

## Pleural vasculitides of microscopic polyangiitis with asbestos-related plaques

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### Keywords

Asbestos, microscopic polyangiitis, MPO-ANCA, pleural effusion, pleural vasculitides.

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### Abstract

A 69-year-old man who had been exposed to asbestos for approximately 40 years presented with the complaint of fever and pleuritic chest pain on the right side on deep inspiration. Chest X-ray films showed pleural effusion in the right side. Initial antibiotic treatment was ineffective. The hyaluronic acid level was high in the pleural effusion but no malignant mesothelioma cells were seen with blind pleural biopsy. Blood chemistry showed a remarkable high titer of myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA) and open renal biopsy suggested crescentic glomerulonephritis. The precise pathological examination on the pleura obtained by the open pleural biopsy showed vasculitides and plaque leading to diagnosis of microscopic polyangiitis (MPA). This is a rare case of MPA seen in the pleural arteries.

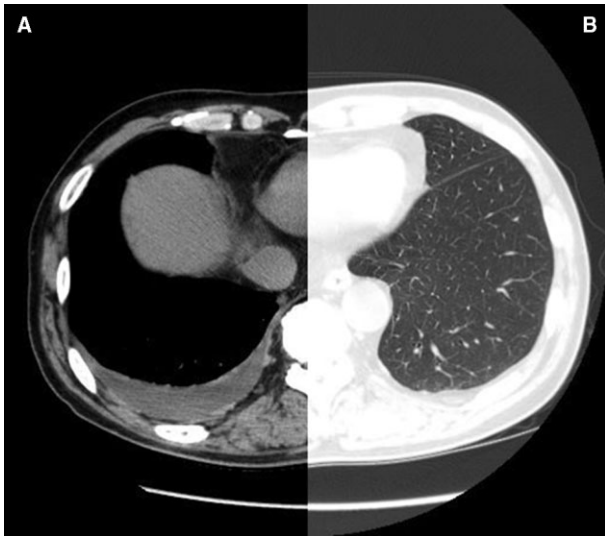
## Introduction

Pleural effusion in patients with a history of asbestos exposure is well recognized as evidence of asbestos-related disease. Asbestos exposure is associated with the onset of microscopic polyangiitis (MPA) [1, 2] but pleural effusion is rare in MPA [3, 4]. Only six cases of MPA with pleuritis as the only pulmonary complication have been reported but none of the patients had previous exposure to asbestos. There have been no reports of histologically proven vasculitides in pleura. This is the first case of MPA with a history of asbestos exposure and histologically proven vasculitides of both the pleura and glomeruli.

## Case Report

A 69-year-old man was presented to our hospital with complaints of fever and purulent sputum as well as pleuritic chest pain on the right side at deep inspiration. He had episodes of 37.8°C night fever for 10 days, and complained of

malaise and anorexia. He was an air conditioning pipe fitter and had been exposed to asbestos for approximately 40 years. Physical examination showed that he was febrile (37.3°C) but normal in heart rate (87 beats/min), blood pressure (131/90 mmHg) and body mass index (BMI) (23.9). Respiratory rate was regular at 18/min and peripheral capillary oxygen saturation (SpO<sub>2</sub>) was 98% on room air. The right bulbar conjunctiva appeared hyperemic. Breath sounds were weak in the right lower lung field. Screening laboratory data showed inflammatory reactions (white blood cells (WBC) 9900/μl with 57.9% neutrophils, 4.2% eosinophils, and C-reactive protein (CRP) 7.7 mg/dl) and elevated serum creatinine (0.81 mg/dl). Urinalysis was positive for blood and protein (31 mg/dl). Chest X-ray films showed costophrenic angle blunting in the right side but almost normal in both lung fields. High resolution computed tomography (HRCT) images of the chest revealed a small amount of pleural effusion in the right side and showed normal in the lung fields (Fig. 1). An antibiotic was started for treatment of pleuritis. Fever and CRP level



**Figure 1.** High resolution computed tomography (HRCT) images of the chest revealed a few volume of pleural effusion in the right side (A) and showed normal in the lung fields (B) as well.

improved immediately, but after a few days, the inflammatory markers elevated again along with increase in pleural effusion. A sample of aspirated pleural effusion was exudative (pH 7.45, protein 5.5 g/dl, LDH 547 IU/l, glu 119 mg/dl) and suggested neutrophilic pleuritis. Pleural adenosine deaminase and various tumor markers were normal and no bacterium was cultured. The level of hyaluronic acid was high at 123,000 ng/ml in the pleural fluid. One month later, pleural effusion also appeared in the left side. Contrast-enhanced HRCT images suggested the presence of thick parietal pleura and pleural plaques. Video-assisted thoracoscopic surgery (VATS) was performed for investigation of malignant mesothelioma. However, pathologic evidence presented no signs of mesothelioma. Additional serum chemistries showed that myeloperoxidase antineutrophil cytoplasmic antigen (MPO-ANCA) was strongly positive (>300 U/ml) and the serum level of creatinine had increased from 0.81 to 1.14 in one month. Open renal biopsy was performed. The renal specimens contained 15 glomeruli, some of which had crescent formations. Specimens obtained by VATS found several clusters of infiltrated neutrophils around the venules and capillaries of the pleura (Fig. 2A) and clusters of lymphocytes in the visceral pleura (Fig. 2B). Mature and incipient vasculitides were seen mixed which suggested that inflammatory reactions had persisted for more than one month. The patient was diagnosed as having a type of MPA. He was treated by high-dose of prednisolone (1 mg/kg/day). The pleural effusion almost disappeared. The serum creatinine and CRP levels were back in normal range. An additional

intensive immunosuppressive therapy, including azathioprine, intravenous cyclophosphamide, and rituximab was also started.

