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Thin-Section CT Findings of Nontuberculous Mycobacterial Pulmonary Diseases: Comparison Between *Mycobacterium avium-intracellulare* Complex and *Mycobacterium abscessus* Infection

We aimed to compare the CT findings of nontuberculous mycobacterial pulmonary diseases caused by *Mycobacterium avium-intracellulare* complex (MAC) and *Mycobacterium abscessus*. Two chest radiologists analyzed retrospectively the thin-section CT findings of 51 patients with MAC and 36 with *M. abscessus* infection in terms of patterns and forms of lung lesions. No significant difference was found between MAC and *M. abscessus* infection in the presence of small nodules, tree-in-bud pattern, and bronchiectasis. However, lobar volume decrease (p=0.001), nodule (p=0.018), airspace consolidation (p=0.047) and thin-walled cavity (p=0.009) were more frequently observed in MAC infection. The upper lobe cavitary form was more frequent in the MAC (19 of 51 patients, 37%) group than *M. abscessus* (5 of 36, 14%) (p=0.029), whereas the nodular bronchiectatic form was more frequent in the *M.* abscessus group ([29 of 36, 81%] vs. [27 of 51, 53%] in MAC) (p=0.012). In conclusion, there is considerable overlap in common CT findings of MAC and *M. abscessus* pulmonary infection; however, lobar volume loss, nodule, airspace consolidation, and thin-walled cavity are more frequently seen in MAC than *M. abscessus* infection.

Key Words : *Mycobacteria, Atypical; Bronchiectasis; Bronchiolitis; Tomograph, X-ray Computed; CT, thin-section; Mycobacterium avium; Mycobacterium abscessus; Tuberculosis*

Myung Jin Chung, Kyung Soo Lee, Won-Jung Koh*, Ju Hyun Lee, Tae Sung Kim, O Jung Kwon*, Seonwoo Kim†

Department of Radiology and Center for Imaging Science; Division of Pulmonary and Critical Care Medicine*, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul; Biostatistics Units†, Samsung Biomedical Research Institute, Seoul, Korea

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Address for correspondence
Kyung Soo Lee, M.D.
Department of Radiology, Samsung Medical Center, Sungkyunkwan University School of Medicine, 50 Ilwon-dong, Gangnam-gu, Seoul 135-710, Korea
Tel : +82.2-3410-2518, Fax : +82.2-3410-2559
E-mail : kyungs.lee@samsung.com

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INTRODUCTION

Nontuberculous mycobacterial (NTM) organisms are widely distributed in the environment and the frequency of NTM pulmonary disease has been reported to be increasing (1, 2). NTM species are divided into slow-growing and rapid-growing species by the Runyon classification (2). Representatives of the slow-growing species include; *M. avium*, *M. intracellulare (Mycobacterium avium-intracellulare* complex: MAC) and *M. kansasii*, while those of the rapid-growing species include; *M. abscessus*, *M. fortuitum* and *M. chelonae*. In the United States, MAC species accounts for more than two thirds of NTM pulmonary diseases caused by slow-growing organisms and *M. abscessus* accounts for most pulmonary diseases caused by rapid-growing organisms (3-5). In Korea, MAC and *M. abscessus* represent the common pathogen in NTM lung disease and *M. kansasii* is relatively uncommon (6-10).

The CT findings of MAC pulmonary disease have been reported and are well known (11-14). Recently CT findings of *M. abscessus* were reported (15). According to these reports, CT findings of pulmonary diseases caused by the organisms of two species are mainly bronchiolitis of tree-in-bud pattern and bronchiectasis (11-16). However, no study has directly compared the CT findings of the pulmonary diseases caused by these two pathogens. Moreover, the treatment of pulmonary disease caused by these organisms is totally different. The pulmonary disease caused by *M. abscessus* needs intravenous antimycobacterial chemotherapy necessitating hospitalization for several weeks, whereas that caused by MAC needs oral antimycobacterial therapy on outpatient basis (2, 5). Therefore, CT differentiation between the diseases caused by these species before definite diagnosis by microbiological culture is important for treatment. In this study, we aimed to analyze the thin-section CT findings of pulmonary NTM diseases caused by MAC and *M. abscessus* and to compare the findings of the two groups.

