

## CASE REPORT

# MYCOBACTERIUM ABSCESSUS LUNG DISEASE IN A PATIENT WITH PREVIOUS PULMONARY TUBERCULOSIS

Duan Hongfei, Huang Xuerui, Wang Jing and Chu Naihui

Department of Tuberculosis, Beijing Chest Hospital, Capital Medical University, Tongzhou District, Beijing, PR China

**Abstract.** Patients with pre-existing lung damage, such as due to pulmonary tuberculosis (PTB), are susceptible to nontuberculous mycobacteria (NTM) infections. For patients with previous PTB, it is difficult to differentiate NTM lung disease from PTB, especially in tuberculosis (TB) high-burdened countries. Here, we report a case of *Mycobacterium abscessus* lung disease with a previous history of PTB. The patient underwent a right upper lobe lobectomy due to disappointing treatment response with anti-tuberculosis therapy. However, the disease worsened after the surgery. Five years later, she was diagnosed with *M. abscessus* lung disease. Successive computed tomography (CT) scans showed the progressing features of *M. abscessus* lung disease. This patient had multiple micronodules adjacent to the pleura with a positive culture for NTM. Bilateral bronchiectasis without lobar predominance are valuable features for distinguishing *M. abscessus* lung disease from other mycobacterial lung disease.

**Keywords:** Mycobacterium, atypical, *Mycobacterium tuberculosis*, lung disease

Nontuberculous mycobacteria (NTM), including *Mycobacterium avium* complex, *M. abscessus*, *M. kansasii*, *M. xenopi*, and *M. chelonae*, are frequently isolated from environmental sources. The isolation of NTM species from a respiratory sample is insufficient evidence to diagnose NTM lung disease. Patients with pre-existing lung damage, such as pulmonary tuberculosis (PTB), are susceptible

to NTM (Sexton and Harrison, 2008). For patients with previous PTB, it is difficult to differentiate NTM lung disease from PTB, especially in tuberculosis (TB) high-burdened countries.

Here, we describe a case of *M. abscessus* lung disease with a previous history of PTB. After being diagnosed with PTB, the patient underwent a right upper lobe lobectomy due to disappointing treatment response from anti-tuberculosis therapy. However, the disease worsened after the surgery. Five years later she was diagnosed with *Mycobacterium abscessus* lung disease. Successive computed tomogra-

Correspondence: Chu Naihui, Department of Tuberculosis, Beijing Chest Hospital, Capital Medical University, Tongzhou District, Beijing 101149, PR China.

E-mail: dongchu1994@sina.com

Table 1

Results of susceptibility testing of 4 strains of mycobacteria isolated from patient.

Drugs	Cut-off value ( g/ml) <sup>a</sup>	Results of susceptibility testing			
		Sep 15, 2003 <i>M. tuberculosis</i>	Sep 24, 2003 <i>M. tuberculosis</i>	Sep 18, 2004 NTM <sup>b</sup>	Mar 24, 2010 <i>M. abscessus</i>
Isoniazid	1	R	R	R	R
Streptomycin	10	S	S	R	R
Ethambutol	5	S	S	R	R
Rifampin	50	R	R	R	R
Kanamycin	10	S	S	S	R
Capreomycin	10	S	R	R	R
Amikacin	10	ND <sup>c</sup>	ND	R	R
Prothionamide	25	R	R	R	S
<i>p</i> -aminosalicylic acid	1	R	R	R	R
Floxacin	5	R	R	R	R
Levofloxacin	2	ND	ND	R	R
Rifapentine	5	ND	ND	R	R

<sup>a</sup>Cut-off value for resistance (R) and susceptibility (S) to the corresponding anti-TB drug. <sup>b</sup>Species unknown; <sup>c</sup>ND: not done

phy (CT) scans showed the progressing features of *M. abscessus* lung disease.

#### CASE REPORT

A 61-year-old female was referred to our hospital in 1999 with a 2-month history of productive cough and mild fever. She was a non-smoker. CT scans shown cavities, small nodules and branching nodular opacities in the bilateral upper lobes of the lungs. A sputum smear was positive for acid-fast bacilli (AFB) and a sputum culture using Lowenstein-Jensen (L-J) medium was negative. The patient was diagnosed with PTB and treatment was given for 12 months from April 1999 to April 2000. The drugs used were isoniazid, rifapentine, ethambutol and levofloxacin. Due to gastrointestinal adverse effects, she was not treated with pyrazinamide. At the end of treatment, the patient had few symptoms negative

AFB smears and a negative culture. A chest x-ray showed a cavity in left upper lobe of the lung and most of the infiltrates had resolved, but cavity in the right upper lobe still existed.

