

Case Report

Myelomatous pleural effusion as an initial presenting sign in a case of multiple myeloma

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ABSTRACT

Multiple myeloma (MM) is a neoplastic disease which mainly affects bone marrow but rarely may infiltrate extramedullary tissues as well. Myelomatous pleural effusions (MPE) develop due to extension of plasmacytoid cell lesions of thoracic bones into pleural tissue and directly presenting as an initial sign in a case of MM is exceedingly rare. It indicates poor prognosis, resistance to treatment and more chance of relapse in spite of aggressive chemoradiotherapy. The effusions of serous cavities in MM generally develop as a late complication of the disease like heart failure, renal failure, pneumonia and amyloidosis. We are reporting a rare case of IgG subtype myelomatous pleural effusion demonstrating abundance of plasmacytoid cells in pleural fluid. Bone marrow smear examination favoured the diagnosis of multiple myeloma with the presence of predominant population of plasma cells with high cellularity. There were also presence of a heterogenous myelomatous mass lesion in the right infratemporal fossae, multiple erosive lesions in ribs, vertebral bodies, skull and pelvic bones. Pleural fluid and serum protein electrophoresis demonstrated the presence of gamma monoclonal protein peaks confirming the diagnosis.

Keywords: Effusion, Myeloma, Plasmacytoma, Pleural

INTRODUCTION

Multiple myeloma (MM) is a plasma cell disorder and accounts for 1% of all malignancies and approximately 10% of all hematologic cancers.¹ Only fewer than 100 cases of true MPE have been reported worldwide.^{2,3} In multiple myeloma proliferated clonal plasma cells produce large amounts of non-functional immunoglobulin chains and eighty percent cases of MPE are associated with IgA subtype followed by those due to IgG.^{4,5,6}

The exact pathogenesis of primary myelomatous effusions is unknown. However, these may arise either

from extension of plasmacytoma of the chest wall, invasion from adjacent skeletal lesions, direct pleural involvement by myeloma or following lymphatic obstruction secondary to lymph node infiltration.^{7,8}

Plasma cells are responsible for both short and long lived antibody responses following antigenic stimulation. Normally clones of plasma cells secrete cytokines and stromal factors through immune regulatory pathways which are necessary for the survival of plasma cells and antibody secretion. It is thought that primary genetic events transform a normal post germinal centre B-cell into the malignant plasma cell. Functionally, these malignant cells are no longer regulated by normal

immunoregulatory mechanisms, with the net result being, the development of an enlarging clones of cells that support their own growth and proliferation via local secretion of cytokines such as IL6, IGF-1, TNF- α and others that are secreted by plasma cells themselves or by the stromal microenvironment within the bone marrow.⁹ Unchecked malignant proliferation of a clone of plasma cells (plasmacytoma) produce destruction and erosive lesions in the bones, that lead to bone pain and pathologic fractures. The myeloma proteins might lead to hyperviscosity syndrome and renal failure. The most common causes of pleural effusion associated with MM are heart failure, renal failure, parapneumonic and amyloidosis. Involvement of the serous cavities is a late manifestation in the natural history of the disease and represents the aggressive behaviour of myeloma. However, actual myelomatous pleural effusions are very uncommon and signify a concurrent disease process, poor prognosis and low possibility of survival.¹⁰ Myelomatous etiology of pleural effusion is usually diagnosed if pleural fluid protein electrophoresis demonstrates gammopathy or presence of abundant numbers of malignant plasma (plasmacytoid) cells in pleural fluid cytology.¹¹ Cytological identification of plasmacytoid cells within the pleural effusion has been considered as a best diagnostic method for diagnosing MPE, especially in the situation when routine blood and pleural fluid biochemical tests are nonspecific. Histological confirmation with a pleural biopsy is inconvenient and shows poor yield due to patchy involvement of pleura by myelomatous tissue.¹²

CASE REPORT

A 65 year old male presented to our hospital with complains of mild breathlessness and non-radiating left side chest pain for last two months, pain and mild swelling around right periorbital area radiating to temporal area for last one month and other constitutional symptoms like fatigue and weakness for last few weeks. He was an ex-smoker and presently kheni (Tobacco) chewer for about one year after quitting smoking. He was diagnosed with hypertension one year back and was on regular medication. Thereafter he had not been evaluated for any other illness. His general examination revealed pallor and mild periorbital swelling around right eye with slightly restricted eyeball movements and diplopia. Respiratory system examination confirmed left sided pleural effusion. Other systemic examinations were non-contributory.

