

# Pulmonary Non-tuberculous Mycobacterial Infections in Category II Failures from National Tuberculosis Programme

Y.N. Dholakia and D.P. Shah

Tuberculosis Unit, Koldongri Municipal Dispensary, Andheri (East), Mumbai, India

## Abstract

Pulmonary infections due to non-tuberculous mycobacteria (NTM) are increasingly being reported. These can mimic drug-resistant tuberculosis. A diagnosis of NTM infections needs a high degree of clinical suspicion and repeated isolation of the organism on culture. NTM infections occur commonly in immunocompromised individuals and in people with lung abnormalities. Currently there are no guidelines on drug combinations and the duration of treatment is not adequately defined.

Two cases of pulmonary infection with NTM in immune-competent individuals are described in the present report. Although the bacteriological, radiological and clinical response to treatment was good; early discontinuation of treatment resulted in recurrence and change in drug susceptibility pattern, suggesting the need for prolonged treatment for achieving cure. [Indian J Chest Dis Allied Sci 2015;57:27-30]

**Key words:** Pulmonary NTM infection, Treatment.

## Introduction

Pulmonary non-tuberculous mycobacteria (NTM) infections are being increasingly detected.<sup>1</sup> This is especially so in settings where the incidence of tuberculosis (TB) is declining.<sup>2</sup> Of 95 species of NTM, around a third are associated with human infections.<sup>3</sup> NTM infection is commonly seen in immunocompromised individuals. In a cohort of drug-resistant TB cases in treatment failures attending our centre, 5 cases out of 34 (14%) were identified as having NTM infections.<sup>4</sup> Isolates from 7% (68/958) cases were reported as NTM in a retrospective cohort study conducted in Seoul.<sup>5</sup> NTM usually involves skin and soft tissue. However, pulmonary infection is not uncommon and may be seen in individuals with underlying lung damage.<sup>6,7</sup>

Presenting with similar clinical and radiological features, these infections could be misdiagnosed as drug-resistant TB.<sup>8</sup>

Treatment of NTM infections depends on drug susceptibility profile of the infecting strain. Currently there are no guidelines on drug combinations and the duration of treatment is not available and these aspects of management are not adequately defined.<sup>9</sup>

We present two cases of pulmonary NTM infection in immune-competent hosts from Category II failures from the National TB Control Programme to highlight problems of diagnosis and management of NTM infections.

## Case Reports

### Case 1

A 32-year-old unmarried male, embroider by occupation was referred to our diagnostic centre for relapse of symptoms after a complete treatment under Category II. The patient had a prior history of anti-TB treatment for suspected right sacro-iliac joint TB for which he took Category I anti-TB treatment at a tertiary hospital in 2007. After three months of regular treatment, he developed pulmonary symptoms and was diagnosed as sputum smear positive pulmonary TB. Since he had deteriorated on a regular treatment, he was advised Category II treatment which he completed successfully and was sputum smear negative with complete clearance of radiological lesions.

In the current episode, his blood counts were normal, diabetes was excluded and test for human immunodeficiency virus done after counselling and consent was non-reactive. Chest radiograph (postero-anterior view) showed cavities in the left upper and middle zones (Figure 1) and sputum smear for acid-fast bacilli (AFB) was positive. However, sputum culture for AFB was performed using BACTEC MGIT 960 TB system by rapid detection and continuous monitoring using fluorescence method. Anti-microbial susceptibility test was done using MIC breakpoints as per CLSI guidelines. Culture was positive for Mycobacteria Other than Tuberculosis (MOTT). Speciation was done and reported as *Mycobacterium*

[Received: July 25, 2013; accepted after revision: March 25, 2014]

**Correspondence and reprint requests:** Dr Yatin N. Dholakia, 2B Saurabh, 24E Sarojini Road, Santacruz (West), Mumbai-400 054, India; E-mail: yatindholakia@gmail.com

