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Case report

Disseminated melioidosis in a patient from Nicaragua

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ABSTRACT

Melioidosis is a disease caused by *Burkholderia pseudomallei*. Highly endemic areas include tropical Australia and Southeast Asia, though cases have been reported in the Americas. To our knowledge this is the first case to have occurred due to presumed exposure in Nicaragua, demonstrating the need for increased awareness. In addition, the severity of melioidosis also varies widely and more research is needed on the pattern of disease particularly in non-endemic regions.

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Introduction

Melioidosis is a disease caused by *Burkholderia pseudomallei*, a gram-negative saprophyte found in wet soil [1]. The bacterium is well known for causing pneumonia, sepsis and multiple abscesses within organs [2]. Infection is usually acquired by percutaneous inoculation, inhalation or ingestion. It is commonly found in the soil and on surface water in highly endemic areas of tropical Australia and Southeast Asia. However, cases have been sporadically reported in the Middle East, Europe, and the Americas [3]. To our knowledge, this is the first case have occurred due to presumed exposure in Nicaragua.

In addition, melioidosis also can have a wide range of clinical manifestations varying from asymptomatic infection, localized skin ulcers, chronic pneumonia mimicking tuberculosis to septic shock with disseminated abscesses in internal organs [4]. It can cause disseminated disease in immunocompromised individuals and has a high relapse rate, even among those treated [3]. Here we report a case of a disseminated melioidosis in a patient with undiagnosed metastatic cancer.

Case description

A 70-year-old woman of Nicaraguan descent with past medical history of type two diabetes mellitus and hypertension arrived from the airport with altered mental status and painless jaundice to the emergency room. She arrived from Nicaragua after a two month stay with relatives in rural areas during the rainy season months of May and June. She had no other travel history and resided only in the United States and Nicaragua. The family reported that she was in her usual state of health prior to the trip and stayed compliant to her insulin. Moreover, she was hospitalized for one week in Nicaragua for liver failure and required blood transfusions for unknown reasons. Unfortunately, further medical records were not available.

On arrival to the emergency department, patient's vital signs were notable for a temperature of 38.6 °C, heart rate of 106 beats per min and blood pressure of 95/57 millimeters of mercury. Physical examination revealed scleral icterus, jaundiced skin, mild asterixis, and anasarca. Patient was only oriented to name. She also had mild suprapubic tenderness on palpation of abdomen. On admission, labs were significant for white blood count of 15.1 K/cumm, INR 2.33, sodium of 123 mmol/L, Creatinine 3.18 mg/dL (unknown baseline), alkaline phosphatase 374 u/L, total bilirubin 18.4 mg/dL, and a direct bilirubin 11.7 mg/dL. Chest x-ray revealed right sided pleural effusion.

Seven hours after arrival, the patient became hypotensive requiring vasopressor support and her antibacterials were broadened to meropenem and vancomycin. Preliminary urine and blood cultures demonstrated gram negative rods. Two days later urine cultures grew out extended spectrum beta-lactamase (ESBL) *Escherichia*

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Fig. 1. Early arterial phase coronal contrast-enhanced CT shows low-attenuation of the lesion in the liver with slight, irregular peripheral rim-enhancement. Differential diagnosis includes metastases versus hepatic abscess.

coli and three days later blood cultures tentatively identified the pathogen as *Burkholderia pseudomallei*. This identification required further confirmation and sensitivities to be sent to the Centers for Disease Control (CDC). In the meantime, meropenem was continued and maintained throughout hospitalization. Because of her increased creatinine, a cat scan (CT) of the abdomen/pelvis without contrast on day two of admission was done and it showed hepatomegaly, moderate amount of ascites, and a liver nodularity concerning for cirrhosis along with an ill-defined area of hypoattenuation in the dome of the liver. In addition, a six-millimeter nodule was seen in left lower lobe of the lung. Follow up imaging of the abdomen with magnetic resonance imaging (MRI) showed numerous T2 hyperintense lesions throughout the liver, concerning for metastatic disease, although liver abscess could not be completely ruled out given her bacteremia (Fig. 1). A subsequent MRI of the liver was obtained to further differentiate abscesses from metastatic lesions (Fig. 2). A liver biopsy was performed on hospital day ten showing evidence of malignant undifferentiated carcinoma rather than abscesses. Labs showed a positive CA-125 of greater than > 3000 u/ml.

Despite continued meropenem, patient's kidney function and mental status declined. Although the patient improved with an initial trial of dialysis, she ultimately deteriorated with multi-organ failure and died twenty-two days after hospitalization.

