Serial CT Findings of *Mycobacterium massiliense* Pulmonary Disease Compared with *Mycobacterium abscessus* Disease after Treatment with Antibiotic Therapy[1]

Hyun Su Kim, MD
Kyung Soo Lee, MD
Won-Jung Koh, MD
Kyeongman Jeon, MD
Eun Ju Lee, MD
Hee Kang, MD
Joonghyun Ahn, PhD

Purpose: To present the serial computed tomographic (CT) findings of lung abnormalities in *Mycobacterium massiliense* pulmonary disease compared with those in *Mycobacterium abscessus* disease.

Materials and Methods: The institutional review board approved this retrospective study and waived informed consent. Serial chest CT scans of *M massiliense* ($n = 34$) and *M abscessus* ($n = 24$) pulmonary diseases were retrospectively reviewed. Patients were treated with clarithromycin-containing combination antibiotics regimen, and sputum examinations were performed regularly. CT scans were obtained at the beginning of antibiotic therapy, at the end of 4-week hospitalization, and at the time of 12-month antibiotic therapy.

Results: All patients with *M massiliense* disease had sputum conversion during treatment, whereas 50% of patients with *M abscessus* disease had sputum conversion. The most common CT findings of *M massiliense* disease at presentation were cellular bronchiolitis ($n = 34$, 100%), bronchiectasis ($n = 34$, 100%), consolidation ($n = 33$, 97%), nodules ($n = 32$, 94%), and cavities ($n = 15$, 44%). These findings were similar in *M abscessus* disease. Thirty (88%) patients with *M massiliense* disease had decrease in overall CT score at 12-month therapy, whereas only eight (33%) patients with *M abscessus* disease had a decrease ($P < .0001$). Improvement was noticeable in cellular bronchiolitis and cavity in *M massiliense* disease.

Conclusion: Common CT findings of *M massiliense* diseases overlap with those of *M abscessus* disease. However, responses to antibiotic treatment are much different; in *M massiliense* disease, negative sputum conversion is accomplished in all patients and serial CT scans show improvement in most patients.

[1] From the Department of Radiology and Center for Imaging Science (H.S.K., K.S.L., E.J.L., H.K.), Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul 135-710, Korea; the Division of Pulmonary and Critical Care Medicine (W.J.K., K.J.), the Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine; the Samsung Biomedical Research Institute (J.A.), Samsung Medical Center, 50 Ilwon-dong, Gangnam-gu, Seoul 135-710, Korea. Received July 13, 2011; revision requested August 22; revision received September 26; accepted November 2; final version accepted November 14. **Address correspondence to** K.S.L. (e-mail: *kyungs.lee@samsung.com*).

Nontuberculous mycobacteria (NTM), also known as environmental mycobacteria, atypical mycobacteria, or mycobacteria other than tuberculosis, are ubiquitous mycobacteria that cause chronic human pulmonary infection other than tuberculosis (1). There are currently more than 140 NTM species, at least 40 of which are associated with lung infection (2). NTM lung diseases are increasing worldwide and the prevalence of NTM lung disease is greater than that of tuberculosis in Canada and the United States (3,4). *Mycobacterium avium-intracellulare* complex (MAC), *Mycobacterium abscessus*, and *Mycobacterium kansasii* are the most frequent causes of NTM lung disease (1).

M abscessus are rapidly growing mycobacteria and the most common cause of rapidly growing mycobacteria lung disease. *M abscessus* lung disease has been regarded as a chronic incurable infection for most patients given the current antibiotic options (1,5,6). *Mycobacterium massiliense* has recently been recognized as a separate species from *M abscessus,* and identification of *M massiliense* has been reported in many countries, including the United States (7). Treatment response rates to combination antibiotic therapy are much higher in patients with *M massiliense* lung disease than in those with *M abscessus* lung disease (8).

Authors of only a few articles have reported the imaging findings of *M abscessus* lung disease (9–11). According to those reports, the main radiographic and computed tomographic (CT) manifestations of *M abscessus* lung disease are bilateral small nodular opacities, bronchiectasis, and cavity formation, and there is considerable overlap in the common CT findings of MAC and *M abscessus* lung disease (9–11). Yet, to our knowledge, there has been no report about the CT findings of *M massiliense* lung disease. The purpose of our study was to present serial CT findings of lung abnormalities in *M massiliense* pulmonary disease, compared with those in *M abscessus* pulmonary disease.

Advances in Knowledge

- The most common CT findings at presentation in patients with *Mycobacterium massiliense* disease are cellular bronchiolitis (n = 34, 100%), bronchiectasis (n = 34, 100%), consolidation (n = 33, 97%), nodules (n = 32, 94%), and cavities (n = 15, 44%); the nodular bronchiectatic form (73%) is more frequent than the upper lobe cavitary form (24%) or the unclassifiable form (3%), and findings are similar to those of *M abscessus* disease.
- In *M massilense* disease, 88% of patients showed a decrease in the overall extent of lung abnormalities at follow-up CT 1 year after antibiotic treatment, while all patients showed negative sputum conversion during antibiotic treatment; in *M abscessus* disease, CT improvement was achieved in only 33% of patients and sputum conversion rates were in 50% of patients.

Materials and Methods

The institutional review board approved this retrospective study, and informed consent was waived for the use of patients' medical data. Patient consent was obtained for performing the initial and follow-up CT studies.

Patients and Diagnoses

All patients with *M massiliense* and *M abscessus* lung disease who were given antibiotic treatment from October 2004 through June 2009 were enrolled. The patients met the diagnostic criteria for NTM lung disease according to the American Thoracic Society guidelines (1). These patients (n = 150) had initially received a diagnosis of *M abscessus* lung disease. On the basis of the precise reclassification of stored bacterial organism isolates with use of sequence analysis targeting the *rpoB* and *hsp65* genes, these organisms were identified as *M massiliense* in 84 patients and as *M abscessus* in 66 patients (8). The reclassification procedure was started and completed from June through August 2009. Of these patients, 34 patients with *M massiliense* (two men, ages 63 and 64 years; 32 women, mean age of 52 years ± 13.6 [standard deviation], age range of 20–72 years) and 24 patients *with M abscessus* (four men, mean age of 53 years ± 9.8, age range of 40–63 years; 20 women, mean age of 56 years ± 14.1, age range of 22–74 years) disease, for whom serial CT scans were available, were included. In these 58 patients, antibiotic therapy for NTM disease was administered for at least 1 year. Thirty-four (59%) of the 58 patients had also been included in a previous study conducted at our institution (8).

