Case Report: A *Burkholderia pseudomallei* Infection Imported from Eritrea to Israel

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Abstract. Although it has been predicted that melioidosis is probably endemic in the Horn of Africa, no confirmed cases have ever been detected in the region. We have recently isolated *Burkholderia pseudomallei* from an Eritrean patient in Israel. The isolate was assigned a novel multilocus sequence type (ST-1479). The observation has important epidemiological implications in an era of massive human migration.

Melioidosis is a severe systemic infection of humans and animals caused by the soil bacterium *Burkholderia pseudomallei*.¹ The disease is endemic in northern Australia and throughout southeastern Asia, northwestern Brazil, and the Caribbean.² Although cases have also been detected in western and southern Africa,³ and more recently in the islands of Madagascar and Mauritius,^{4,5} the disease is conspicuously absent from reports from the Horn of Africa. This apparent lack of morbidity does not necessarily indicate that the organism does not exist in the environment in the northeastern areas of the continent. Rather, because of the lack of adequate medical services, laboratory support, and reliable reporting systems in resource-poor and politically troubled countries, patients may be entirely missed.² On the basis of climatic considerations and soil characteristics, it has been predicted that melioidosis is probably endemic in the region, but no actual cases of the disease have ever been diagnosed in Somalia, Ethiopia, Djibouti, or Eritrea.²

THE CASE

We have recently isolated *B. pseudomallei* from a 45-year-old male Eritrean migrant worker in Israel. He left his country of origin in 2012 and lived in Ethiopia for 2 years. In 2014, he traveled to Israel via Sudan and Egypt. He had chronic hepatitis B infection and abused alcohol, but had no diabetes mellitus and his human immunodeficiency virus serological tests had been persistently negative. The patient presented with a lung infection and subsequently developed skin and subcutaneous abscesses, bacteremia, suppurative arthritis, and septic shock.

Presumptive *B. pseudomallei* organisms were recovered from a lung abscess, respiratory secretions, urine specimens, multiple blood cultures, and synovial fluid aspirates. The isolate identification was confirmed by the VITEK 2 instrument GN card (bioMérieux, Marci l'Étoile, France) with a 92% probability (bionumber 0003653510500011), API 20NE kit (bioMérieux) (probability of 92.6%, biochemical profile number 1156574), and by full sequencing of the 16S ribosomal RNA gene (100% identity), but was misdiagnosed as *Burkholderia vietnamiensis* by the matrix-assisted laser

desorption ionization time of flight mass spectrometry of the VITEK MS system (bioMérieux).

Antibiotic susceptibility of the organism was determined by the VITEK2 system (bioMérieux) and the E-test method,⁶ and interpreted according to the Clinical and Laboratory Standards Institute criteria for *Burkholderia cepacia*.^{6,7} The minimum inhibitory concentrations of the isolates, as determined by the E-test, were as follows: ampicillin: 64 µg/mL, amoxicillin-clavulanate: 3 µg/mL, ceftazidime: 1.5 µg/mL, ceftriaxone: 12 µg/mL, piperacillin-tazobactam: 1.5 µg/mL, meropenem: 0.5 µg/mL, tetracycline 1 µg/mL, trimethoprim-sulfamethoxazole: > 32 µg/mL, and gentamicin: > 256 µg/mL. Medical treatment included life support in an intensive care unit and combined initial antibiotic therapy with ceftazidime and ciprofloxacin. Once the antibiotic susceptibility results were known, the fluoroquinolone administration was stopped. The patient's condition gradually improved, although a small residual pleural effusion remained. Four months after his hospital discharge, the patient is still receiving intravenous ceftazidime through a peripherally inserted central venous catheter, and switch to oral therapy with amoxicillin-clavulanate and doxycycline is planned.

The strain was further characterized by multilocus sequence typing (MLST) analysis of seven housekeeping genes, and the sequencing results were submitted to the public database at <http://pubmlst.org/bpseudomallei/> for allele number and sequence type (ST) assignment. The isolate's allelic numbers were as follows: *ace*: 1; *gltB*: 1; *gmhD*: 10; *lepA*: 2; *lipA*: 5; *narK*: 1; *ndh*: 3. The isolate was given the identification number 4569 and the combination of allele numbers was assigned ST-1479. This ST differs from all other known *B. pseudomallei* STs and is only distantly related to those of western African sources. It shares six allelic numbers with the ST-7 strains Ducrete and 2002721638 from Vietnam, and strain 2002721124 (ST-95) from the United States. In addition, the Eritrean strain shows full identity of five alleles with strains NT08 (ST-26) from Niger, SHCH1135 and MSHR7436 (both belonging to ST-930) from Cambodia and Thailand, respectively, Nig80656 (ST-707) from Nigeria, Gb100 (ST-1127) and C2 (ST-1128) from Gabon, and BpSp (ST-829) from west Africa.

DISCUSSION

Because *B. pseudomallei* is not autochthonous of Israel and the patient had not left the country since his arrival in 2014, he probably represents a truly imported case of melioidosis

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acquired either in Eritrea or Ethiopia, possibly through inhalation, resulting in a dormant lung infection.⁸ The prolonged incubation period (≥ 2 years), followed by a stormy clinical course characterized by lung abscess formation, bacteremia, systemic dissemination of the organism, and development of multiple secondary foci of infection, and complicated by life-threatening septic shock, are fully consistent with human melioidosis.³ As exemplified by the herein-described patient, the infection exhibits unusual clinical severity and the case-fatality rate may reach 60%, and thus, prompt and adequate medical treatment and life support in a well-equipped intensive care unit, when needed, are of paramount importance.⁹ Because of the intrinsic or acquired resistance of *B. pseudomallei* to many first-line agents used to empirically treat community-acquired infections, a high index of clinical acumen, as well as timely and correct identification of isolates by the laboratory, and determination of their antibiotic susceptibility are critical in instituting appropriate therapy.¹⁰

The MLST profile of the isolate showed more similarity to *B. pseudomallei* Asian strains than to those of west African origin. However, because of low-grade resolution of the MLST typing method, high rates of horizontal gene transfer of the species, and potential ST homoplasy, a more discriminatory approach such as genome-wide single-nucleotide polymorphisms analysis is needed to determine the true relationship between strains.¹¹ Interestingly, recent phylogenomic analysis of a large *B. pseudomallei* strain collection strongly supports an ancient Asian origin for African organisms, which possibly crossed the ocean through human migration and trade, or were carried by migratory birds flying along the Asia–east Africa flyway.¹¹

The detection of an imported case of melioidosis in a country with well-resourced medical facilities revealed for the first time that the disease is endemic in the Horn of Africa, and the isolated organism appears to be only distantly related to *B. pseudomallei* strains from the western regions of the continent. The epidemiological implications of the case are dual. On one hand, individuals in peace-keeping forces and nongovernmental organizations travel to this war-torn region to offer medical and humanitarian assistance, and thus, may be exposed to the organism. On the other hand, because of the massive influx of migratory workers and refugees from east Africa currently arriving in European countries where the disease is not prevalent, the possibility of melioidosis should be considered in patients from that origin presenting with a severe clinical infection.

Received June 14, 2016. Accepted for publication August 1, 2016.

Published online August 29, 2016.

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