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Original article

18 Cases of pulmonary *Mycobacterium abscessus*: Clinical difference depending on the presence or absence of *Mycobacterium avium* complex

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ABSTRACT

Background and objectives: It can be difficult to treat respiratory tract infections caused by *Mycobacterium abscessus* (*M. abscessus*) as there is no established treatment strategy. Complications involving other nontuberculous mycobacterial infections such as *Mycobacterium avium* complex (MAC) are also commonly observed.

Methods: We investigated the clinical background and course of 18 cases of pulmonary *M. abscessus* infection treated over 8 years at Kurashiki Central Hospital. Radiological evaluation was performed using NICE scoring system, a method of semi-quantitative evaluation of imaging findings of pulmonary MAC infection.

Results: The mean age of the 18 patients (males, 6; females, 12) was 74.7 years. The median follow-up period was 1316 days (95% confidence interval; 720–1675 days), and 11 patients were concomitantly infected with pulmonary MAC. Among the patients that underwent antibacterial treatment for *M. abscessus*, there was one MAC-complication case and one non-MAC-complication case. All MAC-complication cases underwent antibacterial treatment including clarithromycin. Chest X-ray NICE scores for all cases were 8.50 ± 5.45 and 10.94 ± 6.03 at baseline and follow-up, respectively ($p = 0.0063$). For MAC-complication cases, scores were 8.36 ± 4.74 and 12.00 ± 6.02 at baseline and follow-up, respectively ($p = 0.00818$), and for non-MAC-complication cases, scores were 8.71 ± 6.82 and 9.29 ± 6.13 at baseline and follow-up, respectively ($p = 0.356$). MAC-complication cases were significantly further exacerbated than non-MAC-complication cases ($p = 0.027$).

Conclusions: Some cases of pulmonary *M. abscessus* infection progressed well without undergoing antibacterial treatment. In particular, results suggested that the clinical course of MAC-complication and non-MAC-complication cases differs.

1. Introduction

Mycobacterium abscessus (*M. abscessus*) is a rapidly growing nontuberculous mycobacterium (NTM) that belongs to the Runyon classification group IV [1] [2]. It is indigenous to environments such as soil and water and is known to cause skin and soft tissue infections in addition to respiratory tract infections [3] [4]. In Japan, it

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has been reported that in pulmonary NTM infections, *M. abscessus* is second most common pathogen following *Mycobafcterium Mycobacterium avium* complex (MAC) [5] *Mycobacterium kansasii*. Furthermore, complications with other NTM infections may also be observed. Although skin and soft tissue infections often respond well to antibacterial treatment, it is frequently difficult to treat respiratory tract infections as there is no established protocol for the timing of treatment initiation, selection of the appropriate antibacterial agent, or treatment duration [3]. In recent years, *M. abscessus* using whole genome sequencing of clinically isolated strains, *M. abscessus* is classified into three subspecies; *M. abscessus*, *Mycobacterium massiliense* (*M. massiliense*), and *Mycobacterium bolletii* (*M. bolletii*) [6], which are together known as the *M. abscessus* complex [7]. We retrospectively investigated the clinical course and findings, including the diagnostic imaging results, of 18 cases of pulmonary *M. abscessus* complex infection that occurred over 8 years at Kurashiki Central Hospital. We have discussed our results based on the presence or absence of a complicating MAC infection.

2. Patients and methods

Subjects comprised 18 patients diagnosed with pulmonary *M. abscessus* infection over 8 years between January 1, 2005 and December 31, 2012 at Kurashiki Central Hospital (Kurashiki, Japan). Subsequent progress of the patients was followed-up until March 2015. All cases met the diagnostic criteria for NTM infection, as determined by the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA) [3]. We retrospectively investigated various background factors such as underlying disease, laboratory findings, diagnostic imaging findings, treatment details, and clinical course, based on the medical records of these cases. For imaging findings in particular, two pulmonologists (K.F. and A.I.) evaluated the chest X-ray findings obtained at a date closest to when *M. abscessus* was first detected in respiratory tract specimens and the most recently available chest-ray at Kurashiki Central Hospital. The evaluation method used was the NICE scoring system (N; nodule, I; infiltration, C; cavity, E; bronchiectasis), which was recently proposed by Kurashima et al. for the semi-quantitative evaluation of MAC [8]. In the NICE scoring system, the lungs are divided into six zones (zone 1: area on the upper right above the level of the carina, zone 2: area on the upper left above the level of the carina, zone 3: area on the right between the level of the carina and the lower pulmonary vein, zone 4: area on the left between the level of the carina and the lower pulmonary vein, zone 5: area on the right below the lower pulmonary vein, and zone 6: area on the left below the lower pulmonary vein). Then, imaging findings for each zone are scored from 0 to 4 points based on four factors (N, I, C, E), according to the proportion of each zone that the lesion comprises. For 0%, 0 points are awarded; for 0% to <25%, 1 point; for 25% to <50%, 2 points; for 50% to <75%, 3 points; and for ≥75%, 4 points. The follow-up period in this study was set as the number of days between the two X-ray imaging sessions evaluated with the NICE scoring system. Cases were divided for analysis into those diagnosed as MAC-complication cases diagnosed according to the NTM infection diagnostic criteria of the ATS/IDSA [3] or non-MAC-complication cases.

