

A Young Diabetic Patient With Sepsis After Gardening

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We report a case of soft tissue infection, sepsis, and bacteremia due to *Burkholderia pseudomallei* (melioidosis) in a diabetic young patient and the genomic characterization of *Burkholderia pseudomallei* isolate (COL-5428).

CASE

In July 2018, a 35-year-old man living in a town in the northern region of Colombia (Calamar, Bolivar) was admitted to a tertiary care hospital in Barranquilla (the largest city in Northern Colombia) with fever (101.3°F), chills, headache, and mild pain in the medial area of the right thigh. The initial presumed diagnosis was a viral infection. After 5 days, the patient returned to the hospital with prolonged fever, headache, and disabling pain in the right thigh. There was no evidence of trauma or skin lesions. He had diabetes treated with metformin and vildagliptin. The patient indicated that 10 days before admission, he had worked as a gardener and had been in contact with soil but denied trauma or penetrating injury. Physical exam revealed a temperature of 100.4°F and a heart rate of 104 beats per minute. He was notoriously diaphoretic, and his blood pressure was 130/70. Edema was evident in the distal medial third of the right thigh, which was warm on palpation. Relevant laboratory studies showed leukocytosis (13 140 cell/μL, 94.7% neutrophils, and 2.8% lymphocytes) with hyperglycemia (blood glucose 175 mg/dL), glucosuria, and a serum creatinine of 0.71 mg/dL. Liver

function tests and other laboratories were within normal limits. Ultrasound evaluation on the thigh did not reveal abscess or fluid collections. The patient was started on clindamycin for a presumed diagnosis of myositis. However, the patient deteriorated, remaining febrile, tachycardic, and tachypneic with worsening of limb pain and swelling and was transferred to the intensive care unit. Subsequently, icteric sclera developed (total bilirubin, 4.17 mg/dL; conjugated bilirubin, 4.16 mg/dL) with elevation of transaminases (alanine aminotransferase, 137 U/L; aspartate aminotransferase, 104 U/L). Arterial blood gases revealed high anion gap metabolic acidosis. Magnetic resonance imaging of the right thigh and knee (Figure 1) revealed inflammatory changes in muscle and destructive changes of the bone without presence of gas. Chest x-rays and computed tomography scan of the chest revealed bilateral pleural effusion and multilobar infiltrates with extensive ground glass opacities and a bilateral interstitial pattern (Figure 1). Antibiotics were switched to meropenem (2 g IV q12h) and vancomycin (1.2 g IV q12h). Serologies for hepatitis viruses, HIV, and leptospira were negative. Blood cultures were positive for a gram-negative rod (Figure 1).

DISCUSSION

The final diagnoses were soft tissue infection, sepsis, and bacteremia due to *Burkholderia pseudomallei* (melioidosis). The isolate (COL-5428) was initially identified as *B. thailandensis* in the clinical laboratory using matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF) (Figure 2) [1]. Subsequently, using whole-genome sequencing, the isolate COL-5428 was confirmed as *B. pseudomallei* (Bps) using 16S sequencing, MLST typing, and strain-seeker (Figure 2).

Melioidosis is caused by the environmental gram-negative bacterium *Burkholderia pseudomallei*, which is commonly found in the soil and surface groundwater of many tropical and subtropical regions. The likely exposure of our patient was during the gardening activities. Acquired infections in humans result from exposure through broken skin, inhalation, or ingestion, with a variety of clinical presentations [2–4], including pneumonia, bone, skin/soft tissue, or central nervous system infections. The symptoms are not specific and can affect any organ, with severe presentations clearly described [2–4]. The major risk factors for melioidosis are patients with diabetes mellitus (like our patient) and chronically immunosuppressed states [2–4]. Due to the protean clinical presentations, melioidosis has been reported in the literature as the “great mimicker” [2–4]. Thus, a high index of suspicion is required in patients in endemic areas or with a history of traveling to regions of the world when these infections are common [2–4]. Other risk

