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Abstract

We retrospectively analyzed 1062 respiratory specimens from 214 patients with cystic fibrosis, of whom 5 patients had 36 cultures positive for M. abscessus. Results of molecular typing demonstrated that each of these 5 patients carried a single unique strain (genotype), which suggests that it may not be necessary to segregate patients with CF who are colonized or infected with M. abscessus from those who are not.
Lack of Transmission of *Mycobacterium abscessus* among Patients with Cystic Fibrosis Attending a Single Clinic

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Diseases caused by nontuberculous mycobacteria are found in patients with underlying pulmonary disease, especially those with bronchiectasis. Cystic fibrosis (CF), the most common life-shortening autosomal recessive disorder in populations of European origin, leads to both obstructive and restrictive lung disease. The course and prognosis of CF are largely determined by recurrent infections of the respiratory tract with opportunistic pathogens, most commonly infection with *Pseudomonas aeruginosa*. Various studies have suggested that nontuberculous mycobacteria may worsen CF pulmonary disease [5, 12, 13]. *Mycobacterium chelonae* and *Mycobacterium abscessus* (formerly *M. chelonae* subsp *abscessus*) are among the nontuberculous mycobacteria that have been isolated from the respiratory tract of patients with CF [1, 2, 8]. Most studies have not distinguished between these 2 species, and refer to them as “*M. chelonae* group.” Histological examination provides evidence to distinguish invasive pulmonary disease caused by *M. abscessus* from mere colonization [4, 12]. A series of 154 patients with pulmonary infection caused by rapidly growing mycobacteria included 9 patients with CF; the organism most frequently isolated from these patients (including all 9 patients with CF) was *M. abscessus* [6].

Extensive person-to-person spread of a strain of *Pseudomonas aeruginosa* among patients attending the same CF center has been demonstrated [3]. Therefore, in our clinic, patients who are colonized or infected with *Pseudomonas aeruginosa* are segregated from patients for whom cultures are negative for *P. aeruginosa*. For *Mycobacterium tuberculosis*, the principal route of transmission is from person to person via aerosol. For nontuberculous mycobacteria, the route of transmission is less clear. Therefore, we wished to determine whether person-to-person spread of *M. abscessus* in patients with CF occurs, because if cross-infection were evident, it would be beneficial to segregate patients with CF who are colonized or infected with *M. abscessus* from those who are not.

To address this question, we first identified all patients who attended the CF clinic of the Medical School Hannover during a period of 19 months (from September 1997 through March 1999). During this time period, sputum samples, tracheal aspirates, and specimens obtained by bronchoscopy from patients with CF were routinely processed by the Department of Medical Microbiology, where acid fast bacilli (AFB) smears and culture were performed. After treating with N-acetyl-L-cysteine/sodium hydroxide, AFB smears were performed using the fluorochrome method, and smears with positive results were restained using the Ziehl-Neelsen method. All specimens were incubated in the BACTEC MGIT 960 automated culture system (Becton Dickinson) at 37°C.

Species identification for cultures positive for acid-fast bacilli was performed by means of PCR-mediated amplification of selected sequences of the 16s rRNA gene and direct sequence determination, as described elsewhere [9]. Amplified PCR products were sequenced using an ABI automated sequencer (Applied Biosystems) under conditions recommended by the manufacturer. We differentiated between *M. chelonae* and *M. abscessus* by sequencing an additional 26-bp region of the 16s rRNA gene corresponding to *Escherichia coli* positions 1001 to 1027 [11]. For DNA fingerprinting, genomic DNA was digested with DraI and then separated by pulsed field gel electrophoresis (PFGE) as described elsewhere [14]. Cultures for bacteria and fungi were performed on standard media. Chart reviews of all clinic visits were done for all patients with cultures positive for *M. abscessus*.

A total of 1062 specimens from 214 patients with CF were cultured for mycobacteria, a mean of 5.0 specimens per patient.
Figure 1. Isolation of *Mycobacterium abscessus* from patients with cystic fibrosis who attended a cystic fibrosis clinic during the period September 1997–March 1999. *Times at which specimens from the respiratory tract were cultured for mycobacteria. Boxed asterisks, 36 cultures positive for *M. abscessus*. Arrows, 21 isolates that were subjected to analysis by pulsed-field gel electrophoresis. #Patient C had *Mycobacterium avium* isolated once.

Figure 2. Pulsed-field gel electrophoresis patterns for *Mycobacterium abscessus* isolates from 5 patients with cystic fibrosis. The chromosomal DNA was digested with Dral. Lane 1, isolate from patient B; lane 2, isolate from patient A; lane 3, isolate from patient C; lane 4, isolate from patient D; lane 5, isolate from patient E; lane 6, λ DNA standard.
of infection is minimal—both arguments for nonsegregation policies [7, 13]. Other studies have found that M. chelonae group are among the mycobacterial species most frequently isolated from patients with CF and that M. chelonae group has a higher prevalence among patients with CF than in the general population [1, 6, 8]. Kilby et al. [8] observed that patients with positive AFB smears from whom M. chelonae group was subsequently isolated suffered from a worsening of lung disease. In a necropsy study, active mycobacterial disease was demonstrated in 2 patients infected with M. abscessus [12]. Moreover, in a recent case report, the results of histological examination indicated that invasive pulmonary disease with M. abscessus was present in a patient with CF for several years [4].

In the present study, patient A was treated twice with amikacin and rifabutin after AFB smears of respiratory specimens were highly positive. M. abscessus was isolated, and disease worsened significantly. After both courses of treatment, the patient’s pulmonary function recovered promptly and the mycobacterial burden in the sputum was greatly reduced. It is noteworthy that patient A was not colonized or infected by Pseudomonas at the time. Although the number of patients treated in this study was too small to allow any analysis, the course of disease in patient A suggests that M. abscessus was producing the disease and responded to therapy. Nontuberculous mycobacteria other than M. abscessus were recovered from patients in this study: M. avium-intracellularare, which might also cause pulmonary disease in patients with CF [8], and M. interjectum, M. simiae, and M. gordonae, which are generally considered avirulent [10].

In the retrospective study presented here, nontuberculous mycobacteria were recovered multiple times from 15 of 214 patients with CF; 5 of these 15 were colonized or infected with M. abscessus. The study population was seen in a clinic. We failed to detect evidence that M. abscessus colonization or infection had originated from the same source or that person-to-person transmission had occurred. We conclude that, in this setting, there is no need to segregate patients with CF who are colonized or infected with M. abscessus from those who are not.

References