Mycobacterium chimaera Pulmonary Disease in Cystic Fibrosis Patients, France, 2010–2017

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We report *Mycobacterium chimaera* pulmonary disease in 4 patients given a diagnosis of cystic fibrosis in a university hospital in Montpellier, France. All patients had *M. chimaera*–positive expectorated sputum specimens, clinical symptoms of pulmonary exacerbation, or a decrease in spirometry test results that improved after specific treatment.

M*ycobacterium chimaera* is a member of the *Mycobacterium avium* complex, which was elevated to species rank in 2004. *M. chimaera* was reported by Tortoli et al. (*1*) as a cause of human lung disease but has been widely known as the bacteria responsible for an outbreak of endocarditis and disseminated infection after cardiac surgery in 2013 (*2*).

Although virulence and pathogenicity of *M. chimaera* in lung disease are currently debated, several cases of *M. chimaera* lung infections have been reported in settings of chronic obstructive pulmonary disease, malignancy, or immunosuppression (*3–5*). We found 1 case of *M. chimaera* infection in a patient with cystic fibrosis (*6*). Other nontuberculous mycobacteria (NTM), especially *M. abscessus* and *M. intracellulare*, are well-known pathogens in such a setting (*7*). We report *M. chimaera* pulmonary disease in 4 patients with cystic fibrosis.

After reviewing data for 248 patients who were examined at the Cystic Fibrosis Center of Montpellier, France, during 2010–2017, we observed that 24 (9.7%) of 248 patients had ≥1 respiratory smear sample positive for NTM; for 4 (16.7%) of 24, the sample was positive for *M. chimaera*. The 4 case-patients were Caucasian, age 8–21 years, and who had a newborn diagnosis of cystic fibrosis, preexisting respiratory impairment, and digestive malabsorption. The association of an increased cough and sputum production, breathlessness, and fatigue with a reduction in forced expiratory volume in 1 s (FEV1) or forced vital capacity (FVC) was diagnosed as pulmonary exacerbation (*7*) for all patients (Figure). Diagnosis was confirmed by computed tomography by the presence of bronchiectasis and nodules (tree-in-bud pattern) for case-patients 1 and 3.

Respiratory specimens collected every 3–6 months for 1 year were digested and decontaminated by using the sodium dodecyl sulfate–NaOH method and then centrifuged using fluorescence microscopy. Sputum samples from all patients were negative for acid-fast bacilli. Samples were cultured on solid and liquid media (BACTEC MGIT 960 System; Becton Dickinson Diagnostic Systems, https://www.bd.com) which identified, after 11–41 days, mycobacteria from ≥2 separate sputum samples.

We performed species identification by using a commercial kit (GenoType NTM-DR assay; Hain Lifescience, https://www.hain-lifescience.de) and identified isolates as *M. chimaera*. We also performed molecular identification of isolates as *M. chimaera* as described (*1,8*). All isolates were susceptible to macrolides and aminoglycosides. We also isolated several other microorganisms: *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* from case-patient 1; *Haemophilus influenzae* from case-patient 2; *M. avium* and *Stenotrophomonas maltophila* from case-patient 3; and *M. abscessus*, methicillin-resistant *S. epidermidis*, and *P. aeruginosa* from case-patient 4.

Azithromycin, rifampin, and ethambutol (in combination) and ceftazidime, tobramycin, and inhaled colistin were given to case-patient 1. No antimicrobial drugs were given to case-patient 2. Azithromycin and rifampin (in combination) and inhaled colistin were given to case-patient 3. Clarithromycin and linezolid were given to case-patient 4. All 4 case-patients required physiotherapy.

All case-patients were followed up for ≥1 year after the first positive smears for *M. chimaera* were obtained. We found a substantial reduction in symptoms of pulmonary exacerbations and sterilization of sputum specimens for patients given macrolides and rifampin with or without aminoglycosides after 3 months, as well as improvement in FEV1 and FVC after 6 months. In contrast, patients not given treatment (case-patient 2) or given only partial treatment with an anti-NTM antimicrobial drug regimen (case-patient 4) showed a decrease in FEV1 and FVC after 6 months (Figure) and slight recovery or no change after 1 year.