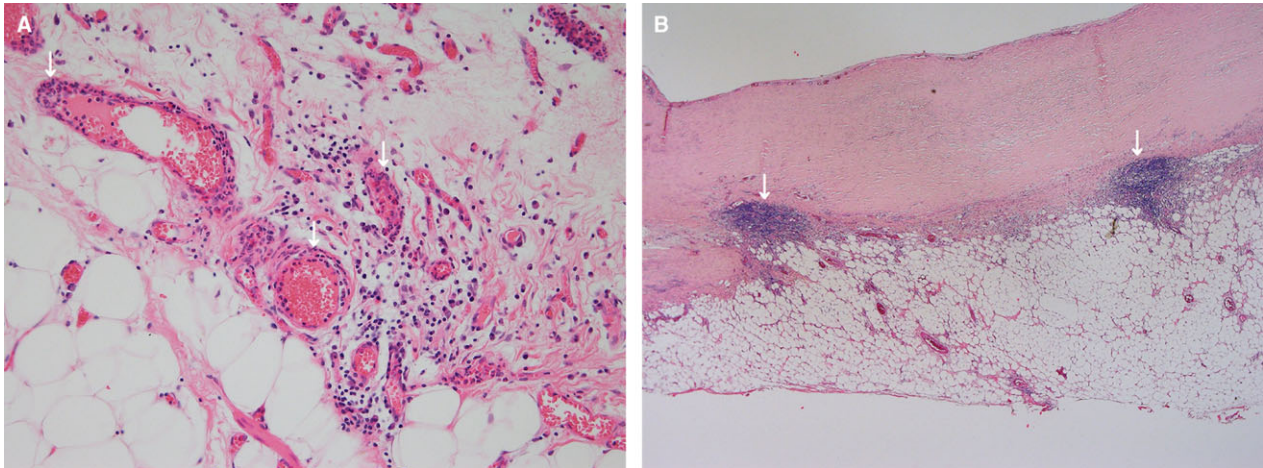
## Discussion

The hyaluronic acid level was high in pleural effusion of this patient, suggesting malignant mesothelioma. However, the pleural tissue obtained by open lung biopsy revealed vasculitides compatible with evidence of angitis. MPA is a disease of the small vasculitides related to MPO-ANCA. Gene, environmental, and microbial pathogens are considered intricately related to its pathogenesis. Asbestos and silica exposure are known environmental factors. One study showed that ANCA was positively detected significantly more frequently in the asbestos-exposed group than in the control group (21.3% vs. 5.1%,  $P=0.034$ ) [1]. Another study showed that morbidity of MPO-ANCA-related angitis and/or nephritis was seen more frequently after Kobe earthquake in 1995 [2]. In this case, his known asbestos exposure represents an environmental risk factor that may have acted as a contributor to the development of this disease. The clinical syndrome was classified as probable MPA in this case, following the criteria established by the Japanese Ministry of Health, Labor and Welfare [5] because pleuritis was the only pulmonary manifestation. After examining pathological findings in the pleura and glomeruli, this case was reclassified as definitive MPA. Pleuritis is a rare complication in MPA. Pulmonary complications have been reported in 60.8% of Japanese MPA (28 of 46 cases) and detail is alveolar hemorrhage in 23.9%, interstitial pneumonia in 43.5% and no pleuritis [3]. The pathological study also reported alveolar hemorrhage in 83%, interstitial pneumonia in 25%, and pleuritis with alveolar hemorrhage and interstitial pneumonia in one case [4]. It has been reported that pleuritis is the only pulmonary complication of MPA in six patients, all of whom had both pleural effusion and high levels of serum MPO-ANCA. None of the patients had asbestos exposure. Renal biopsy had been done in two patients but no pleural biopsy had been done. Our patient had histologically proven MPA with vasculitides of both pleura and glomeruli. Although very uncommon, the presence of a pleural effusion in a patient with known asbestos exposure history should raise the possibility of vasculitides in the differential diagnosis when all other more common causes have been excluded.

## Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.



**Figure 2.** (A) Infiltration of neutrophils around the venules and capillaries as seen in the visceral pleura (hematoxylin and eosin staining,  $\times 200$ ). (B) Two clusters of lymphocytes are also seen in the pleura (hematoxylin and eosin staining,  $\times 40$ ).

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