Travel-Associated *Burkholderia pseudomallei* Infection (Melioidosis) in a Patient with Cystic Fibrosis: A Case Report

Paolo Visca,1 Giantonio Cazzola,2 Andrea Petrucca,2 and Cesare Braggioni1

1Department of Biology, Università Roma Tre–Istituto Nazionale di Malattie Infettive “Lazzaro Spallanzani,” 2Laboratory of Bacteriology and Medical Mycology, Istituto Superiore di Sanità, Rome, and 3Cystic Fibrosis Centre, Verona, Italy

In September 1997, a 25-year-old Italian woman with cystic fibrosis (CF) spent 3 weeks in Thailand. In August 1998, her pulmonary function rapidly declined, with productive cough and intermittent fever. Chest x-ray films revealed diffuse, small, patchy opacities in the upper lobes. *Burkholderia pseudomallei* (BP) was isolated from specimens of the patient’s sputum and was identified by means of 16S rDNA sequencing. The diagnosis of melioidosis was serologically confirmed. Continuous therapy with ceftazidime and co-trimoxazole and maintenance with co-trimoxazole, doxycycline, and chloramphenicol resulted in eradication of BP. We present the issue of whether patients with CF represent a population particularly at risk for melioidosis.

Cystic fibrosis (CF) is the most common inherited lethal disorder to affect the white population (incidence, 1:2500 births). Microbial infection of the respiratory tract is the principal cause of morbidity and mortality among patients with CF [1]. In this report, we describe a case of travel-associated pulmonary melioidosis in a patient with CF in whom *Burkholderia pseudomallei* was identified by means of 16S rDNA amplification and sequencing.

A 25-year-old Italian woman with CF spent 3 weeks vacationing in Bangkok and Phuket, Thailand, during September 1997. After her return, she was hospitalized in the regional CF center because of fever and pulmonary exacerbation. The chest x-ray film revealed diffuse, small, patchy opacities located bilaterally in the upper lobes; it also revealed bronchiectasis. *Pseudomonas aeruginosa* and *Burkholderia cepacia*, which had colonized the patient since 1992, were isolated from sputum samples obtained as late as September 1998; during the last year of colonization, the patient was treated with either ciprofloxacin, piperacillin/tazobactam, meropenem/ticloplatin, or meropenem/tobramycin. From August through October 1998, the patient’s clinical presentation showed progressive deterioration, with productive cough, a decline in pulmonary function, and intermittent fever that relapsed after 2 courses of iv meropenem/tobramycin. No significant change was observed on chest radiographs. Cultures of sputum samples performed in October 1998 yielded *B. cepacia* and a microorganism that reacted as *B. pseudomallei*, according to the API 20NE identification system (profile 1156574). Safety precautions, which required isolation of the patient, were enforced, and the isolate presumed to be *B. pseudomallei* was sent to the Istituto Superiore di Sanità, Rome, for confirmatory tests.

The strain grew on Ashdown’s medium like typical *B. pseudomallei*; it demonstrated bipolar staining, reacted with a *B. pseudomallei*-specific antiserum, and exhibited biochemical reactions characteristic of the species. The 16S rDNA sequence of the isolate (GenBank accession no. AJ131790; available at http://www.ncbi.nlm.nih.gov/Genbank), obtained after amplification by use of universal eubacterial primers [2], was characterized by >99% identity with the 16S rRNA gene sequence of the *B. pseudomallei*-type strain 1026B, and it fully matched the *B. pseudomallei* 16S rDNA signature regions [3]. At 14 of the 15 critical positions, the sequence also differed from the 16S rDNA sequence of the closely related, avirulent *Burkholderia thailandensis* species, which is found in the geographical region visited by the patient [4]. A sample of the patient’s serum taken on October 29 had an IgG titer of 4000, according to ELISA tests that were performed using both the homologous antigen and the standard *B. pseudomallei* lipopolysaccharide antigen (performed by Dr. T. L. Pitt, Laboratory of Hospital Infection, Central Public Health Laboratory, London); this is consistent with the diagnosis of melioidosis. *B. pseudomallei* was resistant to amikacin, cefalothin, cefuroxime, fosfomycin, gentamicin, netilmycin, and tobramycin; it was intermittently resistant to aztreonam, cefepime, ciprofloxacin, and tetracycline; and was sensitive to cefoperazone, cefotaxime, ceftazidime, chloramphenicol, co-trimoxazole, imipenem, meropenem, mezlocillin, piperacillin, rifampicin, and ticarcillin/clavulanic acid.