Implication for Patient Care

- Accurate identification and differentiation of *M massiliense* from *M abscessus* organisms is crucial because common CT findings of the two diseases overlap with each other; patients with *M massiliense* disease show a good response to antibiotic therapy, as reflected by the improvement of lung abnormalities at serial CT, and a high rate of negative sputum conversion and its maintenance after antibiotic treatment.

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Abbreviations:
CI = confidence interval
ICC = intraclass correlation coefficient
MAC = *Mycobacterium avium-intracellulare* complex
NTM = nontuberculous mycobacteria

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Potential conflicts of interest are listed at the end of this article.

Treatment and Sputum Culture

The antibiotic treatment regimens were as follows: all patients were hospitalized for 4 weeks to receive a clarithromycin-containing three-drug oral regimen that included clarithromycin, ciprofloxacin, and doxycycline, along with an initial 4-week course of intravenous amikacin and cefoxitin. After discharge, the patients received a three-drug oral regimen for a total of 24 months. The 24-month regimen usually included at least 12-month therapy after negative conversion of the sputum culture. When the negative conversion was not achieved, especially in *M abscessus* disease, the oral 24-month regimen was extended for the negative conversion. The treatment protocol was modified in January 2008 and then the patients received a two-drug regimen that included clarithromycin and fluoroquinolones (ciprofloxacin or moxifloxacin) after the initial parenteral therapy (5,8,12).

Sputum smear and culture examinations were performed during hospital stay, monthly for the first 6 months after discharge, and then at 3-month intervals until the end of treatment. In all patients, CT scans were obtained three times, namely, at the beginning of antibiotic therapy (time point A), at the end of the 4-week hospitalization (time point B), and at 12 months after the start of antibiotic treatment (time point C).

CT Acquisition

CT scans were obtained by using a helical technique; 64-detecor scanners (Aquilion 64, Toshiba Medical System, Tokyo, Japan [63 scans in 41 patients]; LightSpeed VCT, GE Healthcare, Waukesha, Wis [53 scans in 34 patients]), a 40-detector scanner (Brilliance-40; Philips Medical Systems, Cleveland, Ohio [36 scans in 22 patients]), a 16-detector scanner (LightSpeed 16, GE Healthcare [13 scans in seven patients]), and an eight-detector scanner (LightSpeed Ultra, GE Healthcare [nine scans in eight patients]) were used. Intravenous contrast medium was not administered to any of the patients. Scans were obtained from the level of lung apices to the lung bases. Expiratory CT scans were not obtained. All CT data were reconstructed by using a high-spatial-frequency algorithm. The CT images were obtained with the following parameters: collimation, 1.25 or 0.625 mm; field of view, 36 cm; beam pitch, 1.35 or 1.375; gantry speed, 0.5 or 0.6 sec/rotation; 120 kVp; 150–200 mA; and reconstruction interval, 1–2.5 mm. The image data were reformatted with a 2.5-mm section thickness for transverse images and a 2.0-mm section thickness for coronal images. The scan data were directly displayed on monitors (four monitors, 1536 × 2048 image matrices, 8-bit viewable grayscale, and 60-ft-lambert luminescence) of a picture archiving and communication system (Centricity 2.0; GE Medical Systems Integrated Imaging Solutions, Mt Prospect, Ill) workstation. On the monitors, both the mediastinal (window width, 400 HU; window level, 20 HU) and lung (window width, 1500 HU; window level, −700 HU) window images were available for analysis.

CT Interpretation

Two independent chest radiologists (E.J.L. and H.K., with 2 and 5 years of experience in chest CT, respectively) evaluated retrospectively the chest CT scans. A total of six lung lobes in each patient (the lingular division of the left upper lobe, considered as a separate lobe) were assessed for the presence of lung parenchymal abnormalities. Each lung lobe was evaluated for the presence and extent of parenchymal abnormalities, including bronchiectasis, cellular or inflammatory bronchiolitis, nodules of 10–30 mm in diameter, airspace consolidation, and cavities. The laterality (unilateral or bilateral) and location of the lung lesions were also analyzed. A total of 204 lung lobes in 34 patients (six lobes per patient) with *M massiliense* disease and of 144 lung lobes in 24 patients with *M abscessus* disease were evaluated for the presence of lung lesions.

Bronchiectasis was defined to be present when the bronchial lumen diameter was greater than the adjacent pulmonary artery without tapering of the bronchial lumen diameter. Because bronchial wall thickening and mucus plugging were frequently accompanied by bronchiectasis, they were considered under the subcategory of bronchiectasis. Bronchial wall thickness was estimated by measuring the ratio of the airway wall thickness to the outer diameter of the corresponding bronchus. Mucus plugging was regarded as present when a broad linear or branching attenuating lesion was observed within a proximal airway (lobar, segmental, or subsegmental bronchus) associated with airway dilatation. Cellular bronchiolitis was defined as the presence of centrilobular small nodules (< 10 mm in diameter) and branching nodular structures (ie, tree-in-bud sign) on CT scans. We did not consider tree-in-bud sign (mostly cellular bronchiolitis) as mucus plugging, and so the sign was not included in the scoring of mucus plugging. The presence of other abnormalities, including cavities; nodules (10–30 mm in diameter); and lobular (consolidation of 10–20 mm in diameter with a polygonal shape), peribronchial, or segmental consolidation, was also recorded. 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 of these forms of consolidation were grouped into airspace consolidation (Table 1).

