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Increasing Burden of Nontuberculous Mycobacteria in Korea

Nontuberculous mycobacteria (NTM) are diverse microorganisms of genus Mycobacterium other than M. tuberculosis complex and M. leprae, which are ubiquitous in the environment such as tap water, swimming pools, natural water, room dust, and soil (1). NTM species has been relatively neglected compared to M. tuberculosis complex because NTM species rarely causes human infectious diseases and human-to-human transmission has never been reported to date. However, some of NTM species may cause pulmonary, lymphatic, skin, soft tissue, disseminated, and bone diseases in humans (2).

In the current issue of this journal, Kim et al. (3) reported that the annual rates of NTM isolation increased steadily from 23.9% in 2009 to 48.2% in 2015, at tertiary referral hospitals, south-eastern region of Korea. In addition, the incidence of NTM disease increased significantly from 6.8 to 12.9 per 100,000 patients during the same period, most of which was associated with pulmonary NTM disease (93.1%). Especially, the number of patients with pulmonary NTM disease per 100,000 patients increased over the study period, whereas the number with extrapulmonary NTM disease remained unchanged. This trend of increasing NTM isolation was also observed at other tertiary referral hospitals in Korea, the rates of which increased steadily from 21%-43% in the early 2000s to 47%-70% in the early 2010s (4-8). Moreover, the incidence of pulmonary NTM disease has been increasing worldwide including Korea (9,10).

To date, however, the cause of this increasing trend remains unclear. The increasing rate of NTM isolation and disease is considered to be inversely associated with the decreasing rate of tuberculosis (TB) burden. This explanation is supported by Ide et al.'s study (11) reporting that the incidence of pulmonary NTM disease increased gradually from 4.6 to 10.1 per 100,000 people between 2001 and 2009 in Nagasaki, Japan, whereas the incidence of TB decreased from 32.9 to 22.1 per 100,000 people. On the contrary, the incidence of TB in Korea increased from 86 to 95 per 100,000 people over the same period, despite of the increased rate of NTM isolation and disease. This suggested that the distinct feature of pulmonary NTM disease in Korea as compared with that in Japan was the relatively high percentage of patients with a history of TB, leading to the speculation that structural lung damage by TB infection renders the host vulnerable to NTM disease rather than that exposure to TB provides crossprotection to NTM disease (9). The development of NTM dis-

ease has been reported to be associated with two distinct groups of risk factors (2): 1) host factors such as structural lung disease (e.g., chronic obstructive lung disease, and cystic fibrosis), history of TB, genetic susceptibility, immune defects (e.g., human immunodeficiency virus infection and immunosuppressive drugs), demographic characteristics (e.g., advanced age and male sex), lower body mass index, and higher comorbidity level; 2) environmental factors such as geographic characteristics (e.g., humidity and altitude) and aerosolized water exposure (e.g., showers and hot tubs). Collectively, combination of both host and environmental risk factors could contribute to this increasing trend of NTM isolation and disease.

Analyzing NTM species according to their isolation site, the authors (3) further reported that the most commonly isolated species among pulmonary specimens were M. intracellulare (38.9%), followed by M. avium (23.1%), M. abscessus (8.4%) and M. kansasii (7.7%), whereas those among extrapulmonary specimens were M. avium (25.0%), followed by M. fortuitum complex (20.9%) and *M. intracellulare* (16.6%). This is in line with previous studies from Korea (4,5,7,8,12). M. abscessus-massiliense complex is the second most common etiologic organism in pulmonary NTM disease in Korea (12). Because M. abscessus and *M. massiliense* are equally distributed within this complex in Korea and the treatment success rate is significantly higher in pulmonary NTM disease caused by M. massiliense compared to M. abscessus, precise identification of M. abscessus-massiliense complex to subspecies-level is very important. Sequencing of the hsp65, rpoB, and 16S-23S rRNA internal transcribed spacer genes is necessary, but these molecular methods are more costly and time-consuming. In the future, matrix-assisted laser desorption/ionization-time of flight mass spectrometry could be a rapid identification method for differentiation between M. abscessus and M. massiliense in clinical microbiology laboratories (13).

In conclusion, the rate of NTM isolation and disease has been increasing steadily in Korea. The most commonly isolated NTM species are M. avium-intracellulare complex and M. abscessusmassiliense complex. Therefore, the notification of NTM disease and the introduction of rapid method for subspecies-level identification of NTM to improve treatment success and prognosis of NTM disease are warranted in Korea.

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DISCLOSURE

The authors have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTION

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