

[CASE REPORT]

Pleurisy Caused by *Mycobacterium abscessus* in a Young Patient with Dermatomyositis: A Case Report and Brief Review of the Literature

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Abstract:

M. abscessus is a rapidly growing mycobacteria (RGM) and is the most common cause of pulmonary RGM infection. *M. abscessus* pleurisy is extremely rare. We herein report the case of a young patient with *M. abscessus* pleurisy without any lung lesions. A laboratory analysis of the pleural effusion revealed lymphocyte predominance and increased adenosine deaminase, similar to the findings observed in tuberculous pleurisy. The patient was initially treated for tuberculous pleurisy, which resulted in the partial improvement of the patient's symptoms and pleural effusion. *M. abscessus* pleurisy should be considered, especially in immunocompromised individuals, even in the absence of pulmonary involvement.

Key words: *Mycobacterium abscessus*, pleurisy, dermatomyositis

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Introduction

The rate of nontuberculous mycobacteria (NTM) infection has been increasing worldwide (1-3). The pulmonary diseases associated with NTM infection are commonly caused by *Mycobacterium avium-intracellulare* complex (MAC) and *M. kansasii*, which are slow-growing species (1).

Recently, lung diseases caused by rapidly growing mycobacteria (RGM) have often been recognized in patients with NTM infection. *M. abscessus* (formerly *M. chelonae* subspecies *abscessus*) is the most common cause of pulmonary infection by RGM and has been increasingly commonly identified as a pathogen in both healthy and immunocompromised hosts (1, 4). Morimoto et al. reported that pulmonary *M. abscessus* disease accounted for 2.6% of the pulmonary infections caused by NTM and that the incidence of *M. abscessus* disease was highest in the Kyushu-Okinawa area in a large laboratory-based analysis of Japan (5).

Pleurisy caused by NTM is relatively rare. It is reported to account for only 5% of pulmonary NTM infections (1, 6). In cases of NTM pleurisy, the most frequently identified pathogen is MAC. Thus far, there have only been a few reported cases of RGM pleurisy, which is suggested to be extremely rare (7-11).

We herein report a case of pleurisy caused by *M. abscessus* without infectious lung lesions in a young patient who was undergoing corticosteroid treatment for dermatomyositis.

Case Report

A 28-year-old Japanese man was admitted to our hospital in November 2016 due to a high-grade fever of 38.0-40.0°C that had persisted for 1 week. The patient had received prednisolone treatment for dermatomyositis at a starting dose of 50 mg since October 2014. The dose had been tapered to 10 mg in October 2016. He was a never-smoker, and he had no

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Table 1. The Results of the Peripheral Blood Analysis on Admission.

<Blood cell counts>		<Blood chemistry>		<Serology>		<Infection>	
WBC	6,400 / μ L	TP	7.2 g/dL	CRP	10.79 mg/dL	IGRA	(-)
Neut	84 %	Alb	3.6 g/dL			Anti MAC antibody	(-)
Lymph	10 %	T-bil	0.3 mg/dL	Anti-nuclear antibody	<40		
Eos	1.0 %	AST	26 IU/L	Anti ds-DNA antibody	2.0 IU/mL	β -D glucan	<6.0 pq/mL
RBC	413 \times 10 ⁴ / μ L	ALT	28 IU/L	Anti Sm antibody	1.3 U/mL	Aspergillus antigen	0.1
Hb	12.5 g/dL	LDH	247 IU/L	Anti Scl-70 antibody	<1.0 U/mL	C7-HRP	(-)
Ht	36.7 %	ALP	298 IU/L	Anti Jo-1 antibody	(-)	HIV antibody	(-)
Plt	20.9 \times 10 ⁴ / μ L	γ -GTP	69 IU/L	Anti centromere antibody	<5.0		
		BUN	17 mg/dL	Anti RNP antibody	<2.0 U/mL		
ESR	74 mm/h	Cre	0.51 mg/dL	Anti ARS antibody	(-)		
		Na	141 mEq/L	MPO-ANCA	<10		
		K	4 mEq/L	PR3-ANCA	<10		
		CK	62 IU/L				

IGRA: interferon-gamma-releasing assay

**Figure 1. Chest X-ray obtained on admission showed right pleural effusion and no abnormal shadows in the bilateral lung fields.**

history of traumatic injury. In addition, he had no family history of chronic lung or collagen disease.