After the pattern and distribution of the parenchymal abnormalities seen at CT were analyzed, the diseases were classified into three forms: upper lobe cavitary, nodular bronchiectatic, and unclassifiable. The upper lobe cavitary form was defined when a cavity (or cavities) was present in the upper lobes with findings of emphysematous change in the middle and lower lung zones with or without a volume decrease of the upper lobes and apical pleural thickening (11,13). The nodular bronchiectatic form was defined when bilateral bronchiectasis and cellular bronchiolitis were present mainly in the right middle lobe and lingular division of the left upper lobe, irrespective of the presence of cavities in both lungs. However, in this form, there was neither upper lobar

Table 1

CT Scoring System for Assessment of the Extent of *M massiliense* and *M abscessus* Disease

CT Finding	Score 0	Score 1	Score 2	Score 3
Bronchiectasis (9 points)				
Severity*	Absent	Mild	Moderate	Severe
Extent†	Absent	1–5	6–9	>9
Mucus plugging†	Absent	1–5	6–9	>9
Cellular bronchiolitis (6 points)				
Severity‡	Absent	Mild	Moderate	Severe
Extent†	Absent	1–5	6–9	>9
Cavity (9 points)				
Diameter (cm)	Absent	<3	3–5	>5
Wall thickness (mm)	Absent	<1	1–5	>5
Extent§	Absent	1–3	4–5	>5
Nodules (3 points)†	Absent	1–5	6–9	>9
Consolidation (3 points)†	Absent	<3	3–5	>5

* Mild = bronchus diameter greater than adjacent vessel diameter; moderate = bronchus diameter 2–3 times vessel diameter; severe = bronchus diameter greater than three times vessel diameter.

† Data are the number of segments.

‡ Mild = identifiable, peripheral lung <1 cm from pleura; moderate = definite, involvement greater than 1–3 cm from pleura; severe = extensive, extending to central lung.

§ Data are the number of cavities.

volume loss nor emphysematous change in the remaining lungs (11,13). When the disease did not belong to either the upper lobe cavitary or the nodular bronchiectatic form, it was deemed as unclassifiable. In this form, multifocal lobular or segmental consolidation or consolidation along the bronchovascular bundles might be seen.

Lesion Quantification

The CT scores in terms of the severity of lung involvement in *M massiliense* and *M abscessus* pulmonary diseases (Table 1) were calculated by modifying the previously published scoring system proposed by Song et al (13), which appeared to correlate with measures of functional impairment in patients with MAC pulmonary disease. This modified and detailed scoring system was used, because simple visual quantification at several levels of CT images seemed to be inadequate for assessing the detailed changes in lung abnormalities at serial CT. A total score of 30 was allocated for the overall extent of a lung lesion in each patient. Scores were given by considering the presence, severity, and extent of bronchiectasis, cellular bronchiolitis, cavities, nodules, and consolidation in both lungs. For the cavities, their diameter, wall thickness, and extent were evaluated (Fig 1). The mean overall CT score for each pattern of parenchymal abnormality was defined as the average score of the two observers divided by the total number of patients.

Statistical Analyses

For statistical analyses, SAS for Windows software (version 9.1.3; SAS Institute, Cary, NC) was used. For the frequency of lung lesion laterality and distribution, the readings from the two observers were averaged by rounding. When there were discrepancies in their reading for the three forms of disease, final decisions were reached by consensus. The distribution of the three forms of NTM diseases between *M massiliense* and *M abscessus* was compared by using the Fisher exact test. The proportion of increase, decrease, and no change in the extent of overall disease among the three time points between the two diseases was compared with the Fisher exact test by using permutation method for multiple comparisons.

Because each observer evaluated CT scans three times (time points A, B, and C), we calculated the interobserver agreement in terms of the extent and severity of bronchiectasis, cellular bronchiolitis, cavities, nodules, and consolidation by using repeated measures of data analysis for the intraclass correlation coefficient (ICC), with consideration of the change of the CT findings in each patient at different time points. The 95% confidence intervals (CIs) for the ICC were estimated with the Bootstrap method. ICC was regarded to show poor agreement when it was less than 0.4; moderate agreement, when it was 0.4 but less than 0.75; and high agreement, when it was 0.75 or greater.

We used repeated-measures data analysis with a mixed model to test the significance of differences in CT scores for each parenchymal abnormality among the three time points in both *M massiliense* and *M abscessus* diseases. Tukey-Kramer pairwise comparison was used for posthoc analysis. A *P* value of less than .05 was considered to indicate a significant difference.

Results

Negative sputum conversion and its maintenance for more than 12 months were accomplished in all 34 patients (mean follow-up, 40 months; range, 21–77 months) with *M massiliense* disease, but in 50% (12 of 24) of patients with *M abscessus* disease (mean follow-up, 32 months; range, 24–72 months). The mean time to negative conversion after the initiation of treatment was 10 days (range, 1–230 days; 230 days in one patient and 1–56 days in the remaining 33 patients) in *M massiliense* disease and 299 days (range, 7–920 days) in *M abscessus* disease.

Initial CT Findings

The pattern of the parenchymal findings; frequency, laterality, and location of the lung lesions; and the averaged values from the two observers are summarized in Table 2. In *M massiliense* disease, the most common initial CT