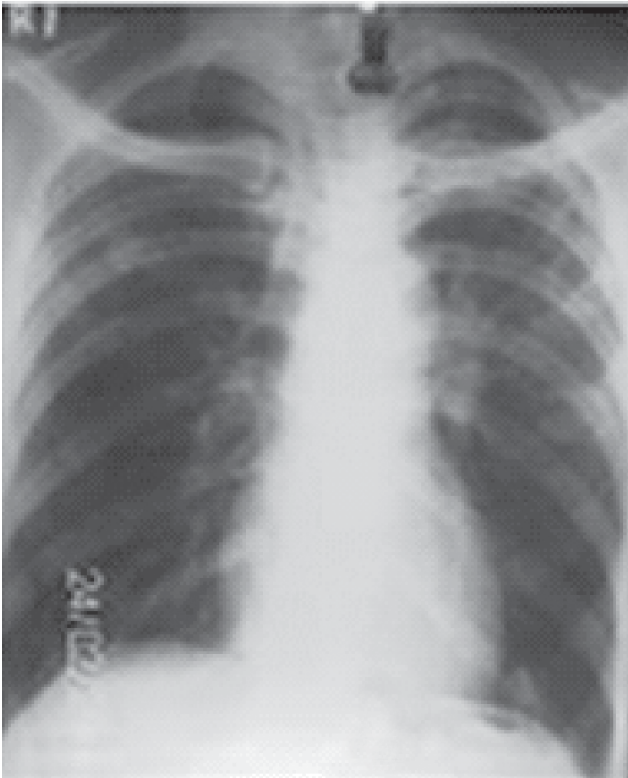


Figure 1. Chest radiograph (postero-anterior view) showing upper and mid zone cavities with infiltrates.

*fortuitum* type II. Results of drug susceptibility test (DST) done in the year 2009 are shown in the table.

On receipt of the culture report, the patient was started empirically on cotrimoxazole and sulfamethoxazole (TMP/SMX) combination along with oral penicillin. After the DST report, the therapy was switched to sparfloxacin and cotrimoxazole and sulfamethoxazole combination. This therapy was given for six months and the patient showed a good clinical response. The smears for AFB were converted to negative after three months of the changed treatment and there was total radiological clearance of the shadows.

The patient returned after three months with relapse of symptoms. He was investigated again and found to be sputum smear positive for AFB, and radiograph showed fresh lesions. Sputum culture was positive for MOTT and speciation again showed *M. fortuitum*. Results of DST done in the year 2010 are presented in the table. He was initiated on three drugs in September 2009. Amikacin was given parenterally, daily for six months with periodic renal function monitoring. The sputum converted after three months; and chest radiograph showed clearance of shadows with good clinical response. The treatment was continued for a total period of 24 months and sputum remained consistently negative. Culture could not be repeated due to financial reasons. Final chest radiograph showed complete resolution of the lesions (Figure 2).

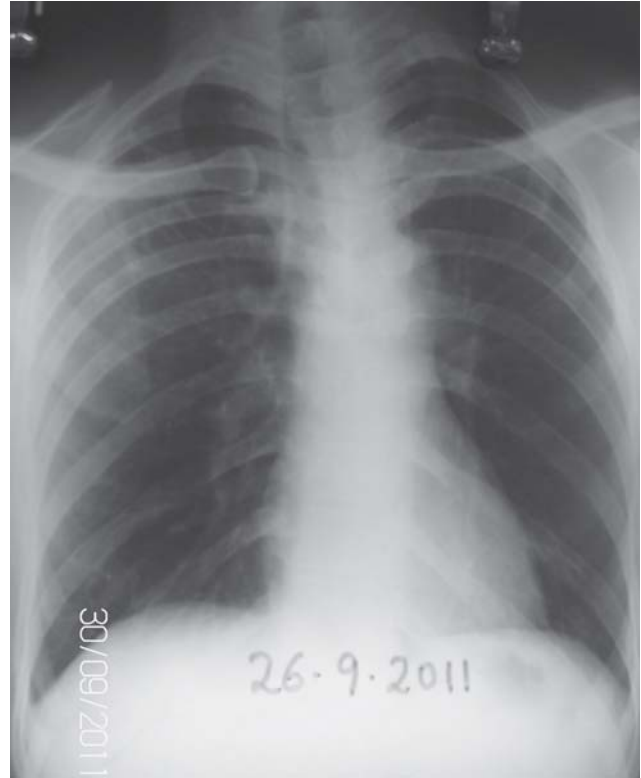


Figure 2. Case 1. Chest radiograph (postero-anterior view) showing complete regression of lesions.

The patient is under regular three monthly follow-up and is asymptomatic till date.

