

[CASE REPORT]

***Mycobacterium avium* Complex Pleuritis with Elevated Anti-glycopeptidolipid-core IgA Antibody Levels in Pleural Effusion**

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Abstract:

Pleuritis caused by nontuberculous mycobacteria is uncommon and difficult to diagnose. We herein report a case of *Mycobacterium avium* complex (MAC) pleuritis with elevated anti-glycopeptidolipid (GPL)-core IgA antibody levels in the pleural effusion. A 73-year-old woman with MAC pulmonary disease presented with massive left pleural effusion. A pleural biopsy by video-assisted thoracoscopic surgery was performed, revealing many noncaseating epithelioid cell granulomas. MAC was not identified by culture of the pleural effusion or specimens, but the anti-GPL-core IgA antibody level was markedly elevated in the pleural effusion. Measurement of anti-GPL-core IgA levels in the pleural fluid may be useful for diagnosing MAC pleuritis.

Key words: *Mycobacterium avium* complex, pleural effusion, glycopeptidolipid

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Introduction

Pleuritis is a rare manifestation of nontuberculous *Mycobacterium* (NTM) infection, and the diagnosis of pleuritis caused by NTM is often difficult (1). A serum anti-glycopeptidolipid (GPL)-core IgA antibody assay kit is highly predictive of *Mycobacterium avium* complex (MAC) pulmonary disease (2). However, there are no data regarding the levels of anti-GPL-core IgA antibodies in pleural fluid. We herein report a case highly suspected of being MAC pleuritis with elevated anti-GPL-core IgA antibody levels in the pleural effusion fluid.

Case Report

A 73-year-old woman was admitted to the hospital due to exertional dyspnea and massive left pleural effusion. She had been diagnosed with nodular bronchiectatic *M. avium* pulmonary disease 10 years previously and had been ob-

served without antibiotic treatment. She was a non-smoker and had no other relevant medical history.

Chest computed tomography taken 1 year before admission showed bronchiectasis and small nodules in the right middle lobe and lingula. In addition, there was a subpleural cavity in the lingula. All vital signs were normal. Her sputum was smear-positive for acid-fast bacilli and culture-positive for *M. avium*. Laboratory findings showed a white blood cell count of 6,990/mm³ with 14.2% lymphocytes, a C-reactive protein level of 4.59 mg/dL, and a serum anti-GPL IgA level 19.0 of U/mL (cutoff 0.7 U/mL). The T-SPOT.TB assay was negative. A human immunodeficiency virus antibody test was negative. Chest X-ray showed massive pleural effusion in the left lung (Fig. 1A). The pleural fluid was yellowish and clear. An analysis of the pleural effusion fluid showed nonspecific cytology, a white blood cell count of 3,599/mm³ with 97.5% lymphocytes, a protein level of 4.8 g/dL, a lactate dehydrogenase level of 300 IU/L, a glucose level of 99 mg/dL, an adenosine deaminase (ADA) level of 100.7 IU/L, and negativity for the T-SPOT.TB as-

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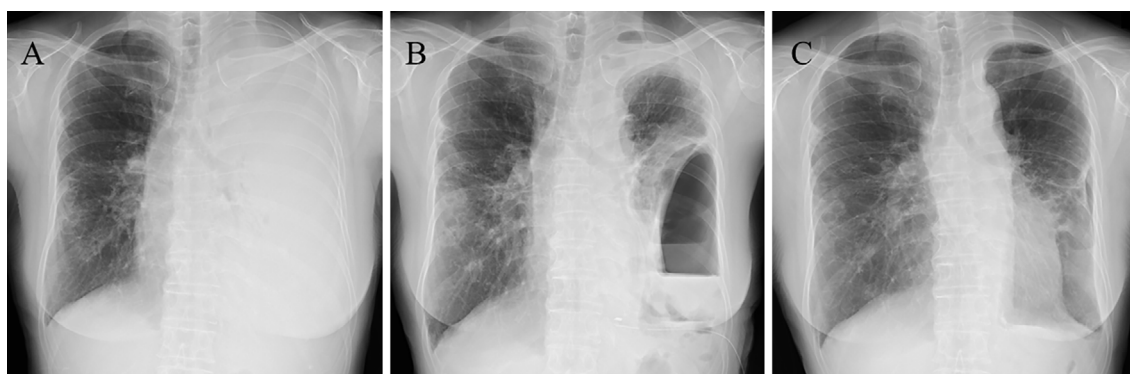


Figure 1. Chest X-ray findings at the time of admission show massive pleural effusion on the left side (A). After thoracoscopic surgery, the left lung was trapped, and the pleural effusion remained in the pleural space (B). At eight months after treatment initiation, the pleural space shrank, and the pleural effusion also decreased (C).

