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Brief Communication

Pulmonary *Mycobacterium kansasii* disease in immunocompetent host: Treatment outcomes with short-course chemotherapy

***C Padmapriyadarsini, D Nair, NS Gomathi, B Velayudham**

Abstract

Mycobacterium kansasii, most virulent of all atypical mycobacteria, causes pulmonary disease identical to the disease caused by *Mycobacterium tuberculosis.* Early identification of the species and prompt initiation of treatment for *M. kansasii* is necessary to prevent morbidity and mortality due to this disease. This case series highlights the similarity in the clinical presentation of both *M. tuberculosis* and *M. kansasii* and response to direct observation of short-course chemotherapy with rifampicin, in the management of pulmonary *M. kansasii* disease. Larger studies are required to evaluate the long-term effect of short-course chemotherapy, especially use of moxifloxacin, in the management of pulmonary *M. kansasii* disease.

Key words: *Moxifloxacin, pulmonary Mycobacterium kansasii, rifampicin, short-course chemotherapy*

Introduction

With new and improved tuberculosis (TB) diagnostic tools, pulmonary infections due to non-tuberculous mycobacterium (NTM) are being increasingly recognised worldwide. The isolation of NTM raises the question of their clinical significance especially in endemic settings like India. Although more than 150 different species of NTM have been described, pulmonary infections are most commonly due to *Mycobacterium avium* complex, *Mycobacterium kansasii* and *Mycobacterium abscessus*.[1]

M. kansasii has been considered the most virulent of the NTM. Pulmonary disease caused by *M. kansasii* is nearly identical to the disease caused by *Mycobacterium tuberculosis*, including chest X-ray (CXR) findings. The American Thoracic Society (ATS) recommends an 18-month regimen of daily isoniazid, rifampin and ethambutol, in the management of *M. kansasii* lung disease.[1] To date, no short-course or intermittent treatment regimen has been approved or endorsed by the ATS. In an *in vitro* susceptibility study of 148 *M. kansasii* strains isolated from clinical specimens, moxifloxacin followed by levofloxacin, clarithromycin and linezolid showed a good therapeutic alternative.[2] Here, we report a series of patients treated with a short-course regimen for *M. kansasii* pulmonary disease, with favourable response at the end of 2-year of follow-up.

Case Reports

Patients reported here were enrolled in a randomised controlled clinical trial that assessed the efficacy of moxifloxacin in shortening the duration of TB treatment in new sputum smear positive, non-HIV-infected patients. As per the trial protocol, based on sputum smear status and CXR findings, they were randomised to either a 3- or 4-month regimen of daily moxifloxacin [M], isoniazid [H], rifampicin [R], ethambutol [E] and pyrazinamide [Z] ($3MHREZ_7$ or $2MHREZ_7/2MHR_7$ or $2MHREZ_7/2MHR_3$) or 6-month of thrice-weekly regimen ($2EHRZ_3/4RH_3$).

After starting treatment under direct observation, sputum samples were subjected to Lowenstein–Jensen solid culture for acid-fast bacilli. Following the growth of mycobacteria, species were identified using high-performance liquid chromatography technique. Patients, who grew *M. tuberculosis* in their sputum, were retained in the clinical trial while those showing NTM were considered as pre-treatment exclusions. However, by

*Corresponding author (email: <pcorchids@gmail.com>)
Departments of Clinical Research (PC, DN, BV) and Bacteriology (NSG), National Institute for Research in Tuberculosis, Chennai, Tamil Nadu, India
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the time culture results were available patients had already completed more than 2 months of treatment and/or had become sputum culture negative. Further management of these patients was individualised based on the presence of symptoms or CXR deterioration. Sputum conversion was defined as three consecutive negative cultures at the end of treatment. All patients were followed for 24 months. Recurrence was defined as two consecutive positive cultures 1 month apart, after culture conversion. National Institute for Research in Tuberculosis's (NIRT's) Institutional Ethics Committee approval was obtained for the clinical trial and informed written consent was taken from all patients before enrolment to the study.

Table 1 gives the clinical details of all the nine cases whereas Table 2 shows their response to treatment and follow-up.