Continuous antibiotic therapy with iv ceftazidime and co-
trimoxazole was started in October 1998 and continued for 6 weeks. Oral maintenance treatment with co-trimoxazole, doxycycline and chloramphenicol was then administered for 30 weeks. The patient exhibited remission of fever and respiratory symptoms and substantial improvement of the pulmonary function to the baseline values. The serological markers of inflammation gradually normalized in the period from October through December 1998 (erythrocyte sedimentation rate and C-reactive protein levels decreased from 91 mm/h to 18 mm/h and from 0.143 g/L to 0.003 g/L, respectively), and tests of sputum samples taken in November 1998 yielded negative results for B. pseudomallei. These laboratory results are prognostic of successful antibiotic therapy and resolution of the infection [5]. In fact, the patient had no recrudescence of melioidosis during 1 year of follow-up, and no secondary cases were observed.

The isolation of B. pseudomallei from patients with CF is a unique event with relevant microbiological, clinical, and epidemiological implications. The genus Burkholderia includes mostly plant pathogenic species, some of which can cause opportunistic infections in humans. B. cepacia has increasingly been associated with respiratory infection in patients with CF [1], whereas the highly pathogenic B. pseudomallei causes melioidosis, a disease with protein clinical manifestations. Melioidosis is endemic in southeast Asia and northern Australia, but it is extremely rare in temperate countries and, so far, is unrecognized in Italy [6]. This implies that our patient acquired B. pseudomallei in Thailand, presumably by means of accidental inhalation, and that the infection went undiagnosed for approximately 1 year after her return. Dance et al. [7] recently reviewed 15 cases of culture-positive melioidosis imported into England and Wales during the past decade. All patients had a history of travel in southeast Asia, and 1 had CF as an underlying disease. These findings pose the intriguing question of whether patients with CF are predisposed to melioidosis due to an unknown tropism for the CF respiratory tissue shared by B. cepacia and B. pseudomallei. B. pseudomallei and B. cepacia are related with regard to ecological niche, resistance to intrinsic antibiotics, and cell surface lipid composition [8, 9]. Existing damage to the CF respiratory epithelium could facilitate bacterial colonization by adhesion mechanisms that are similar in these 2 species. It is interesting to note that mucinophilic properties have been reported for both P. aeruginosa and B. cepacia [1, 10].

Successful management of melioidosis largely depends on early laboratory diagnosis. However, the diagnosis of pulmonary melioidosis in patients with CF is complicated for several reasons. First, underlying bacterial infection can distort the early bronchopneumonic presentation of the disease. Second, empiric antibiotic therapy (which was administered to our patient from October 1997 through October 1998) can reduce the B. pseudomallei population in the lung and can result in subclinical disease. Furthermore, B. pseudomallei can easily be overlooked or misidentified as B. cepacia in routine cultures of sputum samples obtained from patients with CF. Finally, a lack of familiarity with melioidosis is common in Western countries. Our case would not have been diagnosed if the culture not been sent to a specialized laboratory. Given the microbiological complexity of the sputum of patients with CF, a DNA-based approach is advisable for reliable identification of an uncommon pathogen like B. pseudomallei. Because patients with CF are particularly at risk for melioidosis, we urge physicians either to inform patients with CF of this risk or to consider melioidosis in the differential diagnosis of febrile respiratory illness in patients returning from endemic areas.

References