MATERIALS AND METHODS

Patient selection

Between July 1999 and March 2004, we diagnosed a total of 105 patients with NTM pulmonary diseases and who underwent chest CT. Of these 105 patients, 51 patients had MAC infection; 25 men with mean ages, 66 yr (range; 46-87 yr) and 26 women with mean ages, 56 yr (range; 25 to 74 yr). Thirty-six had *M. abscessus* infection; 9 men with mean ages, 51 yr (range; 21-75 yr) and 27 women with mean ages, 56 yr (range; 32-77 yr). Of the remaining 18 patients, seven had *M. kansasii* infection, six M. *fortuitum* complex, two *M. chelonae*, two *M. szulgai*, and one *M. celatum*.

We retrospectively reviewed the CT findings of these 87 patients with MAC and *M. abscessus* infection. The 87 patients met the diagnostic criteria of the American Thoracic Society inclusion criteria for NTM pulmonary disease: 1) clinical signs and symptoms; 2) compatible radiologic findings; and 3) multiple positive sputum cultures, recovery of NTM in large amounts on microbiologic smears and cultures of bronchoscopic samples, or compatible histopathology with a positive NTM culture (2).

The interval between the isolation of MAC and initial CT examination ranged from 0 to 328 days (mean, 22 days; median, 0 day), whereas that between the isolation of *M. abscessus* and initial CT examination ranged from 0 to 173 days (mean, 10 days; median, 0 day).

CT Imaging evaluation

All CT examinations were obtained using a Light Speed Advantage Q/xi Scanner (General Electric Medical Systems, Milwaukee, WI, U.S.A.). None of the patients were administered an intravenous injection of contrast medium. All CT data were reconstructed using a bone algorithm. Helical volumetric scan data, using multidetector-row CT (120 kVp, 70 mA, 2.5-mm collimation, and pitch of 0.875), were obtained through the thorax. Data were reconstructed with 2.5-mm thickness for transaxial images. The scan data were directly displayed on monitors (four monitors, 1,536 × 2,048 image matrices, 8-bit viewable gray scale, and 60-ft-lambert luminescence) of a picture archiving and communication system (PACS) (Centricity 1.0, General Electric Medical Systems Integrated Imaging Solutions, MT. Prospect, IL, U.S.A.). On the monitors, both mediastinal (window width, 400 H; window level, 20 H) and lung (window width, 1,500 H; window level, -700 H) window images were available for analysis.

Two chest radiologists (T.S.K. and M.J.C. with seven and six years of experience, respectively), who were unaware of any clinical information, except that the patients had NTM pulmonary disease, assessed the CT images together, and reached final decisions by consensus. The presence of the patterns of parenchymal abnormalities in each lobe (six lobes: the right upper lobe, right middle lobe, right lower lobe, left upper lobe, lingual segment, and left lower lobe) in each patient was recorded. The evaluated patterns of parenchymal abnormalities included well-defined small nodules (less than 10 mm in diameter), branching centrilobular nodules (tree-in-bud pattern), nodules of 10-30 mm in diameter, airspace consolidation, thin-walled (less than 5 mm in thickness) cavities, bronchiectasis, and volume decrease. Regardless of size or distribution [lobular (0.5-3.0 cm in diameter and polygonal), segmental (pleura-based and polygonal or truncated-cone appearance), or peribronchial (along the bronchovascular bundles)], all forms of consolidation were grouped into airspace consolidation. When a nodule contained cavity, it was designated a cavitary nodule, and when consolidation contained cavity, it

Fig. 1. A 66-yr-old man with *M. avium-intracellulare* complex pulmonary disease. (A) Transaxial thin-section (2.5-mm thickness) CT scan obtained at level of great vessels shows multiple large thin-walled cavities in both lung apices. Also note several small nodules (arrows) in right lung. (B) CT (2.5-mm thickness) scan obtained at level of suprahepatic inferior vena cava shows multiple small nodules and branching centrilobular nodules, so-called tree-in-bud pattern (arrows), in lingular segment of left upper lobe and left lower lobe. Small nodule (arrowhead) is also seen in right middle lobe.

was designated a cavitary consolidation. In addition, the presence of mediastinal or hilar lymph node enlargement and pleural effusion or thickening was recorded.