Discussion

We report nine immunocompetent patients suffering from *M. kansasii* pulmonary disease. The clinical and radiologic findings were indistinguishable from *M. tuberculosis*. Most reported patients of *M. kansasii* infection are males with a history of heavy smoking and pre-existing pulmonary conditions such as bronchiectasis, chronic bronchitis, TB or pneumoconiosis.[3-5] Smoking may influence the cilia and macrophage function in airways while prior lung infection with TB or pneumoconiosis can provide a nidus for *M. kansasii* infection. *M. kansasii* being more pathogenic can readily establish significant infection in relatively normal lung tissue also. In our case series, all were males with 6 of them being smokers with none showing any pre-existing pulmonary conditions.

Table 1: Clinical details of cases

Case number	Age (years)/ gender	Smoking/ job	Symptoms/duration	Prior TB	Contact with PTB	BMI	CXR	Sputum AFB smear	Treatment
1	22/male 89,163	Yes/ electrician	Cough, LOA haemoptysis - 2 weeks	No	Yes Father	15.1	Cavity: Upper lobe Infiltrates: Two zones left lung	+	$2HREZ_3/4RH_3$
2	25/male	Yes/painter	Cough, fever - 2 weeks	No	None	15.3	Cavity: Upper lobe Infiltrates: Three zones, both lungs	++	$2HREZ_3/4RH_3$
3	29/male 93,187	No/courier services	Cough, LOA, Weight loss - 3 months	No	Yes Uncle	20	Cavity: Upper lobe Infiltrates: Three zones, left lung	+++	$2HREZ_3/4RH_3$
4	55/male	Yes/ plumber	Cough, fever, breathless - 2 weeks	No	No	17.5	Cavity: Upper lobe Infiltrates: Three zones both lungs	++	$2HREZM_7/2RHM_7$
5	28/male 91,814	Yes/driver	Cough 8 months, fever, LOA, haemoptysis, breathless - 1 month	No	Yes Father	17.8	Cavity: Upper lobe Infiltrates: One zone left lung	++	$2HREZM_7/2RHM_3$
6	56/male	Yes/retired	Cough, fever, chest pain - 2 weeks	No	No	14.5	Cavity: Nil Infiltrates: Three zones both lungs	+	$2HREZM_7/2RHM_7$
7	34/male	No/ electrician	Cough 6 months, breathless - 1 month	No	No	14.9	Cavity: Middle lobe Infiltrates: Four zones, both lungs	+	$2HREZM_7/2RHM_3$
8	50/male	Yes/ camera-man	Cough, fever, weight loss - 1 month	No	Yes Mother Brother	12.9	Cavity: Nil Infiltrates: Six zones both lungs	++	$3HREZM_7$
9	40/male	No/tailor	Cough, fever, breathless, chest pain - 3 weeks	No	No	16.1	Cavity: Nil Infiltrates: Five zones both lungs, right pleural effusion	++	$2HREZM_7/2RHM_3$

BMI: Body mass index, AFB: Acid fast bacilli, LOA: Loss of appetite, H: Isoniazid, R: Rifampicin, E: Ethambutol, M: Moxifloxacin, Z: Pyrazinamide, CXR: Chest X-ray, PTB: Pulmonary tuberculosis, TB: Tuberculosis