His baseline investigations confirmed anaemia with Hb 7.7 g/dL, mild leucocytosis with TLC 12300/cmm. Differential count showed Neutrophil 59%, Lymphocytes 30%, Eosinophils 0%, Monocytes 1%, Basophils 5%, Mylocytes 2% and spillage of plasmacytoid cell (>1%) with basophilic cytoplasm and large eccentric nuclei (Figure 1).

RBCs were normocytic with rouleaux formation. Platelet count in the blood smear was adequate (1.88 lacs/cmm).

Renal function tests were mildly elevated with serum urea 37 mg/dl and creatinine 2.1 mg/dl. Liver function tests showed total protein 8.1 gm/dL with raised globulin (6.3 gm/dl) and reduced albumin (1.8 gm/dl). Other blood biochemical tests showed normal values, with S. Na- 135 mmol/dl, S.K.-4.4 mmol/dl, S. Calcium 8.9 mg/dl, S. Phosphorus 5.5 mg/dl, APTT 24.7 (control 18.8), Prothrombin Test -15.1 (control - 11.3) and INR -1.301.

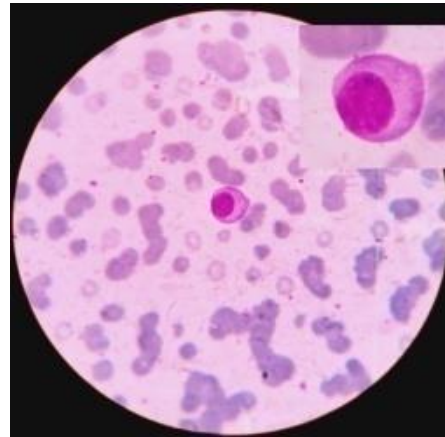


Figure 1: Spillage of plasma cells in peripheral blood smear.

Chest X-ray was suggestive of left sided mild pleural effusion (Figure 2). On thoracocentesis about 350 ml. of mildly pinkish-reddish, non-turbid freely flowing pleural fluid was aspirated without any trauma.

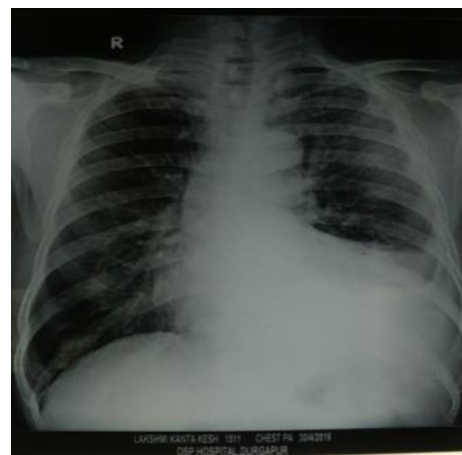


Figure 2: Chest X-ray PA view showing left side pleural effusion.

Biochemical analysis of pleural fluid showed glucose 29 mg/dl, Protein 8.9 gm/dL, LDH 3.7 U/dl and ADA 26.1 IU/l. Pleural fluid protein electrophoresis revealed the presence of monoclonal protein spike (M-spike gamma protein 3.8 gm/dl). Pleural fluid cytology showed predominantly presence of plasmacytoid cells with eccentric nuclei, cart-wheel or clock-face chromatin pattern with variable number of mesothelial cells and lymphocytes on a fibrinous background (Figure 3).

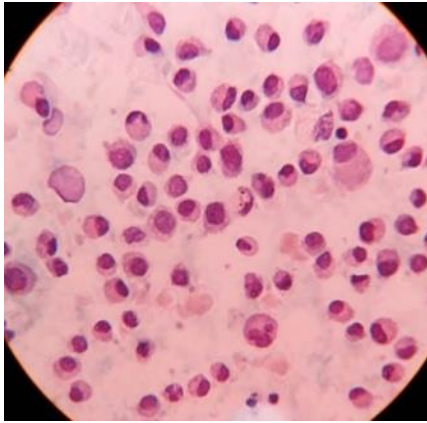


Figure 3: Plasmacytoid cells with eccentric nuclei in pleural fluid.