#### Case 2

A 62-year-old male reported to our clinic with a past history of multiple episodes of TB in 2004, 2005, 2007 and 2008 that were treated at private clinics. Culture reports at various time points reveal rapidly growing bacilli, as shown in the table. He was started on Category II treatment under Revised National Tuberculosis Control Programme (RNTCP) at our centre to which he did not respond and was declared a failure. He was a non-diabetic and test for HIV done after pre-test counselling was negative. Chest radiograph (postero-anterior view) at this point showed right upper zone fibro-cavitary lesions with pleural effusion and left mid-zone cavitary lesions. Sputum AFB culture, done as described in the first case showed NTM (rapid growing). Speciation showed *Mycobacterium chelonae*. DST was done by MIC method and is shown in the table. Based on DST results, he was started on amikacin (0.5 g) daily intramuscularly and TMP/SMX combination in February 2009. Renal functions were monitored periodically. In January 2010, he complained of diminished hearing and amikacin had to be discontinued. Treatment with TMP/SMX was continued till August 2010. Sputum smear converted to negative in December 2009 and remained negative till the end of treatment in August

Table. Bacteriology results of the Cases

Date	Culture	Susceptible to	Resistant to
<i>Case 1</i>			
2009	Growth – MOTT – <i>M. fortuitum</i> type II	Sparfloxacin, ws* PZA, OFL	SM, KAN and AMK; RMP, Rifabutin, INH, EMB, ETA, CLY, PAS, Clarithromycin and Roxithromycin
2010	Growth – MOTT – <i>M. fortuitum</i>	AMK, Clarithromycin and Ciprofloxacin	SM, KAN; RMP, Rifabutin, INH, EMB, ETA, CLY, PAS, and Roxithromycin
<i>Case 2</i>			
8.12.2007	Growth within 3 weeks	ND	ND
31.08.2008	Growth	NIL	SM, INH, RMP, PZA, EMB, KAN, CAP, ETA, PAS and OFL
14.02.2009	Growth – <i>M. chelonae</i>	AMK,TMP/SMX, LNZ	Clarithromycin, Cefoxitin, Ceftriaxone, Imipenem, Minocycline, Tobramycin, Ciprofloxacin, Gatifloxacin and Amoxicillin
01.09.2011	Growth – rapid growing	AMK, Tobramycin, LNZ and Clarithromycin,	TMP/SMX, Cefoxitin, Ceftriaxone, Imipenem, Minocycline, Ciprofloxacin, Gatifloxacin and Amoxicillin

*Definitions of abbreviations:* \*ws=Weakly sensitive; MOTT=Mycobacteria Other Than Tuberculosis; PZA=Pyrazinamide; OFL=Ofloxacin; SM=Streptomycin; KAN=Kannamycin; AMK=Amikacin; RMP=; INH=Isoniazid; EMB=Ethambutol; ETA=Ethionamide; CLY=Cycloserine; PAS=Para-amino-salicylic acid; ND=Not done; CAP=Capreomycin; TMP/SMX=Trimethoprim/Sulphamethoxazole; and LNZ=Linezolid

2010. Radiologically there was regression in the lesions in the right upper zone, the pleural effusion resolved and there was a thin-walled cavity in the left mid zone.

In February 2011, he came back with the recurrence of symptoms. Now sputum smear was positive for AFB. The patient was advised to undergo culture and DST for atypical mycobacteria. However, he did not comply and was initiated on Category II treatment with which he had severe drug intolerance. After repeated counselling, he agreed to culture and DST. He was culture positive for atypical mycobacteria (rapid growing). Speciation could not be done. He was started on linezolid and clarithromycin as per the DST report. Currently he is on treatment with regular periodic follow-up.

## Discussion

Non-tuberculous mycobacteria infections occur usually in patients with pre-existing lung disease,<sup>6,7</sup> such as bronchiectasis, cystic fibrosis or healed cavities from previous TB and in those with reduced immunity. The first patient did not have any of these conditions. The radiograph at the end of the first episode of TB did not have any residual lesions. The second patient did have residual lesions when he presented to us. However, his bacteriological studies from the first episode pointed to NTM infection.

A reliable diagnosis of NTM infection is based on highly suspicious clinical presentation.<sup>10</sup> Multiple isolates are needed from non sterile sites to obtain a diagnosis of NTM infections.<sup>3</sup> In our first case, same organisms were isolated at two different time points

suggesting that the disease was indeed due to NTM infection. In the second case, since the beginning, rapid growing organisms were cultured although the organisms were not typed prior to reporting to us. We could identify *M. chelonae* in one sample. However speciation could not be confirmed with the NTM isolate obtained at a later stage, thus, precluding a firm diagnosis.