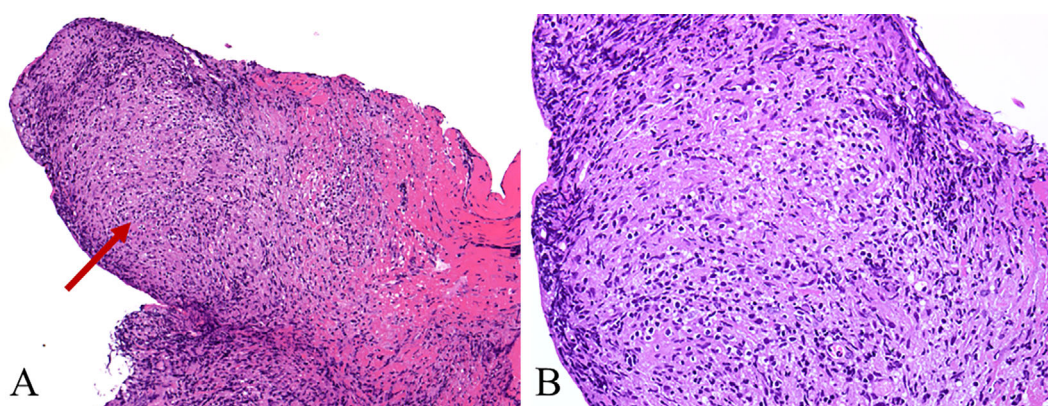


Figure 2. Hematoxylin and Eosin staining of pleural biopsy specimens: A histopathological examination showed noncaseating epithelioid cell granulomas and Langhans giant cells in the granulomas (A, arrow, 100 \times) and (B, 200 \times).

say. Although cultures of the pleural effusion were negative for bacteria, fungi and mycobacteria, the anti-GPL IgA level in the pleural effusion fluid was elevated to 12.8 U/mL.

A pleural biopsy by video-assisted thoracoscopic surgery was performed to confirm the diagnosis. There were thick fibrin formations between the visceral and parietal pleura. Ziehl-Neelsen staining and cultures of pleural biopsy specimens were negative for mycobacteria. However, a histopathological analysis of the pleural specimen revealed many noncaseating epithelioid cell granulomas and Langhans giant cells in the granulomas (Fig. 2), which were compatible with MAC pleuritis. Accordingly, treatment was started with rifampin 450 mg/day, ethambutol 625 mg/day, clarithromycin 600 mg/day and amikacin 500 mg three times per week.

After thoracoscopic surgery, the left lung was trapped, and the pleural effusion remained in the pleural space (Fig. 1B). However, after treatment, the pleural space gradually shrank, and the pleural effusion also decreased (Fig. 1C).

Discussion

This is the first reported case of elevated anti-GPL-core IgA antibody levels in pleural effusion fluid from a patient with MAC pleuritis. Because NTM pleuritis is an uncommon condition that exhibits varying clinical features, there are no established diagnostic criteria for this disease (1). Concurrent MAC lung disease, the presence of epithelioid cell granulomas in pleural biopsies and a good response to the standard treatment regimen for MAC disease support the diagnosis of the present case. In this case, although MAC was not identified by culture of pleural effusion fluid or pleural biopsy specimens, the level of anti-GPL IgA in the pleural effusion fluid was markedly elevated. These facts suggest the utility of the anti-GPL-core IgA test on pleural fluid for the diagnosis of MAC pleuritis.

When diagnosing NTM disease, it is important to differentiate tuberculosis (TB). However, differentiating between TB pleuritis and NTM pleuritis based on clinical or histopathological findings is often difficult. The pleural fluid findings of NTM pleuritis, e.g., a high percentage of lympho-

cytes and elevated ADA levels, as in this case, are similar to those of TB pleuritis (3). Patients with NTM pleuritis frequently have fibrocavitary-type lung disease (1), which is similar to the radiological findings of pulmonary TB. Furthermore, pleural biopsy specimens in both diseases present chronic granulomatous inflammation, and the histopathological difference is unclear (3, 4). Accordingly, confirmation by culture results is the most important factor for the differential diagnosis between TB pleuritis and NTM pleuritis. However, the sensitivity of pleural fluid culture for *M. tuberculosis* is low (less than 40%) (3). Although the positive rate for NTM culture in pleural fluid remains uncertain due to the lack of diagnostic criteria, some researchers have set criteria that do not require culture positivity because such cultures are often negative in cases compatible with NTM pleuritis (1, 5). Therefore, a specific diagnostic marker for NTM pleuritis is needed.

In this case, the levels of anti-GPL IgA antibodies in both the serum and pleural fluid were elevated. Because a positive test for serum antibodies reflects the presence of MAC lung disease, the test cannot be used to diagnose pleuritis. Whereas several studies have reported the using interferon gamma release assays, which are blood tests that detect *M. tuberculosis* infections, to test pleural fluid to diagnose TB pleuritis (6, 7), there are no reports regarding the use of the anti-GPL-core IgA antibody tests with pleural fluid. Takikura et al. reported a case of MAC pleuritis with an elevated level of IL-6 in the pleural effusion fluid (8). Reportedly, GPL from *M. avium* can induce the secretion of IL-6 primarily by monocytes in human peripheral blood monocytes (9), and the upregulation of IgA at mucosal sites in humans is induced by IL-6 (10, 11). Immune responses similar to those observed in peripheral blood might occur in pleural fluid and lead to high anti-GPL IgA antibody levels.

This is the first reported case showing elevated levels of anti-GPL-core IgA antibodies in pleural fluid from a patient with MAC pleuritis. Measurement of the anti-GPL-core IgA levels in pleural fluid may be useful for the diagnosis of MAC pleuritis. However, given the findings in this case, we cannot deny the possibility that antibody positivity in pleural effusion merely reflected exudation of the antibody in the blood. To determine whether or not pleural fluid positivity truly reflects the presence of MAC pleuritis, it is necessary to prove that the antibody level in the pleural effusion is not elevated due to other causes in patients with an elevated

blood antibody level. Further studies comparing the antibody levels in pleural effusion fluid with various causes are necessary to confirm the diagnostic accuracy of this test.

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

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