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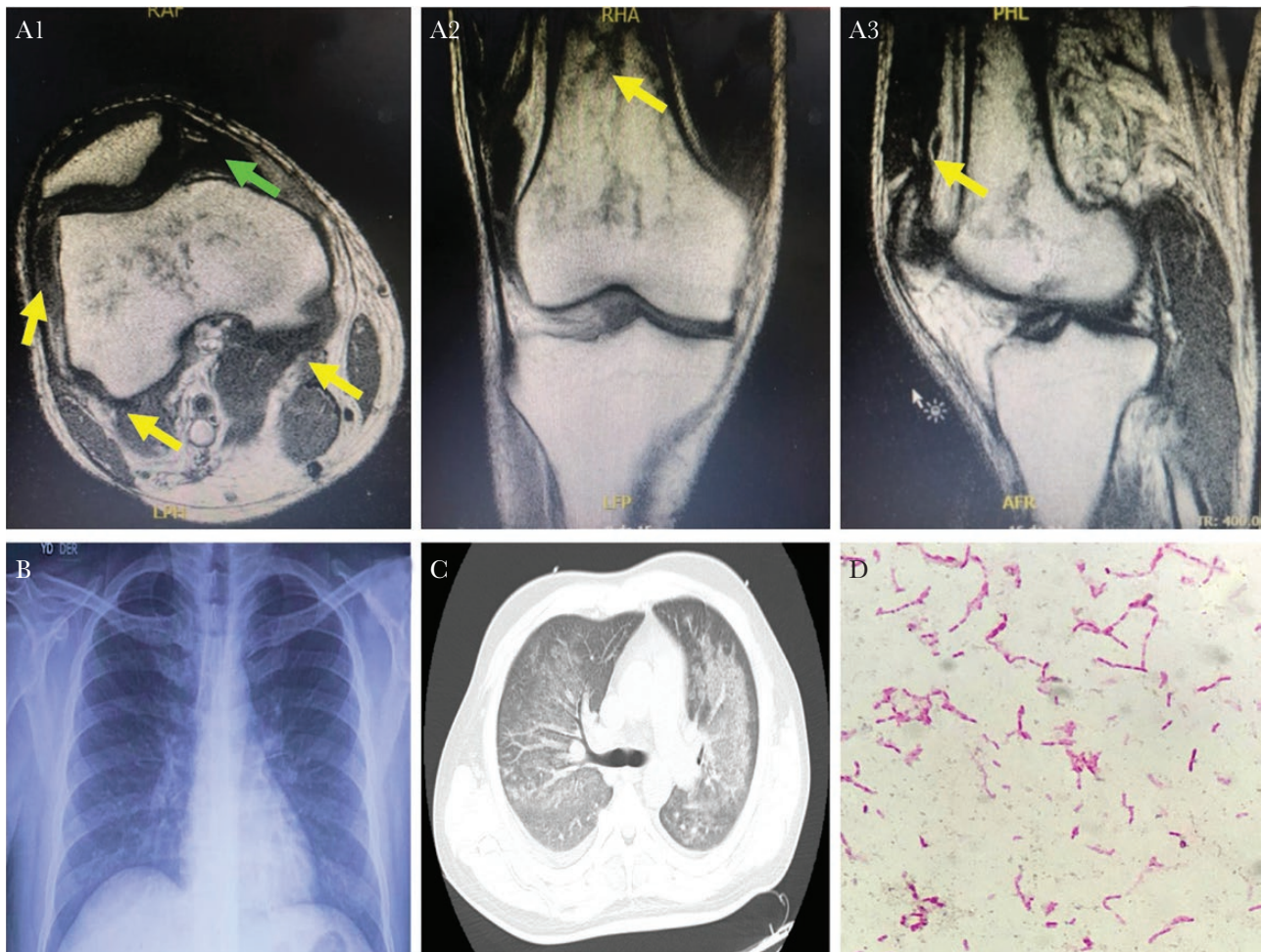


Figure 1. A1, Patellofemoral joint face level with free fluid in the cavity at the lateral face (green arrow). Inflammatory changes in periarticular soft tissues are shown with yellow arrows (axial section image, T1 sequence). A2, Femoral bone metaphysis and diaphysis showing a moth-eaten appearance due to destructive changes of the bone (coronal section image, T1 sequence). A3, Joint leak of the knee at the level of the prepatellar face (yellow arrow; sagittal section, T1 sequence). B, Chest x-ray showing bilateral infiltrates. C, Computed tomography scan of the chest showing alveolar and interstitial infiltrates with ground glass opacities. D, Gram stain of the organism showing a gram-negative rod with a “safety pin” staining pattern.

