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Multi-systemic melioidosis in a patient with type 2 diabetes in non-endemic areas: A case report

Ni HY *et al*. Multi-systemic melioidosis

Huan-Yu Ni, Ying Zhang, Dong-Hai Huang, Feng Zhou

Abstract

BACKGROUND

Melioidosis, an infectious disease caused by *Burkholderia pseudomallei* (*B. pseudomallei*), occurs endemically in Southeast Asia and Northern Australia and is a serious opportunistic infection associated with a high mortality rate.

CASE SUMMARY

A 58-year-old woman presented with scattered erythema on the skin of her limbs, followed by fever and seizures. *B. pseudomalle*i was isolated successively from the patient's urine, blood, and pus. Magnetic resonance imaging showed abscess formation involving the right forehead and the right frontal region; subsequently, abscess resection and drainage were performed. The patient showed no signs of relapse after 5 months of follow-up visits post-treatment.

CONCLUSION

We present here a unique case of multi-systemic melioidosis that occurs in non-endemic regions in a patient who has no recent travel history. Hence, it is critical to enhance the awareness for melioidosis in non-endemic regions.

Key Words: Melioidosis; *Burkholderia pseudomallei*; Endemic; Diabetes; Case report

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Core Tip: This case describes a patient with no history of travel to melioidosis-endemic areas, who accidentally contracted *Burkholderia pseudomallei* (*B. pseudomallei*) due to trauma caused by a fall in a non-endemic area, leading to a multisystem melioidosis. This case is beneficial in enhancing the understanding of melioidosis, which suggests that *B. pseudomallei* could emerge in other non-endemic regions with climate change.

INTRODUCTION

Melioidosis is an endemic disease caused by *Burkholderia pseudomallei* (*B. pseudomallei*), mainly in tropical and sub-tropical areas, such as Southeast Asia, Northern Australia, and India, and is extremely rare in temperate regions[1-3]. *B. pseudomallei* is an environmental saprophyte found in soil, surface water, and groundwater[4]. Humans are likely infected through contaminated scratches and abrasions or the occasional aspiration of fresh water. Infections typically occur in the epidemic areas; sporadic cases are very rare, and melioidosis reported in other areas is essentially from imported cases of travelers or immigrants[5]. The most significant risk factors of melioidosis include diabetes, excessive alcohol use, chronic lung disease, chronic renal disease, thalassemia, immunosuppressive therapy, and cancer[6,7]. Melioidosis has been dubbed "the Great Imitator" given the absence of specific clinical features. Clinical and laboratory diagnoses of melioidosis are challenging[7,8]. Although melioidosis is a serious opportunistic infection, the mortality rate is very high[7,9,10]. Timely diagnosis and treatment are key to reducing the mortality rate. Herein, we report the clinical details of a patient with multi-systemic melioidosis caused by *B. pseudomallei* in Wuhan, Hubei Province of China, which is a non-endemic region.

CASE PRESENTATION

Chief complaints

The patient was admitted due to a 6-d history of fever.

History of present illness

Twenty days after the incident, she experienced painful erythematous swelling of the bilateral lesser thenar and erythema on her limbs (Figure 1). She was diagnosed with undifferentiated connective tissue disease because of limb skin erythema, left knee joint pain, and positive Sjogren's syndrome antigen B antibody (anti-SSB). She began to take 30 mg prednisone daily for treatment. About 3 wk after prednisone therapy, the patient presented with chills, fever, headaches, frequent micturition, and other uncomfortable

symptoms, with the highest temperature reaching 39.2℃. Despite oral antibiotic therapy with 0.5 g amoxicillin (Amoxil) thrice daily, the fever and headache did not subside.

History of past illness

She has had type 2 diabetes for over 5 years, with no chronic kidney dysfunction or blood system diseases, among other conditions.

Physical examination

Upon examination, the patient was apyretic (body temperature: 36.5℃), but generally unwell. The patient had a small erythematous patch with tenderness on the right forehead. She was hemodynamically stable, and the results of her respiratory and cardiovascular examinations were perfectly normal. Her abdomen was soft, with no hepatosplenomegaly. She had scattered skin rashes on her limbs. The result of her neurological examination was normal.

Laboratory examinations

Blood biochemistry revealed elevated C-reactive protein (CRP) and erythrocyte sedimentation rate and normal white cell count and neutrophils. However, the red and white blood cell count was positive in urine sediment analysis (Table 1).

