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Myelomatous Effusion with Poor Response to Chemotherapy

While pleural effusion in multiple myeloma is relatively infrequent, myelomatous pleural effusion is extremely rare. We experienced a 61-year-old woman with IgD-λ multiple myeloma and pleural effusion. The diagnosis was made originally by pleural biopsy, pleural fluid cytology and immunoelectrophrosis of pleural fluid. Transient improvement of the pleural effusion was observed after administration of combination chemotherapy of vincristine, melphalan, cyclophosphamide, pednisone (VMCP) / vincristine, cyclophosphamide, adriamycin, prednisone (VCAP). Two months later, myelomatous pleural effusion recurred and no response to salvage therapy was observed. We reviewed the clinical feature of this case and literature concerning myelomatous pleural effusion.

Key Words: *Multiple Myeloma; Pleural Effusion; Drug Therapy*

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INTRODUCTION

Multiple myeloma is a disorder in which malignant plasma cells accumulate in the bone marrow and produce an immunoglobulin, usually monoclonal IgG or IgA (1). Malignant plasma cells usually invade the bone marrow but may involve other areas as well. The thorax may be invaded by myeloma, producing thoracic skeletal abnormalities, plasmacytoma, pulmonary infiltrates and pleural effusion. Pleural effusion in multiple myeloma is relatively infrequent and myelomatous pleural effusion is extremely rare. We recently experienced a patient with IgD-λ multiple myeloma with pleural involvement which responded poorly to chemotherapy. We reviewed the clinical feature of this case and literatures on myelomatous pleural effusion.

CASE HISTORY

A 61-year-old woman complained of a one-month history of dull left lower chest pain and exertional dyspnea. No hemoptysis, fever or weight loss was present. On physical examination, she appeared to be chronically ill. The temperature was 36.7℃, pulse 80 per min, respirations 20 per min, and blood pressure 120/70 mmHg. Examination revealed dullness and decreased breath sounds in the left lung base.

On admission, hemoglobin was 9.5 g/dL, Hct 26.7%, white blood cells 4,200/μL with a normal differential count and platelet 66,000/μL. Total protein was 3.9 g/dL, albumin 2.5 g/dL, globulin 1.4 g/dL, blood urea nitrogen 7.7 mg/dL, creatinine 1.0 mg/dL, calcium 7.4 mg/dL, lactate dehydrogenase 415.4 IU/L and urate 5.6 mg/dL.

Serum protein electrophoresis did not demonstrate a M-spike. Serum immunoglobulins quantification revealed diminished level of immunoglobulins: IgG 356 mg/dL, IgA 21 mg/dL, IgM 68 mg/dL, but serum immunoelectrophoresis showed abnormally bowed precipitin arcs in the IgD and Lambda chain. Urinary protein electrophoresis demonstrated monoclonal peak in beta immunoglobulin region and urinary immunoelectrophoresis showed an abnormal arc in the Lambda light chain.

Radiographic examinations showed left pleural effusion and osteolytic lesion in skull series. A thoracic CT scan showed enhanced posterior pleural wall thickening without bony destruction as well as a large pleural effusion in the left lower hemithorax (Fig. 1).

Thoracentesis was performed and revealed bloody fluid with a glucose level of 74 mg/dL, lactate dehydrogenase level of 608.2 IU/L and protein level of 3,166 mg/dL.

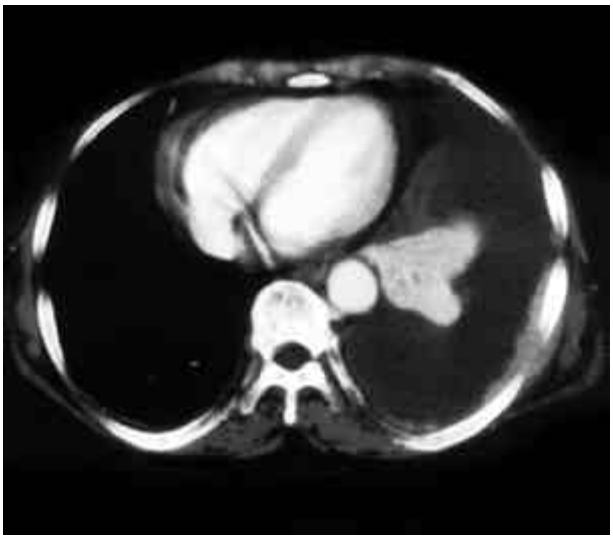

Fig. 1. Thoracic CT scan. Contrast-enhanced CT scan shows a posterior pleural-based enhanced mass encasing ribs without bony destruction as well as a large pleural effusion in left lower hemithorax.

