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Concurrent Myelomatous Pleural Effusion and Extramedullary Mediastinal Involvement as an Initial Manifestation of Multiple Myeloma

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Patient: Female, 72
Final Diagnosis: Myelomatous pleural effusion
Symptoms: Dyspnea
Medication: —
Clinical Procedure: Thoracentesis
Specialty: Pulmonology





Objective: Rare disease
Background: Myelomatous pleural effusion (MPE) is a rare occurrence in patients with multiple myeloma (MM). Fewer than 20 cases of MPE have been reported as an initial manifestation of MM. Extramedullary plasmacytoma (EMP) occurs in fewer than 5% patients with MM, and mediastinal EMP is even rarer, with only about 80 cases reported in the literature. We present a case study involving a patient with concurrent MPE and mediastinal EMP as an initial manifestation of MM.

Case Report: The patient was a 74-year-old nonsmoking female with a 3-month history of exertional dyspnea and back pain. On exam, the patient was afebrile (temperature 37.2°C), blood pressure was 160/74 mm Hg, heart rate was 92 bpm, respiratory rate was 22/min, and oxygen saturation was 87% on room air. Patient was in mild distress and had decreased breath sounds over right lung fields about halfway up with dullness to percussion. Computed tomography of the chest showed a moderate-sized right pleural effusion and an anterior mediastinal mass. Thoracentesis showed a lymphocyte-predominant exudate. Cytology showed numerous plasma cells including immature forms. Stains for CD138 were positive, confirming plasma cell origin of cells. The anterior mediastinal mass was also biopsied and showed diffuse infiltrate of lymphocytes with plasma cell features that were also positive for CD138. Systemic protein electrophoresis showed a monoclonal immunoglobulin G kappa spike, and bone marrow biopsy was consistent with MM.

Conclusions: MPE and EMP are extremely rare manifestations in MM. In addition, it is extremely rare for these to be the presenting features of MM. We report concurrently occurring MPE and EMP in a patient as her initial manifestation of MM.

MeSH Keywords: Multiple Myeloma • Plasmacytoma • Pleural Effusion, Malignant

Full-text PDF: <http://www.amjcaserep.com/abstract/index/idArt/898849>

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Background

Pleural effusions are reported in about 6% patients with multiple myeloma (MM). The majority of these are benign and related to heart failure, renal failure, and hypoalbuminemia. Among patients with MM, 0.8% develop myelomatous pleural effusion (MPE) [1], and fewer than 100 cases of MPE have been reported in the literature. MPE usually develop during the treatment course of MM, and fewer than 20 cases of MPE have been reported at the time of diagnosis of MM [2–4]. Fewer than 10% of patients with mediastinal extramedullary plasmacytoma (EMP) have concurrent MM. In addition, EMP very rarely involves the mediastinum, with fewer than 15 cases in the literature [1,5]. We report a patient whose initial manifestation of MM was an MPE and a mediastinal EMP.

Case Report

A 74-year-old African American female with a previous history of renal cell carcinoma (status post right nephrectomy 8 years prior to presentation) presented to our institution for complaints of worsening exertional dyspnea and right-sided back pain for 3 months. She also had a dry cough and had had a 15-pound unintentional weight loss during this period. The back pain was described as stabbing and radiating to right anterior chest, and was worsened with any movement. Her initial vitals were as follows: temperature, 37.2°C; blood pressure, 160/74 mm Hg; heart rate, 92 bpm; respiratory rate, 22/min; oxygen saturation 87% on room air. She was in mild distress but speaking in full sentences. Chest exam revealed absent breath sounds over lower right lung field posteriorly extending about halfway up with dullness to percussion. No axillary or cervical lymphadenopathy was palpated. There was no point tenderness over the spine. She had no clubbing or edema in her extremities. Initial labs were as follows: white blood cell count $6.5 \times 10^9/L$ (74% neutrophils, 25% lymphocytes, 1% monocytes); hemoglobin 9.2 g/dL; platelet count $154 \times 10^9/L$; total protein 8.5 g/dL; albumin 2.4 g/dL; calcium 8.4 mg/dL. Computed tomography scan of the chest showed a moderate right pleural effusion with pleural nodules posteriorly (Figures 1, 2). There was a mediastinal mass noted as well along with a right posterior paraspinal mass, which was confirmed on subsequent magnetic resonance imaging (Figure 3). She underwent a thoracentesis of the right pleural fluid, and the fluid was consistent with a lymphocyte-predominant exudate. Cytology of the fluid showed numerous plasma cells, including immature forms (Figures 4, 5). Staining for CD138 confirmed plasma cell origin of the cells (Figure 6). Transthoracic needle aspiration of the mediastinal mass was performed, and biopsy showed diffuse infiltrate of lymphocytes with plasma cell features (Figure 7). These cells also were stained for CD138. The patient underwent a serum protein electrophoresis, which showed a monoclonal immunoglobulin G (IgG) kappa spike.