Imaging examinations

Head computed tomography (CT) measurements were normal (Figure 2A). Brain magnetic resonance imaging (MRI) showed a T2-weighted-fluid-attenuated inversion recovery (Figure 2B) signal that was slightly hyperintense, involving the right frontal region with a 7.6 mm × 33 mm strip, suggesting subdural hematoma. The right frontal skin showed swelling (Figure 2C). A second brain MRI was performed one week after the first one and showed that the subdural hematoma and subcutaneous swelling at the right frontal region worsened (Figures 2D and E).

FINAL DIAGNOSIS

Multi-systemic melioidosis; Type 2 diabetes.

TREATMENT

Blood and urine cultures were performed on the second day of admission. On the third day of admission, the patient presented with sudden loss of consciousness and generalized seizure for a few seconds. The patient was diagnosed with epileptic seizure and treated with diazepam. On the fifth day of admission, blood and urine cultures revealed a gram-negative bacillus, *B. pseudomallei*, which is sensitive to ceftazidime, levofloxacin, cotrimoxazole, and meropenem. Ceftazidime (2 g every 8 h) was given according to the drug sensitivity test. The patient's fever resolved, and the rashes gradually subsided after therapy. After 1 wk of ceftazidime treatment, the patient again developed high fever (highest recorded temperature: 39.0℃). Ceftazidime was discontinued and replaced with meropenem. The patient was treated with incision and drainage of the subcutaneous abscess in the right frontal region.

OUTCOME AND FOLLOW-UP

The patient showed no signs of relapse at the 5-month follow-up visit.

DISCUSSION

Melioidosis is regarded endemic to Southeast Asia and Northern Australia. In China, melioidosis often occurs in the southern areas, namely Hainan, Guangdong, Guangxi, and Fujian[11], and is very rare in other parts of China. Most of the sporadic cases reported in other parts of China are of patients with a travel history of endemic melioidosis. Although it is an endemic disease, melioidosis is a life-threatening disease caused by *B. pseudomallei*. Our patient presented multi-systemic involvement, including the skin and soft tissue, genitourinary system, and central nervous system (CNS).

Cutaneous melioidosis (CM) has been rarely described compared with other systemic melioidosis[12]. CM may be a primary cutaneous infection or a disseminated

secondary skin infection[13]. The common presentations of CM include ulcers, skin abscesses, single pustules, crusted erythematous lesions, and dry asymmetric erythematous flat lesions[13,14]. CM is often misdiagnosed as other diseases in non-endemic areas, because the skin manifestations and histologic results of CM are non-specific[15,16]. The dry asymmetric erythematous flat lesions in this patient were considered the main evidence for the diagnosis of undifferentiated tissue disease. The risk factors of melioidosis includes diabetes mellitus, excessive alcohol consumption, liver disease, chronic lung disease, chronic kidney disease, and steroid use[5,7,17-19]. Melioidosis patients with known diabetes have poor diabetic control and show a stunted *B. pseudomallei*-specific cellular response during acute illness compared with those without diabetes[20]. Uncontrolled blood sugar and steroid therapy are also important risk factors for the spread of melioidosis[19]. This patient showed typical melioidosis skin lesions such as painful erythematous swelling of the bilateral lesser thenar and erythema on the limbs, but the patient's condition was aggravated by misdiagnosis, diabetes, and steroid therapy.

Genitourinary melioidosis is common, accounting for 3.2%-14%[7,21] of all melioidosis cases. Genitourinary melioidosis occurs more frequently in male patients with complications, such as prostatitis, prostatic abscess, renal abscess, epididymo-orchitis, and sepsis[7,22]. The clinical manifestations are mainly urinary frequency, dysuria, urinary retention, and swelling of the scrotum[22,23], and some patients may present septic shock[24]. Much white and red blood cells can be observed in urine[25]. Genitourinary melioidosis can be ruled out if the patient has no urinary symptoms or a negative urine test[26]. This patient also presented with urinary frequency and white and red blood cells in the urinalysis.

