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Clinical Characteristics and Treatment Outcomes of *Mycobacterium kansasii* Lung Disease in Korea

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Purpose: While *Mycobacterium kansasii* is a common cause of nontuberculous mycobacterial (NTM) lung disease in many developed countries, *M. kansasii* is infrequently isolated in Korea. We investigated the clinical and radiological features and treatment outcomes of *M. kansasii* lung disease in Korea retrospectively. **Materials and Methods:** We identified 41 patients with *M. kansasii* lung disease who met the diagnostic criteria for NTM lung disease in two tertiary referral hospitals in Seoul, Korea, between January 1998 and December 2007. **Results:** Their median age was 63 years [interquartile range (IQR) 51-75 years] and 33 (81%) were men. Twenty-three patients (56%) were smokers and 13 patients (32%) had previous pulmonary tuberculosis. The most common radiographic findings were nodules (n = 22, 54%) and consolidation (n = 22, 54%). Cavitation was present in 13 patients (32%). Thirty-one patients (76%) were treated with isoniazid, rifampin, and ethambutol. The median treatment duration was 16 months (IQR 9-18 months). The negative conversion rate after 12 months of treatment was 95%. **Conclusion:** Clinicians should be aware of the various radiographic manifestations of *M. kansasii* lung disease. With appropriate treatment, these patients have a good prognosis.

Key Words: Nontuberculous mycobacteria, *Mycobacterium kansasii*, treatment outcome

INTRODUCTION

Mycobacterium kansasii is the second most common nontuberculous mycobacteria (NTM) after the *Mycobacterium avium* complex in the United States and Japan,[1,2] and is the most common cause of NTM lung disease in the United Kingdom and Western Europe.[3,4] Infection with *M. kansasii* probably occurs via an aerosol route. Moreover, unlike other NTM, *M. kansasii* is much more difficult to recover from natural water supplies.[5] Tap water is likely a major reservoir for *M. kansasii* causing human infection, and thus an association may exist between clinical disease and potable water supplies.

Mycobacterium kansasii usually presents as lung disease that is nearly identical to tuberculosis. Cavitation was found in about 90% of cases in older reports,[6-8] while recent survey of 56 adults with *M. kansasii* lung disease in Israel between

1999 and 2004 noted cavitation in 54% only.[9] A variety of radiologic findings have been reported in *M. kansasii* lung disease, including non-cavitary or nodular/bronchiectatic lesions.[10,11]

In Korea, *M. kansasii* is infrequently isolated and a relatively uncommon cause of NTM lung disease.[12-15] Although small numbers of cases have been reported,[16,17] little is known about the detailed clinical and radiological characteristics or treatment outcomes in Korea. This study investigated the clinical and radiological features and treatment outcomes of *M. kansasii* lung disease in Korea.

MATERIALS AND METHODS

Study subjects

This retrospective study included 41 patients with *M. kansasii* lung infection who attended two tertiary referral hospitals in Seoul, Korea, between January 1998 and December 2007: Samsung Medical Center and Asan Medical Center. All patients met the diagnostic criteria of NTM lung disease,[1] and we reviewed their medical records and radiographs. This study was approved by the institutional review board of Samsung Medical Center and Asan Medical Center, both of which waived the requirement for informed consent of the individual patients due to the retrospective nature of the study.

Microbiological examination

Mycobacterial stains and cultures were performed using standard methods.[18] The results of smear microscopy were reported semiquantitatively. A positive smear was defined as one with > 1 acid-fast bacilli (AFB) per 100 high-power fields. Respiratory specimens were decontaminated using N-acetyl-L-cysteine/2% NaOH, and processed specimens were plated onto 3% Ogawa medium. Inoculated tubes were incubated at 37˚C and then inspected weekly for 8 weeks. To distinguish between *M. tuberculosis* and NTM, all AFB isolates were assessed according to growth rates, colony morphology, and pigmentation, as well as with a commercial polymerase chain reaction-based assay system (MTB-ID; M&D, Wonju, Korea). NTM species were identified using a polymerase chain reaction and restriction fragment length polymorphism methods based on the *rpoB* gene, as described previously.[14]

Evaluation of clinical and radiographic findings

The medical records of all study patients were reviewed, including information such as age, sex, body mass index (BMI), respiratory and constitutional symptoms, smoking history, underlying illness, pulmonary function tests, tuberculosis history, results for human immunodeficiency virus (HIV) antibody, and treatment history.

Chest radiographs and computed tomography (CT) images were those obtained closest in time to the date of the first positive respiratory culture result. The chest X-ray and CT images were evaluated in terms of the presence of nodules, consolidation, cavitation, and pleural effusion. In addition, hilar or mediastinal lymphadenopathy and bronchiectasis was evaluated on CT.

