Malignant Pleural Mesothelioma Presenting as Acute Empyema with Severe Leukocytosis

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Five months after the treatment for acute empyema, a 75-year-old woman was referred to our hospital because of marked elevation of the white blood cell (WBC) count and C-reactive protein (CRP) level, and a right pleural mass detected by chest computed tomography. At this time, the WBC count and CRP level had increased to 60400/μl and 18.2 mg/dl, respectively. We performed biopsy and the tumor was diagnosed as sarcomatoid malignant pleural mesothelioma. Malignant pleural mesothelioma occasionally presents the symptoms and findings like an acute empyema. We demonstrated the case of malignant pleural mesothelioma which had presented the symptoms and laboratory findings very similar to acute empyema and had treated as acute empyema.

Keywords: malignant mesothelioma, empyema, leukocytosis

Introduction

Malignant pleural mesothelioma occasionally presents the symptoms and laboratory findings similar to acute empyema. We experienced a case of malignant pleural mesothelioma with severe leukocytosis and presented a clinical course similar to acute empyema.

Case Report

A 75-year-old woman consulted a local physician because of continuous right chest pain and productive cough. She had suffered from rheumatoid arthritis for 25 years and had been treated with oral steroid. She had no history of asbestos aspiration. She was an ex-smoker and her smoking pack-year was 15. Because chest computed tomography (CT) demonstrated low density mass with right pleural effusion (Fig. 1) and her laboratory data showed a high white blood cell (WBC) count and C-reactive protein (CRP) level, she was treated as having lung abscess and pleuritis. Although antibiotics were administered, her symptoms and laboratory data did not improve, and therefore chest tube drainage was done. Examination of the pleural effusion demonstrated neutrophil-dominant cytological class II exudates. Histological examination using cell blocks of the pleural effusion showed only fibrin clots and necrotic tissue without malignant cells. Many gram-positive and gram-negative bacteria were evident histologically. Because the patient’s laboratory data did not improve after chest tube drainage and antibiotic treatment, she underwent thoracoscopic treatment of empyema. After thoracoscopic dissection of the empyema cavity and decortication of the thickened visceral and parietal pleura, her serum WBC count and CRP level decreased immediately to normal, and the findings of chest roentgenography improved.

Five months after thoracoscopic dissection, she was referred to our hospital because of severe elevation of the WBC count and CRP level, and a right pleural mass evident by chest CT (Fig. 1). At this time, the WBC count and CRP level was increased to 60400/μl and 18.2 mg/dl, respectively (Fig. 2). Because chest CT demonstrated an isodense mass in the right lateral chest...
wall, we biopsied the mass and the tumor had a very rich blood supply. Histological examination revealed an increased number of spindle-shaped cells with nuclear atypia and mitosis. Immunohistochemistry demonstrated positivity for CAM5.2 and negativity for calretinin and carcinoembryonic antigen (CEA) (Fig. 3). Accordingly, the tumor was diagnosed as sarcomatoid malignant pleural mesothelioma. Although the patient demonstrated severe leukocytosis, immunohistochemistry for anti-granulocyte colony stimulating factor (G-CSF) antibody was negative. As the patient had chronic rheumatoid arthritis and her performance status was too poor to allow chemotherapy or surgical resection, she received only supportive care and died of malignant mesothelioma 5 months after diagnosis. 

Discussion

Although chest pain and productive cough are symptoms usually present in patients with infectious diseases such as pleuritis and empyema, they are also characteristic of malignant pleural mesothelioma. In the present case, examination of pleural effusion at first admission in local physician demonstrated neutrophil-dominant exudates and no atypical cells. She had no history of asbestos aspiration and she was immunocompromized patient with administration of oral steroid due to rheumatoid arthritis for 25 years. Histological examination using cell blocks also yielded no evidence of malignant cells, and many gram-positive and gram-negative bacteria were present in the pleural effusion. Moreover, at surgery, many fibrin clots, necrotic tissue and white uniformly thickened pleura were found in the empyema cavity without evidence of tumor. All of these findings were typical for acute empyema. After surgical treatment of the empyema, the serum WBC count and CRP level decreased immediately to normal and reincreased. 5POD: 5 post-operative day; 3m: 3 months after surgery; 5m: 5 months after surgery.
normal, and the findings of chest roentgenography improved. Because this course was typical for acute empyema, it was thought that the treatment for acute empyema succeeded. In this case, it was considered that occult malignant pleural mesothelioma had already been presented at the time of initial treatment and if a histological examination had been performed at surgery, a diagnosis of malignant pleural mesothelioma might have been possible. Histological examination is thus important and should be performed even in the cases that considered to be acute empyema clinically.

Five months after initial surgery, the serum WBC count and CRP level increased again, and an enlarged mass shadow in the right chest wall became evident. At that time, chest CT demonstrated the solid and isodense mass in the right chest wall. Biopsy diagnosis of this mass was sarcomatoid malignant pleural mesothelioma. Although immunohistochemistry for G-CSF in the biopsy material was negative, the specimen represented only a small portion of the tumor and not all the tumor cells would have been evaluable on that basis alone. Because no bacteria were found in the biopsy specimen at second admission and no other inflammatory focus was detected in the patient’s body, G-CSF or other inflammatory cytokines from the mesothelioma cells might have led to severe leukocytosis and high CRP level in this case.

Several cases of G-CSF-producing malignant pleural mesothelioma have been reported to cause severe leukocytosis. Cases of malignant pleural mesothelioma expressing G-CSF receptor or the inflammatory cytokine IL-6 have also been documented and the high serum levels of IL-6 was correlated with the levels of CRP. Inflammatory cytokines such as G-CSF and IL-6 might cause leukocytosis and CRP elevation even in patients with malignant mesothelioma. Although we did not measure the levels of these cytokines in the patient’s serum, it was assumed that the level of G-CSF or IL-6 was elevated, in view of the severe leukocytosis and very high CRP level in this case. Evidence also suggests that IL-6 might play a role in the induction of VEGF production. Adachi, et al. demonstrated that IL-6 and IL-6 receptor stimulation increased expression of VEGF in 80% of malignant mesothelioma cell lines. VEGF is a potent inducer of angiogenesis and its critical role in a tumor progression is well established. Inflammatory cytokines such as G-CSF, IL-6, and VEGF may promote

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### Fig. 3

Histological examination of resected specimen demonstrated an increased number of spindle-shaped cells with nuclear atypia and mitosis (A, H-E stain, ×100). Immunohistochemistry demonstrated positivity for CAM5.2 (B, ×400) and negativity for calretinin and carcinoembryonic antigen (C and D, ×400).
tumor growth and proliferation. \(^{10,11}\) Indeed, in patients with malignant pleural mesothelioma, it is reported that high WBC count and elevated CRP level associated with poor survival. \(^{12,13}\) Also, in this patient, the tumor had a very rich blood supply and the prognosis was poor. Although G-CSF production from the mesothelioma cells was not apparent and the levels of other inflammatory cytokines were not measured, an immune response in the area might have contributed to progression of the malignancy. Because possible auto-proliferation of malignant pleural mesothelioma through inflammatory cytokines has been reported, \(^{11}\) further investigation of the relationship between inflammatory cytokine production and proliferation of malignant pleural mesothelioma cells is warranted, so that more effective therapeutic approaches can be sought.

**Conclusion**

We have presented a rare case of malignant pleural mesothelioma with severe leukocytosis and high CRP level that presented as acute empyema. Histological examination should be done even if acute empyema was surely considered in clinically.

**Disclosure Statement**

None declared.

**Reference**


