Melioidosis: Can Tropical Infections Present in Nonendemic Areas? A Case Report and Review of the Literature

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INTRODUCTION

Melioidosis is an infectious disease that affects both humans and animals. It is caused by *Burkholderia pseudomallei*, a small, motile, aerobic, intracellular, nonspore-forming, Gram-negative and oxidase-positive rod-shaped bacterium with exopolysaccharide capsule. *B. pseudomallei* is most commonly found in wet soil and stagnant water, particularly rice paddy fields.[1-3] Melioidosis is an important cause of sepsis in tropical areas of Eastern Asia, mainly affecting immunocompromised adults. Diabetes mellitus is the most important host risk factor. Here, the authors report a case of a 54-year-old Saudi male with uncontrolled diabetes mellitus for 10 years who presented to our hospital with a 6-week history of fever, cough, night sweats and weight loss. The patient was a frequent traveler to the Philippines, with his last visit being during the rainy season 2 weeks before the onset of symptoms. Definite diagnosis of melioidosis was not made because of insufficient facility to culture the organism in our laboratory; nevertheless, a diagnosis of melioidosis was made based on the cumulative clinical scenario. The patient was discharged on trimethoprim-sulfamethoxazole and doxycycline for 3 months and showed significant improvement at follow-up. For prompt diagnosis and treatment, clinicians must maintain a high index of suspicion for melioidosis in febrile patients with a history of traveling to endemic areas, especially diabetic patients.

CASE REPORT

A 54-year-old Saudi male, with a history of uncontrolled diabetes mellitus for the past 10 years presented to the King Fahd Hospital of the University, Al Khobar, Saudi Arabia, with a 6-week history of irregular fever pattern, dry cough, night sweats and weight loss. No other respiratory, genitourinary or gastrointestinal symptoms were reported. In the past 5 years, the patient

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traveled to the Philippines 2–3 times a year, with his last visit being during the rainy season 2 weeks before the onset of symptoms. The patient had no history of contact with animals or sick patients as well as had no extramarital sexual contacts, intravenous (IV) drug abuse or blood transfusions. Despite seeking medical advice and receiving multiple oral and IV antibiotics, the patient had no improvements.

Physical examination of the lungs revealed decreased air entry in the right upper and middle zone posteriorly, with minimal fine inspiratory crepitations. Complete blood count as well as renal and liver function tests were normal, except for white blood cells, which were $13.2 \times 10^9$/L with normal differential count. Complete bacteriology and virology screening were negative. Blood and sputum cultures were also negative.

Imaging in pan-computed tomography (CT) scan revealed multiple, bilateral pleural-based nodules and multiple splenic hypodensities, representing possible abscesses [Figures 1 and 2]. The patient underwent flexible bronchoscopy with right video-assisted thoracoscopic surgery. The lung biopsy showed noncaseating granuloma with negative malignant cells, and acid-fast bacilli and fungal cultures were negative. Minimal clinical improvement was observed during a 21-day course of empirical therapy with IV ceftriaxone, but fever continued to spike at lower grades.

Although definite diagnosis could not be made because of insufficient facility in our laboratory, a provisional diagnosis of melioidosis was made based on the cumulative clinical scenario. Accordingly, the patient was discharged on trimethoprim–sulfamethoxazole (TMP–SMX) and doxycycline for 3 months. At the outpatient follow-up, significant improvements were observed with respect to fever and inflammatory markers. For definitive diagnosis, the authors attempted to send another specimen to a more advanced laboratory; however, the patient was lost to follow-up.

**DISCUSSION**

Melioidosis is endemic in tropical areas, especially in Southeast Asia (including Thailand, Malaysia, Singapore and Vietnam) and northern Australia. In Thailand, melioidosis represents the most common cause of fatal community-acquired pneumonia and septicemia, with an annual incidence of 50 per 100,000, making it the third most common cause of death from infectious disease, following HIV and tuberculosis.[2-4] Recently, there has been a sudden increase in sporadic cases reported in countries located between the latitudes 20° N and 20° S.[6]

Several isolations of *B. pseudomallei* have been reported from the Middle East, but none have been confirmed. In Saudi Arabia, Shibl *et al.*[7] reported a human case, while Barbour *et al.*[8] reported an animal case. In addition, a few isolated cases have also been reported in the United Arab Emirates, Egypt and Turkey.[9]

The most common mode of transmission is by direct inoculation from contaminated soil or water through skin abrasions. Inhalation and ingestion are other known modes of transmission.[6] Human-to-human transmission is very rare, but vertical transmission at childbirth, by mothers with mastitis and as a sexually transmitted infection, have been reported.[1,3,4] Other rare routes of
transmission include near-drowning experience as well as nosocomial and laboratory transmissions.[9]

