

Letter to the Editor

A Rare Pulmonary Manifestation of Kahler's Disease

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Sir,

Kahler's disease also known as Multiple Myeloma (MM) is a neoplastic plasma-cell disease known for its infiltration of malignant plasma cells in the bone marrow (BM) accompanied by multiorgan dysfunction. The median age at diagnosis is approximately 70 years.^[1] Less than 2% of the patients are younger than 45 years of age at diagnosis.^[2] MM may present as a diffuse disease of the bone (myelomatosis) or may be as a single plasmacytoma of bone or as an extramedullary plasmacytoma (EMP). The very common thoracic involvement by MM is the bone involvement or infiltration of the lungs secondary to an infection. Although the pulmonary parenchyma is quite a rare site of extramedullary involvement in MM patients, interstitial lung disease (ILD) as a pulmonary manifestation of MM is even rarer. Only few proved cases have been reported in the literature so far. Therefore, we present a rarest case possible of a MM presenting as ILD.

A 40-year-old female with a history of hypothyroidism and hypertension had presented to the hospital with dyspnea, neck pain, and vomiting. Her dyspnea worsened on exertion, with no positional variations and no nocturnal/diurnal variations and was not associated with any chest pain. She was having around 5–6 vomiting per day which was non-projectile, non-bilious with the absence of blood in vomiting and was also afebrile. On physical examination, she was afebrile, pale, tachypnoeic (22/min), tachycardic (104 beats/min), and with the presence of bilateral basilar crackles.

The patient was initially treated with intravenous (IV) fluids, non-invasive ventilation (NIV) support, antiemetics, and antacids. Further management included carotid massage,

adenosine, diltiazem, amiodarone infusion for paroxysmal supraventricular tachycardia (PSVT), IV fluids, diuretics, zoledronic acid, calcitonin, and dialysis for hypercalcemia. After MM has been confirmed, the patient was treated with chemotherapy of six cycles of bortezomib (2 mg), dexamethasone (10 mg) regimen, and zoledronic acid (4 mg) with each cycle.

Investigations showed anemia (hemoglobin of 7.4 g/dl), raised erythrocyte sedimentation rate, hypercalcemia (20.60 mg/dl) while electrocardiogram showed ST depression, T wave inversions in V4-6, Lead II and I, and AVL and QS complexes in Lead III.

During the course, despite the ongoing treatment, she developed recurrent junctional tachycardia and worsening of respiration due to ILD. Chest X-ray showed bilateral lung infiltrates. Computed tomography (CT) chest showed patchy ground-glass opacification with interlobular septal thickening in bilateral perihilar lung parenchyma with multiple osteolytic lesions in vertebrae and sternum [Figure 1].

Bronchoalveolar lavage (BAL) tested positive for myeloma cells in the lungs bilaterally. BM biopsy showed plasma cells. Immunohistochemistry (IHC) showed plasma cell population in both BAL fluid cell block (positive for CD 138) and BM biopsy [Figures 2 and 3].

Plasma protein electrophoresis showed M spike (2.74 g/dl) and increased gamma globulin (3.41 g/dl) [Figure 4].

Serum immunofixation electrophoresis showed IgG kappa chain dominance (148.20 mg/L) and increased kappa/lambda ratio (19.32) [Figure 5].

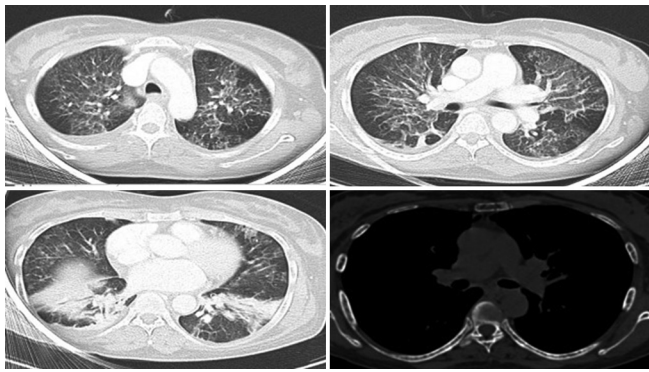


Figure 1: Patchy ground-glass opacification with interlobular septal thickening in bilateral perihilar lung parenchyma with multiple osteolytic lesions in vertebrae and sternum

cycles of dexamethasone (10 mg), bortezomib (2 mg), and zoledronic acid (4 mg) regimen.

The patient responded significantly well to the treatment with improvement. After four cycles of chemotherapy, plasma protein electrophoresis showed a decrease in M spike (0.80 g/dl) [Figure 6].