In March 2003, she was again referred to our hospital with productive cough. A chest x-ray showed a cavity in the right upper lobe of the lungs and bilateral nodular infiltrates in the lower lungs. Her sputum was positive on AFB smear and on L-J medium culture; the species identified was *M. tuberculosis*. Susceptibility was tested using the absolute two-concentration method, showing the bacillus was resistant to several first-line and second-line drugs (Table 1). She could not tolerate many second-line drugs due to gastrointestinal side effects and resultant albuminuria. Based on susceptibility testing and consultation with senior clinicians, the patient was treated

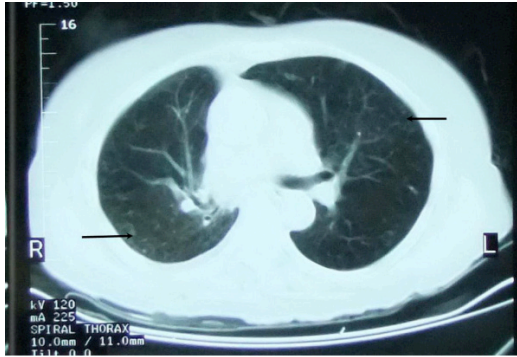


Fig 1—Chest computed tomography scan on June 18, 2005 (3 days after surgery). Transverse CT scan (10-mm collimation) shows nodules and branching nodular opacities (arrow) bilaterally in lobes connected with the pleura.

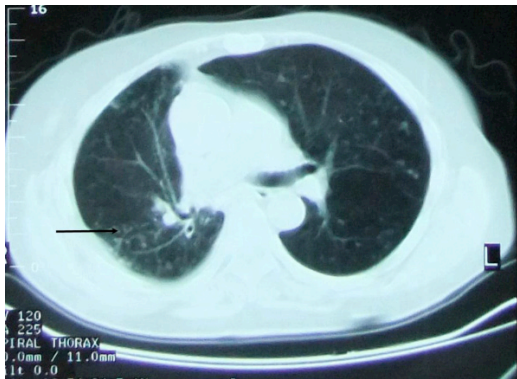


Fig 2—Chest computed tomography scan on December 23, 2005 (6 months after surgery). Transverse CT scan (10-mm collimation) showing bilateral well-defined micronodules, and branching nodular opacities (arrow).

with isoniazid for 11 months, rifampicin for 7 months, rifapentine for 10 months, ethambutol for 17 months, prothionomide for 8 months, pasiniazide for 16 months, clarithromycin for 16 months, *p*-aminosalicylic acid for 7 months, amoxicillin/clavulanate for 6 months, levofloxacin for 6 months and moxifloxacin for 7 months. Her symptoms did not improve and the

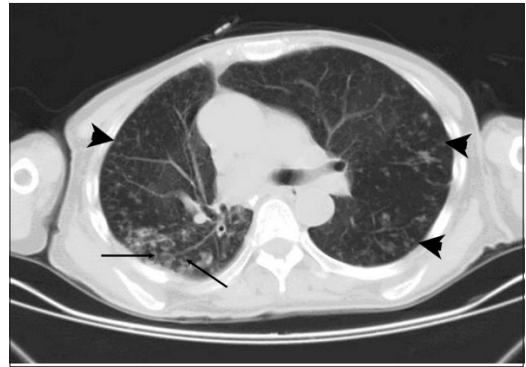


Fig 3—Chest computed tomography scan on March 28, 2010 (5 years after surgery). Transverse CT scan (7.5-mm collimation) shows bilateral cylindrical bronchiectasis (arrow), well-defined micronodules, and branching nodular opacities (arrowhead).

sputum remained positive for AFB. On September 18, 2004, NTM was isolated from her sputum, but was believed to be of little clinical significance.

On June 15, 2005, she underwent a right upper lobe lobectomy due to hemoptysis. After the surgery, she still had cough productive of sputum and had a mild fever. A CT scan showed disease progression (Figs 1, 2). Since there were few drugs suitable for her, her treatment regimen consisted of rifapentine for 16 months, ethambutol for 49 months, pasiniazide for 65 months and clarithromycin for 16 months. The sputum continued to be positive on AFB smear and negative with L-J medium culture. On March 24 and March 27, 2010, colonies of mycobacteria were identified in her sputum with L-J medium. The bacilli proved to be *M. abscessus*, diagnosed by commercial DNA probe (GenoType Mycobacterium CM, Hain Lifescience, Nehren, Germany). A CT scan showed volume loss in the right middle lobe of the lung and bronchiectasis with multiple small nodules in both lungs (Fig 3). With a diagnosis of *M. abscessus*

lung disease, the regimen was changed to clarithromycin, imipenem, 2 weeks later followed by cefoxitin for 2 weeks, doxycycline and levofloxacin from April, 2010 to October, 2011. She was not treated with amikacin due to albuminuria. Three months later, her symptoms improved and she had negative sputum cultures for mycobacterium. By the end of treatment, the patient had few symptoms and negative AFB smears and cultures. She was discharged due to cure.