Serum protein electrophoresis revealed total serum protein 12.05 g/dl including total Albumin 3.17 g/dl and Globulin 8.8 gm/dl. Serum electrophoretogram showed monoclonal gamma pathology pattern (M spike gamma protein 5.43 gm/dl). There was IgG Lambda light chain restriction in immunofixation electrophoresis. Immunoassay showed the serum IgG 9413 mg/dl, IgA <40.0 and IgM <25 mg/dl. Bone marrow smear samples from left iliac crest showed bone marrow plasmacytosis. There were approximately 10% of the plasma cells with deep basophilic cytoplasm with eccentric nuclei in the nucleated cell population of the bone marrow (Figure 4).

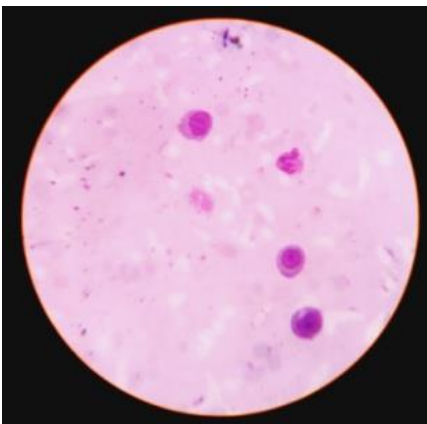


Figure 4: Bone marrow Smear showing plasma cells with eccentric nuclei.

CT Scan - head revealed multiple lytic lesions in skull (Figure 5A) with heterogenous mass lesion in the right infratemporal fossa extending into right retro-orbital region, ethmoid and sphenoid sinus and causing erosion of adjacent bones, suggesting neoplastic etiology (Figure 5B and 5C).

These findings were further evaluated with MRI of right orbit, which revealed a soft tissue mass causing proptosis and compression of the optic nerve. There were myelomatous deposits and erosion of bilateral greater wing of sphenoid, bilateral pterygoid plates, clivus and basioociput with focal erosion of cella and multiple lytic

lesions in the calvaria. Further CT Scan of thorax, whole spine and pelvis showed multiple lytic lesions involving 2nd and 3rd right rib, L4 and L5 vertebral bodies and bilateral iliac and pubic bones. Multiple compression fractures were noted through the dorsal vertebrae with degenerative disc disease at level D2, D5 and D10 (Figure 6 and 7).

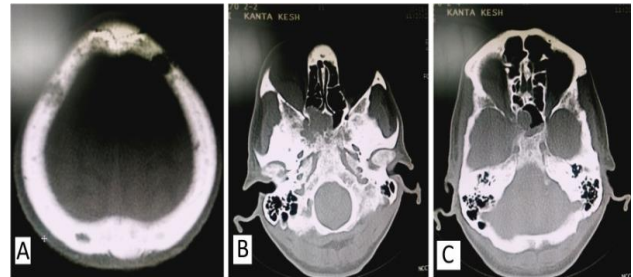


Figure 5: (A) Multiple lytic lesions in skull bone. (B and C) Heterogenous mass lesion in the right infratemporal fossa region extending into right retroorbital region, ethmoid and sphenoid sinus causing erosion of adjacent bone, suggesting neoplastic etiology.

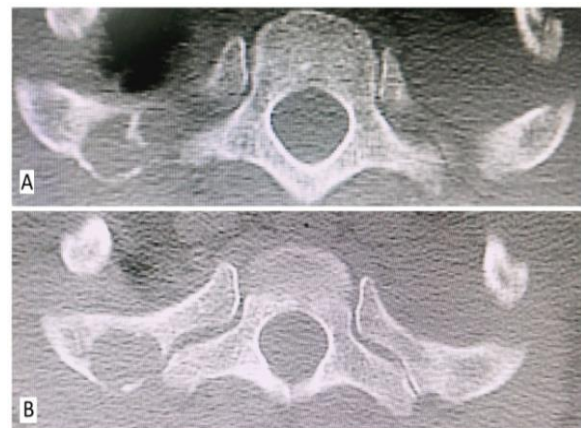


Figure 6: Multiple lytic lesions involving 2nd and 3rd ribs.

