

Mycobacterium kansasii Pulmonary Diseases in Korea

Mycobacterium kansasii is one of the most common cause of pulmonary diseases due to nontuberculous mycobacteria. We investigated the changing in the number of isolation of *M. kansasii* and the clinical characteristics of *M. kansasii* pulmonary disease in Korea. Through searching the database of the Korean Institute of Tuberculosis, we identified the cases of isolated *M. kansasii* from 1992 to 2002. The number of *M. kansasii* isolation had increased from once in 1992 to 62 in 2002. Fifteen patients with *M. kansasii* pulmonary disease were identified during the period January 1997 to December 2002. Twelve patients (80%) were male and fourteen (93%) were from highly industrialized areas. The most common symptom was a cough. Seven patients (47%) had a cavitory lesion and right upper lobe was most commonly involved. Patients responded well to isoniazid and rifampicin based regimens both bacteriologically and radiographically. In conclusion, *M. kansasii* isolation has increased, especially in highly industrialized areas, as well as other nontuberculous mycobacteria in Korea.

Key Words : *Mycobacterium kansasii*; *Mycobacterium Infections*, Atypical; *Mycobacteria*, Atypical; Korea

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INTRODUCTION

Mycobacterium kansasii is a slow growing photochromogen, usually isolated from various water sources (1-4). *M. kansasii* is the second most commonly isolated nontuberculous mycobacteria (NTM) after *M. avium-intracellulare* in the United States and Japan (5-8). Furthermore, it is the most common NTM in some areas (9, 10).

The incidence or detection of the disease caused by NTM usually increases with decreasing the prevalence of tuberculosis (TB). Although the prevalence of active TB has dramatically decreased from 5.1% in 1965 to 0.5% in 2002 (11) during the past 40 yr in Korea, there has been no recent report on the change of the annual numbers of NTM isolation including *M. kansasii*. In this study, we evaluated changes in the number of *M. kansasii* isolation and examined the clinical characteristics of patients with pulmonary disease due to *M. kansasii* in Korea.

MATERIALS AND METHODS

Isolation of *M. kansasii*

To determine the annual number of isolation of *M. kansasii*

in clinical samples, we searched the database of the Korean Institute of Tuberculosis, the referral tuberculosis laboratory. The identification of individual NTM has only been possible because the Korean Institute of Tuberculosis started to identify individual species of NTM through 1992 to 2002; thus we searched the database from 1992 to 2002 and collected data on the annual isolations of the each species of NTM including *M. kansasii*. During the period from 1992 to 2000, mycobacterial species identifications were performed by the traditional biochemical method (12). From January 2001, the species identification of mycobacteria was performed by the PCR-restriction fragment length polymorphism (RFLP) of the polymorphic region of the *rpoB* gene (13).

M. kansasii pulmonary disease

We identified patients from whom *M. kansasii* was isolated from January 1997 to December 2002. Among these, patients with a *M. kansasii* positive culture on 2 or more times were defined to have a *M. kansasii* pulmonary disease as suggested before (9). A questionnaire was sent to the responsible physicians, which requested details on; demographic patient characteristics, symptoms, signs, laboratory findings, radiographic findings, treatment regimen, and treatment response.

Patients with positive *M. tuberculosis* culture in the same period, incomplete clinical record were excluded for the analysis, and patients with no response to isoniazid and rifampicin-based chemotherapies were also excluded, because we wanted to exclude those NTM simply colonized in their lungs with previous tuberculosis sequelae.

RESULTS

The number of isolation of *M. kansasii* and other NTM

The total number of mycobacterial colonies referred to Korean Institute of Tuberculosis for identification decreased from 18,970 in 1992 to 5,181 in 2002. In 1992, *M. kansasii* was identified once (0.2%) from among 448 NTM, and this increased to 62 times (3.6% out of 1,737 colonies) in 2002. During the same period, the number of NTM detections increased from 448 to 1,737. *M. avium-intracellulare* was found to be the most common through 1992 to 2002, and showed an increasing tendency. *M. fortuitum*, *M. abscessus* and *M. goodii* were also found to increase.

M. kansasii pulmonary diseases

During the period January 1997 to December 2002, *M. kansasii* was isolated 204 times from 150 patients. Among these, the number of patients positive for *M. kansasii* by culture 2 or more times was 30. Among these 30 patients, we excluded 7 from analysis because of insufficient clinical data and another 2 due to a positive *M. tuberculosis* culture in same period. Of the other 21 patients, 6 patients were excluded

because their pulmonary lesion in chest radiographs did not improve after at least 6 months of isoniazid and rifampicin-based treatment. Even though *M. kansasii* was isolated more than twice from the sputum of these 6 patients, we decided that in these patients *M. kansasii* might be a colonizer rather than a true pathogen.