Neurological melioidosis is rare but has a high mortality rate[27,28]. In a patient series of 540 melioidosis, neuro-melioidosis accounts for only 3%-5%, but accounts for 21% of the mortality[7]. The neurological manifestations of melioidosis often include meningoencephalitis, myelitis, and spinal epidural abscess but rarely brain abscess[29,30]. Although the radiographic features of neurological melioidosis are not specific, CNS

imaging is essential for locating lesions and identifying those that can be treated with surgery or biopsy so that appropriate treatment can be initiated in a timely manner[31,32]. In this case, head CT presented no abnormalities, and cerebral hemorrhage was misdiagnosed on head MRI. However, the subsequent head MRI revealed the progression of melioidosis and recorded the evolution of the patient's intracranial abscess. MRI is more sensitive for diagnosing neurological melioidosis than CT[33]. Therefore, serial head MRI is one of the important methods of diagnosing neurological melioidosis.

The isolation of *B. pseudomallei* from clinical specimens is the gold standard for the diagnosis of melioidosis. However, *B. pseudomallei* can be easily thought of as a contaminant or confused with other bacteria[5], resulting in the misdiagnosis or delayed diagnosis of melioidosis. Blood cultures are the most important, but the positive rate of *B. pseudomallei* is only 50%-70% in blood culturre[34,35]. In one series, only 29% of the brain tissue or puts and 19% of the CSF samples were culture positive[29]. *B. pseudomallei* was isolated from the samples of this patient's blood, urine, and right frontal subcutaneous abscesses, but not from CSF and intracranial abscess samples.

The laboratory markers associated with poor prognosis include leucopenia (especially lymphopenia), a normal or only slightly raised CRP, raised transaminases, bilirubin, urea, and creatinine, hypoglycemia, and acidosis[36,37]. CRP estimations may be helpful in ascertaining active infection in patients with low serum levels of specific IgM antibody[38], however, a normal level of CRP cannot be used to exclude acute, chronic, or relapsed melioidosis in febrile patients in endemic regions[39]. In this case, the level of CRP gradually decreased with the improvement of the patient's disease, and no serious increase in transaminases, bilirubin, and creatinine was noted.

Because melioidosis is a serious threat to patients' health, commencement of treatment should be immediate, rather than wait until the culture results. The treatment of melioidosis consists of an intensive phase of at least 10-14 d of intravenous administration of ceftazidime, meropenem, or imipenem, followed by oral eradication therapy, usually with trimethoprim-sulfamethoxazole for 3-6 months[40,41]. Attention

should also be paid to the risks of long-term antibiotic treatment. *B. pseudomallei* is resistant to penicillin, ampicillin, first-generation and second-generation cephalosporins, gentamicin, tobramycin, streptomycin, macrolides, and polymyxins[42,43], Thus, no therapeutic effect was noted when the patient first took amoxicillin. This patient was initially given ceftazidime according to the susceptibility testing upon admission, which was switched to meropenem because of fever during treatment with ceftazidime. The failure of ceftazidime treatment may be related to the suppression of the immune system by steroid therapy and poor blood glucose control. Festic *et al*[44] showed that glucocorticosteroids impact biofilm formation and antibiotic tolerance. Physicians who are unfamiliar with the treatment of melioidosis should follow the course of treatment recommended by the guidelines[45,46]. Although antibiotics are preferred for the treatment of multiple intracranial abscesses in melioidosis[47]. Adjunctive abscess drainage was performed in 58% cases. After treatment, 37% patients with CNS melioidosis recovered completely or nearly completely, 31% had moderate neurological improvement, while 13% did not recover and suffered neurological disability[48]. In our patient, the intracranial abscess gradually increased during the course of antibiotic treatment, so intracranial abscess drainage was performed, resulting in no further adverse neurological prognosis.

CONCLUSION

We present here a rare case of multi-systemic melioidosis in a female patient without a travel history in a non-endemic area. In this case, cutaneous and genitourinary melioidosis infection as well as intracranial melioidosis infection occurred. For melioidosis with poor response to antibiotics, the aggravation of infection leads to intracranial abscess for which abscess excision and drainage are an effective measure. We believe that this report will help improve the traditional understanding of melioidosis among the medical staff in non-endemic areas and provide an account of the clinical experience for the diagnosis and treatment of multi-systemic melioidosis.

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"Imported Melioidosis in South Korea: A Case Series with a Literature Review", Osong Public Health and Research Perspectives, 2015
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17 Gibney, KatherineB., AllenC. Cheng, and BartJ. Currie. "Cutaneous Melioidosis in the Tropical Top End of Australia: A Prospective Study and Review of the Literature", Clinical Infectious Diseases, 2008.
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