

Tanaffos (2007) 6(2), 68-72

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Myelomatous Pleural Effusion

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ABSTRACT

Multiple myeloma (MM) is a common hematologic malignancy. Pleural effusion is a rare presenting feature of multiple myeloma which carries a poor prognosis. Few cases of multiple myeloma with pleural involvement have been reported in the medical literature. We report a patient with MM diagnosed by cytologic examination of pleural fluid. Our patient was a 64-year old man with multiple myeloma who was receiving chemotherapy. He had developed dry coughs and exertional dyspnea about a month prior to the admission. Radiographic examination showed left pleural effusion with mediastinal shift to the opposite side. Diagnostic thoracentesis of pleural fluid was performed for the patient. Pathologic examination of pleural fluid showed plasmacytes and plasmablast type mononuclear cells with atypical nuclei, consistent with the diagnosis of pleural effusion due to multiple myeloma. In view of multiple etiologies of pleural effusion in malignant diseases, rare etiologies should also be considered in order to treat the effusion appropriately. (Tanaffos 2007; 6(2): 68-72)

Key words: Multiple myeloma, Pleural effusion, Plasmablast

INTRODUCTION

Multiple myeloma (MM) comprises about 1% of all malignancies as well as 10% of hematologic malignancies. The mean age of affliction is 65 years (1).

Multiple myeloma is a malignant proliferation of β (type) plasma cells which results in production of monoclonal immunoglobulins. This disease causes clinical signs and symptoms due to the tumoral mass. Accumulation of protein in organs (kidneys and heart) causes the disease manifestation and reduces the secretion of natural immunoglobulins by the normal plasma cells which eventually results in

hypogammaglobulinemia. Hematogenesis is deranged and osteolytic lesions appear resulting in hypercalcemia and renal dysfunction (1). Clinical signs and symptoms are heterogenous and vary from a slowly progressive form to a very aggressive type with extramedullary symptoms (1). Prognosis is correlated with the level of β_2 microglobulin (β_2M), C-reactive protein (CRP), lactate dehydrogenase (LDH), albumin, hemoglobin, platelets and the tumoral mass (5). Extramedullary symptoms and signs include involvement of liver, lymph nodes, spleen, kidneys, skin, meninges and the brain.

Malignant pleural effusion is extremely rare in multiple myeloma patients and the first case was reported in 1994 (3). Almost 80 cases of myelomatous pleural effusion have been reported in the medical literature up to 2005 (7).

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Received: 27 January 2007

Accepted: 3 March 2007

CASE REPORT

A retired 64-year old man residing in Mashhad presented to our hospital complaining of diffuse pain of extremities and swelling of the left ankle joint. The patient was suffering from pain in his legs and his left ankle joint for eight months. Nocturnal pain was not relieved by ordinary analgesics.

The patient developed skin lesions in the form of 2-10 mm purple plaques two months prior to admission. He also gave a history of non-productive coughs and exertional dyspnea one month earlier.

The patient did not recall any specific diseases in his past medical history. In review of systems, the patient mentioned a 3-5 kg weight loss during the last 4 months which was associated with fatigue and malaise. He denied having fever or sweating.

Diffuse skin lesions in the form of purple plaques were detected all over the body which were painless and asymptomatic. Jugular vein pressure (JVP) and thyroid examination were normal. Auscultation of the heart was unremarkable. Decreased breath sounds in the lower lobe of the left lung were found upon auscultation. The abdomen was soft without organomegaly. Peripheral pulses were normal in the extremities. Ankle swelling was not associated with any limitation of movement.

The patient underwent evaluation and paracentesis of synovial fluid which was mostly lymphocytic and negative for TB bacilli, crystals or malignant cells. Thyroid, liver, and kidney function tests and serum electrolytes were all normal. Serum protein electrophoresis was performed for the patient which showed a monoclonal gammopathy. Urinalysis (U/A) was negative for Bence Jones protein, but contained lambda M component monoclonal IgG. In the bone scan osteolytic lesions were detected in the extremities.

In the complete blood count (CBC) normocytic anemia with Hb=7 g/100cc, WBC= 2440/mm³ (PMN: 54%, Lymph= 34%) and platelet= 56,000/mm³ was noted. ESR was 146mm/h and PPD test was negative. Abdominal sonography was

normal. In the serum immunoelectrophoresis, albumin and betaglobulin had decreased to 3.2 gr/100 ml and 0.83 gr/100 ml and gammaglobulin had increased to 6.1 gr/100 ml (monoclonal gammopathy). On radiography of the skull, sclerotic lesions were detected in some areas. No lytic lesions were detected.

