



Multiple Myeloma Presenting as Bilateral Malignant Pleural Effusion

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Abstract:

Pleural effusions in multiple myeloma are relatively infrequent and more so myelomatous ones. It is usually a late complication and associated with a poor prognosis. A 74-year-old male presented with dyspnoea and fever of two months duration. On examination he had bilateral pleural effusion. The diagnosis of myelomatous effusion was made by cytological examination of the aspirated pleural fluid.

Key words: Malignant effusion, Multiple myeloma, Plasmablast, Pleural effusion.

Introduction

Multiple myeloma presenting initially as malignant pleural effusion is extremely rare. Diagnosis of such cases is usually made by the presence of neoplastic plasma cells. Recognition of atypical plasma cells in fluids is critical for therapeutic and prognostic considerations as their presence indicates a poor prognosis. We report a case of multiple myeloma initially diagnosed by exfoliative cytology of pleural fluid and later confirmed by protein electrophoresis and bone marrow studies.

Case Report

A 74 year old male belonging to upper middle socio-economic strata presented to the chest OPD with dyspnoea, tachypnoea and low to moderate grade fever since two months. On examination he had bilateral pleural effusion. A clinical diagnosis of tubercular effusion was initially considered. Pleural fluid aspiration yielded a haemorrhagic fluid. The total protein content was 3.9 g/dl with an increased globulin contents, sugar levels were 15 mg/dl and chlorides 90 mmol/L. The total cell counts were approximately 600 cells/mm³. Centrifuged smears prepared from the fluid showed more than 80% atypical plasma cells [Fig.1].

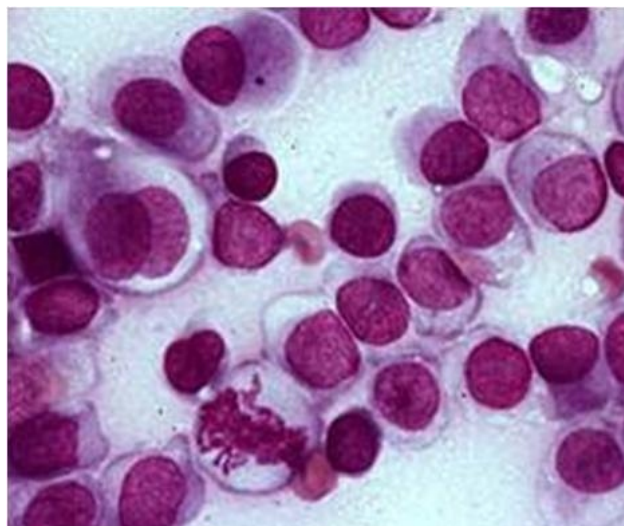


Fig. 1: Malignant plasma (Myeloma) cells in pleural fluid (MGG X 400)

Further examination revealed right inguinal lymphadenopathy, right posterior triangle cervical lymphadenopathy and bony tenderness. The FNAC smears prepared from both the inguinal and posterior triangle neck lymph nodes showed similar cytological findings. There was presence of round to oval cells with high N/C ratio, deep blue cytoplasm, eccentric nuclei, granular nuclear chromatin and one to two prominent nucleoli. Mitosis was frequent. Abnormal binucleated and multinucleated forms were also noted.

On further investigations, CT scan chest showed multiple osteolytic lesions at D3-D7 level. A large 7.6×4.0 cm lobulated homogeneously enhancing soft tissue lesion was seen in the right para-vertebral region located against D3-D6 level. The mass was seen extending to azygo-oesophageal recess. Scalloping with destruction of adjacent vertebral body was noted. Large 33×28 mm enhancing mass was seen in the right para-tracheal location as well. Carina appeared displaced anteriorly with mild extrinsic impression on the right main branches. Few small pre-carinal and pre-tracheal lymph nodes were observed.

Haematological investigations showed Haemoglobin 9.4 g%, PCV 27%, TLC 5500 cells/mm^3 , Differential $P_{66}L_{32}E_1M_1$, ESR 72 mm in 1st hour by Wintrobe's method and the peripheral smear showed marked rouleaux formation. The platelet counts were reduced (0.81 lacs/mm^3). Serum Protein electrophoresis showed a suspicious non-discrete protein band in the gamma globulin region (? Monoclonal gammopathy'M'spike). Beta 2 microglobulin levels were very high $3723 \mu\text{g/L}$ (N=570-1470 $\mu\text{g/L}$). Bone marrow aspiration, trephine biopsy and bone scan confirmed the diagnosis of multiple myeloma (plasmablastic type). The patient received chemotherapy but despite that he showed a downhill course and expired one month later.