Cytologic examination of pleural fluid revealed various sized immature plasma cells on bloody background (Fig. 2). Specimens from pleural biopsy demonstrated clusters of immature plasma that revealed positive findings for most of the cells on immunohistochemical staining of antibody lambda chain (Fig. 3). Bone marrow aspiration and biopsy showed high cellularity and 53% of immature plasma cells (Fig. 4).

After first cycle of combination chemotherapy with vincristine, melphalan, cyclophosphamide, prednisone (VMCP)/vincristine, cyclophosphamide, adriamycin, prednisone (VCAP), chest radiograph showed a reduction of pleural effusion. After two months, the pleural effusion increased again. Therapy was changed to salvage chemotherapy with vicristine, doxorubicin, dexamethasone (VAD) regimen, but no response was observed. Her disease progressed.

DISCUSSION

Multiple myeloma is a malignant proliferation of plasma cells that accumulate in the bone marrow and produce monoclonal immunoglobulin or immunoglobulin fragments (1, 2). Malignant plasma cells usually invade the bone marrow but may involve other areas as well. Despite the common occurrence of rib and sternal lesion in multiple myeloma, pulmonary parenchymal or pleural involvement has been reported infrequently (3-5). Pleural effusions in multiple myeloma occur in about 6 percent of patients and are due to several etiologies. The most common cause is congestive heart failure, due to either amyloidosis or atherosclerotic heart disease and the other causes are pulmonary embolism, chronic renal failure, second neoplasm and pleural myelomatous involvement (6).

In a review of 958 patients at the Mayo Clinic from 1960 to 1974, only eight cases (0.8%) were reported as myelomatous pleural effusion, and pleural effusion as the first manifestation of multiple myeloma is absolutely exceptional (7). In the literature reporting myelomatous pleural effusions, 80 percent of then were due to IgA