Figure 1

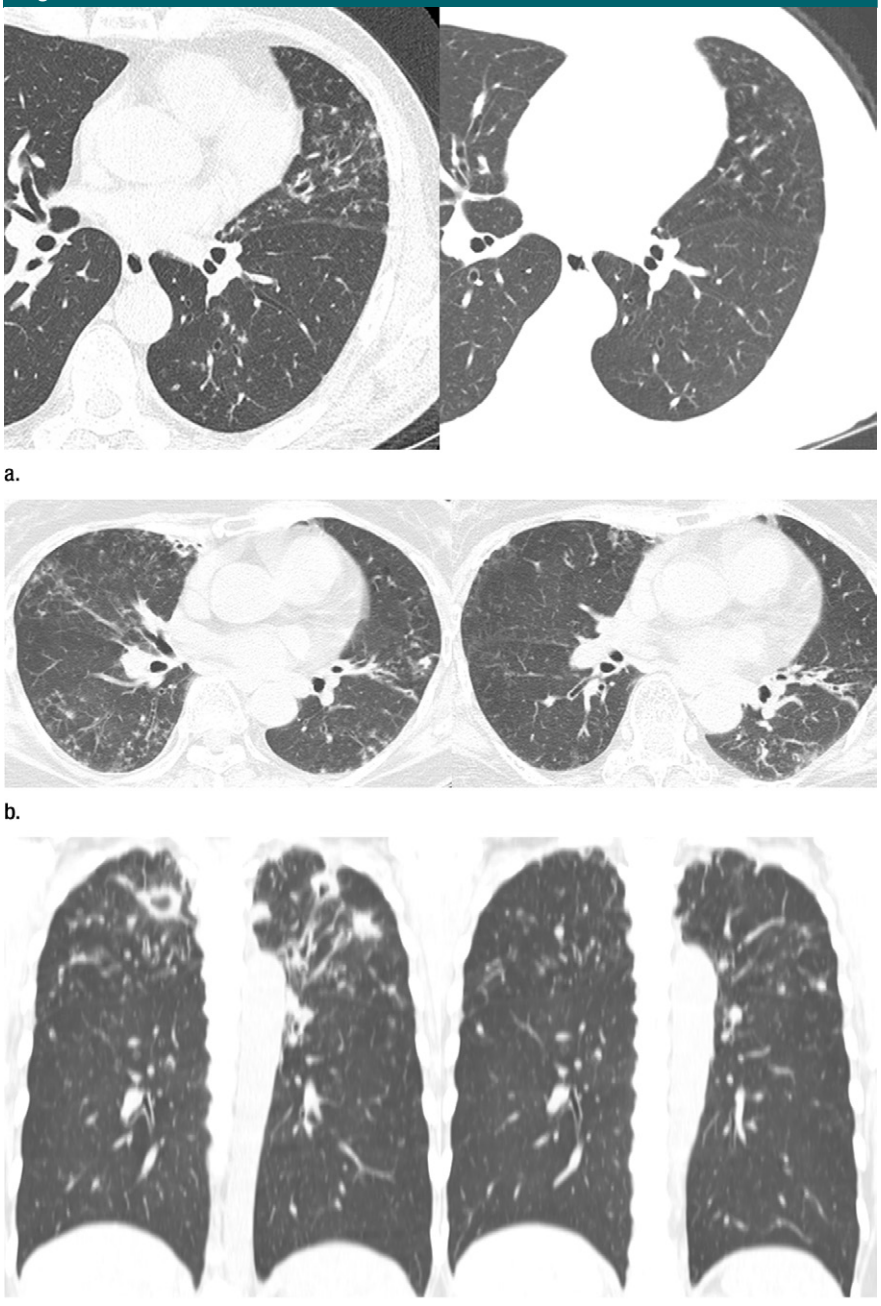

Figure 1: Serial CT scans of *M massiliense* diseases at time points A (left) and C (right). **(a)** Scans in 63-year-old man show interval improvement of wall thickening of dilated bronchi (severity) in the lingular division of left upper lobe. There was no change in the number (extent) of involved lobes. Total (severity, extent, and mucus plugging) scores for bronchiectasis were 5 (score of 2, 2, and 1, respectively) for time point A and 3 (score of 1, 2, and 0, respectively) for time point C. **(b)** Scans in 72-year-old woman. Note associated bronchiectasis. Total (severity and extent) scores for cellular bronchiolitis were 5 (score of 3 and 2, respectively) for time point A and 2 (score of 1 and 1, respectively) for time point C. Interval improvement in severity and extent (from seven to four segments involved, not shown here) is overt in both lungs. **(c)** Scans in 48-year-old woman. Total scores (severity, wall thickness, and extent) for cavitary lesions were 7 (score of 2, 2, and 3, respectively) for time point A and 4 (scores of 1, 2, and 1, respectively) for time point C. Cavities showed obliteration and decreased number of segmental involvement (not shown here).

findings were cellular bronchiolitis and bronchiectasis (n = 34, 100%), followed by consolidation (n = 33, 97%), nodules (n = 32, 94%), and cavities (n = 15, 44%). In *M abscessus* disease (n = 24), the CT findings were bronchiectasis (n = 24, 100%), followed by cellular bronchiolitis (n = 23, 96%), consolidation (n = 19, 79%), nodules (n = 17, 71%), and cavities (n = 12, 50%). In both diseases, cellular bronchiolitis and bronchiectasis were bilateral in distribution in more than 80% of patients, and they involved more than two-thirds of all lung lobes. In *M massiliense* disease, 25 (73%) patients had the nodular bronchiectatic form, eight (24%) had the upper lobe cavitary form (Fig 2), and one (3%) had the unclassifiable form. In *M abscessus* disease, 14 (58%) patients had the nodular bronchiectatic form (Fig 3), four (17%) had the upper lobe cavitary form, and six (25%) had the unclassifiable form. The distribution of the three forms of NTM diseases between *M massiliense* and *M abscessus* diseases was not significantly different (P = .05).

Changes in CT Findings after Treatment

The CT scores recorded by both observers are shown in Figure 4. In *M massiliense* disease, none of the patients had an increased CT score at follow-up. Thirty (88%) of 34 patients had a decrease in the overall score (Figs 1,2) and four (12%) had no change in the total CT score at time point C. In *M abscessus* disease, 10 (42%) of 24 patients had an increase (Fig 3), eight (33%) had a decrease, and six (25%) had no change in the overall CT score at time point C. Those changes were significantly different between the two diseases ($P < .0001$). Between time points A and B, 28 (82%) patients had improvement and six (18%) had no change in the extent of *M massiliense* disease, whereas two (8%) patients had an increase in the overall score, eight (33%) had a decrease, and 14 (58%) had no change in the extent of *M abscessus* disease (P = .0003). In *M massiliense* disease, prominent improvement of lung abnormality was noticed in consolidation (observer 1) and

Table 2

Pattern and Distribution of Parenchymal Abnormalities at Initial CT

CT Pattern	No with *M massiliense* Disease	No with *M abscessus* Disease	Laterality of *M massiliense* Involvement			Laterality of *M abscessus* Involvement		Location of *M massiliense* Disease*								Location of *M abscessus* Disease*							
								Right Lung			Left Lung			Total		Right Lung			Left Lung			Total	
			Unilateral	Bilateral	Unilateral	Bilateral		Upper	Middle	Lower	Upper	Li†	Lower	(*n* = 204)	Upper	Middle	Lower	Upper	Li†	Lower	(n = 144)	
Bronchiectasis	34 (100)	24 (100)	5	29	4	20		20	29	15	17	30	20	131	17	22	13	11	21	15	99	
Bronchiolitis	34 (100)	23 (96)	5	29	1	22		29	25	24	25	24	30	157	18	19	20	14	20	19	110	
Cavity	15 (44)	12 (50)	13	1	6	6		7	1	3	8	3	4	26	8	1	4	8	5	5	31	
Nodules	32 (94)	17 (71)	15	17	6	11		18	11	14	13	12	24	92	7	5	12	4	5	10	43	
Consolidation	33 (97)	19 (79)	10	23	7	12		20	17	8	14	20	16	95	9	13	6	5	12	4	49	

Note.—Unless otherwise indicated, data are number of patients and data in parentheses are percentages.