On admission, the patient's height and body weight were 167.0 cm and 66.1 kg, respectively. A physical examination revealed the following findings: body temperature, 37.6°C; heart rate, 80 beats/min; blood pressure, 117/64 mmHg; and oxygen saturation, 95% in room air. On auscultation, the respiratory sounds in the right lower lung field were weak. In addition, facial flushing, Gottron-like eruption, and Raynaud syndrome of the maniphalanx were observed; however, these findings were not obviously aggravated in comparison to the time in which he was afebrile, before the dose of prednisolone had been reduced (from 11 mg/day to 10 mg/day). The laboratory findings on admission (Table 1) demonstrated a normal white blood cell count (6,400/ μ L) and creatinine kinase level (62 IU/L) but an elevated C-reactive protein level (CRP) (10.79 mg/dL). The patient was negative for anti-Jo-1 and anti-aminoacyl tRNA synthase antibodies. In addition, the results of an interferon-gamma releasing assay (IGRA) for *M. tuberculosis* (T-SPOT[®]), anti-MAC anti-

bodies, β -D glucan, and C7-horseradish peroxidase (HRP) were all within the normal ranges. Chest X-ray on admission showed right pleural effusion (Fig. 1), and chest computed tomography (CT) on admission also demonstrated right pleural effusion with no abnormal pulmonary or lymph node lesions (Fig. 2A, B and C). The right pleural effusion was a purulent pale yellow color. A laboratory analysis of the pleural effusion demonstrated lymphocyte predominance (54%) and a marked increase in the lactic acid dehydrogenase level (1,919 IU/L) (Table 2). In addition, no bacteria were detected in bacterial cultures or by Ziehl-Neelsen staining of the pleural effusion. At 1 week after admission, an analysis of the pleural effusion revealed that the adenosine deaminase (ADA) level was increased (132.7 U/L).

Meropenem (3.0 g/day) was initiated after admission to treat the right pleurisy. However, with the exception of right pleurisy, no other obvious infectious foci were seen. Despite the treatment, there was no obvious change in the patient's febrile condition. Although the IGRA for *M. tuberculosis* was negative, the elevated ADA level and the lymphocyte predominance of the right pleural effusion was suggestive of tuberculous pleurisy. Given the clinical and laboratory findings, isoniazid (INH) (300 mg/day), rifampicin (RFP) (450 mg/day), ethambutol (EB) (750 mg/day), and pyrazinamide (PZA) (1.2 g/day) were started on the ninth day after admission. He did not show symptoms of cough or sputum production at this time and sputum was not obtained. After the initiation of treatment with anti-tuberculosis agents (INH, RFP, EB, and PZA), the patient's high-grade fever and serum CRP level improved to around 37.0°C and 3.0-4.0 mg/dL, respectively, on the 20th day after admission (11 days after starting treatment with INH, RFP, EB, and PZA). The patient was discharged from our hospital on the 29th day after admission (Fig. 3).

At two weeks after the examination of the right pleural effusion, a mycobacterial culture of the right pleural effusion was found to be positive. *M. abscessus* was finally identified on the 48th day, based on the nucleic acid identification of