Discussion

To date, this is the first reported case of melioidosis due to presumed exposure in Nicaragua. Although endemic to Southeast Asia and northern Australia, cases have been reported throughout Central

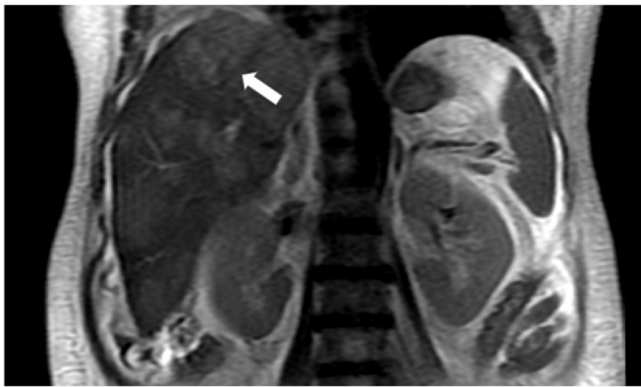


Fig. 2. Coronal T2 weighted single-shot fast spine-echo (SSFSE) sequence shows slightly increased, heterogenous signal within this lesion, indicating a metastatic lesion. A hepatic abscess would show more marked, homogenous T2 hyperintensity.

America, South America and more recently the United States. The magnitude of melioidosis in the Americas however remains unclear due to underreporting. The cases that have been identified so far have mainly originated from Brazil, El Salvador and Mexico [5,6]. Limmathurotsakul et al. reports that incidence of disease in Mexico and El Salvador could be as high as 550 and 114 per 100,000 respectively [7]. Moreover, several cases have also been reported in the United States among individuals with no travel history. As of August 2021, the CDC identified four cases spread across different states, linked together by a common source of exposure based on genomic analysis [8]. Reports have also suggested that melioidosis can have a latency period of months to years; therefore, a comprehensive travel and exposure history is crucial [9]. Because of the increasing prevalence, our patient could have acquired melioidosis in the United States. However, her extensive travel history to rural Nicaragua especially in the rainy season makes it more likely she acquired melioidosis in Nicaragua. In addition, our patient's metastatic cancer could have activated a latent form of the bacteria, which she could have acquired much earlier in her previous trips. Overall however, the global distribution of cases is expanding, and increased awareness of the growing prevalence may be helpful to avoid misidentifying the pathogen or causing delays in management.

Identification of *B. pseudomallei* in culture was a key diagnostic step in our patient. Despite the prompt diagnosis, our case highlights the need to maintain a broad differential, including one of malignancy. For hospital systems not accustomed to identifying *B. pseudomallei*, delay or misidentification the pathogen are not uncommon [4]. These delays can be fatal, especially since empirical antibiotics do not provide adequate coverage for *B. pseudomallei*. The bacteria are inherently resistant to penicillin, ampicillin, first-generation and second-generation cephalosporins, gentamicin, tobramycin, streptomycin, and polymyxin [10]. In addition, cure is often difficult and melioidosis can have a protracted course, requiring more than three months of antibiotic therapy. Current treatment recommendation calls for 2–8 weeks of ceftazidime or meropenem followed by a 3–6-month oral eradication phase with trimethoprim-sulfamethoxazole and amoxicillin-clavulanic acid [9]. Minimization of treatment failure and relapse in patients depends on an appropriate duration of initial intensive therapy followed by an adherence to the eradication phase [11]. In our patient, her risk factors of recent travel within the rainy season, diabetes, and advanced age helped to broaden antibiotics. The presumed diagnosis of melioidosis and appropriate initiation of antibiotics were made within seventy-two hours of admission, with a confirmation by the CDC on day nine. Once a diagnosis is confirmed, imaging the abdomen and pelvis is recommended to search for organ abscesses. Adjunctive therapy for abscesses if found includes drainage, aspiration and washout [1]. For our patient however, imaging alone was not sufficient for diagnosis because the patient's liver lesions were due to underlying malignancy, not abscesses. With a biopsy confirming a previously unknown undifferentiated metastatic cancer, our case demonstrates the need for a differential broad, even in the setting of disseminated melioidosis.

The severity of melioidosis varies widely and more research is needed on the pattern of disease particularly in non-endemic regions. These variations may reflect many factors including patients' underlying conditions, geographical variation of the bacterial strain and virulence patterns. The presentation of disease for example can range from a localized skin infection, to chronic infection mimicking tuberculosis or cancer, to an acute lethal sepsis [12]. In the largest case series of 540 patients over 20 years, pneumonia however was the most common presentation, followed by infections of the genitourinary system, skin, blood stream, septic arthritis/osteomyelitis and central nervous system [13]. There is also a multitude of evidence that host factors play a crucial role in the pattern of disease. Established risk factors in melioidosis include diabetes, heavy alcohol consumption, chronic pulmonary disease, chronic renal disease, thalassemia, glucocorticoid use and cancer [1]. Currie et al. identified that the predictors

of mortality appear to be age ≥ 50 and presence of any risk factor [14]. The geographic variation in the pattern of disease has also been reported. For example, prostatic abscesses and neurological melioidosis are more frequently found in Australia and suppurative parotitis is more often seen in East Asia. Our patient travelled to Nicaragua and developed septic shock, multiorgan failure and died. The pattern and severity of melioidosis in Nicaragua and the Americas is less clear and ongoing research is needed.

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Consent

Written informed consent was obtained from the patient's daughter for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

CRedit authorship contribution statement

Tejasvi Pasupneti: Conceptualization, Writing – original draft, Writing – review & editing. **Mark Munekata:** Writing – original draft, Writing – review & editing. **Sunita Saith:** Writing – review & editing, Visualization. **Scott Filler:** Writing – review & editing, Supervision.

Declaration of Competing Interest

None.

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