* Data are the number lobes.

† Li = lingular division of left upper lobe.

cellular bronchiolitis (observer 2). Mild improvement of bronchiectasis was also observed. The mean decrease in the total extent of lung lesions between two time points (A and B) seen by the two observers was 1.98. In *M abscessus* disease, the decrease in mean score was slight, and the mean decrease in the overall extent was 0.58. Between time points B and C, 32 (94%) patients with *M massilense* disease showed improvement and two (6%) showed no change, whereas 11 (46%) patients with *M abscessus* disease showed an increase, seven (29%) showed no change, and six (25%) showed a decrease in the total score ($P < .00001$). In *M massiliense* disease, cellular bronchiolitis had marked improvement in its score, followed by cavities and consolidation. The mean decrease in the overall extent of lung lesions between time points B and C seen by two observers was 3.87. In other words, the lung abnormalities demonstrated noticeable improvement between time points B and C, compared with time points A and B (Fig 4). Specifically for cavitary lesions, the wall thickness, size, and number of cavities showed improvement, with a decrease in their scores. In *M abscessus* disease, only cavity showed slight improvement (mean decrease, 0.27) and the rest of lung abnormalities showed slight increase, most prominently in cellular bronchiolitis (mean increase, 0.27). The mean change in the score in the overall extent of lung lesions between time points B and C seen by the two observers was a 0.33 increase (Fig 4).

In *M massiliense* disease, a high level of interobserver agreement was demonstrated for bronchiectasis (ICC, 0.87; 95% CI: 0.83, 0.92), cavities (ICC, 0.85; 95% CI: 0.76, 0.95), and the total score. The level of agreement was moderate for bronchiolitis (ICC, 0.70; 95% CI: 0.62, 0.83), nodules (ICC, 0.73; 95% CI: 0.62, 0.84), and consolidation (ICC, 0.59; 95% CI: 0.50, 0.72). The same tendency in interobserver agreement was also noted in *M abscessus* disease evaluation (Table 3).

Significant differences in the scores for bronchiectasis, bronchiolitis, cavities, nodules, and consolidation

Figure 2

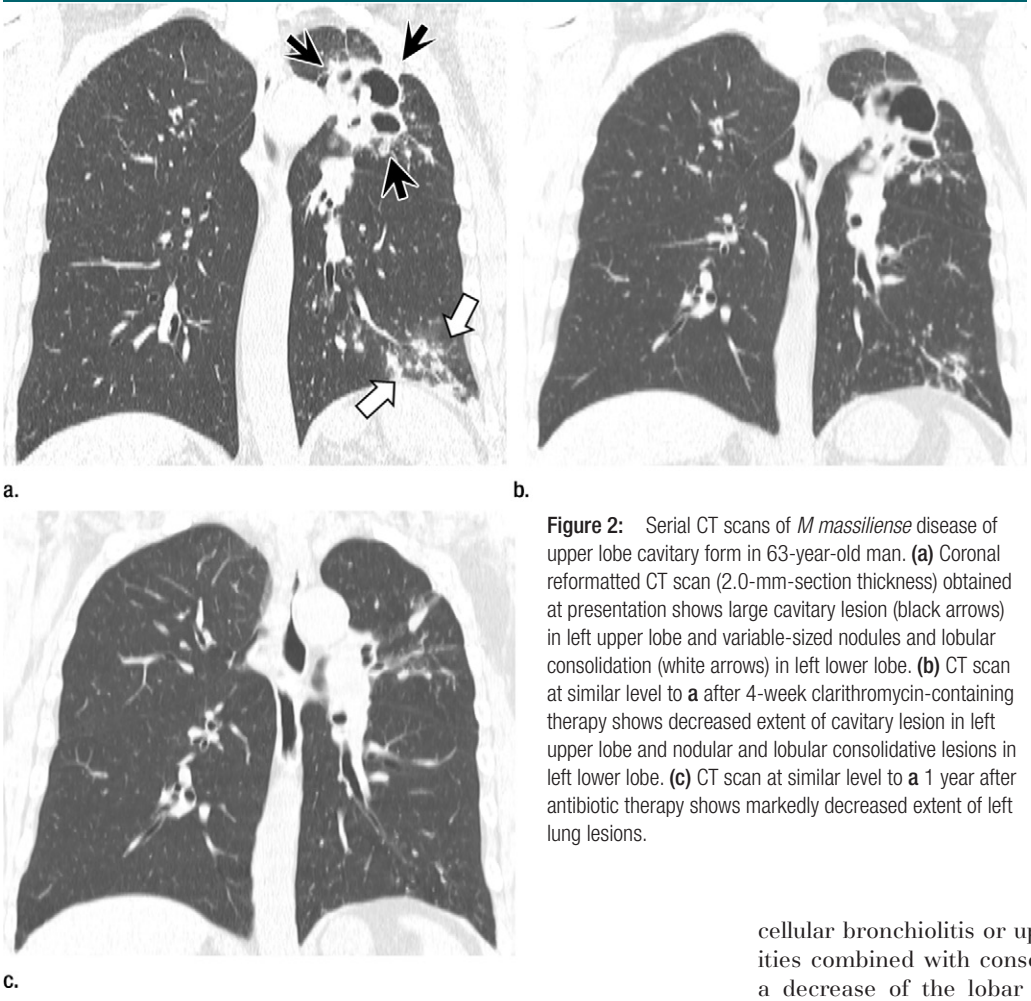

Figure 2: Serial CT scans of *M massiliense* disease of upper lobe cavitary form in 63-year-old man. **(a)** Coronal reformatted CT scan (2.0-mm-section thickness) obtained at presentation shows large cavitary lesion (black arrows) in left upper lobe and variable-sized nodules and lobular consolidation (white arrows) in left lower lobe. **(b)** CT scan at similar level to **a** after 4-week clarithromycin-containing therapy shows decreased extent of cavitary lesion in left upper lobe and nodular and lobular consolidative lesions in left lower lobe. **(c)** CT scan at similar level to **a** 1 year after antibiotic therapy shows markedly decreased extent of left lung lesions.