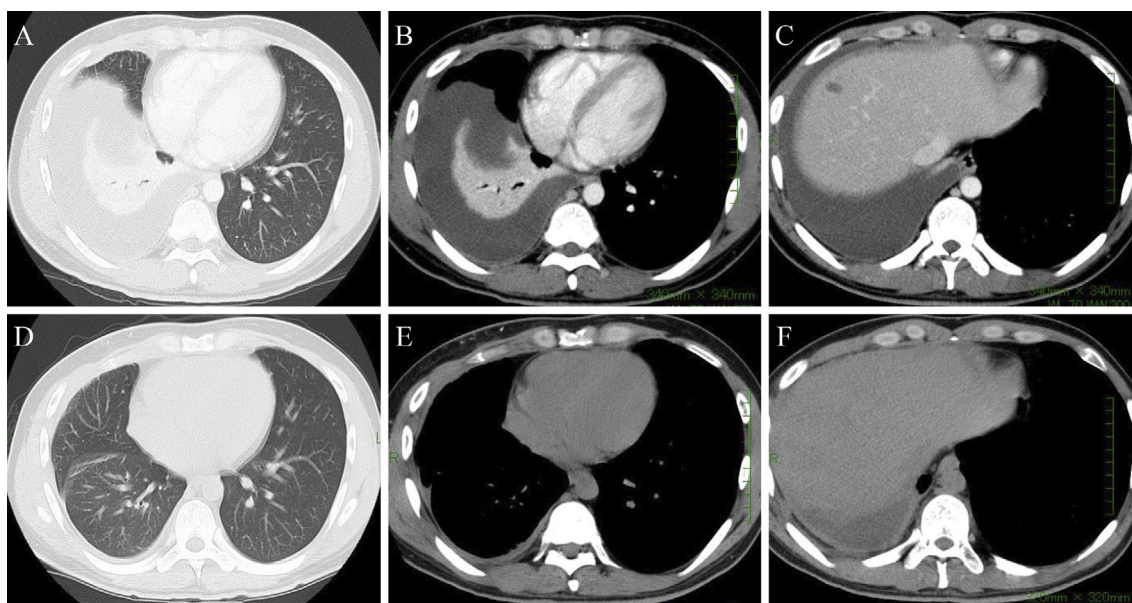


Figure 2. Chest computed tomography (CT) obtained on admission (November, 2016) (A, B and C) revealed right pleural effusion but no abnormal findings in the bilateral lung fields or lymph nodes. Chest CT performed at two months after the start of antimicrobial treatment (INH, RFP, EB, PZA) (January, 2017) (D, E and F) demonstrated a decrease in right pleural effusion and thickening of the right pleura.

Table 2. The Results of the Right Pleural Effusion Analysis on Admission.

Color	Yellow	<Bacteriological examination>		<Drug sensitivity for <i>M. abscessus</i> >		
Cell count	1,995 / μ L	Bacterial culture	No growth		MIC	(S/R)
Neut	3 %			Clarithromycin	S	2 (8/32)
Lymph	54 %	Acid-fast bacilli		Amikacin	S	8 (16/64)
Eos	0 %	Smear	(-)	Rifampicin	R	>32 (0.5/2)
TP	5.5 g/dL	Culture (2w)	(+)	Rifabutin	R	8 (1/4)
Alb	3.1 g/dL	DDH	<i>M. abscessus</i>	Ethambutol	R	4 (4/8)
LDH	1,919 IU/L			Streptomycin	R	32 (4/32)
BS	84 mg/dL			Kanamycin	I	8 (4/32)
Anti-nuclear antibody	<40			Levofloxacin	R	4 (1/4)
ADA	132.7 U/L					

DDH: nucleic acid identification of Mycobacterium group, MIC: minimum inhibitory concentration, S: sensitive, I: intermediate, R: resistant

the *Mycobacterium* group.

After discharge from our hospital, the patient started to feel bilateral femoral muscle pain, which was exacerbated with time. In addition, his low-grade fever (approximately 37.0°C) and increased serum CRP level (approximately 3.0-6.0 mg/dL) continued after discharge. He was therefore readmitted to our hospital in January 2017. On readmission, chest CT demonstrated an obvious decrease in the right pleural effusion (Fig. 2D, E and F). Based on the mycobacterial culture results, INH was switched to clarithromycin (CAM) (800 mg/day) and moxifloxacin (400 mg/day) in addition to RFP (450 mg/day) and EB (750 mg/day) to treat an *M. abscessus* infection. However, there was no obvious improvement in the patient's low-grade fever or in the increased CRP level. At the same time, recurrence of dermato-

myositis was suspected. In February 2017, intravenous immunoglobulin treatment resulted in the improvement of the low-grade fever, bilateral femoral muscle pain, and serum CRP level (approximately 1.0 mg/dL).