factors include exposure to soil, typhoons, or a concurrent skin-lung infection. Due to the lack of a specific clinical presentation, the differential diagnosis is broad and includes common acute skin and soft tissue bacterial infections caused by *Staphylococci*, *Streptococci*, and *Aeromonas* spp., among others. Additionally, tuberculosis should be considered when less acute presentations are observed. Leptospirosis should be taken into consideration, particularly in patients who present with cholestasis and ictericia. Infections that concomitantly affect the lung and skin with the proper exposures and epidemiological history in a diabetic patient should raise suspicion of melioidosis [5].

Commonly reported in Southeast Asia and Northern Australia, melioidosis is an environmental emergent disease in the Americas, and its increased prevalence has been associated with major climatic changes of the 21st century. After Brazil, Colombia seems to have a high number of reported cases of melioidosis [6–8]. In a study conducted in 2017, the

reported prevalence was 2.4 cases per 10 million habitants, with 12 strains identified in 4 different regions of Colombia [8]. The presentation of our patient is typical of a severe case of sepsis caused by melioidosis, including soft tissue infection and pneumonia. Regional differences in clinical presentations of melioidosis have been described. For example, prostate abscess and encephalomyelitis are common in Australia, while parathyroid abscess and hepatosplenic purulent secretion are more frequent in Thailand [9].

Although microbiological culture is the gold standard for diagnosis of melioidosis, identification may require 48 hours to 7 days, with poor performance of automated systems [1, 10, 11]. Indeed, these organisms are often misidentified as *Pseudomonas* spp., *Chromobacterium violaceum*, or *Burkholderia cepacia* complex. MLST typing of our isolate revealed a new sequence type, ST1714 (a single locus variant of ST951) [10], suggesting emerging lineages of the Bps species in Colombia, consistent