were demonstrated ($P < .0001$, $P < .0001$, $P = .0005$, $P < .0001$, and $P < .0001$, respectively) between *M massiliense* and *M abscessus* diseases among the three time points. Posthoc analysis regarding *M massiliense* disease revealed significant differences in all scores for each pattern of parenchymal abnormality between time points A and B ($P < .0001$, $P < .0001$, $P = .0249$, $P = .0491$, and $P < .0001$, respectively) and time points B and C ($P = .0004$, $P < .0001$, $P = .0009$, $P = .0005$, $P < .0001$, respectively). However, in *M abscessus* disease, it revealed no significant differences in the scores for each pattern of parenchymal abnormality between time points A and B ($P = .6846$, .9355, .9607, .8786, and .9266, respectively) or time points B and C ($P = .9243$, $P = .323$, $P = .6314$, $P = .8786$, and $P = .6291$, respectively).

Discussion

MAC pulmonary disease has been divided into two distinct subtypes: the upper lobe cavitary form and the nodular bronchiectatic form (12). However, there have been few studies regarding the subtyping of pulmonary diseases caused by rapidly growing mycobacteria, including *M abscessus,* into these two different forms of disease. Considerable overlap exists in the imaging findings between MAC and *M abscessus* pulmonary disease (10,11). In both diseases, bilateral multilobar bronchiectasis and cellular bronchiolitis or upper lobe cavities combined with consolidations and a decrease of the lobar or segmental volume are the predominant manifestations. However, lobar volume loss, consolidation, nodule(s), and thin-walled cavity are more frequently seen in MAC pulmonary disease than in *M abscessus* disease. Additionally, the upper lobar cavitary form is more frequently observed in MAC pulmonary disease (10,11).

Similar to previous reports, the most common CT findings in *M massiliense* pulmonary disease in our study were bilateral cellular bronchiolitis and bronchiectasis ($n = 34$, 100%). Cavities were noted in 14 (41%) patients. Also in *M abscessus* disease, the most common CT findings were bronchiectasis ($n = 24$, 100%) and cellular bronchiolitis ($n = 23$, 96%). Cavities were seen in 12 (50%) patients. In *M massiliense* disease, the nodular bronchiectatic

Figure 3

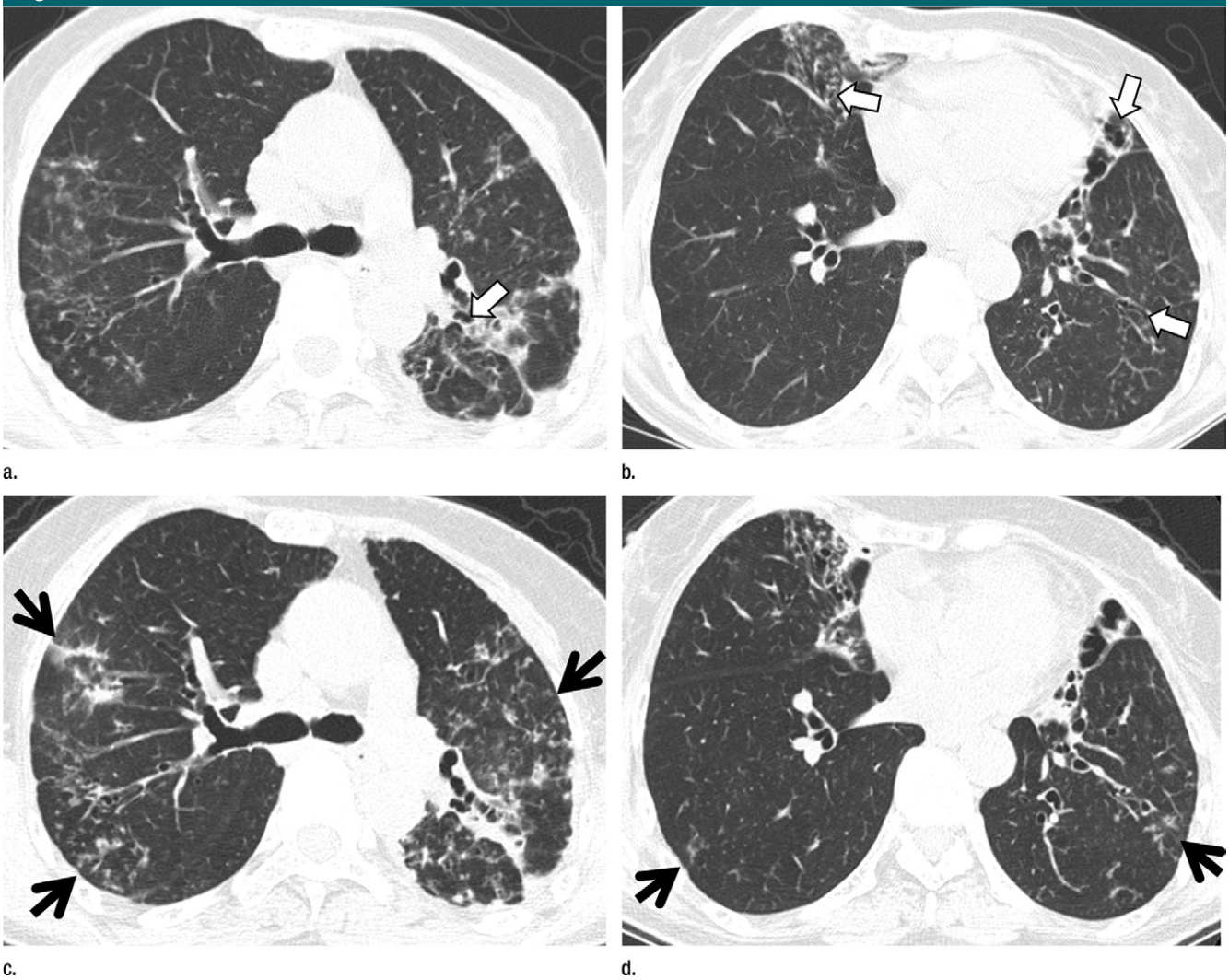

Figure 3: Serial CT scans of *M abscessus* disease of nodular bronchiectatic form in 65-year-old woman. **(a, b)** Transverse CT scans (2.5-mm-section thickness) obtained at presentation at levels of **(a)** right upper lobar bronchus and **(b)** right inferior pulmonary vein show extensive cellular bronchiolitis with tree-in-bud signs in both upper lobes and left lower lobe. Also note bronchiectasis (arrows) in right middle lobe, lingular division of left upper lobe, and left lower lobe. **(c, d)** CT scans obtained at similar levels to **a** and **b**, respectively, 1 year after clarithromycin-containing therapy show rather increased extent of cellular bronchiolitis (arrows) in both lungs.