The laterality (unilateral or bilateral) and the locations of lung lesions were also analyzed. A total of 306 lung lobes in 51 patients (six lobes per patient; the lingual segment was taken as a separate lobe) with MAC infection and 216 lobes in 36 patients with *M. abscessus* infection were evaluated for the presence of lung lesions. Each lung lobe was evaluated with regard to the presence or absence of each parenchymal abnormality.

After analyzing the pattern and distribution of parenchymal abnormalities at CT, diseases were classified into three forms: upper lobe cavitary, nodular bronchiectatic, and an un-

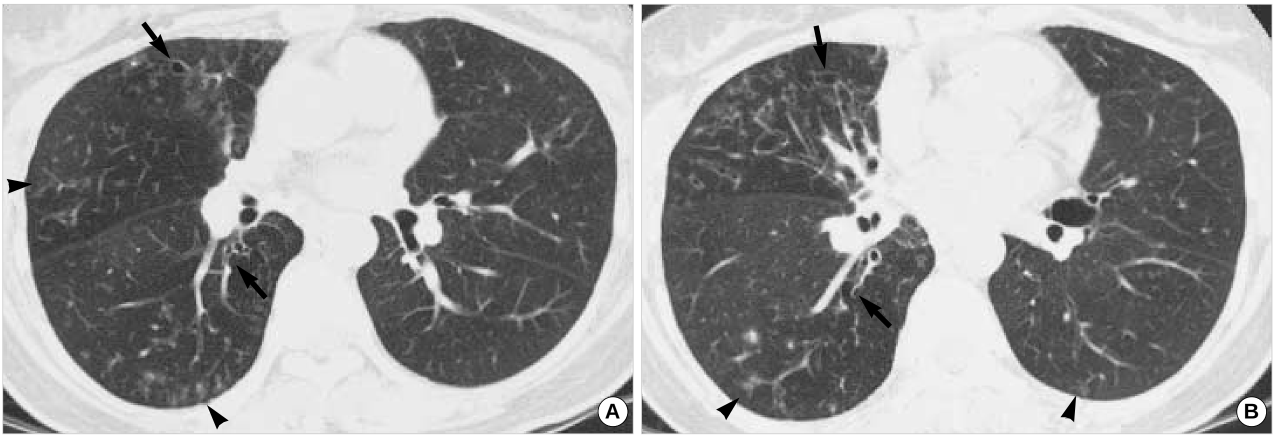
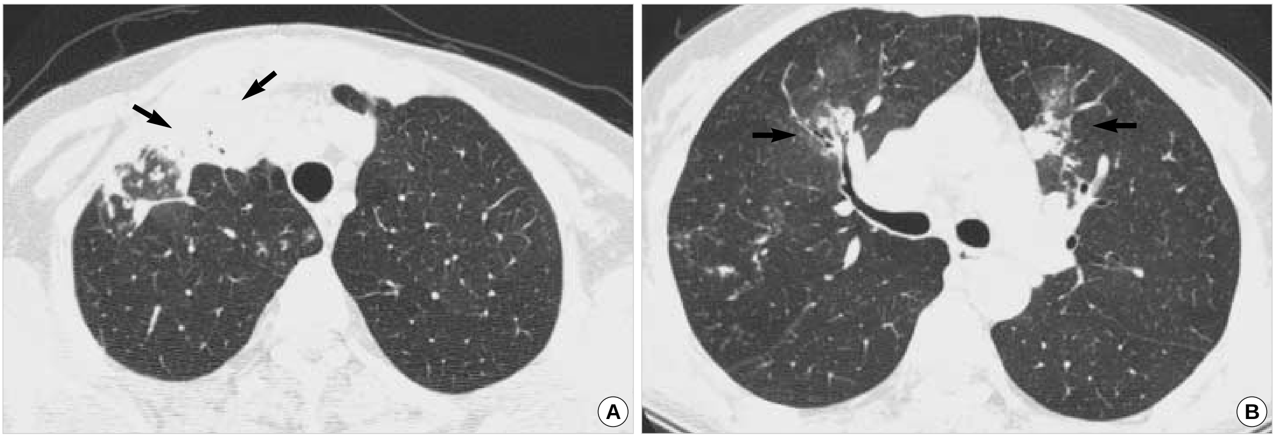