Further MRI of whole body for metastatic evaluation revealed focal diffuse lesions in multiple dorsal and lumbosacral vertebrae, ribs, bilateral femur and pelvic bones. Focal lesions were also present in left Glenoid and lateral 1/3rd of left clavicle. There were no focal lesions in the cervical vertebrae and the body of sternum.

Patient was treated with CTD chemotherapy (Cyclophosphamide + Thalidomide + Dexamethasone) and palliative radiation for right orbital region administered (400 cGy/day for 5 days) to preserve vision and minimize diplopia. Patient responded well initially with improvement in diplopia and swelling around the orbit but later on general condition gradually deteriorated over a period of last six months. Patient succumbed to death probably due to renal failure at his home after about seven months from start of treatment.

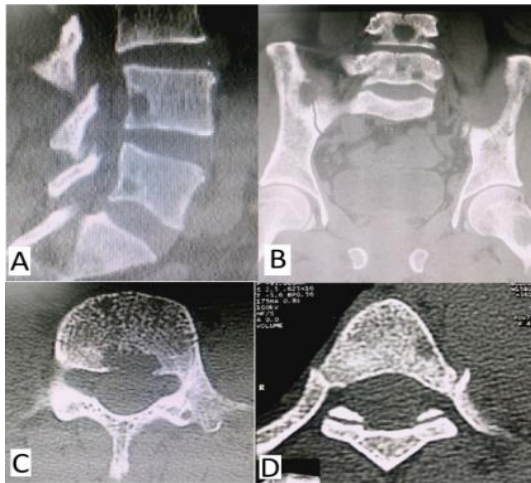


Figure 7: (A and B) Multiple lytic lesions involving L4 and L5 vertebral bodies and bilateral pelvic and femur bones. (C and D) Compression fractures and lytic lesions in dorsal vertebrae with degenerative changes.

DISCUSSION

The effusions of serous cavities in MM generally develop as a late complication of the disease like heart failure, renal failure and amyloidosis. This patient presented with initial signs of left sided pleural effusion. Usually the features of thoracic involvement in MM include chest pain and frequent recurrent pneumonia but intrathoracic plasmacytoma is rare. 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.¹³

Suspicion of multiple myeloma was aroused when we found elevated levels of pleural fluid total protein with increased globulin levels, presence of anemia and raised serum creatinine levels. Myelomatous etiology of pleural effusion was confirmed when pleural fluid cytology showed abundance of plasmacytoid cells with eccentric nuclei and monoclonal gamma protein peak in pleural fluid protein electrophoresis in absence of other obvious causes of pleural effusion.

However, on further evaluation we demonstrated multiple skeletal lytic lesions, serum monoclonal gammopathy and raised serum levels of IgG immunoglobulins that confirmed the diagnosis of multiple myeloma with myelomatous pleural effusion. Present patient had IgG subtype of myelomatous etiology. We presume that the myelomatous effusion in our case was due to extension of plasmacytoid cell lesions of chest wall and ribs. We demonstrated presence of atypical plasma cells in pleural fluid and spillage of plasma cells in blood smears. Bone marrow smears also revealed high cellularity with a predominant plasmacytoid cell population that favoured the diagnosis of myelomatous etiology over a reactive

one. This was further supplemented by the presence of monoclonal gammopathy detected in in pleural fluid and serum protein electrophoresis. Pleural biopsy was not done because of inconvenience and poor yield. Lower diagnostic yield of pleural biopsy is because of patchy pleural involvement of myelomatous tissue in the pleura.¹³

CONCLUSION

Although myelomatous pleural effusions are extremely rare as a presenting sign of multiple myeloma, yet plasma cell neoplasms should be considered in the differential diagnosis of pleural effusions. It indicates advanced stage of disease and a poor prognosis. Cytological evaluation is a useful tool in its diagnosis. Usually plasma cells accumulate predominantly in the bone marrow; rarely, they may invade other areas especially the thorax as a result of which myelomatous pleural effusion, even though very rare, might become the first clue to the diagnosis.

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