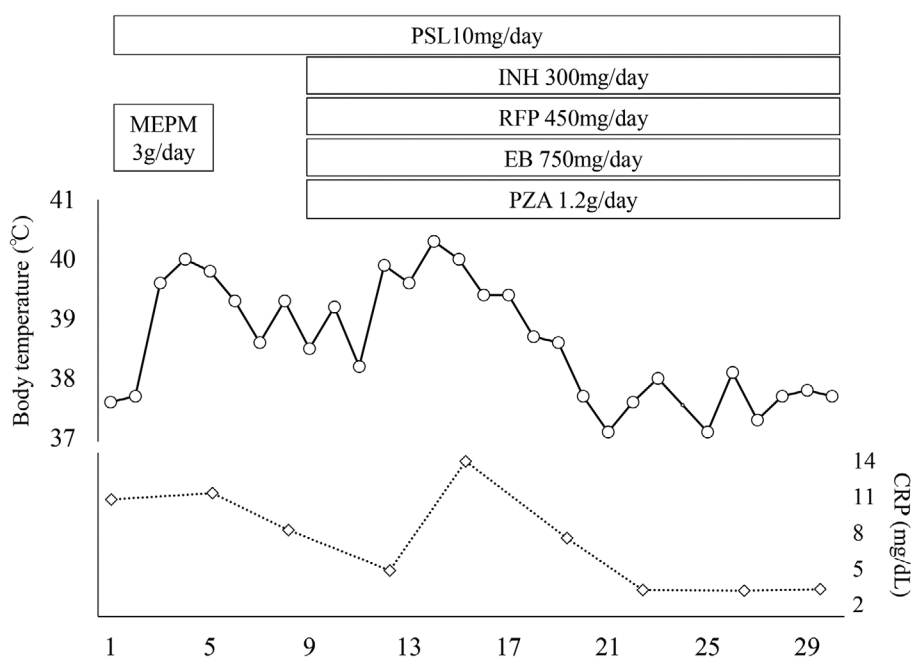
Discussion

Pleurisy caused by *M. abscessus* was first reported in a lung transplant patient by Fairhurst et al., and a total of six case reports, including our own, have been published (Table 3) (3, 11-14). These cases are characterized by complication with pulmonary infectious lesions and comorbid diseases. In addition, only the case reported by Lai et al. and our patient showed no obvious pulmonary involvement. Therefore, physicians should consider *M. abscessus* pleurisy

Table 3. Reported Cases of *M. abscessus* Pleurisy.

Reference	Age (y)	Sex	Presentation	Comorbidity	Cultured part of <i>M. abscessus</i>	Pleural effusion		Antibiotics used for outcome	Outcome
						Predominant cell type	ADA (U/L)		
12	66	M	Lung infection + empyema	Lung transplant recipient	Pleural effusion, BALF	Lymphocyte	-	CAM, CFX, CPMX	Died
11	68	F	Lung infection + empyema	Liver cirrhosis	Pleural effusion, sputum	Neutrophil	101	CAM, AMK, IPM/CS	Improved
13	57	M	Lung infection + empyema necessitatis	Old tuberculosis	Pleural effusion, sputum	Neutrophil	-	CAM, CFX, AMK, CPMX	Improved
14	50	F	Lung infection + pleural effusion	Organizing pneumonia	Sputum	Lymphocyte	79.7	CAM, AMK, IPM/CS	Partially improved
3	44	M	Empyema + bacteremia	Diabetes mellitus, liver cirrhosis	Pleural effusion, blood	Neutrophil	-	CAM, AMK, IPM/CS	Improved
Present case	28	M	Pleurisy	Dermatomyositis	Pleural effusion	Lymphocyte	132.7	INH, RFP, EB, PZA	Partially improved

CAM: clarithromycin, CFX: cefoxitin, CPMX: ciprofloxacin, AMK: amikacin, IPM/CS: imipenem/cilastatin sodium, INH: isoniazid, RFP: rifampicin, EB: ethambutol, PZA: pyrazinamide

**Figure 3. The clinical course of the patient.**

in patients with pleural effusion with comorbid disease, even if lung disease is absent.