Bone marrow biopsy was performed for the patient which contained:

PMNs= 26% bands=6% blasts= 1-2%
erythroblasts= 32% plasma cells=15%
lymphocytes= 19%

Also, the bone marrow contained mononuclear cells and cells with side nuclei and obvious atypical changes. In the serum protein electrophoresis, the Kappa component was negative but the Lambda component was positive in 95% of the cells. The patient underwent systemic therapy for diagnosis of plasma cell myeloma. On further evaluation, CRP was positive, level of β_2 microglobulin had increased to 11.8 (normal range 0-3), serum albumin 3.2 gr/100, LDH=682 and alkaline phosphatase 86. According to the aforementioned rates, the patient was in stage 3 of IPI staging (considering the level of β_2 microglobulin more than 5.5) (4-5). Also, the skin biopsy reported plasmocytoma.

Chest radiography obtained 4 months prior to admission was normal. But considering the patient's symptoms including cough and dyspnea another chest x ray was obtained at the time of admission on which heart size was normal and left pleural effusion was observed. No lesion was detected in the parenchyma and soft tissue and thoracic cavity were normal (Figure 1). No parenchymal involvement was seen on the CT-Scan.

Due to the presence of pleural fluid, diagnostic paracentesis of the pleural fluid was performed for the patient. The fluid was cloudy and bloody and contained the following elements:

Protein=2.6 gr/dl glucose= 62 mg/dl
cholesterol= 52 mg/dl WBC=420 (L=85% P=16%)
LDH= 754 hematocrit= 0.2%

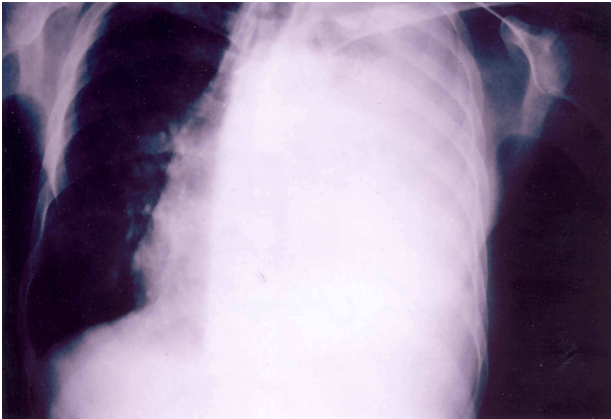


Figure 1. Chest-x-ray of patient.

Cytologic examination of the pleural fluid revealed a large number of plasmocyte and plasmoblast type mononuclear cells with large atypical nuclei which was consistent with the diagnosis of pleural fluid plasmocytoma (Figures 2 and 3).

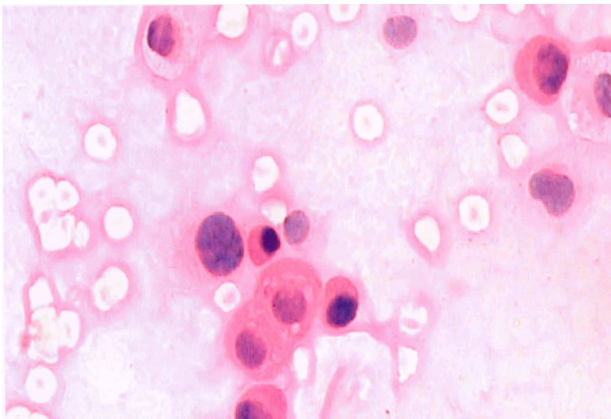


Figure 2. Cytologic examination of the pleural fluid.

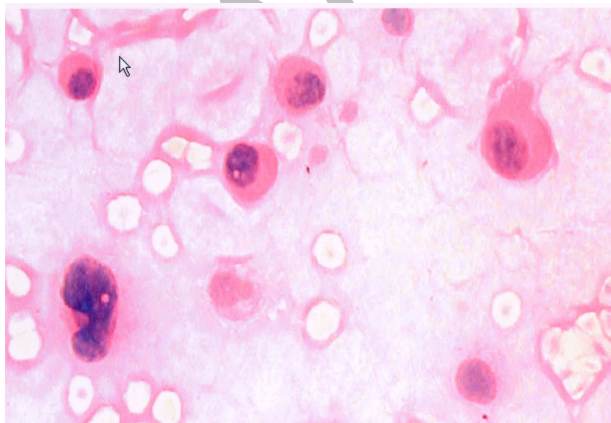


Figure 3. Cytologic examination of the pleural fluid.