Fig. 2. A 45-yr-old woman with *M. abscessus* pulmonary disease. (A) Transaxial thin-section (2.5-mm thickness) CT scan obtained at level of proximal lower lobar bronchus shows bronchiectasis (arrows) and multiple small nodules and branching centrilobular nodules, so-called tree-in-bud pattern (arrowheads) in right lung. (B) CT (2.5-mm thickness) scan obtained at level of basal trunk shows bronchiectasis (arrows) and multiple small nodules and branching centrilobular nodules, so-called tree-in-bud pattern (arrowheads) in both lungs.



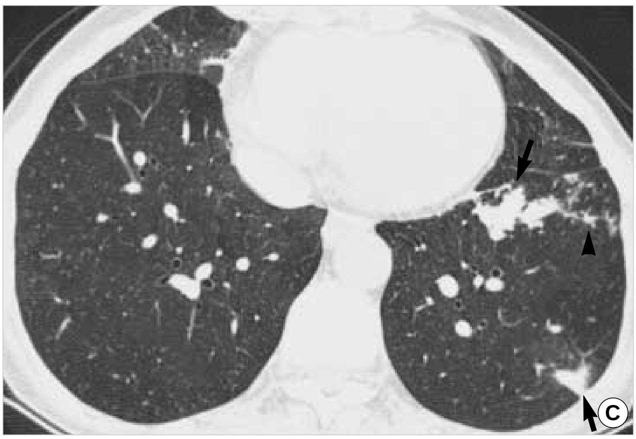


Fig. 3. A 52-yr-old woman with *M. avium-intracellulare* complex pulmonary infection. (A) Transaxial thin-section (2.5-mm thickness) CT scan obtained at level of great vessels shows subsegmental consolidation with open bronchus sign in right upper lobe (arrows). (B) CT (2.5-mm thickness) scan obtained at level of right upper lobar bronchus shows airspace consolidation with surrounding ground-glass opacity (arrows) along bronchovascular bundles in anterior segments of both upper lobes. Also note small nodules in right upper lobe. (C), CT (2.5-mm thickness) scan obtained at lung base shows lobular consolidation in left lower lobe (arrows). Also note lesion of tree-in-bud pattern (arrowhead) in left lower lobe and small nodules in right middle lobe.

Table 1. Laterality and distribution of parenchymal lesions in patients with MAC (n=51) and *M. abscessus* (n=36) disease

	MAC (n=51)									*M. abscessus* infection (n=36)								
	Laterality+		RUL	RML	RLL	LUL	Li	LLL	Sum*	Laterality+		RUL	RML	RLL	LUL	Li	LLL	Sum*
	Uni	Bi								Uni	Bi							
Small nodules	13	21	25	22	18	15	12	17	109	15	15	18	14	21	14	10	16	93
Tree-in-bud pattern	13	20	22	20	17	13	12	15	99	15	15	18	14	21	14	10	16	93
Bronchiectasis	13	35	39	32	23	21	28	22	165	11	22	23	22	18	14	18	19	114
Volume decrease	11	10	11	13	1	3	8	1	37	2	1	1	2	0	0	1	0	4
Nodule	6	4	3	5	3	2	2	4	19	1	0	0	1	0	0	0	0	1
Cavitary nodule	13	7	10	3	9	7	3	6	38	7	1	4	0	2	3	1	0	10
Airspace consolidation	12	13	9	7	10	8	6	10	50	7	3	4	1	3	4	0	4	16
Cavitary consolidation	4	1	1	1	3	2	0	1	8	1	1	2	0	0	1	0	0	3
Thin-walled cavity	17	3	14	0	1	9	0	0	24	5	0	3	0	0	2	1	0	6

MAC, *Mycobacterium avium-intracellulare* complex; Uni, unilateral; Bi, bilateral; RUL, right upper lobe; RML, ight middle lobe; RLL, right lower lobe; LUL, left upper lobe; Li, lingular segment; LLL, left lower lobe; +, number of patients; *, number of involved lobe (of total 306 lobes in MAC and 216 lobes in *M. abscessus* infection).