Among the 150 patients positive for *M. kansasii*, 76 (51%) lived in Seoul, the largest city in Korea (Fig. 1A). Other highly industrial cities such as, Ulsan (18 patients, 12%), Busan (16 patients, 11%) and Incheon (16 patients, 11%) were also represented. The other patients came also from highly industrialized areas or large cities, only 4 patients lived in rural areas. Fourteen of 15 patients with *M. kansasii* pulmonary disease were from highly industrialized cities (Fig. 1B).

The median age of the 15 patients with *M. kansasii* pulmonary disease was 41 yr (range; 26-70) and 12 were men (Table 1). 75% of them were current or ex-smokers and 9 (60%) had a history of previous tuberculosis. Two patients had been diagnosed as having bronchiectasis. Their most common symptom was a cough, of which eight (53%) patients complained; hemoptysis, dyspnea, and fatigue followed. Seven (47%) of 15 patients had cavitory lesions in chest radiographs, 7 patients had nodulostreaky lesions and 1 had consolidation without a cavity. The most frequently involved lung site was the right upper lobe, 52% of all described lesion was found in the right upper lobe.

A combination of isoniazid, rifampicin, pyrazinamide and ethambutol were prescribed initially for 11 patients, and streptomycin was used in combination with these for another 1 patient. Rifampicin, cycloserine, prothionamide and ofloxacin were prescribed initially in one, rifampicin, pyrazinamide, ethambutol and ofloxacin in another, and rifampicin, pyrazi-

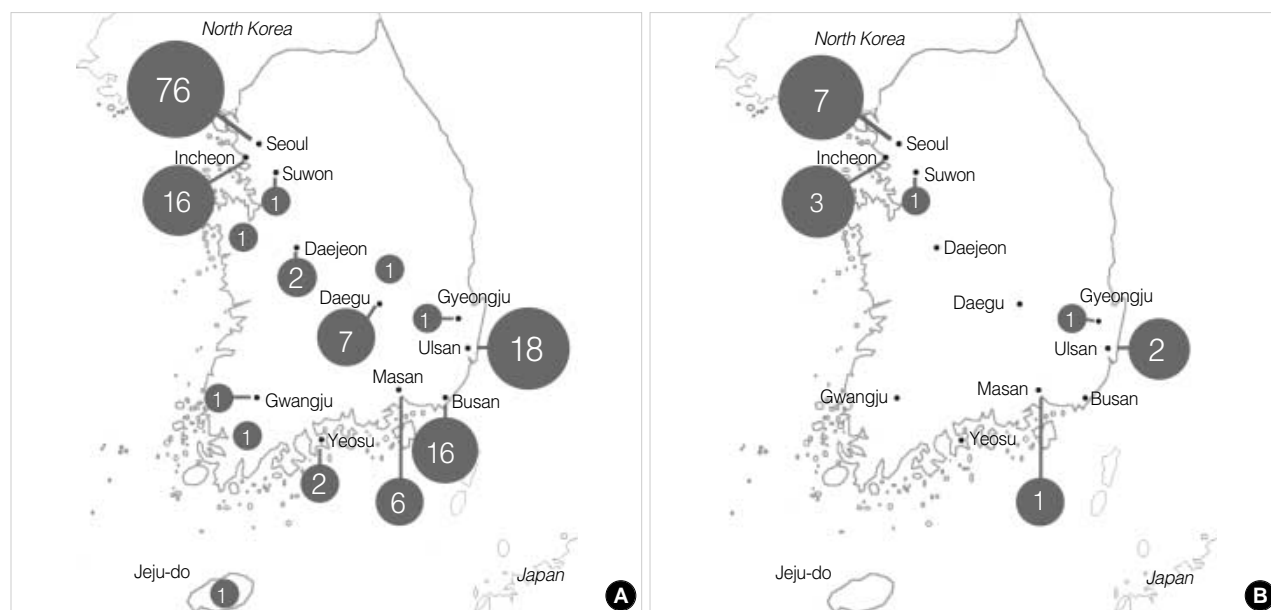


Fig. 1. Geographic distribution of patients with a *M. kansasii* positive culture (A) and probable *M. kansasii* pulmonary disease (B). Patients not matched with a city were from rural areas.