Pleural biopsy showed diffuse fibrosis, hypercellular calcified centers containing fibroblasts and fibrinous pleuritis. Pleural fluid was negative for TB (smear and culture). Pleural fluid adenosine deaminase (ADA) activity was normal and polymerase chain reaction (PCR) was negative for TB. Systemic chemotherapy was continued for the patient and due to the development of dyspnea, therapeutic paracentesis of pleural fluid was performed twice resulting in relative improvement of dyspnea. On both occasions, evaluation of pleural fluid was negative for TB. The patient underwent thoracoscopy and pleurodesis because of the recurrence of pleural effusion causing dyspnea.

DISCUSSION AND CONCLUSION

Pleural effusion is a rare manifestation of multiple myeloma. The first case of pleural effusion and involvement of serous cavities in multiple myeloma was reported in the Chest Journal in 1994 by Rodriguez and colleagues.

It was the first case of multiple myeloma with raised IgA light chain Kappa (IgA-k). In the literature, 80 percent of myelomatous pleural effusions (MPE) were due to IgA MM (3-7).

Pleural involvement in these cases carries a poor prognosis. Involvement of serous cavities (pleural effusion and ascites) in myeloma currently has no standard effective treatment regimen (2). Chemotherapy and pleurodesis are effective in resolving malignant pleural effusion but survival is short (7). Pleural effusions in MM occur in about 6 percent of patients due to several etiologies requiring different types of therapy. Myelomatous pleural effusion is rare and occurs in less than 1% of cases. Pulmonary and pleural infiltrations are rare and might originate from the soft tissue plasmacytoma or present as a parenchymal mass, airway lesion or pleural effusion (8-11).

Myelomatous pleural effusion develops within 12

months of diagnosis of MM. All patients had high-risk disease (2-7). The initial diagnosis of myelomatous pleural effusion is based on positive cytology. Pleural tissue infiltration is found on pleural biopsy (7).

In every patient with malignancy who develops pleural effusion, diagnostic paracentesis of pleural fluid should be performed. Pleural effusion in myeloma may be due to plasma cell infiltration of the pleura, pulmonary embolism, nephrotic syndrome, secondary neoplasms, congestive heart failure concomitant with primary malignant disease, infections (parapneumonia), tuberculosis or other exudative or transudative causes (8, 9).

In view of these multiple etiologies, diagnostic thoracentesis should be performed to treat the effusion appropriately. Pleural effusion can be a complication of myelomatous ascites (2). In our patient, abdominal sonography was normal without ascites.

Extramedullary symptoms of multiple myeloma consist of involvement of organs such as liver, lymph nodes, spleen, kidneys, skin, brain, meninges and blood disorders (hemorrhage and thrombosis). Multiple myeloma is an uncommon cause of malignant pleural effusion. Electrophoresis and immunoelectrophoresis of the pleural fluid may be diagnostic. The most common thoracic disorders associated with myeloma are bone involvement or pulmonary infiltrates secondary to complicating infectious processes. Primary thoracic involvement by myeloma occurs in less than 1% of the cases. Reported patterns of extramedullary plasmacytoma of the thorax include lung mass, multiple pulmonary nodules, diffuse reticulonodular infiltration by myeloma cells, lymphadenopathy and mediastinal mass, pleural effusion and nodular pleural thickening and tracheobronchial infiltration (6). If the fluid is exudative (according to Mr. Light's criteria) the next step should be the cytologic examination of the

pleural fluid, determining cellular differentiation and pleural biopsy if required. In this patient, cytologic examination was performed after aspiration of the pleural fluid which was positive for plasmacytoma. To our knowledge, myelomatous pleural effusion has never been reported in Iran and this is the first case of multiple myeloma presenting with malignant plasmacytoma effusion. Malignant pleural effusion (MPE) in patients with MM heralds a poor prognosis and short survival. These patients usually die about four months from onset of MPE (7).

The first case of multiple myeloma was reportedly IgA-Kappa (3); whereas our patient had IgA-lambda multiple myeloma. Myelomatous pleural effusion in multiple myeloma is rare. Approximately 80 cases have been reported (till 2005) (7). Systemic chemotherapy in these patients is effective in resolving pleural effusion. However, pleurodesis may be required as well.

Our patient improved clinically after two thoracentesis. After a few days he developed pulmonary symptoms again (dyspnea and cough) which was treated with pleurodesis. Pleural biopsy revealed fibrinous pleuritis. Determination of the etiology of pleural effusion is significantly important in order to treat the effusion appropriately. Rare etiologies of pleural effusion are also noteworthy.

Acknowledgement

We would like to thank Dr. Ghaffarzadegan for his sincere cooperation in preparing the photographs.

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