Figure 1. Computed tomography scan of chest showing moderate right pleural effusion and mediastinal mass.



Figure 2. Computed tomography scan of chest showing right pleural effusion with pleural nodules and masses.

Subsequent bone marrow biopsy confirmed a diagnosis of MM with more than 30% plasma cells seen in the marrow. Because of the poor overall prognosis and advanced nature of disease, the patient chose to go home with home hospice and passed away within a month of diagnosis.

Discussion

Pleural effusions are fairly common in MM (6% of patients). However, the majority of these are benign and related to heart failure, renal failure, and hypoalbuminemia [6]. Fewer than 1% patients with MM develop MPE [1]. MPE usually develops during the treatment course of MM and is associated with an extremely poor prognosis, with a median reported survival of fewer than 4 months [7]. Fewer than 20 cases of MPE have been reported at the time of diagnosis of MM [2–4]. A total of 17

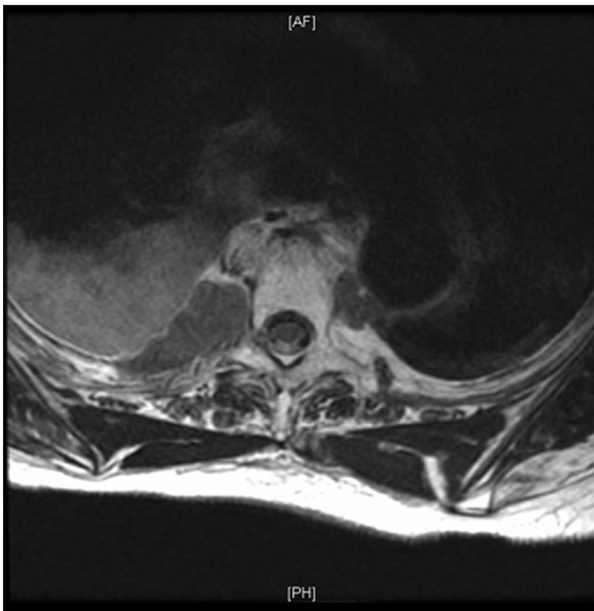


Figure 3. Magnetic resonance imaging study of chest showing posterior paraspinal mass adjacent to the pleura.

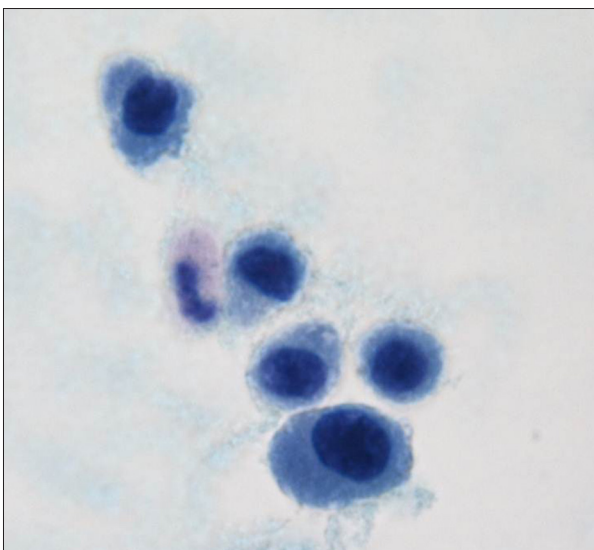


Figure 4. Papanicolaou smear of pleural fluid showing several plasma cells, including a large immature plasma cell at the bottom.

patients with MPE as initial manifestation were analyzed [3] in a recent review of all patients presenting with MPE as initial manifestation of MM since 2000. Males were more common (11/17), and left-sided pleural effusions were most common (8/17). IgG kappa gammopathy was the most frequently noted condition (7/17 patients).

Various mechanisms have been proposed for MPE, chief among these being tumor infiltration of the pleura, extension from chest wall plasmacytomas, invasion from adjacent skeletal

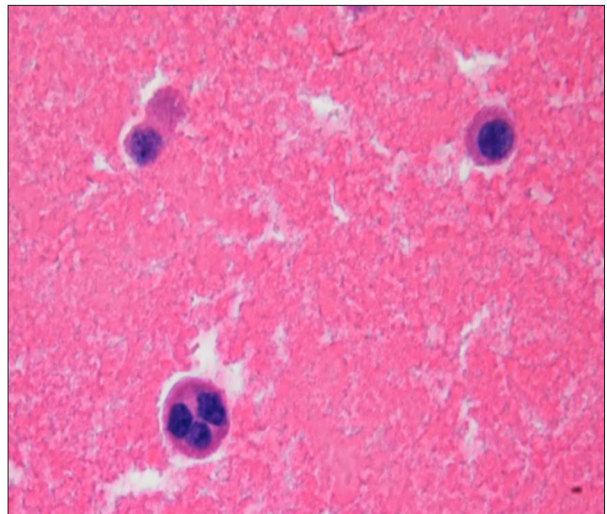


Figure 5. Hematoxylin and eosin stain of pleural fluid showing abnormal trinucleated plasma cell in lower left corner.