Nodules (≤ 3 cm in diameter) were considered present when a rounded opacity was observed, either well or poorly defined. Consolidation was defined as a homogeneous increase in pulmonary parenchymal attenuation that obscures the margins of vessels and airway walls. A cavity was regarded as present when a gas-filled space was seen within pulmonary consolidation, a mass, or a nodule. Bronchiectasis was defined as bronchial dilatation relative to the accompanying pulmonary artery, a lack of tapering of bronchi, and bronchi identified within 1 cm of the pleural surface.[19]

The distribution (upper vs. middle and lower lung zone) and laterality (unilateral vs. bilateral infiltrates) of the lung lesions were also analyzed. Lesions were considered to be in the upper zone of the lung if cephalad to the aortic arch, in the lower zone if caudad to the inferior pulmonary vein, and in the middle zone if between these two zones.[20]

Assessment of microbiological responses

Sputum conversion was defined as three consecutive negative cultures within 6 months, with the time of conversion defined as the date of the first negative culture. If the patient could not expectorate sputum during the treatment period, the sputum was considered to have converted to negative. Sputum relapse was defined as two consecutive positive cultures after sputum conversion.[21]

RESULTS

Clinical characteristics

The baseline characteristics of the patients are shown in Table 1. The median age was 63 years [interquartile range (IQR) 51-75 years] and 33 (81%) were men. Twenty-three (56%) patients were current or ex-smokers. None of the patients were HIV positive. Comorbid conditions included previous pulmonary tuberculosis in 13 (32%) patients, chronic obstructive pulmonary disease in 13 (32%), underlying malignancy in nine (22%), and diabetes mellitus in two (5%). The most common presenting symptoms were cough (n = 27, 66%) and sputum (n = 26, 63%). Ten (24%) patients had dyspnea and four (10%) had hemoptysis.

The diagnosis was confirmed by obtaining an adequate number of positive sputum cultures (n = 37, 90%). Patients,

Table 1. Clinical Characteristics of 41 Patients with *M. kansasii* Lung Disease

Variables	Number (%)
Age, yrs	63 (51 - 75)
Male	33 (81)
Body mass index, kg/m^2	20 (18.3 - 22.6)
Current or ex-smoker	23 (56)
Comorbid conditions	
Tuberculosis history	13 (32)
Chronic obstructive pulmonary disease	13 (32)
Malignancy	9 (22)
Diabetes mellitus	2 (5)
Symptoms at presentation	
Cough	27 (66)
Sputum	26 (63)
Dyspnea	10 (24)
Hemoptysis	4 (10)
Weight loss	2 (5)
Fever	2 (5)

The data are presented as the median (interquartile range) or number (%).

who were either unable to produce sputum or had negative sputum cultures, were diagnosed using bronchial aspirates (n = 3, 7%) or lung tissues (n = 1, 2%). Sputum AFB smear examinations were positive in 11 patients (27%). Testing for rifampin susceptibility was performed on *M. kansasii* isolates recovered from 28 patients and 89% (25/28) were susceptible to rifampin.

Radiographic and CT findings

All 41 patients had abnormal chest radiographic findings at the time of diagnosis (Table 2). The most common radiographic findings were nodules (n = 22, 54%) and consolidation (n = 22, 54%). Cavitation was present in 13 patients (32%) and pleural effusion in four (10%). Radiographic abnormalities were confined to the upper lung zones in 15 patients (37%), and 21 patients (51%) had bilateral disease.

A chest CT was available in 36 patients (88%). The most common CT finding was nodules (n = 25, 69%). Consolidation and cavitation were present in 16 patients each (44% each). Combined bronchiectasis was found in 12 patients (33%).

Management of patients

Ten (24%) patients did not receive anti-mycobacterial drugs after the diagnosis of *M. kansasii* disease. Of these, eight patients had mild symptoms and no significant change on their radiographs during the follow-up period. One patient was lost to the follow-up 1 month after the diagnosis. The upper lobar consolidation resolved spontaneously without antibiotic therapy in one patient (Table 3).

Table 2. Radiographic and CT Findings of 41 Patients with *M. kansasii* Lung Disease

Variables	Number (%)
Chest radiograph	
Nodules	22 (54)
Consolidation	22 (54)
Cavitation	13 (32)
Pleural effusion	4 (10)
Chest CT*	
Nodules	25 (69)
Consolidation	16 (44)
Cavitation	16 (44)
Hilar or mediastinal lymphadenopathy	3 (8)
Bronchiectasis	12 (33)
Pleural effusion	3 (8)
Distribution	
Upper lung zone(s)	15 (37)
Middle and/or lower lung zone(s)	9 (22)
Both	17 (41)
Unilateral	20 (49)
Bilateral	21 (51)

*Chest CT was available in 36 patients.