In diagnosing tuberculous pleurisy, an increased lymphocyte-to-neutrophil ratio (>0.75 lymphocytes/neutrophils) and an ADA level of >40 U/L (especially >70 U/L) are considered to be useful (15), and a meta-analysis revealed that the diagnostic odds ratio of an elevated ADA level was 110.08 (95% confidence interval: 69.96-173.20) (16). In comparison to tuberculous pleurisy, the characteristics of NTM-associated pleurisy are unknown (3, 14, 17, 18). In the five reported cases of *M. ab-*

scensus pleurisy, the predominant cell types of pleural effusion were different. In addition, the ADA levels in the pleural effusion were only described in two patients, although both showed an increase in these levels (Table 3) (3, 11-14).

The combination of intravenous amikacin and cefoxitin or imipenem, in addition to CAM or azithromycin, was recommended for the treatment of *M. abscessus* infection in the 2007 American Thoracic Society (ATS)/Infectious Disease Society of America (IDSA) guidelines. However, no consensus treatment regimen has been established for extrapulmonary NTM diseases (2), and poor outcomes of patients

with *M. abscessus* disease have been reported (19). Similar to our patient, anti-tuberculosis regimens were often used initially in patients with NTM pleurisy including *M. abscessus*, but RGMs are reported to show no susceptibility to treatment with these first-line agents (10, 12). A few reports have shown the clinical effect of combined treatment with CAM, EB, and RFP on patients with pulmonary NTM infection (20, 21), and improvements in the pleural effusion and high-grade fever were achieved by treatment with first-line anti-tuberculosis medications in our case. *M. abscessus* is generally resistant to RFP and EB *in vitro*, but the *in vitro* susceptibility of agents do not always represent the *in vivo* clinical activity in patients with NTM (1). However, Hsieh et al. reported a case in which an incomplete response to anti-tuberculosis drugs in patients with pulmonary NTM infection caused empyema (7). The subsequent response to treatment should therefore be carefully monitored.

An apparent response to treatment with anti-tuberculosis drugs was recognizable after approximately two weeks in our patient. During this early stage of treatment, other possible causes of the patient's pleural effusion were considered, including comorbidities associated with dermatomyositis; however, pleural effusion due to dermatomyositis is thought to be extremely rare (22). In the present case, we made a diagnosis of *M. abscessus* pleurisy based on the results of mycobacterial culture, but tuberculous pleurisy could not be ruled out from the clinical course because *M. tuberculosis* is often uncultured in patients with tuberculous pleurisy, and *M. tuberculosis* can be missed in cases in which RGM is first cultured. In addition, the blood IGRA has been reported to not be very useful in identifying patients with tuberculous pleurisy (15); in a meta-analysis, the sensitivity and specificity of the blood IGRA for tuberculous pleurisy were 0.80 and 0.72, respectively (23). Therefore, physicians should take particular care in diagnosing *M. abscessus* pleurisy.

Only the pleural effusion obtained in the first thoracentesis procedure was positive for *M. abscessus*, and pleural mycobacterial cultures after starting anti-tuberculosis agents were negative. Shu et al. reported that the prognosis of NTM pleurisy patients with single and multiple positive results were not markedly different (2). Thus, the finding of more than one positive mycobacterial culture might be sufficient to start treatment for NTM pleurisy.

The precise pathogenetic mechanism of *M. abscessus* pleurisy is unknown; however, development from a lung parenchymal infection with *M. abscessus* and/or minor chest trauma is usually considered the pathway in patients with NTM pleurisy (17). Other mechanisms, such as the entrance of NTM into the pleural cavity through transient bacteremia or by contiguous spread from a small subpleural focus, have also been proposed (18).

In conclusion, we presented a case of *M. abscessus* pleurisy in a young patient complicated with dermatomyositis. Even in patients without preceding *M. abscessus* lung disease, *M. abscessus* pleurisy should be considered in the differential diagnosis of the cause of pleural effusion, espe-

cially in immunocompromised patients and aging individuals.

The authors state that they have no Conflict of Interest (COI).

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