Therefore, we hypothesized that *M. chimaera* showed virulence and pathogenicity in our patients because of their clinical picture and evolution. We are aware that the diagnosis of NTM diseases according to American Thoracic Society criteria (*9*) might not be made with complete certainty because definitive exclusion of other diagnoses was often
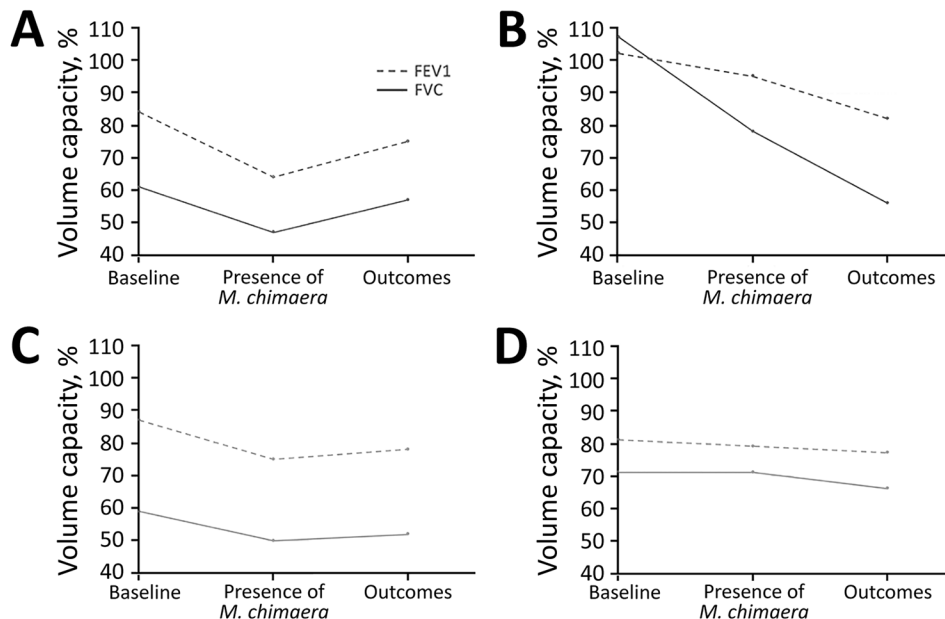
Figure. Evolution of lung function for 4 cystic fibrosis patients with *Mycobacterium chimaera* pulmonary disease, France, 2010–2017. A) Case-patient 1, B) case-patient 2, C) case-patient 3, D) case-patient 4. Case-patients 1 and 3 were given specific treatment for *M. chimaera* disease for 3 months; case-patient 2 was not given specific treatment; case-patient 4 was given only partial treatment. FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity.

difficult for cystic fibrosis patients. Several confounding factors, such as co-infection with conventional pathogens, were observed, which could explain the observed favorable outcome. However, specific treatment against NTM improved outcome, which strengthens our presumption of the potential pathogenic role of *M. chimaera* in lung disease of patients with cystic fibrosis.

Cystic fibrosis transmembrane conductance regulator disorder results in mucus retention and bronchiectasis that favor repeated respiratory tract infection, including NTM diseases (*7*). In these circumstances, cystic fibrosis might promote *M. chimaera* infection in a similar manner to that in patients with chronic obstructive pulmonary disease. The lack of improvement of respiratory function for case-patient 4, who had been given treatment for infection with other pathogens, but only partially for *M. chimaera*, supports our hypothesis. However, whether *M. chimaera* is only a surrogate of respiratory impairment without any virulence or a real pathogenic microorganism remains unknown. In conclusion, *M. chimaera* lung disease should prompt physicians to consider this bacteria as an emergent pathogen in cystic fibrosis patients.