classifiable form. The upper lobe cavitary form was defined when thin-walled cavity (or cavities) were present in the upper lobes with findings of emphysematous change in the lower lung zones with or without volume decrease of the upper lobes and apical pleural thickening (2) (Fig. 1). The nodular bronchiectatic form was defined when bilateral bronchiectasis and bronchiolitis were present, irrespective of the presence of cavities in both lungs. However, in this form, there was neither upper lobar volume loss nor emphysematous change in the remaining lungs (2) (Fig. 2). When the disease did not belong to either the upper lobe cavitary or the nodular bronchiectatic form, it was deemed unclassifiable. In this form, multi-focal lobular or segmental consolidation or consolidation along the bronchovascular bundles was seen (Fig. 3).

We evaluated difference in male to female ratios in MAC and *M. abscessus* infections using the chi-square test. The difference in forms (upper lobe cavitary, nodular bronchiectatic and unclassifiable) in MAC and *M. abscessus* infection was compared using the Fisher's exact test. The significance of differences in the presence of each pattern of parenchymal abnormality in the MAC and *M. abscessus* pulmonary diseases was tested using the Mann-Whitney test. We tested difference in the extent of involvement (i.e., the number of involved lobes) of each pattern of parenchymal abnormality between the two groups using the chi-square test.

RESULTS

Women were more frequently affected than men (p=0.003) in *M. abscessus* infection, whereas there was no sex difference in MAC infection (p=0.889).

Nineteen (37%) of 51 MAC patients had the upper lobe cavitary form, 27 (53%) the nodular bronchiectatic form, and 5 (10%) the unclassifiable form. Five of 36 *M. abscessus* patients (14%) had the upper lobe cavitary form, 29 (81%) the nodular bronchiectatic form, and 2 (5%) the unclassifiable form. The upper lobe cavitary form was relatively more frequent in the MAC group than *M. abscessus* (p=0.029), whereas the nodular bronchiectatic form was more frequent in the *M. abscessus* group (p=0.012).

Table 2. Comparison of CT findings in terms of patients with and the extent of each pattern of parenchymal abnormality

	Number of patients involved		*p* value	Number of involved lobes		*p* value
	MAC (n=51)	*M. abscessus* (n=36)		MAC (n=306)	*M. abscessus* (n=216)	
Small nodules	34 (67*)	30 (83)	0.083	109 (36)	93 (43)	0.086
Tree-in-bud pattern	33 (65)	30 (83)	0.056	99 (32)	93 (43)	**0.013**
Bronchiectasis	48 (94)	33 (92)	0.657	165 (54)	114 (53)	0.796
Volume decrease	21 (41)	3 (8)	**0.001***	37 (12)	4 (2)	**< 0.001***
Nodule	10 (20)	1 (3)	**0.018***	19 (6)	1 (0)	**< 0.001***
Cavitary nodule	20 (39)	8 (22)	0.095	38 (12)	10 (5)	**0.002**
Airspace consolidation	25 (49)	10 (28)	**0.047**	50 (16)	16 (7)	**0.002**
Cavitary lobular consolidation	5 (10)	2 (6)	0.384*	8 (3)	3 (1)	0.262*
Thin-walled cavity	20 (39)	5 (14)	**0.009***	24 (8)	6 (2)	**0.014**

*Numbers in parentheses are percentages. *p* values were calculated by Chi-square test. †*p* values were calculated by Fisher's exact test.

The laterality and distribution of each type of parenchymal abnormality (e.g., bronchiectasis, small nodules, and tree-in-bud pattern) are summarized in Table 1. The results and comparisons with regard to the presence of each parenchymal abnormality and the extent of each parenchymal lesion on a lobe basis in the MAC and *M. abscessus* groups are summarized in Table 2.