form is more frequent than the upper lobe cavitary form. Twenty-five (73%) of 34 patients had the nodular bronchiectatic form, eight (24%) had the upper lobe cavitary form, and one (3%) had the unclassifiable form. In *M abscessus* disease, 14 (58%) of 24 patients had the nodular bronchiectatic form, four (17%) had the upper lobe cavitary form, and six (25%) had the unclassifiable form. However, the distribution of the three forms of NTM diseases between *M massiliense* and *M abscessus* diseases was not statistically different ($P = .05$).

In a report (14) about the natural history of nodular bronchiectatic MAC pulmonary disease, 34 (60%) of 57 patients showed deterioration with either progressive nodules or consolidation at CT or a positive conversion of MAC culture in the sputum. Twenty-three (40%) patients had stable disease with no change in the extent of CT findings or sputum bacteriology during the observation period of approximately 28 months. None showed spontaneous improvement. Therefore, without treatment, most of the patients with MAC pulmonary disease have progressive disease. There have been a few studies reporting the serial changes in the extent of CT findings of NTM pulmonary disease with antibiotic therapy. According to a study (15) that analyzed chest CT scans before and after clarithromycin-containing therapy in 30 patients with MAC pulmonary disease, bronchial wall thickening

Figure 4

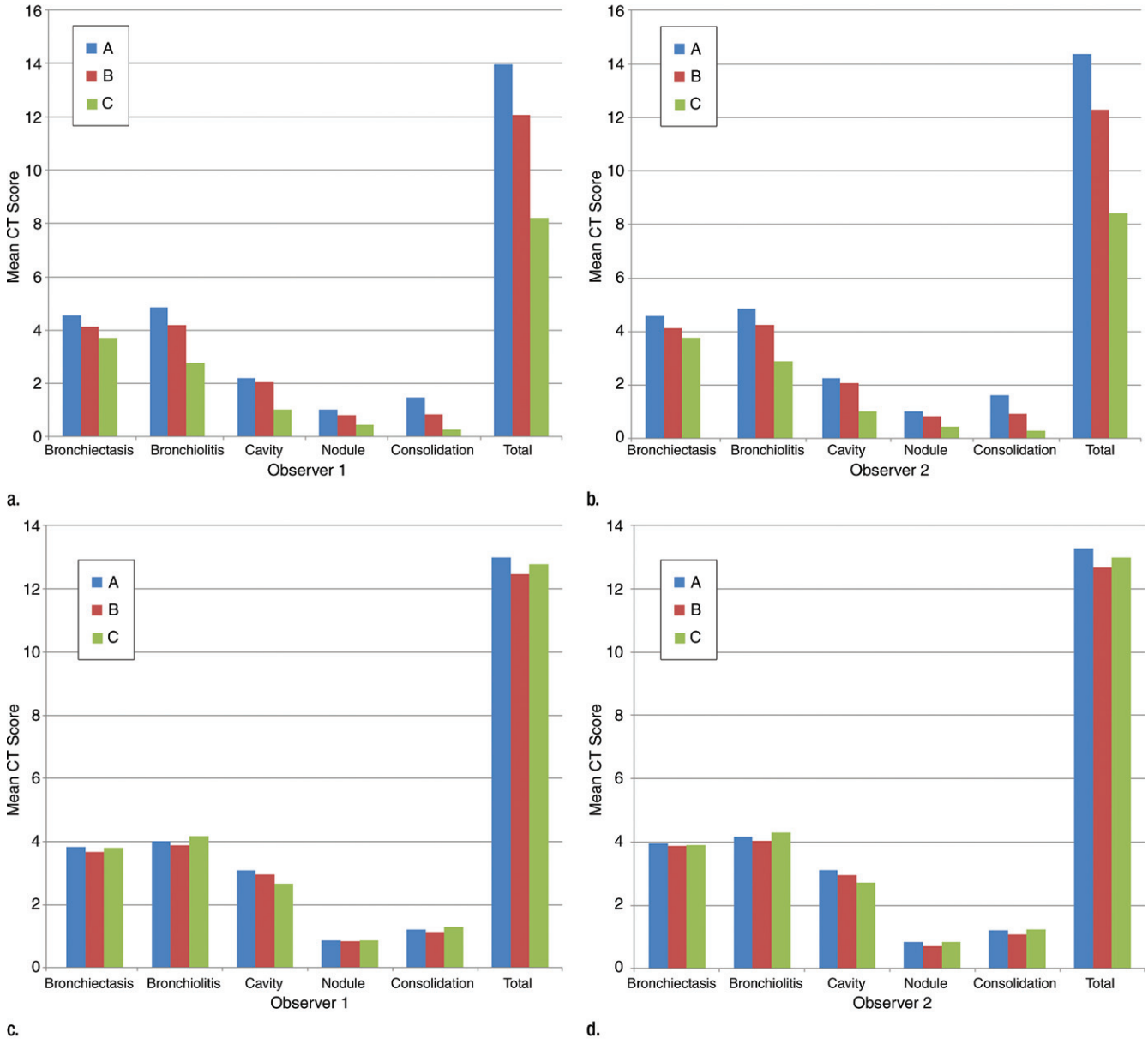

Figure 4: Graphs show changes in mean CT scores in terms of disease patterns after antibiotic therapy. **(a, b)** Evaluation of *M massiliense* disease in 34 patients by **(a)** observer 1 and **(b)** observer 2. For both observers, decrease in overall extent of lung lesions and extent of cellular bronchiolitis and cavitary lesions is prominent. **(c, d)** Evaluation of *M abscessus* disease in 24 patients by **(c)** observer 1 and **(d)** observer 2. For both observers, decrease in overall extent of lung lesions is minimal. Extent of cellular bronchiolitis and consolidation is rather increased. Mean CT score is a subtotal score of each category divided by the number of involved patients at each time point. *A, B,* and *C* = time points A, B, and C, respectively.

and small nodules showed improvement, whereas pleural thickening did not. Most cavitary lesions (five of six) showed no change or deterioration.