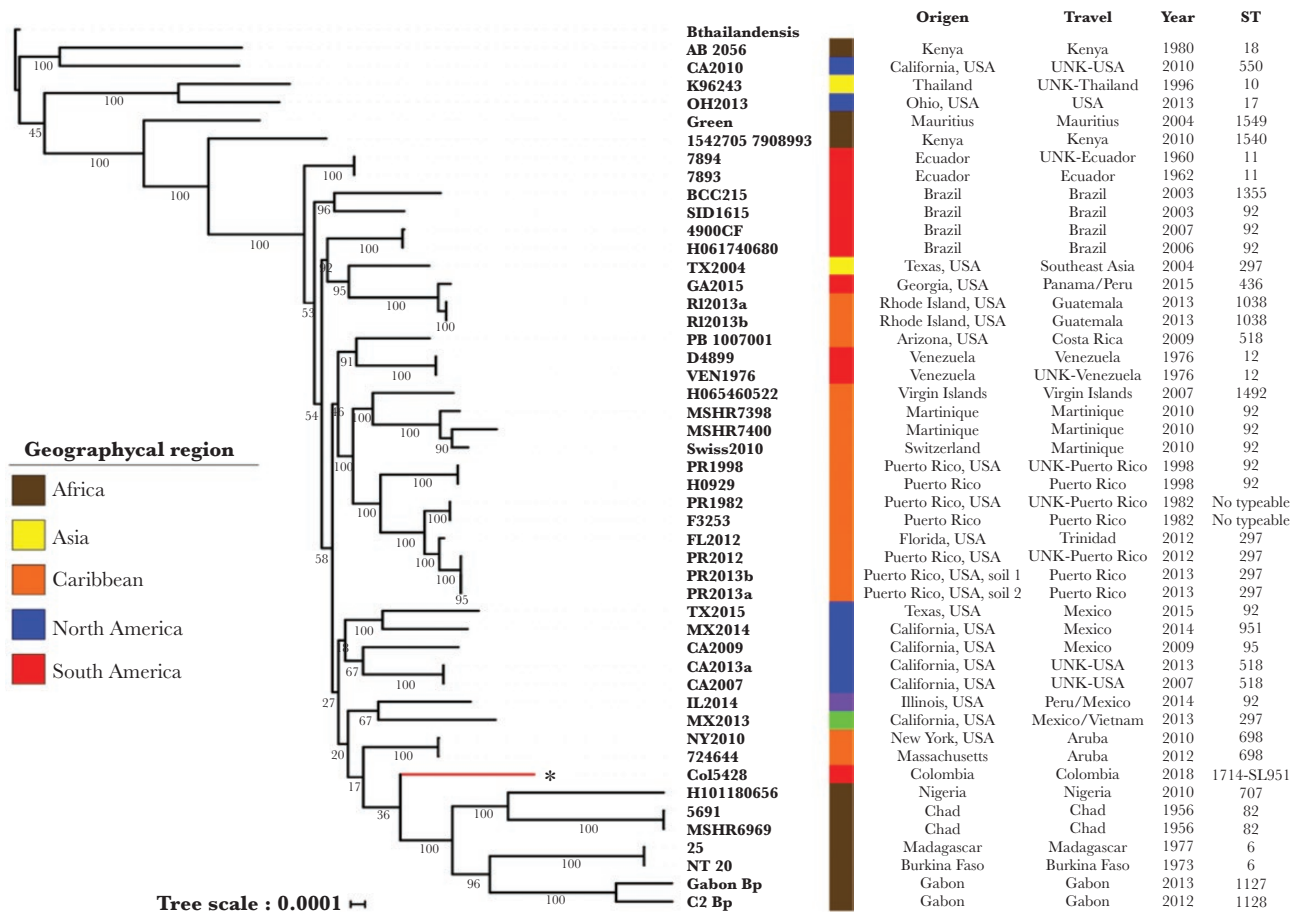


Figure 2. Confirmation of *Burkholderia pseudomallei* (Bps) by whole-genome sequencing. Maximum likelihood phylogenetic tree with bootstrap values of Bps Col-5428 isolate (red branch with asterisk) and 48 other publicly available genomes from other regions in America, the Caribbean, and Africa.

with the genomic plasticity typical of this pathogen, but without any clinical significance [8, 10, 11]. Whole-genome sequencing of COL-5428 identified 46 previously reported virulence determinants in Bps, including genes involved in adherence, invasion, phagosome escape, actin-based motility, and intracellular survival [2]. In terms of antibiotic resistance determinants, only bla-OXA-59 was detected in COL-5428, but no evident phenotypic resistance was identified, as the isolate was susceptible to all tested antibiotics.

The patient was treated with trimethoprim-sulfamethoxazole (TMP-SMX; 320 mg IV q8hr) and levofloxacin (750 mg IV q24h) for 14 days. After 3 days of combination therapy, complete resolution of the infection was noted, with negative blood cultures, hemodynamic stabilization, improvement of the respiratory pattern, and significantly decreased edema and pain in the limb. Finally, when the patient was discharged, treatment was continued with TMP-SMX for 12 weeks. Of note, *B. pseudomallei* is resistant to first- and second-generation cephalosporins, ampicillin, penicillin, aminoglycosides (gentamicin, tobramycin, and streptomycin), macrolides, and polymyxins [2–4]. Most of isolates are susceptible to ceftazidime, meropenem, imipenem, and amoxicillin-clavulanate, although the bactericidal activity

of these drugs varies, they are almost always susceptible to doxycycline, chloramphenicol, and TMP-SMX [2–4]. For patients who require intensive care unit (ICU) admission, the recommended therapies are ceftazidime or meropenem for 10–14 days. For patients with nonpulmonary organ sites of infection, such as neurologic, prostatic, bone, joint, cutaneous, and soft tissue, trimethoprim-sulfamethoxazole appears to be the drug of choice [3]. Suppressive therapy for melioidosis with TMP-SMX for at least for 3 months is considered necessary to prevent relapse. For patients with more severe presentations, including neurological, arterial, and bone melioidosis, suppressive therapy is usually extended for 6 months [2–4, 12]. Lastly, reactivation of latent melioidosis may represent a source of infection in nonendemic areas and is responsible for causing severe opportunistic infections with a high mortality rate among immunocompromised hosts [13].

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