Table 3. Management of 41 Patients with *M. kansasii* Lung Disease

Management	Number (%)
Followed without antibiotic therapy	10 (24)
No significant changes	8
Improved	1
Lost to follow-up	1
Antibiotic therapy	31 (76)
Treatment completion and cure	16
Remained on the treatment	4
Lost to follow-up during treatment	9
Death during treatment*	2

*Two patients died of causes unrelated to *M. kansasii* lung disease during antibiotic therapy.

Thirty-one (76%) patients received antibiotic therapy including isoniazid, rifampin, and ethambutol. Of these, 16 patients completed the treatment and were followed for a median of 13 months (IQR 7-28 months) without relapse. Sputum relapse occurred after treatment completion in one patient who had no history of pulmonary tuberculosis and the isolate of *M. kansasii* was sensitive to rifampin. Four patients remained on the treatment as of the end of May 2009. Nine patients were lost to the follow-up after antibiotic therapy for a median of 6 months (IQR 2-10 months) and two patients died of causes unrelated to *M. kansasii* lung disease during antibiotic therapy (Table 3). Three

patients had rifampin-resistant *M. kansasii* lung disease. One patient was lost to follow-up after 1.5 months of therapy with isoniazid, rifampin, and ethambutol before drug susceptibility results were available. Treatment regimens were changed to clarithromycin and levofloxacin in two patients after the confirmation of resistance to rifampin. However, one patient was lost to the follow-up and the other patient died of causes unrelated to *M. kansasii* lung disease during antibiotic therapy.

The median time for negative culture conversion was 1 month (IQR 1-3 months) in patients who achieved negative conversion. For 21 patients who received antibiotic therapy for more than 12 months, the median treatment duration was 16 months (IQR 9-18 months) and the 12-month culture conversion rate was 95% (20/21).

DISCUSSION

In Korea, *M. kansasii* constitutes only 2-4% of NTM organisms isolated from clinical specimens,[13-15] although the isolation of *M. kansasii* has increased steadily in recent years.[15] In this study, we found that *M. kansasii* lung disease had diverse radiographic findings. Nodules and consolidation were the most common radiographic features, while cavitation was seen on the chest X-ray in only 32% of patients. A rifampin-containing three-drug regimen was effective, especially in patients treated for more than 12 months.

The radiographic features of *M. kansasii* lung disease are frequently reported as being indistinguishable from those of tuberculosis.[8,22,23] Older studies found cavitation in 75-96% of patients with *M. kansasii* lung disease,[3,8,23-25] while the proportion of cavitary lesions was about 50% in recent studies.[9,17] In our series, cavitation was seen in only 32% of patients on chest X-rays. This discrepancy might be explained by recent improvements in the diagnosis and microbiological isolation of the organism.[9] Moreover, some studies have reported that patients with *M. kansasii* lung disease can present with non-cavitary or nodular/bronchiectatic lesions as a major features of *M. avium* complex lung disease, which is the most common etiology of NTM lung disease.[3,10,11]

In addition to the low proportion of cavitation, we found that *M. kansasii* lung disease had diverse radiographic features. Upper lobe lesions were not predominant and pleural effusions were seen in four patients (10%). NTM infection is rarely accompanied by pleural involvement, although a few case reports have described pleural effusion caused by *M. kansasii*.[26-28] Pleural effusion was associated with parenchymal consolidation in three of four patients in our study. On the chest CT, more nodular and cavitary lesions surrounded by consolidation were found in these patients.

Regarding the antibiotic treatment for *M. kansasii* lung disease, a three-drug combination consisting of isoniazid, rifampin, and ethambutol is recommended and these antibiotics should be maintained for at least 12 months after negative sputum conversion.[1] The key to successful therapy for *M. kansasii* lung disease is to include rifampin in a multidrug regimen. Adding isoniazid and ethambutol to rifampin is essential for preventing the emergence of resistance to rifampin.[9]

A prospective trial of 28 patients compared treatment for 12 or 18 months with this three-drug regimen.[29] Only one relapse occurred; the patient was in the 12-month chemotherapy group. In a series of 56 adults with *M. kansasii* lung disease in Israel, the mean treatment duration was 21 ± 7 months.[9] Another case series of 75 patients with *M. kansasii* lung disease in Spain showed that a 12-month multidrug treatment regimen, including isoniazid, rifampin, and ethambutol, supplemented with streptomycin during the first 2-3 months, was effective in most cases of *M. kansasii* lung disease, although five patients (7%) relapsed.[30]

We found that the rifampin-based multidrug regimen was effective, especially in patients treated for more than 12 months. Those patients had a 95% culture conversion rate after a median treatment duration of 18 months. Relapse occurred in one patient. However, the relapse rate may be an underestimate because the loss to follow-up was high in our study.

In summary, the radiographic characteristics of *M. kansasii* lung disease in recently diagnosed patients are diverse in Korea. Nodules and consolidation are found more frequently than cavitary lesions. A three-drug combination regimen containing rifampin for more than 12 months is effective in patients with *M. kansasii* lung disease.

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