CT findings in MAC and *M. abscessus* groups overlapped. The commonest CT findings were bronchiectasis (48 of 51

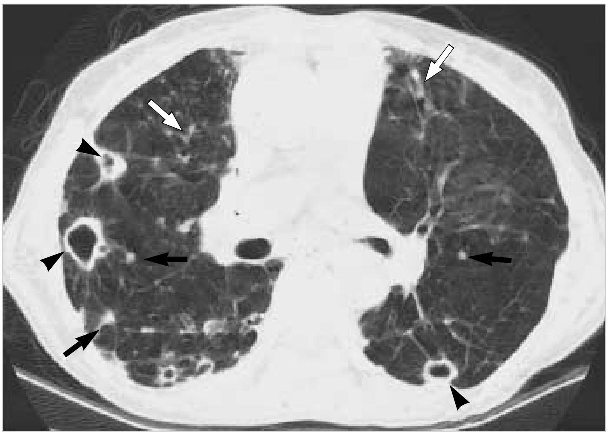


Fig. 4. A 69-yr-old woman with *M. avium-intracellulare* complex pulmonary disease. Transaxial thin-section (2.5-mm thickness) CT scan obtained at level of bronchus intermedius shows multiple cavitary nodules (arrowheads) in both lungs. Also note small nodules (arrows) and bronchiectasis (white arrows).

patients [94%] in MAC infection and 33 of 36 [92%] in *M. abscessus* infection), small nodules (34 of 51 patients [67%] in MAC infection and 30 of 36 [83%] in *M. abscessus* infection), and tree-in-bud pattern (33 of 51 patients [65%] in MAC infection and 30 of 36 [83%] in *M. abscessus* infection) (Fig. 1, 2). No significant difference was observed between MAC and *M. abscessus* groups in the presence of parenchymal abnormalities on person basis except for lobar volume decrease (p=0.001), nodule (p=0.018), airspace consolidation (p=0.047) (Fig. 3) and a thin-walled cavity (p=0.009) (Fig. 4). These three abnormalities were more frequently seen in the MAC group (Table 2).

With regard to the extent of lobe involvement for each parenchymal abnormality, tree-in-bud pattern (p=0.013) were observed in more lobes in *M. abscessus* pulmonary disease than in MAC, whereas lobar volume loss (p<0.001), nodule (p<0.001), cavitary nodules (p=0.002), airspace consolidation (p=0.002) and thin-walled cavity (p=0.014) were observed in more lobes in MAC than *M. abscessus* (Table 2).

DISCUSSION

In MAC pulmonary disease, two distinct radiologic subtypes, the upper lobe cavitary form and the nodular bronchiectatic form, have been noted (2). The former, the traditional and most widely known presentation of MAC pulmonary disease, is usually seen in white, middle-aged or elderly men who smoke or abuse alcohol. Underlying disorders commonly include chronic obstructive pulmonary disease, previous tuberculosis, and silicosis. The second clinical presentation, the so-called nodular bronchiectatic form, was recognized more recently (1), and occurs predominantly in nonsmoking middle-aged or elderly women who also present with a chronic productive cough. Interestingly, previous or underlying lung disease has not been noted in these patients (17, 18). However, because CT findings of the upper lobe cavity and nodular bronchiectasis are frequently observed in the same patient (19) and CT findings of predominantly airspace pattern are seen in patients with NTM pulmonary disease, it is sometimes difficult to divide MAC pulmonary disease into two different forms of disease based on the above forms of the disease, and therefore, we introduced an unclassifiable disease form. In our study, all three forms of disease (upper lobe cavitary, nodular bronchiectatic and unclassifiable forms) were observed in MAC and in *M. abscessus* infection, although the nodular bronchiectatic form was dominant in both. Moreover, the nodular bronchiectatic form was significantly more frequent in patients with *M. abscessus* infection.