Table 1. The number of NTM isolates from clinical specimens requested for the identification to the Korean Institute for Tuberculosis, 1992-2002

Organism \ year	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002
<i>M. kansasii</i>	1	9	21	18	16	12	22	26	35	47	62
<i>M. avium-intracellulare</i>	245	302	329	287	266	253	551	499	593	693	769
<i>M. fortuitum</i>	49	66	60	41	27	20	47	62	56	92	184
<i>M. chelonae</i> complex	32	34	43	55	23	28	63	92	88	166	279
<i>M. chelonae</i>	n-a	n-a	n-a	n-a	n-a	n-a	n-a	n-a	n-a	8	18
<i>M. abscessus</i>	n-a	n-a	n-a	n-a	n-a	n-a	n-a	n-a	n-a	158	261
<i>M. scrofulaceum</i>	1	3	15	2	3	0	4	0	0	0	2
<i>M. terrae</i> complex	14	25	43	27	8	5	32	25	35	3	52
<i>M. szulgai</i>	3	2	9	5	0	6	6	13	18	12	15
<i>M. goodii</i>	5	12	21	10	15	9	22	39	18	31	126
<i>M. celatum</i>	0	0	0	0	0	0	12	8	11	7	10
<i>M. marinum</i>	0	0	0	0	0	2	1	0	1	1	0
<i>M. smegmatis</i>	0	0	0	0	0	0	0	0	0	0	0
Unidentifiable	98	250	608	403	558	752	422	400	314	559	63
Total	448	791	1,149	848	916	1,087	1,182	1,164	1,169	1,611	1,737

*n-a, non-applicable.

namide, cycloserine, and prothionamide in the remaining patient. The median duration of treatment was 10.5 months, 3 patients experienced hepatotoxicity, and one of these was moved on to other regimen. Three patients experienced myalgia, pruritus or gastrointestinal disturbance, respectively. In 10 of 15 patients with *M. kansasii* pulmonary diseases, a follow-up mycobacterial culture was performed. Negative conversion of the mycobacterial culture was observed in all 10 patients at 4.0 months (median). In another 3 patients, only follow-up AFB smears were performed, and smear conversion was reported in all 3 at 2.0 months (median) after the initiation of treatment. Neither a subsequent AFB smear nor a culture was performed in the other 2 patients.

Complete resolution of the radiographic lesion was observed in 2 patients, one of these had a cavitary lesion, and the other had a nodulo-streaky lesion. The other 13 patients experienced definite radiographic improvement, but incomplete resolution.

DISCUSSION

M. kansasii is a slow growing photochromogen, which grows over a temperature range from 32 to 42°C. The biochemical identification of *M. kansasii* has been based on its ability to produce catalase and nitrate reductase, and to hydrolyze Tween 80 (14). *M. kansasii* has been recovered from water sources. Drinking water distribution systems, tap water and shower heads has been reported to be sources of *M. kansasii* (1-4). These reports of *M. kansasii* isolations from water distribution systems, and the fact that this organism can survive in water for up to 12 months (15) support the hypothesis that infection by *M. kansasii* occurs via an aerosol route (16).

Our results show that the number of isolation of NTM increased from 448 in 1992 to 1,562 in 2002, while the prevalence of active TB over the same period decreased from 1.8%

to 0.5% (11). This increase could be due, more probably, to the advances in laboratory methodology and physicians' concern for NTM rather than the decreased prevalence of tuberculosis. In addition, the number of isolation of NTM could be biased because not all mycobacterial colonies isolated had been requested to Korean Institute of Tuberculosis. However, the fact that the total number of mycobacterial colonies requested for identification decreased from 18,970 in 1992 to 5,181 in 2002 suggests the possibility of real increase of NTM prevalence in Korea.

Pulmonary disease caused by *M. kansasii* is known to be more common in urban areas than in rural areas (10, 17), which concurs with our findings. The Korean patients with *M. kansasii* in the lung, regardless as to whether it was as a pathogen or as a colonizer, were predominantly living in highly industrialized cities. Half of the patients with *M. kansasii* lived in Seoul, the largest Korean city of over 10 million people, the next most common location was Ulsan, which is the 7th largest city in Korea, but is heavily industrialized. Other cities represented were Incheon and Busan, which are also highly industrialized. In contrast, few patients were found to be domiciled in the cities of south-west and north-east region of Korea, where agriculture remains the main occupation. This distribution is in accord with a Japanese observation published in 1983 (18) and a study, which reported that 56% of patients with *M. kansasii* pulmonary disease were employed in heavy industry (19).

The clinical characteristics of *M. kansasii* pulmonary disease patients in the present study were similar to those of previous reports including Korean cases (10, 19, 20). Thus, the present study confirms an association between *M. kansasii* pulmonary disease with, a male gender, an urban setting, a history of tuberculosis or of another lung disease as a risk factor, a cough as a common symptom, the presence of a cavitary lesion usually in the right upper lobe, and a response to an isoniazid

and rifampicin based regimen

In conclusion, the number of *M. kansasii* isolation seems to be increasing in Korea. Most of the patients were domiciled in industrialized urban communities, and the clinical characteristics of the patients were similar to those reported previously.

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