Discussion

Malignant pleural effusion in multiple myeloma is rare and seen in less than 1% of cases [1-4]. There have been very few reported cases of multiple myeloma with pleural effusion as the initial presentation similar to that of our case [1-7]. Identification of scanty and mature appearing atypical plasma cells in body fluids is important and may be missed. The cytomorphology of the plasma cells along with the clinical profile are helpful in differentiating reactive from malignant plasma cell infiltrates. High cellularity with a predominant plasma cell population in a haemorrhagic or necrotic background favours a malignant effusion [1-3]. Morphological features of malignant plasma cells are nuclear pleomorphism, prominent nucleoli, frequent mitosis and asynchronous maturation of the nucleus in relation to the cytoplasm. Malignant effusions in myeloma patients are usually resistant to treatment and often relapse in spite of aggressive chemo-radiotherapy necessitating pleurodesis [5,6]. A malignant effusion in myeloma patients places the patient in advanced Salmon Durie stage. This is an alarming presentation, signifying dismal prognosis. Death usually occurs within few months. These effusions occur as a late manifestation in the natural history of multiple myeloma or are an expression of the aggressive behaviour of the disease [1,3,4-6].

Pleural effusion in multiple myeloma is due to several aetiologies requiring different types of therapy. These aetiologies include - heart failure secondary to amyloidosis, chronic renal failure, secondary neoplasm and pleural myeloma associated involvement. The exact pathogenesis of myeloma associated effusion is still unknown [1,4]. Proposed mechanisms include invasion from adjacent skeletal lesions, extension from chest wall plasmacytomas and direct pleural involvement by myeloma. Our patient had rib, vertebral and sternal lesions on CT scan supporting the first mechanism of pleural effusion described above. The best means of diagnosis is cytological identification of malignant plasma cells within the pleural fluid as observed in our case.

Differential diagnoses on cytology include other non-myeloma associated conditions that present with pleural effusion e.g. Non-Hodgkin's Lymphoma, acute and chronic lymphoid leukaemias, especially those with concomitant mediastinal involvement [5,7]. A pure population of poorly differentiated plasma cells may be difficult to distinguish from acute leukaemia, large cell lymphoma and adenocarcinoma. Acute leukaemia shows cells with a high nuclear:cytoplasmic ratio and a thin rim of cytoplasm. Adenocarcinoma shows cellular cohesion and morula formation. Large cell lymphoma shows nuclei with prominent nucleoli and moderate amount of cytoplasm. Such cells may be difficult to distinguish from neoplastic plasma cells; immunocytochemistry may then be necessary to classify them. Pleural fluid electrophoresis, flow cytometry and immunocytochemistry aid in confirming the monoclonality of the plasma cells [8]. Reactive plasmacytosis, as seen in tuberculosis and Hodgkin's lymphoma, is usually accompanied by neutrophilic leucocytes, lymphocytes, reactive mesothelial cells, which seldom exceeds 15-20% of the cells and have few or no abnormal features. Presence of reactive plasmacytosis was easily ruled out in our patient due to the presence of neoplastic plasma cells in all the smears including pleural fluid and lymph node aspirations.

When immunocytochemistry is not available, Immuno-electrophoresis of the pleural fluid may prove to be a useful adjunct in making the diagnosis. A preliminary report of multiple myeloma by exfoliative cytology is seldom made. Myeloma associated pleural effusion as an initial presentation although extremely rare, should always be considered in presence of atypical plasma cells in body fluids irrespective of age. Malignant myeloma usually occurs in elderly patients (mean age 71 years) and the usual presentation is bone pain along with pathological fracture. A purely morphologic diagnosis of myeloma associated pleural effusion can be made if the cytological features are sufficiently distinctive. The present case is rare because the patient had bilateral myeloma associated pleural effusion as the initial presentation.

In conclusion, presence of atypical plasma cells in the body fluids should be carefully interpreted and such patients should be thoroughly assessed for multiple myeloma. Since, benign pleural effusions are common in multiple myeloma; the diagnosis of serous cavity involvement is critically important due to poor prognostic implications.

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