### DISCUSSION

NTM are ubiquitous environmental organisms. Local factors that exacerbate damage to the mucosal surface or that increase the tissue burden of NTM may promote disease (Sexton and Harrism, 2008). A previous history of pulmonary TB is also associated with NTM lung infection (Sexton and Harrison, 2008). During anti-TB treatment, NTM may be isolated from TB patients (Huang *et al*, 2009; Jun *et al*, 2009). A one-time isolation of NTM from the sputum is often considered to be due to contamination or colonization. Few patients have two or more positive cultures for the same NTM species, which is usually *M. abscessus* (Jun *et al*, 2009). Co-infection with pulmonary TB and relatively virulent NTM species, such as *M. abscessus*, does occur. In this patient NTM was isolated from sputum of this patient prior to surgery. Genotyping of mycobacteria was not widely performed in China at that time, so the species of NTM is unknown. However, the susceptibility pattern of that strain was similar to the *M. abscessus* isolated later. It is possible the patient had a co-infection with *M. tuberculosis* and *M. abscessus* prior to surgery.

We believe *M. tuberculosis* caused her disease prior to surgery. *M. tuberculosis* was isolated from this patient twice. Ra-

diographic and clinical improvement was observed after the first anti-tuberculosis treatment. NTM does not respond to these drugs. Susceptibility testing of these isolates showed multi-drug resistant *M. tuberculosis*, which could lead to an unsatisfying treatment response.

The diagnosis of NTM lung disease must rely on clinical, radiographic and microbiological criteria. The American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) revised the criteria of diagnosing an infection due to NTM in 2007. This case meets all the criteria of the ATS 2007 guidelines, including pulmonary symptoms, multifocal bronchiectasis with multiple small nodules and positive culture results from at least two separate expectorated sputum samples (Griffith *et al*, 2007).

After the surgery the sputum culture remained negative for a long time, leading to a delay in diagnosis. The rate of false-negative sputum cultures is high in patients with the nodular bronchiectatic form of NTM lung disease. Incubation at 37°C is not suitable for rapidly growing mycobacteria. As a result, many patients with NTM disease, especially patients with the nodular bronchiectatic form, may not have a definite bacteriological diagnosis, especially in high TB-burden countries, in which NTM disease is likely to be underestimated.

Tanaka *et al* (2001) found with NTM lung disease the original nodules or branching nodular opacities were connected with the pleura. NTM then spread transbronchially along the draining bronchus or toward the pleura to produce lesions, including new nodules, bronchiectasis and volume decrease due to severe bronchiectasis. In this case, we observed micronodules adjacent to the pleura prior to surgery, and then produced branching

nodular opacities and bronchiectasis. We speculate that the micronodules are caused by *M. abscessus* infection prior to surgery. Bronchiectasis may also be caused by *M. abscessus*. The lesions may spread to other lobes.

NTM pulmonary disease accounts for at least one-third of patients with well-defined micronodules, branching nodular opacities (tree-in-bud pattern) and bronchiectasis (Han *et al*, 2003; Koh *et al*, 2005). The radiographic findings in *M. abscessus* lung disease are similar to those of *M. avium* complex lung disease except in patients with *M. avium* lung disease, most nodular bronchiectasis was either isolated to or most severe in the middle lobes or the lingular segment (Han *et al*, 2003). However, the findings in patients with *M. abscessus* lung disease are most commonly bilateral and showed no lobar predominance. Many patients with *M. abscessus* lung disease have no bacteriological evidence of infection on sputum examination. Based on our experience with this patient, multiple micronodules adjacent to the pleura with a positive culture for NTM are likely to be NTM. Bilateral bronchiectasis and bronchiectasis without lobar predominance may help distinguish *M. abscessus* lung disease from other mycobacterial lung disease.

*M. abscessus* is often resistant to many antibiotics and the optimal therapeutic regimen has yet to be established. Isolates are usually susceptible only *in vitro* to parenteral amikacin, cefoxitin, imipenem and oral macrolides (clarithromycin and azithromycin). Jeon *et al* (2009) found a standardized combination antibiotic regimen together with an initial 4-week course of cefoxitin and amikacin, was moderately effective in treating *M. abscessus* lung disease; the response rates to treatment were 83% for symptoms, 74% for high-resolu-

tion computed tomography and 58% for sputum conversion. Based on our experience, a combination regimen, including a clarithromycin-containing drug regimen along with an initial 4-week course of intravenous antibiotics is effective against *M. abscessus* lung disease.

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