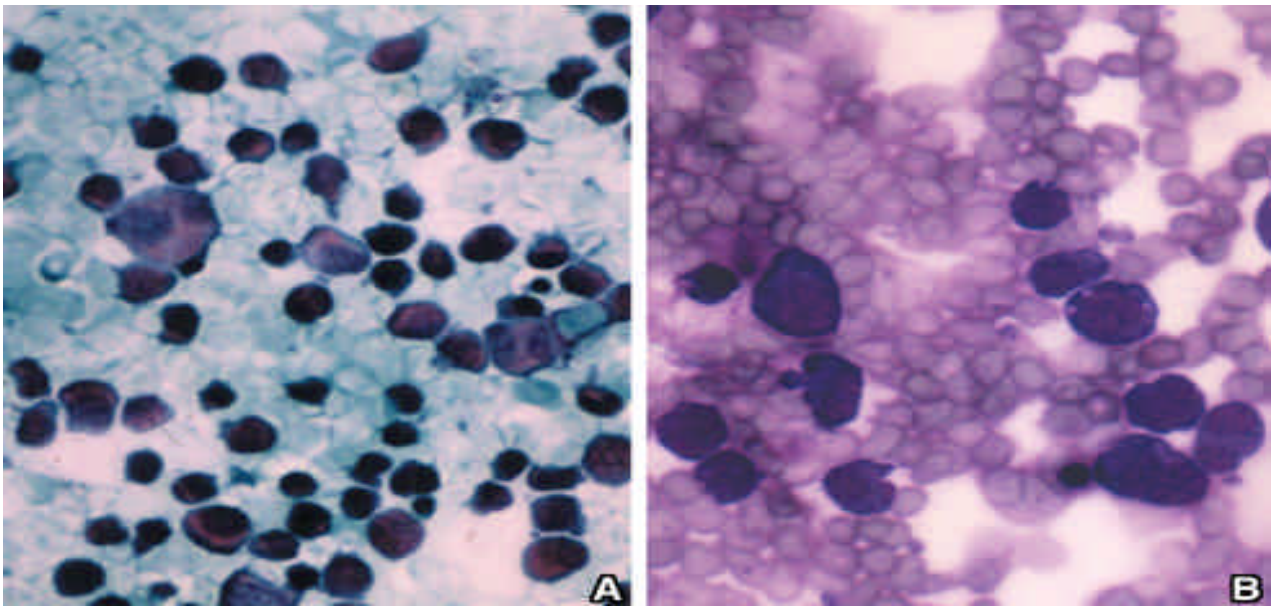

Fig. 2. Cytologic findings of pleural fluid. Various sized immature plasma cells with eccentric nuclei and occasional multinucleated forms are noted on bloody background (A: Papanicolau, ×400; B: Giemsa, ×1,000).

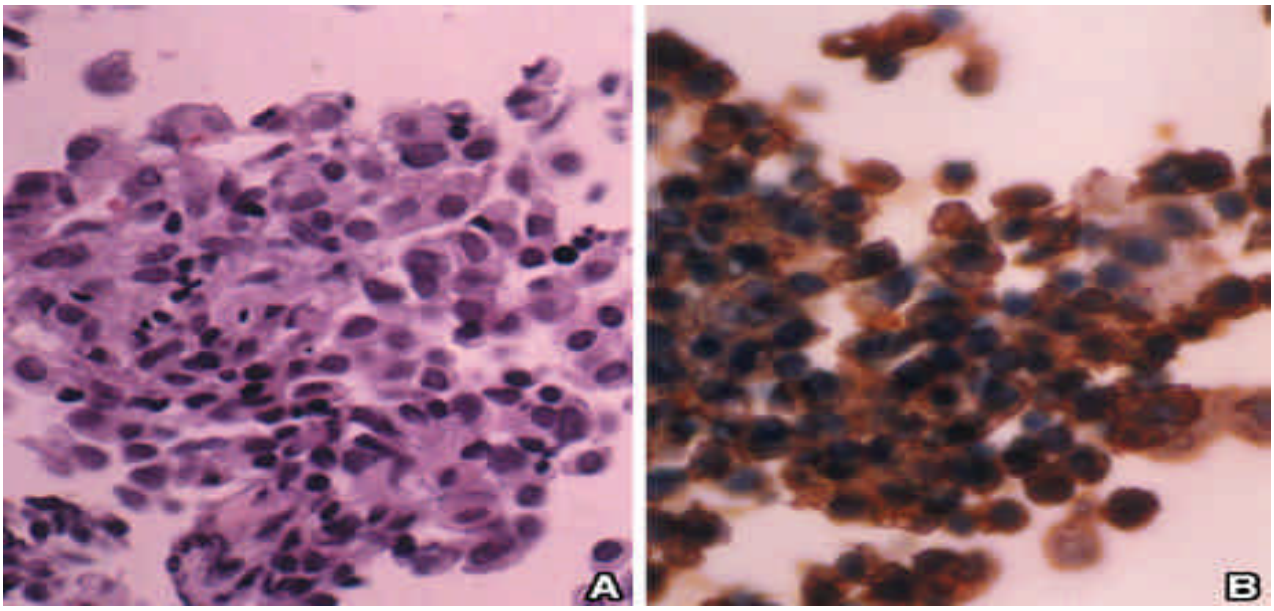

Fig. 3. Histologic findings of pleural biopsy. A: Clusters of immature plasma cells show eccentric nuclei and abundant eosinophilic cytoplasm (H&E, ×400). B: Immunohistochemical staining of antibody for lambda chain reveals positive finding for most of the cells (Immunoperoxidase, ×400).

