Mycobacterium paraffinicum causing symptomatic pulmonary infection

Austin W. Chan (1), Sarah Kabbani (2), Gerald Staton (3), Colleen S. Kraft (2)

(1) Department of Medicine, Emory University, Atlanta, GA
(2) Division of Infectious Diseases, Emory University, Atlanta, GA
(3) Division of Pulmonary Medicine, Emory University Atlanta, GA

Running Title: Bronchiectasis caused by M. paraffinicum

Corresponding author:
Colleen Kraft, MD
Emory University Hospital, F145C
1364 Clifton Rd, NE
Atlanta, GA 30322
Office: 404-712-8889
FAX: 404-712-4632
collen.kraft@emory.edu

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Abstract

*M. paraffinicum* has been newly recognized as a species. A case of symptomatic pulmonary infection caused by *M. paraffinicum* is described, and as far as we know, is the first case of the organism as a human pathogen.
Case Report

In May of 2012, an 85-year-old female presented to our tertiary referral hospital with acute shortness of breath. Her past medical history included hypertension for which she was not treated. She noted progressive generalized weakness, malaise, anorexia, and a chronic cough productive of white sputum for the past six years. On review of systems, she reported no fevers, chills, night sweats, or hemoptysis. She denied any history of smoking (but lived with a smoker), pneumonia or other lung infections, tuberculosis exposure, homelessness, healthcare work, history of imprisonment, or recent travel. On physical exam, the patient had a temperature of 37.0°C, blood pressure of 158/88 mmHg, a heart rate of 109 bpm, a respiratory rate of 20 and a 93% oxygen saturation by pulse oximetry on ambient air. On exam the patient had moderate kyphosis and pectus carinatum with no cervical lymphadenopathy. There was a 3/6 holosystolic murmur present at the cardiac apex, and bibasilar rales on the left lung greater than the right with no evidence of egophony. She exhibited 5/5 strength throughout all extremities. Laboratory data was as follows: white blood cell count 16,400/uL with a differential of 1% band forms, 94% segmented neutrophils, 3% lymphocytes, and 2% monocytes, hemoglobin of 11.4 g/dL, platelet count 507,000/uL, sodium 129 meq/L, potassium 3.6 meq/L, glucose 131 mg/dL, creatinine 1.1 mg/dL. The patient was started on ceftriaxone and azithromycin for treatment of community acquired pneumonia which was consistent with her presentation. On the second day of hospitalization, a computed tomography (CT) of the chest, abdomen, and pelvis with contrast revealed near-complete occlusion of the left main bronchus with associated atelectasis of the lingula, cylindrical and cystic bronchiectasis within the left lower lobe and right middle lobe (Figure 1). Also present were numerous nodules within the atelectatic lung with central hypoattenuation, numerous additional nodules with central hypoattenuation present bilaterally,
and moderate bilateral pleural effusions. A transthoracic echocardiogram was also obtained revealing an impaired relaxation pattern of diastolic filling, and elevated right ventricular systolic pressure. On the fourth day, the patient underwent bronchoscopy with bronchoalveolar lavage (BAL) of the left lower lobe revealing severe mucous plugging of the left lung and thick mucoid secretions without evidence of endobronchial lesions, which grew 3+ *Candida spp*. Acid fast (Kinyoun) stain of the BAL fluid revealed rare acid fast bacilli. The infectious disease service was consulted and polymerase chain reaction (PCR) testing by laboratory-developed test of the primary BAL sample was requested and was negative for tuberculosis (TB). Her shortness of breath improved significantly with treatment for heart failure and pneumonia, which were thought to be responsible for her acute presentation to the hospital, and she was discharged to follow up with the outpatient pulmonary service regarding culture results of the atypical mycobacterium that was yet unidentified. The BBL™ MGIT™ (Mycobacteria Growth Indicator Tube, Becton, Dickinson and Company, Franklin Lakes, New Jersey) was positive after 9 days, as was pinpoint growth on Middlebrook 7H11 and the Accuprobe Culture Identification Test (Gen-Probe, Inc., San Diego, CA) was negative for *M. tuberculosis*, and MAC. Seven days later, a yellowish tint was observed and probes were performed for *M. kansasii* and *M. gordonae* and were negative (Figure 2). The isolate was sent to the National Jewish Health mycobacteriology laboratory for identification and susceptibility testing. One month after discharge the patient was started on an airway clearance device to help mobilize secretions. Three months after discharge, the organism was identified by the National Jewish laboratory as *Mycobacterium paraffinicum*. Repeated sputum samples continued to grow *M. paraffinicum* and the patient was started on an empiric regimen of azithromycin, ciprofloxacin, and linezolid. The organism demonstrated susceptibility to ciprofloxacin, clarithromycin, linezolid and doxycycline. The mycobacterium
had intermediate susceptibility to rifabutin and rifampin and was resistant to ethambutol, streptomycin, amikacin and imipenem. It was susceptible to rifampin and ethambutol when tested in combination. Unfortunately, the patient was unable to tolerate the oral regimen due to nausea and vomiting and decided to discontinue treatment. A cause for her underlying bronchiectasis was never determined. She was last seen in pulmonary clinic in September 2013 where she remained with chronic symptoms, with an occasional productive cough with green phlegm. The lowest oxygen saturation after a 6-minute walk was 88%.

