melioidosis in non-endemic regions is challenging because signs of the disease are non-specific and similar to those of more common diseases, such as tuberculosis [12]. In addition, laboratory diagnosis is also challenging. In this case, *B. pseudomallei* grew readily in culture. However, the VITEK-2 Compact didn't provide definitive species identification; we recheck the identification of *B. pseudomallei* by 16S rDNA gene sequencing analysis. What's more, cultures and analysis of *B. pseudomallei* isolates were both manipulated in biosafety level two plus laboratory.

Melioidosis is endemic to the Pacific region and Southeast Asia [13,14]. Most cases reported in other non-endemic regions are imported [15]. In Thailand, where the patient had travelled, the number of cases increased from 11.5/100,000 inhabitants in 1997 to 21.3/100,000 in 2006 [16]. The main routes of transmission are flooding, a risk factor for melioidosis, as for this case-patient.

Melioidosis may affect healthy persons, but melioidosis infection is closely related to underlying diseases, especially related to diabetes [12]. Diabetic patients are prone to concurrent infections due to malnutrition, hypoalbuminemia, and blood glucose fluctuations that can easily damage defence mechanisms and reduce immune function. In a case-control study in northern Australia, diabetes was associated with an adjusted odds ratio of 13.1 [17]. With the prevalence of diabetes projected to increase constantly in many developing countries and the increased international travel [18], the global reach of melioidosis may expand. To sum up, the immunocompromised travellers might be first sentinels for ongoing endemic diseases. When the travellers return with uncommon diseases, physicians should check for underlying diseases such as melioidosis.

Conclusions

Given the frequency of travel between China and other countries, the existence of imported cases from endemic countries until now is striking, and physicians should be aware of its varied manifestations. In particular, melioidosis should be considered when diabetic patients returning from endemic countries, even without risk factors predisposing to severe disease. And this study finally indicates that this melioidosis acquired by the traveller to Thailand.

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