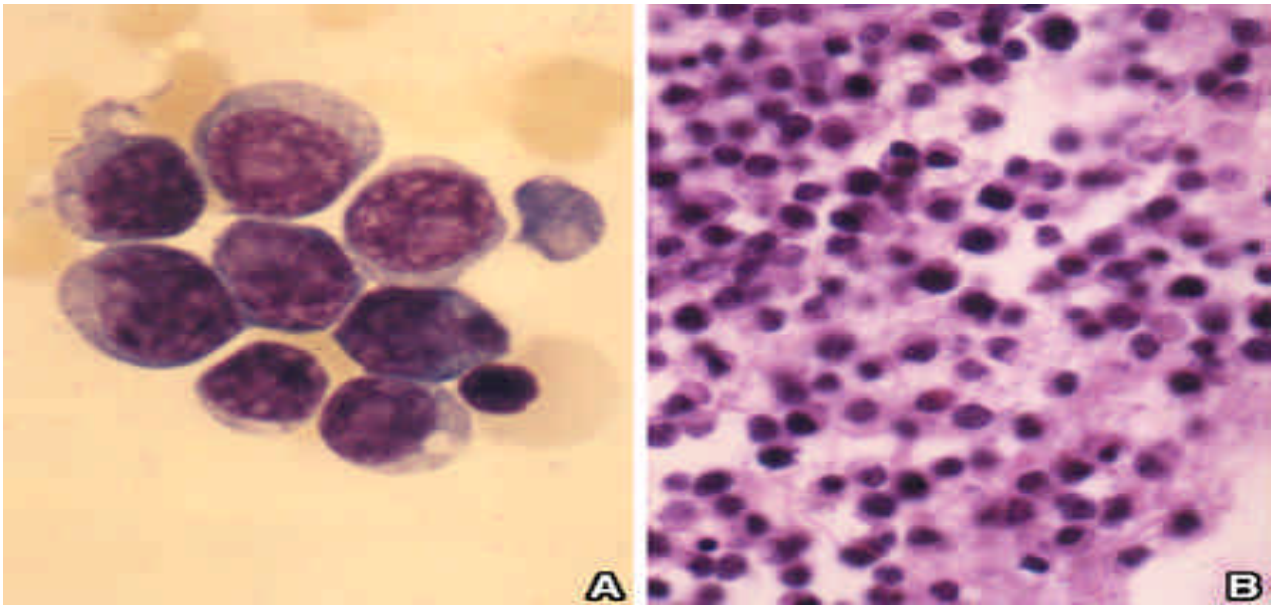

Fig. 4. Bone marrow aspiration and biopsy findings. Immature small and large plasma cells and large plasma cells with eccentric nuclei and prominent nucleoli are seen in the smear (A) and biopsy (B) (A: Giemsa, ×1,000; B: H&E, ×200).

while the others are mostly due to IgG. One exceptional case was caused by κ light chain and IgD myeloma (8, 9). In the present case, IgD-λ multiple myeloma was presented as myelomatous pleural effusion as the first manifestation in multiple myeloma.

Myelomatous pleural effusion is a rare isolated finding in multiple myeloma. The chest wall, mediastinum, or pulmonary parenchyma are frequently involved. Also, lytic lesion in the skeleton is usually present (10). Therefore, it was proposed that a major determinant in the development of myelomatous effusion is the production of large quantities of immunoglobulin by malignant plasma cells in or near the pleura which raises the colloid osmotic pressure of the fluid to such a level that normal absorption can not take place (11). In the present case, myeloma involved the pleura and chest wall.

The diagnosis of myelomatous pleural effusion was established confidently by the demonstration of mono-

clonal protein in pleural fluid electrophoresis, the detection of atypical plasma cells in pleural fluid and histologic confirmation using pleural biopsy specimen or autopsy (12, 13). In our case, we could find immature plasma cell in pleural fluid and infiltration by atypical plasma cell to show λ light chain monoclonal staining in pleural biopsy.

Multiple myeloma associated with myelomatous pleural effusion was very poor in the prognosis. Myelomatous pleural effusion was thought as a late manifestation in the natural history of multiple myeloma or an expression of the aggressive behavior of the disease (8). Reported length of survival generally has been less than four months. Because myelomatous effusion is in fact dependent on excess production of monoclonal protein by malignant plasma cell, one can expect to decrease pleural effusion with combination chemotherapy by decreasing production of monoclonal protein (11). In this case, pleural effusion was decreased after the first cycle of combination chemotherapy. But the pleural effusion increased again, and there was no response to salvage chemotherapy.

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