The majority of affected patients are immunocompromised and have continuous occupational exposure to soils and ground water.[2,8] Diabetes mellitus is the most important host risk factor, accounting for 37%–70% of the cases.[2,6] Other host risk factors include chronic renal disease, pulmonary disease (cystic fibrosis), thalassemia, congestive heart failure, liver cirrhosis, alcoholism, corticosteroid/immunosuppressant therapy and malignancy (leukemia and lymphoma).[2,4] Although melioidosis has not been reported to be associated with HIV infection, immunocompetent individuals are at risk of infection if the exposure load is high.[4] The incubation period ranges from 1 to 21 days postexposure, with a mean of 9 days.[4]

The clinical presentation of melioidosis can range from acute (<2 months), fulminant febrile illness to chronic (>2 months), debilitating or localized infection and is characterized by abscess formation.[2,4] Over half of the patients have bacteremia on presentation, and septic shock develops in approximately one-fifth of the cases.[4] Chronic infection accounts for 11% of all cases and may mimic cancer, tuberculosis or fungal infections, with symptoms such as fever, weight loss and a productive cough with or without hemoptysis.[2,4] Exacerbation of melioidosis can occur after months or even years.[3] Almost every organ may be involved in the disease, but the most common are lungs, spleen and liver, whereas the least common are central nervous system organs. The musculoskeletal and cardiovascular systems may be involved in the disease.[9]

Lungs account for roughly half of all cases (51%), presenting with productive cough and fever, resulting from pneumonia or lung abscess.[6] The severity of the condition varies widely from septic shock to mild undifferentiated pneumonia. However, it is difficult to determine if the lung consolidation is due to primary pneumonia or secondary septicemia.[4,6] Exacerbation of melioidosis can occur after months or even years.[3] Almost every organ may be involved in the disease, but the most common are lungs, spleen and liver, whereas the least common are central nervous system organs. The musculoskeletal and cardiovascular systems may be involved in the disease.[9]

Pneumonia is followed by genitourinary infections in about 14% of the cases, skin infections in about 13%, bacteremia without evident focus in 11%, septic arthritis or osteomyelitis in 4% and neurologic involvement in 3%, whereas the remaining 4% of the patients do not have any evident focus of infection.[4]

Abscess formation can occur in any organ, but the most common sites are spleen, liver, skeletal muscle and prostate.[4] Spleen is the most common extrapulmonary visceral organ to be affected, where lesions are usually multiple, small and discrete.[6,10] Splenic abscesses are found in melioidosis more than any other infectious disease, especially if there is also a concurrent liver abscess.[10] Liver is the second most commonly affected visceral organ, where the radiological appearance is as a single, multiple discrete or multiloculated lesions. However, unlike the spleen, it is usually a part of a multiorgan involvement rather than a single organ involvement.[10,11]

The mortality rates for melioidosis are approximately 40% in Northeast Thailand (35% in children), while in Australia, it is about 14%.[4] Predictors of death were age at diagnosis, presence of pneumonia as well as abnormal serum urea, serum bilirubin, lymphocyte count and serum bicarbonate.[12]

Definitive diagnosis is made when there is a positive culture for B. pseudomallei from any site of the body.[8] However, to date, there is no “gold standard” for the identification of B. pseudomallei. Samples are obtained from blood, sputum, urine, pus culture and throat swab.[2] Direct immunofluorescence microscopy of infected sputum, urine or pus is 98% specific and 70% sensitive compared with culture, but allows a diagnosis to be made within 30 min, which is helpful for initiating early treatment. Polymerase chain reaction may also be used for rapid differentiation.[12] Indirect hemagglutination assay is the most sensitive and is serodiagnostic, but not useful in endemic areas, where they may be positive in up to 50% of cases. However, a high titer (>1:640) is suggestive of an active disease.[12,6,13]

Imaging is often very useful to ascertain the extent of the disease; for example, the use of chest radiography for evidence of nodular infiltrates or consolidation. Ultrasound or CT scans are also recommended to check for subclinical abscesses.[1,2]

With regard to the treatment, B. pseudomallei is resistant to various antibiotics such as penicillin, ampicillin, gentamicin and first-/second-generation cephalosporins. Further, most of its strains are sensitive to amoxicillin–clavulanic acid, piperacillin, carbapenems, third-/fourth-generation cephalosporins, doxycycline and TMP–SMX.[2] There are two phases for treatment: the first is the IV-intensive phase using ceftazidime or carbapenems with TMP–SMX for 10–14 days. Amoxicillin–clavulanate is an alternative, but with a higher failure rate.[2,4] The second is the oral eradication phase using TMP–SMX for 5 months with or without doxycycline. Recurrence, mainly due to reinfection, has been found in 6% and 13% of cases at 1- and 10-year follow-up, respectively.[12,14]
CONCLUSION

Melioidosis is a very rare disease in Saudi Arabia and its diagnosis may be easily overlooked. Thus, for prompt diagnosis and treatment, physicians must maintain a high index of suspicion for melioidosis in febrile patients with a history of traveling to endemic areas with predisposing factors, especially diabetes mellitus.

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Conflicts of interest
There are no conflicts of interest.

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