*M.paraffinicum* was initially isolated from a soil sample in 1956(4). The organism as a long, slender, strongly acid-fast rod showing Much's granules with Ziehl-Neelsen stain; yellow, waxy, wrinkled colonies; no growth on nutrient-agar media, glycerol, or methane(4). Interestingly, in 1971, *M.paraffinicum* lost its standing as a species because it was determined that the isolate could not be reliably distinguished from *M. scrofulaceum*(14). In 1991, in the fourth report of the International Working Group on Mycobacterial Taxonomy (IWGMT), it was determined that the isolate deemed *M. paraffinicum* had different biochemical responses from *M. scrofulaceum* and belonged to a discrete environmental species(15). In 2010, multiple molecular sequence analyses comparing *M. paraffinicum* to *M. scrofulaceum*, *M. nebraskense*, and *M. seoulense* via 16S rRNA gene sequences were conducted, and *hsp65* and *rpoB* gene sequencing, and the name *M.paraffinicum* was reinstated ending what was referred to as "more than five decades of taxonomic confusion"(11). Along with *M. paraffinicum*, other species of non-tuberculous mycobacteria also utilize paraffin and other complex hydrocarbons as a sole carbon source (8, 9). The reports of *M. paraffinicum* in the clinical setting are limited. The only study reporting *M. paraffinicum* in a clinical setting described a pseudo-outbreak of *M. paraffinicum* at a university-
affiliated, tertiary care facility(12, 13). *M. paraffinicum* was isolated from sputum and stool samples from 21 patients over 2.5 years with identification of the hospital water system as the source of the contamination. *M. paraffinicum* was not implicated as a pathogen in any of the 21 patients.

Non-tuberculous mycobacteria, such as *M. paraffinicum*, demonstrate very different susceptibility patterns that differ between species(2). In deciding antibiotic regimens for pulmonary infections caused by non-tuberculous mycobacteria, it is helpful to first divide these organisms into the categories of rapid growing mycobacteria (RGM) and slow growing mycobacteria (SGM). Antibiotic regimens for RGM are dictated primarily by the susceptibility patterns of *M. abscessus* and *M. fortuitum*(7, 10). Both *M. abscessus* and *M. fortuitum* exhibit inducible macrolide resistance which is believed to work through activation of the *erm* gene(6).

In the case of *M. paraffinicum*, because of its recent reclassification as a distinct species, there is no previous susceptibility data to guide therapy. Even when extrapolating from close biological relative, *M. scrofulaceum*, the data remains limited. The empiric regimen for this patient of azithromycin, ciprofloxacin, and linezolid was chosen in order to give the patient an oral regimen with activity against SGM. Many documented SGM species demonstrate susceptibility to macrolides, and these agents are now a cornerstone of most SGM regimens(2). Linezolid demonstrates high oral drug availability and good *in vitro* susceptibility against a broad range of SGM, but it differs depending on the strain of non-tuberculous *Mycobacterium* that is being treated (1, 3). Finally, ciprofloxacin is relatively well tolerated with a low side effect profile and has a relatively broad coverage of the SGM group at achievable MICs(5). The choice of this regimen was corroborated when susceptibility testing returned.
Conclusion

As far as we know, this is the first reported case of *M. paraffinicum* as a pathogen. Given the recent re-instatement of *M. paraffinicum* as a separate and distinct species, we believe that this organism represents a new addition to the list of SGM that are capable of causing human disease.


Figure 1. CT scan demonstrating diffuse bronchiectasis of the left lower lobe and right middle lobe.
Figure 2. Growth of M. paraflinicum demonstrated on Middlebrook 7H11 agar.