Monitoring of treatment should ideally be done with periodic cultures. This was not possible due to limited resources. Both cases were monitored with periodic sputum smear examinations, which is considered as a surrogate for culture from a DOTS Plus pilot site.<sup>11</sup>

There are no guidelines on the management of NTM infections as to the drug combinations and duration of therapy.<sup>12</sup> The optimum duration of treatment is poorly defined in the literature.<sup>9</sup> Treatment duration of antibiotic therapy varies widely from 1 month to 12 months.<sup>13</sup> Treatment is based on DST reports and is usually a combination of multiple drugs. Our patients responded well to the medicines selected as per the DST results with sputum conversion and total clearance of lesions on chest radiograph in Case 1. He was free of all symptoms and had a weight gain. Therapy was given for six months only. This duration proved short for the eradication of the infection, as the patient had a relapse within three months of stopping the treatment. The second case was given treatment for 18 months also with good clinical, radiological response and sputum conversion after 10 months of treatment. His symptoms recurred after six months. The

first case is currently symptom free with no evidence of relapse after a 24-month therapy, indicating that treatment for NTM needs to be of a prolonged duration. Prospective studies are required to determine the optimum duration of the treatment.

Notably, both the cases described in this report had shown a change in the drug susceptibility pattern. This could be possibly due to genetic mutation. This needs further molecular biological studies for validation.

To conclude, suspicion of NTM infections should be high in cases not responding to regular anti-tuberculosis treatment.<sup>8</sup> Isolation of the same organism at different time points is indicative of its role in the disease causation and should be confirmed by repeated cultures.

Treatment should be prolonged; premature discontinuation of treatment even on achieving bacteriological, clinical and radiological quiescence is likely to result in reactivation of disease and development of further drug resistance.

## References

1. Thomson RM. Changing epidemiology of pulmonary nontuberculous mycobacteria infections. *Emerg Infect Dis* 2010;16:1576–83.
2. Saleeb P, Olivier KN. Pulmonary nontuberculous mycobacterial disease: new insights into risk factors for susceptibility, epidemiology, and approaches to management in immunocompetent and immunocompromised patients. *Curr Infect Dis Rep* 2010;12:198–203.
3. Katoch VM. Infections due to non-tuberculous mycobacteria (NTM). *Indian J Med Res* 2004;120:290–304.
4. Dholakia Y, Shah D. Clinical profile and treatment outcomes of drug-resistant tuberculosis before directly observed treatment strategy plus: lessons for the program. *Lung India* 2013;30:316–20.
5. Jun HJ, Jeon K, Um SW, Kwon OJ, Lee NY, Koh WJ. Nontuberculous mycobacteria isolated during the treatment of pulmonary tuberculosis. *Respir Med* 2009;103:1936–40.
6. Marras TK, Daley CL. Epidemiology of human pulmonary infection with nontuberculous mycobacteria. *Clin Chest Med* 2002;23:553–67.
7. Prevots DR, Shaw PA, Strickland D, Jackson LA, Raebel MA. Nontuberculous mycobacterial lung disease prevalence at four integrated health care delivery systems. *Am J Respir Crit Care Med* 2010;182:970–6.
8. Mistry NF, Dholakia Y, D'Souza DTB, Taylor M, Hoffner S, Birdi TJ. Rhodococcus and Mycobacterium tuberculosis: masquerade or mixed infection. *Int J Tuberc Lung Dis* 2006;10:351–3.
9. Piersimoni C, Scarparo C. Pulmonary infections associated with non tuberculous mycobacteria in immunocompetent patients. *Lancet Infect Dis* 2008;8:323–34.
10. Bimben C, Coskun M, Gunduz AT, Senol G, Cirak AK, Tibet G. Nontuberculous mycobacteria isolated from pulmonary specimens between 2004 and 2009: causative agent or not. *New Microbiologica* 2010;33:399–403.
11. Sarin R, Singla R, Visalakshi P, Jaiswal A, Puri MM, Khalid UK, et al. Smear microscopy as surrogate for culture during follow up of pulmonary MDR TB patients on DOTS plus treatment. *Indian J Tuberc* 2010;57:134–40.
12. Subcommittee of the Joint Tuberculosis Committee of the British Thoracic Society. Management of opportunist mycobacterial infections: Joint Tuberculosis Committee guidelines 1999. *Thorax* 2000;55:210–18.
13. Jiang SH, Roberts DM, Dawson AH, Jardine M. Mycobacterium fortuitum as a cause of peritoneal dialysis-associated peritonitis: case report and review of the literature. *BMC Nephrol* 2012;13:35.