During an analysis of CT findings of MAC pulmonary disease in 55 patients, in which two forms (upper lobe cavitary and nodular bronchiectatic) of disease were placed together, Lynch et al. (13) noted nodules (49 of 55 patients, 89%), airspace consolidation (44, 80%), bronchiectasis (40, 73%), and cavities (66%) are predominant findings. In their study, the presence of widespread bronchiectasis was found to allow the differentiation of MAC infection from pulmonary *M. tuberculosis* infection. In another similar study, Obayashi et al. (14) analyzed the CT findings of MAC pulmonary disease in 25 patients (both lungs in each patient were divided into 10 zones), and also combined the two forms of disease. Centrilobular small nodules (167 of 250 zones), bronchiectasis (133 of 250 zones), nodules (81 of 250 zones), airspace consolidation (30 of 250 zones), and cavity (11 of 250 zones) were common CT findings. Therefore, in MAC pulmonary disease, airspace consolidation and cavity are common CT findings in addition to bronchiectasis and centrilobular nodules (tree-in-bud pattern). These observations were further corroborated by our study. In addition, the present study showed a significantly higher frequency of airspace consolidation and thin-walled cavity in MAC than *M. abscessus* pulmonary disease (Table 2). Moreover, lobar volume decrease especially in the right middle lobe and lingular segment of the left upper lobe was observed more frequently in MAC infection than *M. abscessus* infection (Table 1, 2), in keeping with the results of previous reports (20, 21).

The reported CT findings of *M. abscessus* pulmonary disease are bilateral multi-focal bronchiectasis, bronchiolitis [small nodules (<5 mm) and branching centrilobular lesions (so-called tree-in-bud pattern)], and focal areas of consolidation (15). In the current study, bronchiectasis, small nodules and tree-in-bud patterns were the dominant findings of this disease. Although cavitary nodule, lobular consolidation, thin-walled cavity, and peribronchial consolidation were also seen in *M. abscessus* infection, they were present in less than 30% of patients and occurred less frequently than in MAC infection.

When comparing the CT findings of MAC and *M. abscessus* infection, their common findings were bilateral small nodules, tree-in-bud pattern, and bronchiectasis. No significant difference was observed between MAC and *M. abscessus* groups in the presence of these three parenchymal abnormalities on person basis except for a lobar volume decrease, nodule, airspace consolidation and a thin-walled cavitary. The latter four abnormalities were more frequently seen in the MAC group. With regard to the extent of lobe involvement for each parenchymal abnormality, tree-in-bud pattern was observed in more lobes in *M. abscessus* disease than in MAC disease, whereas lobar volume loss, nodule, cavitary nodules, airspace consolidation and thin-walled cavity were observed in more lobes in cases of MAC disease.

The relative applicability of the CT distinction between patients with MAC and *M. abscessus* infection needs to be elaborated. Although only one third or one half of patients with bilateral bronchiolitis and bronchiectasis prove to have NTM pulmonary infection, thin-section CT findings of bronchiectasis plus bronchiolitis involving more than 5 lobes, especially when associated with lobular consolidation or a cavity, are highly suggestive of NTM pulmonary infection (22). In this condition, the distinction may be important. Moreover, when sputum or bronchial washing fluid shows positive acid-fast bacilli staining or transbronchial lung biopsy specimen demonstrates tissue acid-fast bacilli staining positivity or chronic granulomatous inflammation, the above-mentioned CT findings strongly suggest NTM pulmonary infection. In this condition, the CT distinction is helpful for guiding treatment and for predicting the prognosis of patients, because the treatment and prognosis of NTM pulmonary infection differ according to etiologic organisms.

Patients with pulmonary disease caused by MAC are treated with combined regimen of clarithromycin or azithromycin, refampin or rifabutin, and ethambutol on an outpatient basis and with a relatively good response (2). In contrast with MAC infection, patients with *M. abscessus* infection need hospitalization for treatment with administration of parenteral antibiotics such as amikacin and cefoxitin for several weeks. Unfortunately, however, *M. abscessus* pulmonary disease is extremely difficult to eradicate, and it responds best to surgical resection of localized disease (2, 5). Therefore, CT differentiation between the diseases caused by these species before definite diagnosis with microbiological culture is important, taking into consideration of treatment options and prognoses.

In conclusion, there is considerable overlap in CT findings between MAC and *M. abscessus* pulmonary diseases and nodular bronchiectatic form with bilateral tree-in-bud pattern and bronchiectasis is commoner for both infections than upper lobe cavitary form. However, the upper lobe cavitary form is relatively more frequent in MAC infection. And patterns of lobar volume loss, nodule, airspace consolidation, and thin-walled cavity are more frequently associated with MAC infection. Whereas there is no sex difference in MAC infection, women are more frequently affected than men in *M. abscessus* infection.

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