All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Kanda, 2012), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria, version 2.13.0) [9]. Follow-up periods were reported as median and 95% confidence interval (CI), and compared using logrank test. Other absolute data were reported as mean ± standard deviation. Categorical variables were compared using Fisher's exact test. Continuous variables were compared using t test. All p values were two-sided, and p values of ≤0.05 were considered statistically significant.

This study was approved by the Ethics Committee of Kurashiki Central Hospital, Approved Number 1941.

3. Results

A total of 19 patients were diagnosed with pulmonary *M. abscessus* infections over the 8-year observation period. Of these, the underlying disease in one patient was a chest wall tumor (solitary fibrous tumor). This case was excluded from our analysis due to the influence of the tumor on chest contrast images. The backgrounds and bacteriological basis for making a diagnosis of pulmonary *M. abscessus* infection in the remaining 18 cases that were subject to analysis are shown in Table 1. Subjects included six males and 12 females, with a mean age of 74.7 years. There were 11 cases (cases 1–11) that were complicated by pulmonary MAC infection either before diagnosed or during the course of pulmonary *M. abscessus* infection. Of the seven cases that were not complicated by pulmonary MAC infection (cases 12–18), one was complicated by pulmonary *M. kansasii* infection (case 17). Underlying diseases included diabetes in three patients and active, malignant tumors in three patients (one lung cancer, one prostate cancer, and one gastric cancer). Furthermore, two patients were being administered corticosteroids (prednisolone (PSL) 12 mg/day for one case of vasculitis, and PSL 5 mg/day for one case of interstitial pneumonia). Data indicated that none of the patients had problems related to room air oxygenation except for one (case 13) who had originally undergone long-term oxygen therapy for pulmonary thromboembolism. The bacteriological basis for making a diagnosis of pulmonary *M. abscessus* infection included two consecutive positive results for sputum culture (14 cases), a positive result for bronchoalveolar lavage fluid culture (two cases), a positive result from the tissue culture of the surgical specimen of a simultaneously diagnosed lung cancer (one case), and two positive results for sputum culture together with a positive result from he bronchoalveolar lavage fluid culture (one case).

Table 2 shows the treatment details, follow-up periods and outcomes for each case. All of the MAC-complication cases (cases 1–11) except for case 7, received antibacterial treatment for MAC, which mainly included clarithromycin (CAM), rifampicin (RFP), and ethambutol (EB). Only case 2 was treated with imipenem/cilastatin (IPM/CS), amikacin (AMK), and CAM for *M. abscessus*, but the treatment was discontinued due to fatigue approximately one month after starting treatment. Thus, no MAC-complication cases received sufficient treatment for *M. abscessus*. Only one case (case 9) died during the observation period due to disseminated infection of MAC.

With regard to the non-MAC-complication cases (cases 12–18), only case 17 received two rounds of treatment with IPM/CS, AMK, and CAM for *M. abscessus*, and the treatment periods were 5 and 4 months, respectively. Although the sputum culture turned negative after the first round of treatment, a subsequent repeat sputum culture indicated growth of *M. abscessus* again. Therefore, a second round of treatment was performed, after which the sputum culture turned negative again. However, *M. kansasii* was also later detected in the sputum. During the observation period, only one case (case 17) died, but the cause of death was unclear. The median follow-up period for all cases was 1316 days (95% CI; 720–1675 days). The median follow-up periods for MAC-complication cases and non-MAC-complication cases were 1468.5 days (95% CI; 644–1820 days) and 995.0 days (95% CI; 417–1638 days), respectively ($p = 0.245$).

Total NICE score results were 8.50 ± 5.45 at baseline (the time when *M. abscessus* was firstly detected in culture results) and