Table 2: Response to treatment and 24-month follow-up

Case number	Lowenstein-Jensen culture and HPLC species identification	Sputum culture converted	End of treatment					Follow-up till 24 months	
			Weight gain (kg)	Symptom	Sputum		CXR	Symptom	Sputum smears and culture
					Smear	Culture			
1	*M. kansasii*	1 month	8.0	Asymptomatic	Negative	Negative	Improvement	Free	Negative
2	*M. kansasii*	2 months	4.0	Asymptomatic	Negative	Negative	Improvement	Free	Negative
3	*M. kansasii*	2.5 months	6.0	Asymptomatic	Negative	Negative	Improvement	Free	Negative
4	*M. kansasii*	1.5 months	4.0	Asymptomatic	Negative	Negative	Improvement	Free	Negative
5	*M. kansasii*	1 month	2.0	Asymptomatic	Negative	Negative	Improvement	Free	Negative
6	*M. kansasii*	1 month	4.1	Asymptomatic	Negative	Negative	Improvement	9th month: Relapse with *M. kansasii, M. fortuitum, M. peregrinum* started retreatment and cured	
7	*M. kansasii* (DST showed H resistance)	2 months	4.0	Asymptomatic	Negative	Negative	Improvement	12th month: Relapse with H-resistant *M. kansasii* Started retreatment and cured	
8	*M. kansasii*	No, only smear converted	2.0	Asymptomatic	Negative	Positive	No change	Smears negative, culture, grew NTM <20 colonies 18th month, patient developed respiratory insufficiency and died	
9	*M. kansasii*	No	While on Rx, patient developed severe respiratory insufficiency due to extensive lung lesions and expired within a week					Not applicable	

DST: Drug susceptibility testing, NTM: Non-tuberculous mycobacteria, H: Isoniazid, HPLC: High-performance liquid chromatography *M. kansasii: Mycobacterium kansasii*, CXR: Chest X-ray, *M. fortuitum: Mycobacterium fortuitum, M. peregrinum: Mycobacterium peregrinum*

Similar to TB, *M. kansasii* lung disease presents with productive cough, heamoptysis, fever and loss of appetite.[1,2] Unilateral disease, right-sided involvement, cavity and lesser parenchymal infiltrate than *M. tuberculosis* are the most commonly reported CXR pattern.[4,6] Most of our patients were young, had symptoms of productive cough and fever with three having an episode of haemoptysis. All our patients had parenchymal infiltrates, with six of them having bilateral lesions and thin walled cavity in the upper lobe, mimicking TB disease.

Treatment against pulmonary TB should be instituted without delay when TB is suspected, even before the complete workup is available. Hence, all our 9 patients were started on anti-tuberculosis treatment (ATT), as per the trial protocol, before the results of sputum cultures revealed *M. kansasii*. However, as the treatment of *M. kansasii* consists of the same drugs as for *M. tuberculosis*, namely rifampicin, isoniazid and ethambutol, the patient got the benefit of ATT and started responding. Of our nine patients, five patients on short-duration ATT (three patients, cases 1, 2 and 3, received thrice-weekly regimen for 6-month [$2EHRZ_3/4RH_3$] and two patients, cases 4 and 5, received 4 months of moxifloxacin along with other drugs [$2EHRZM_7/2HRM$]) improved with satisfactory clinical, bacteriological and radiological clearance of the disease and were declared cured. Two patients on 4-month intermittent moxifloxacin regimen relapsed but got cured with retreatment of 12-month duration with multidrug regimen. One patient died early in the course of disease, due to extensive disease.

Currently, ATS and the Infectious Diseases Society of America recommend maintaining chemotherapy with a multidrug regimen, for 18 months or at least for 12 months after achieving sputum culture negativity for pulmonary NTM disease.[1] Another study concluded that a 12-month, fixed-course treatment with HRE (supplemented with streptomycin during first 2–3 months), is better in younger patients without debilitating conditions while longer periods of treatment, guided by periodic sputum cultures, is advisable for the rest to avoid relapse.[7] The British Thoracic Society recommends a 9-month course of rifampicin and ethambutol as treatment for *M. kansasii* lung disease in immunocompetent patients.[8] Like clarithromycin, moxifloxacin has also been shown to have activity against clinical isolates of *M. kansasii* and could be used as an alternative drug as well as short-course

or intermittent therapy of *M. kansasii* lung disease.[9,10] Whether relapses can be prevented with longer duration of treatment is not known. Cases considered as relapses may actually be exogenous re-infections. In fact, *M. kansasii* is a ubiquitous pathogen to which people may be repeatedly exposed and become infected more than once. It may, therefore, not be possible to avoid new episodes of active disease completely even with treatments of longer duration. However, in our present series, none of the seven patients alive relapsed till 24-month of post-treatment follow-up, which supports the idea that a shorter duration of treatment can be effective in the management of pulmonary *M. kansasii* disease.

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Conflicts of interest

There are no conflicts of interest.

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