Acknowledgments

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Biomphalaria pfeifferi Snails and Intestinal Schistosomiasis, Lake Malawi, Africa, 2017–2018

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Two surveys conducted in 2017 and 2018 demonstrated *Biomphalaria pfeifferi* snails in Lake Malawi in Africa. Epidemiologic examination of 175 local children at 3 primary schools confirmed emergence of intestinal schistosomiasis. These findings highlight autochthonous transmission of *Schistosoma mansoni* flukes in Lake Malawi and the need to revise international travel advice.

Throughout sub-Saharan Africa, *Biomphalaria pfeifferi* snails are freshwater intermediate hosts for *Schistosoma mansoni* blood flukes, which cause intestinal schistosomiasis (*1*). Geographic distribution of *B. pfeifferi* snails delineates actual or potentially active zones of *S. mansoni* fluke transmission (*2*). Other than a report of a single *Biomphalaria* shell at Karonga in the far northern portion of Lake Malawi (*3*), considered to be from a marginal swamp (*4*), *B. pfeifferi* snails have not previously been found in Lake Malawi (*5*). However, in November 2017, during malacologic surveillance for intermediate hosts of schistosomiasis in the Mangochi District, Malawi, along the southernmost tip of Lake Malawi, 2 discrete populations of *Biomphalaria* snails were unexpectedly encountered in submerged beds of *Vallisneria* spp. plants (Figure, panel A). DNA sequence analysis of the mitochondrial cytochrome oxidase subunit 1 (*cox*1) (*6*) indicated that the *cox*1 sequences (1,006 bp) of those snails differed from sequences of *B. pfeifferi* snails from Chiweshe, Zimbabwe (GenBank accession nos. DQ084829 [HCO/LCO region] and DQ084872 [Asmit1/2 region]) by only 3 synonymous single-nucleotide polymorphisms.

In May 2018, to confirm *B. pfeifferi* colonization within the lake and suspected risk for intestinal schistosomiasis, we undertook a conjoint malacologic and parasitologic survey with ethics approvals from the Liverpool School of Tropical Medicine, UK (application 17-018) and the Ministry of Health and Population, Malawi (application 1805). Reinspection of all prior malacologic sampling locations and another 43 sites found further populations of *B. pfeifferi* snails (Figure, panel A); large numbers (>50), along with innumerable dead shells, were again found at site 9. All snails were inspected for shedding cercariae, and although cercariae from snails at site 5 were seen, identification by microscopy (×100) was unsuccessful. Supplementary analysis indicated that *cox*1 sequences from 9 snails from sites 2, 5, 7, 10, and 11 were identical.

We conducted an epidemiologic survey of 175 schoolchildren, 5–15 years of age, equal numbers of boys and girls, from 3 primary schools closest to site 9 (Figure, panel B). Mean prevalence of intestinal schistosomiasis, calculated by detection of *S. mansoni* circulating cathodic antigen (CCA) on urine dipstick testing, was 34.3% (95% CI 27.9–41.3); prevalence rates by school were Samama, 46.7% (95% CI 36.7–56.7); Mchoka, 25.0% (95% CI 15.0–36.7); and Palm Beach, 9.1% (95% CI 0.0–22.7). We requested fecal samples from 60 *S. mansoni*–positive children and received samples from 46. Duplicate Kato-Katz examinations confirmed *S. mansoni* ova in 7 children; infection intensities were graded as light (<100 eggs/g feces). All urine samples were inspected for *S. haematobium* ova by syringe filtration (10 mL); general prevalence was 14.9% (95% CI 9.8–20.1); 52% of these samples were also positive by CCA urine dipstick, indicative of *S. mansoni* co-infection. To further determine autochthonous transmission of *S. mansoni* flukes, 2 egg-positive children from Samama and Mchoka took us, on foot, to the shoreline where they regularly swam, which corresponded to snail