In MAC pulmonary disease, it is reported that the species of pathogen (*M avium* vs *M intracellulare*) and type (the upper lobe cavitary or nodular bronchiectatic form) do not significantly affect the sputum conversion rate (16). However, a clinically important difference in terms of the response to antibiotic therapy has been reported between *M abscessus* and *M massiliense* lung diseases. Koh et al (8), in their study comparing clarithromycin-containing antibiotic treatment outcomes between 64 patients with *M abscessus* lung disease

Table 3

ICC for Each Pattern of Parenchymal Lung Abnormality

	M massiliense		*M. abscessuss*	
Pattern	ICC	95% CI*	ICC	95% CI*
Bronchiectasis	0.87	0.828, 0.923	0.88	0.841, 0.925
Bronchiolitis	0.70	0.624, 0.832	0.71	0.658, 0.796
Cavity	0.85	0.757, 0.947	0.91	0.877, 0.954
Nodule	0.73	0.626, 0.841	0.72	0.644, 0.827
Consolidation	0.59	0.480, 0.724	0.59	0.517, 0.716
Total CT score	0.86	0.780, 0.946	0.85	0.817, 0.899

* Estimated by using Bootstrap method.

and 81 patients with *M massiliense* lung disease, reported higher radiographic improvement rates in patients with *M massiliense* infection (82%, 27 of 33 patients) than in those with *M abscessus* infection (42%, 10 of 24 patients). Induced resistance to clarithromycin may help explain the lack of efficacy of clarithromycin-containing antibiotic therapy against *M abscessus* pulmonary disease (8). In our study, negative sputum conversion was accomplished in all patients with *M massiliense* pulmonary disease with antibiotic treatment, whereas it was achieved in 50% of patients with *M abscessus* disease. Moreover, serial CT scans showed improvement in 88% of patients with *M massiliense* disease, particularly in the extent of cellular bronchiolitis and cavities. The improvement was achieved in only 33% of patients with *M abscessus* disease. The difference in CT improvement rates was significantly different between the two diseases.

In our study, the mean decrease in the total CT score in *M massiliense* disease was more prominent between studies obtained at time points B and C than between those obtained at time points A and B (observer 1 score, 3.85 vs 1.91; observer 2 score, 3.88 vs 2.06). Therefore, continuous antibiotic therapy may be needed for at least 1 year. In addition, the most noticeable decrease in the CT score in terms of disease pattern between time points B and C was cellular bronchiolitis (observer 1 score, 1.44; observer 2 score, 1.38) and cavity (observer 1score, 1.03; observer 2 score, 1.06). This implies that in *M massiliense* pulmonary disease, cellular bronchiolitis and cavitary lesions are the two main patterns of disease that are readily reversible with antibiotic therapy. In *M abscessus* disease, the decrease in the mean score between time points A and B was slight (score, 0.58). Moreover, the mean change in the score in the overall extent of lung lesions between time points B and C was rather a slight increase (score, 0.33), and lung abnormalities other than cavity showed interval aggravation. Eleven (46%) of 24 patients showed an increase in the overall score and seven (29%) patients showed no change in the total score between the two time points. Furthermore, these changes in extent among the three time points were significantly different between *M massiliense* and *M abscessus* diseases.

The response of upper lobe cavitary lesions in NTM pulmonary disease to antibiotic therapy has not been well described. In our study, *M massiliense* disease did show improvement with antibiotic therapy, starting with wall thickness thinning in the cavitary lesion and then subsequent improvement in the size and extent of the lesions. Because all patients with cavitary lesions showed cavity contraction, none was a candidate for surgical treatment. None had significant complication or resistance to the therapy. This is in contrast to the results of a previous study (5), in which three (5%) of 65 patients with *M abscessus* lung disease of the upper lobe cavitary form who received clarithromycin-containing therapy had complications of chronic necrotizing pulmonary aspergillosis. In our study, cavitary lesions in *M abscessus* disease showed poor response to the treatment. Of 12 patients with cavitary lesions, only six (50%) patients showed a slight decrease in extent; the remaining six patients showed a slight increase or no change in the CT score at the time of 12-month therapy. Also in MAC pulmonary disease, it has been reported that cavitary lesions show no change or an increase in their extent even with antibiotic treatment (15).

There were several limitations in our study. First, all 34 patients with *M massiliense* disease showed negative sputum conversion during the follow-up period. Thus, we could not evaluate the CT findings of lung abnormality in patients infected with a resistant *M massiliense* strain. However, considering the high negative sputum conversion rate of *M massiliense* reported in previous studies (8), it would be difficult to include a large number of patients with treatment-resistant *M massiliense* pulmonary disease. However, it is well known that the sputum conversion rates in patients with MAC and *M abscessus* pulmonary disease are approximately 25%–90% (16–21) and 48%–58% (5,6,8), respectively. Second, our study was retrospective in design, thus it may have had selection bias. We included only patients who had serial CT studies at the selected three time points. Therefore, more patients with *M abscessus* disease might have been excluded, because these patients had more chance of early surgical treatment for localized cavitary lesions and thus more chance of exclusion (did not have three serial CT studies).

In conclusion, the most common CT findings at presentation in patients with *M massiliense* pulmonary disease are cellular bronchiolitis, bronchiectasis, nodules, consolidation, and cavitary lesions, in the decreasing order of frequency. The nodular bronchiectatic form is more frequent than the upper lobe cavitary form. Most patients with *M massiliense* disease show improvement of the CT findings and all patients demonstrate negative sputum conversion during antibiotic treatment. These observations in *M massiliense* disease are sharply in contrast to those in *M abscessus* disease, in which CT finding

improvement and sputum conversion are seen in 33% and 50% of infected patients, respectively. Because patients with pulmonary disease due to the *M massiliense* organism show a good response to antibiotic therapy both in the sputum and on imaging studies, accurate differentiation of *M massiliense* from *M abscessus* or MAC organisms during microorganism culture and identification process is mandatory.

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