Unilateral Massive Pleural Effusion: A Presentation of Unsuspected Multiple Myeloma

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Abstract Pleural effusion in case of multiple myeloma is usually multifactorial but effusion due to myelomatous deposition of pleura is extremely uncommon. We are reporting a unique case of unsuspected multiple myeloma presenting as left sided massive pleural effusion due to myelomatous deposit in pleura and a rare M-band in the alpha-2 region in serum protein electrophoresis. A 61 year lady presented with cough, weakness and progressive shortness of breath. Examination revealed mild pallor and left sided massive pleural effusion that re-accumulated despite treatment. PAP stained smear of pleural fluid showed a large number of plasma cells and pleural biopsy revealed infiltration of plasma cells. Fiber-optic bronchoscopy was inconclusive. Blood examination revealed high value of alpha-2 globulin. Serum electrophoresis showed M band in alpha-2 region and urine electrophoresis showed faint monoclonal light chain pattern. X-ray skull

showed multiple punched out osteolytic lesions. Bone marrow examination revealed hypercellular marrow with atypical plasma cells including binucleate forms in large number (above 55% of nucleated cell population).

Keywords Myelomatous deposits of pleura · Pleural effusion · M-band in the alpha-2 region

Introduction

Multiple myeloma (MM) usually presents with bone pain, pathological fractures and anemia though the symptoms may be nonspecific. Weakness, infection, bleeding and weight loss are reported in as many as 82%, 13%, 13% and 24% of patients, respectively [1]. Pleural effusion occurs in around 6% of patients with myeloma, and aetiology is multifactorial [2]. Pleural effusion due to myelomatous involvement is rare, occurring in <1% of cases [2]. Unilateral pleural effusion as a presentation of unsuspected MM has not been reported.

Ninety-seven percent of myeloma patients have an intact immunoglobulin (Ig) or a free light chain that can be detected by protein electrophoresis, immunoelectrophoresis, or immunofixation studies of the serum or urine [3]. M spike in the region of alpha-2 globulin is very rare. We are reporting a case of MM with an extremely rare presentation of left sided massive pleural effusion, and the case is characterized by presence of M spike in the alpha-2 region in serum electrophoresis.

Case Report

A 61 year lady presented with acute onset of cough with little mucoid expectoration, shortness of breath and intense

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weakness for 2 weeks. She denied history of chest pain, fever, wheeze or weight loss. General survey revealed mild pallor, blood pressure 130/80 mm of Hg, pulse rate 86/min, respiratory rate 24/min and no peripheral lymphadenopathy. Respiratory system findings were consistent with left sided massive pleural effusion. Other systems were essentially normal. Routine blood examination showed Hb-9.5 g%, WBC-4,200/cmm, DLC-N-72, L-24, E-2, M-2, B-0, platelet-3,04,000/cmm, erythrocytes-mild hypochromic with anisocytosis and ESR-45 mm in first hour. Routine blood biochemistry revealed random blood glucose-91 mg/dl, urea-23 mg/dl, creatinine-1.4 mg/dl, serum bilirubin-0.4 mg/dl, SGOT-67 IU/l, SGPT-108 IU/l, alkaline phosphatase-174 IU/l and serum calcium-9.7 mg/dl. X-ray chest PA view showed left sided massive pleural effusion with mediastinal shift towards opposite side (Fig. 1). Straw color exudative pleural fluid was aspirated, and anti-tubercular chemotherapy was started with isoniazid, rifampicin, pyrazinamide and ethambutol, on the basis of mononuclear cell predominance (98%) and high ADA level (142.6 U/l) in pleural fluid. But there was recurrence of effusion. Total four liter of fluid was aspirated on several occasions, and ultimately inter-costal tube was introduced. PAP stained smear of pleural fluid showed a large number of plasma cells, including multinucleated ones admixed with lymphoid cells and a few reactive mesothelial cells (Fig. 2). Pleural biopsy revealed fibrocollagenous tissue with infiltration of plasma cells (Fig. 3). Fiber-optic bronchoscopy revealed no intra luminal growth. Broncho-alveolar lavage fluid showed predominantly lymphoid cells without any malignant cell. Blood examination revealed total serum protein 6.1 g/dl, albumin 3.73 g/dl, globulin-2.37 g/dl, alpha-1 globulin-0.31 g/dl, alpha-2 globulin-1.16 g/dl, beta globulin-0.51 g/dl and gamma globulin-0.39 g/dl. Serum

Fig. 1 PA view of chest X-ray showing massive pleural effusion involving the *left side* and shifting mediastinum towards *opposite side*

Fig. 2 Smear of pleural fluid showing many plasma cells, including a binucleate form, mixed with lymphoid cells and a few reactive mesothelial cells (PAP, $\times 100$)

Fig. 3 Histological section of the pleural biopsy illustrating fibrocollagenous tissue infiltrated by plasma cells (H&E, $\times 400$)

electrophoresis showed M band in alpha-2 region and urine electrophoresis showed faint monoclonal light chain pattern (Fig. 4). X-ray skull showed multiple punched out osteolytic lesions. Bone marrow examination revealed hypercellular marrow; depression of erythropoiesis and leucopoiesis; adequate megakaryopoiesis; and large number of atypical plasma cells including multinucleate forms (above 55% of nucleated cell population). Centrifuged deposit of pleural fluid showed plenty of atypical plasmacytoid cells. Therefore the final diagnosis was multiple myeloma with myelomatous involvement of pleura.

Discussion

Presence of plasma cells in pleural effusion is uncommon. In a series of 18 effusions with more than 5% plasma cells, four were due to malignant disease, three to tuberculosis, three to congestive cardiac failure, three to pulmonary

Fig. 4 Serum and urine electrophoresis showing a monoclonal M band in alpha-2 region and a faint monoclonal light chain pattern, respectively

embolization, two to pneumonia, one to sepsis, and two were of undetermined origin [4]. Smaller numbers of plasma cells are not of any particular diagnostic importance but the presence of many plasma cells with abnormal morphology in the pleural fluid suggests multiple myeloma. Recognition of atypical plasma cell (with nuclear pleomorphism, prominent nucleoli, frequent mitosis, asynchronous maturation of the nucleus in relation to cytoplasm) in fluid is critical for differentiating malignant from reactive plasma cell infiltration [5].

Among the features of thoracic involvement in MM, chest pain and recurrent pneumonia are frequent, and intrathoracic plasmacytoma is rare. Herskovic and associate reviewed the

records of 303 patients of MM seen at the Mayo Clinic over 5-year period, and found 21 (6.9%) of those patients had intra thoracic plasmacytoma [6]. Malignant pleural effusion due to myelomatous pleural infiltration is a rare and late complication in the course of the disease. It indicates a poor prognosis, resistance to treatment and more chance of relapse in spite of aggressive chemo-radiotherapy, and may necessitating pleurodesis [5].

Ninety-three percent of MM has monoclonal protein detectable in their serum. Approximately 70% of them have monoclonal protein or fragments detectable in the urine. In a series of 1,027 newly diagnosed cases of myeloma, the Ig types were IgG, IgA, IgD and free light chain only (Bence Jones myeloma) in 52%, 20%, 02% and 16% of cases respectively [3].

The present case of unsuspected MM presented with unilateral pleural effusion, and pleural involvement was established by the findings of pleural fluid cytology and pleural biopsy showing atypical plasma cell infiltration. Furthermore occurrence of M band in an uncommon location (alpha-2 region) in serum electrophoresis makes this case unique.

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