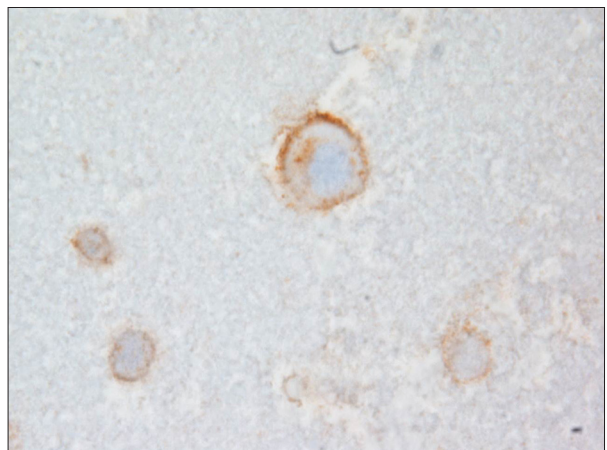


Figure 6. CD138 staining of pleural fluid showing positive (brown) staining of the cytoplasmic membrane, confirming cells as plasma cells.

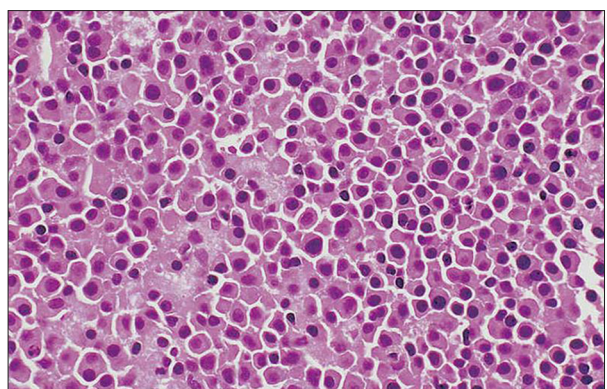


Figure 7. Biopsy of mediastinal mass showing partially crushed tissue with diffuse infiltrate of lymphoid cells with plasma cell features.

lesions, and mediastinal lymph node involvement [4]. However, the exact mechanism of pathogenesis remains unknown.

The best way to diagnose MPE is to identify malignant plasma cells within a cytological sample. On hematoxylin and eosin stains, plasma cells typically have basophilic cytoplasm with large eccentric nuclei and prominent nucleoli. Immature plasma cells may also be seen and tend to correlate with more aggressive disease [7]. Using morphological characteristics alone can be challenging, especially in the setting of large number of immature cells and potential *in vitro* degeneration [8]. Immunophenotyping can be an additional tool to determine lineage of abnormal cells. Classically, MM cells express CD38 and CD138 kappa or lambda light chains but do not express CD19 or CD20. In the event that cytology is unrevealing, pleural biopsy has been used to make a final diagnosis [3]. In our patient the initial diagnosis was made on the basis on morphological features on pleural fluid cytology and confirmed with immunohistochemistry with the cells staining heavily for CD138.

The incidence of EMP in newly diagnosed MM is estimated around 7% to 18% [9]. Most common sites for EMP are in the oropharynx and paranasal sinuses [10]. EMP very rarely involves the mediastinum, with fewer than 20 cases in the literature [1,5]. The occurrence of EMP in the setting of MM is considered the mark of an aggressive disease. Our patient had a mediastinal mass that was biopsied and found to be consistent with the diagnosis of EMP based on morphological characteristics and staining with CD138.

MPE has a median survival time of about 4 months (range: 3–50 months) [3]. Survival rates are poorer compared with

stage III MM [7]. There are case reports of using systemic chemotherapy with or without chest tube and pleurodesis for palliation [7]. There appears to be no benefit of radiotherapy. Anecdotal reports of using thalidomide, bortezomib, and adriamycin have been published, but overall response seems to be temporary with recurrence noted soon after [3,11].

Our patient was unique as she presented with multiple intrathoracic manifestations of MM at the same time that her MM was diagnosed. In addition, MPE and mediastinal EMP are rare entities in and of themselves and even rarer when occurring in combination in a patient newly diagnosed with MM.

Conclusions

MM is a common hematological disorder. Patients can present in variety of ways that are not typically thought to be consistent with MM. We describe the case of an elderly female who presented with a right-sided pleural effusion and a mediastinal mass that was diagnosed to be secondary to MM. She had various intrathoracic manifestations of MM, all of which are rare and require a high index of suspicion to diagnose. Overall, a lymphocyte-predominant exudative pleural effusion must be carefully evaluated with proper cytological and immunohistochemical markers to properly diagnose an MPE.

Statement

No financial support was available, no conflict of interest exists, and no off-label or research drug was used.

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