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Chronic Melioidosis in a Patient with Cystic Fibrosis

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***Burkholderia pseudomallei*, the causative agent of melioidosis, is endemic in Southeast Asia and northern Australia, where it can be found in soil and surface water. We report a case of chronic pulmonary melioidosis in a patient with cystic fibrosis who had traveled to an area where *B. pseudomallei* is endemic.**

CASE REPORT

The patient was a 38-year-old white male with cystic fibrosis (CF) who had undergone middle-lobe resection of the lung for bronchiectasis at the age of 17. During the following 10 years he has had only mild pulmonary symptoms. Since his lung function worsened during each winter season he started to spend the winter months in warmer areas: 1989 and 1990 in Indonesia and 1990 and 1991 in Mexico, the Dominican Republic, California, and Costa Rica. On returning from Thailand in the spring of 1992 he was severely ill with fever, cough, and malaise and was admitted to Freiburg University Hospital. The patient's sputum sample yielded a gram-negative rod that was identified by API 20NE (code 1140474) as a *Pseudomonas* sp. Since then he had 13 documented exacerbations with gram-negative rods that were reported to be either *Pseudomonas* sp. *Pseudomonas aeruginosa*, or *Burkholderia cepacia*. In each case, he was treated for a maximum of 2 weeks with anti-pseudomonas antibiotics (ceftazidime, piperacillin-tazobactam, or piperacillin with or without aminoglycosides or ciprofloxacin) administered intravenously (i.v.) with only moderate effect. The isolated strains were susceptible to the drugs used with the exception of aminoglycosides. A detailed travel history was not documented, and *B. pseudomallei* and melioidosis were never suspected by the microbiologists and clinicians, respectively, associated with this case.

In November 1998 a new screening plate for *Burkholderia* species (3) had been implemented in the diagnostic laboratory, and a sputum isolate was sent to a reference laboratory (Munich, Germany). There, as in our own laboratory, *Burkholderia pseudomallei* was identified on the basis of biochemical tests (API 20NE code @48h 1156577) and by means of 16S rRNA gene sequencing and comparison to the type strain 1026b (GenBank accession number U91839). Moreover, the isolate gave a positive reaction in a recently developed *B. pseudomallei*-specific latex agglutination test (11) which was not available in the diagnostic laboratory at the time of isolation. The isolate was susceptible to ceftazidime, imipenem, trimethoprim-sulfamethoxazole, tetracycline, and ampicillin-sulbactam and was resistant to all aminoglycosides, fosfomycin, and colistin. Bacteriological reports were reviewed, and all previous isolates were found to have an identical susceptibility pattern (ampicillin-sulbactam not tested on all isolates), indicating that *B. pseudomallei* was probably misidentified earlier. Moreover, a serum sample collected in 1992 was tested in an enzyme-linked immunosorbent assay for immunoglobulin G antibodies with specificity for the galactose- and 3-deoxy-D-*manno*-2-octulosonic acid-containing *B. pseudomallei* exopolysaccharide (8) and found to be highly positive (titer, $1:10^6$), providing further evidence that the patient had been suffering from melioidosis since 1992. After a diagnosis of melioidosis was made the patient was treated with i.v. ceftazidime for 2 weeks. In December 1999 the patient's condition deteriorated again, and a 2-week regimen of meropenem and clarithromycin was started, followed by oral ampicillin-sulbactam. Despite 20 weeks of oral therapy he relapsed, and although meropenem was recommended again the patient declined further therapy.

Melioidosis, a tropical disease caused by *B. pseudomallei*, may present itself in a variety of unusual ways, such as neck lumps (5), brain abscess (6), or infection of the placenta, resulting in transplacental mother-to-child transmission (J. M. Orendi, F. C. H. Abbink, and A. J. de Beaufort, abstr. MoP 130, Clin. Microbiol. Infect. **6**(Suppl. 1)**:**43, 2000). The potential for diagnostic confusion of *B. pseudomallei* infection with other diseases may be high in such cases. We report here the first case of chronic *B. pseudomallei* infection in a patient with CF. This case also highlights the need for a careful microbiological diagnosis to discriminate the expected from the unexpected.

In contrast to antipseudomonas therapy in CF, the optimal combination therapy for severe melioidosis has not been conclusively determined (10). It remains unclear whether an earlier recognition of the causative agent in this patient, resulting in an initial i.v. therapy with cefazidime or carbopenems (9), followed by long-term maintenance with amoxicillin-clavulanate, would have had a positive effect on the course of the disease. It has been reported that *B. pseudomallei* can be identified by a combination of the commercial API 20NE biochemical kit and a simple screening system involving Gram stain, the oxidase reaction, resistance to colistin and gentamicin, and typical growth characteristics on Ashdown medium (2). However, the need to perform repeated testing of some strains with

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the API 20NE kit in order to get the correct identification has been reported (2), as well as misidentifications of *B. pseudomallei* as other species (4). A review of bacteriological reports in our case revealed that the API 20NE profiles of some former isolates were recorded after 24 h. Dance et al. have reported that 48 h of incubation of the panel is crucial for a correct identification of *B. pseudomallei* (2). We think it is reasonable to confirm a presumptive identification of *B. pseudomallei* based on biochemical results and resistance pattern by using serological methods such as the monoclonal antiexopolysaccharide antibody-based *B. pseudomallei*-specific latex agglutination test (11). This might be especially true for laboratories where only occasional imported strains have to be identified. This case also demonstrates that testing patient sera for *B. pseudomallei*-specific antibodies might be a helpful tool for confirming the diagnosis.

Recently, imported melioidosis has been reported in patients with various underlying diseases (1), including one CF patient, but no history or clinical details were provided. It is highly suggestive that our patient became infected in Thailand, although we cannot completely rule out the possibility of a primary infection occurring during his visits to countries where *B. pseudomallei* is also endemic before he went to Thailand. Colonization and infection with *Burkholderia* species belonging to the *B. cepacia* complex and with *B. gladioli* is a well-recognized problem in CF patients and is associated with decreasing lung function and disease progression (7). One might speculate as to whether the changes in CF lungs predispose individuals to infection with *B. pseudomallei*. As a result of better management options for CF patients, the quality of life and life expectancy is increasing, and therefore patients' travel activities may be increasing as well. Detailed history taking is crucial, and one should not be biased by the underlying disease when interpreting the biochemical results and susceptibility data. Awareness of melioidosis should be heightened since, as this case demonstrates, diagnosis may be delayed, therapy is difficult, and the outcome uncertain.

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