CT chest showed a significant improvement [Figure 7].

The patient is currently under regular follow-up since 2 years with no new complaints.

MM presenting as ILD has been documented in very rare occasions till date. Interestingly, MM has a potential to involve the thorax through various ways, but the involvement of the pulmonary parenchymal is rather rare. In literature, it was observed that MM's thoracic manifestations included abnormal skeleton structure, pleural effusions, diaphragmatic dysfunction because of peripheral neuropathy, and plasmacytomas.

In a review conducted by Kintzer *et al.* on 958 patients with MM, the thoracic manifestations were specifically reported.^[3] The most common manifestation was osteolytic lesions of ribs or vertebrae's which was observed in 267 (28%) patients followed by pulmonary infiltrates (95 patients [10%]). Otherwise, the pleural effusions were also present in 58 patients (6%) while EMPs were observed in 11 (1%). Only four patients from this study showed diffuse infiltrates which was thought to be caused by plasma cell infiltrate (proven in only one case). This explains the rare phenomenon of ILD in case of MM. In the present case, the observed diffuse infiltrates throughout the lung fields were also caused by plasma cells.

A similar presentation of MM as ILD was reported in a case by Ma *et al.*^[4] and Nitu *et al.*^[5]

Standard medical management of symptomatic MM involves chemotherapy with or without an autologous stem-cell transplant for patients under the age of 70.^[6] IV administration of bisphosphonates are used in conjunction with chemotherapy and have been shown to decrease the progression of osteolytic lesions. Bisphosphonate treatment is recommended for patients with radiological evidence of osteolytic lesions or osteoporosis and is continued monthly for a period of 2 years.^[7] Supportive therapy for patients with MM may include maintenance of fluid and electrolytes with regular hydration, erythropoietin and transfusions to replace red blood cells and platelets, pain control using analgesics (non-steroidal anti-inflammatory drugs are contraindicated due to potential for renal complications), promotion of mobility to prevent osteoporotic fractures, spinal decompression surgery for spinal complications, and radiation therapy for focal skeletal lesions.^[8]

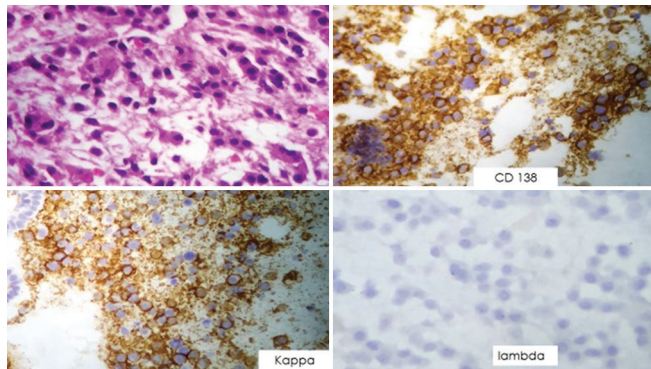


Figure 2: Bronchoalveolar lavage fluid cell block

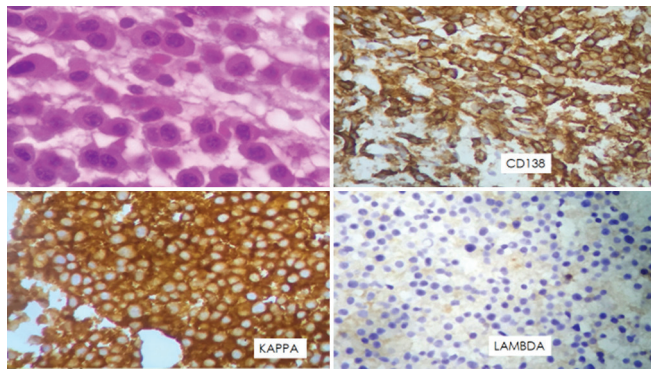


Figure 3: Bone marrow biopsy showing monomorphic plasma cells with occasional binucleated forms

Serum beta-2 macroglobulin was 3143 mg/dl. Thus, the diagnosis of MM with myeloma cells infiltrates in lung showing ILD pattern was made.

The patient was initially treated with IV fluids, NIV support, antiemetics, and antacids. Further management included carotid massage, adenosine, diltiazem, amiodarone infusion for PSVT, calcitonin, IV fluids, diuretics, zoledronic acid, and dialysis for hypercalcemia. After the diagnosis of MM was confirmed, the patient was started on chemotherapy of six

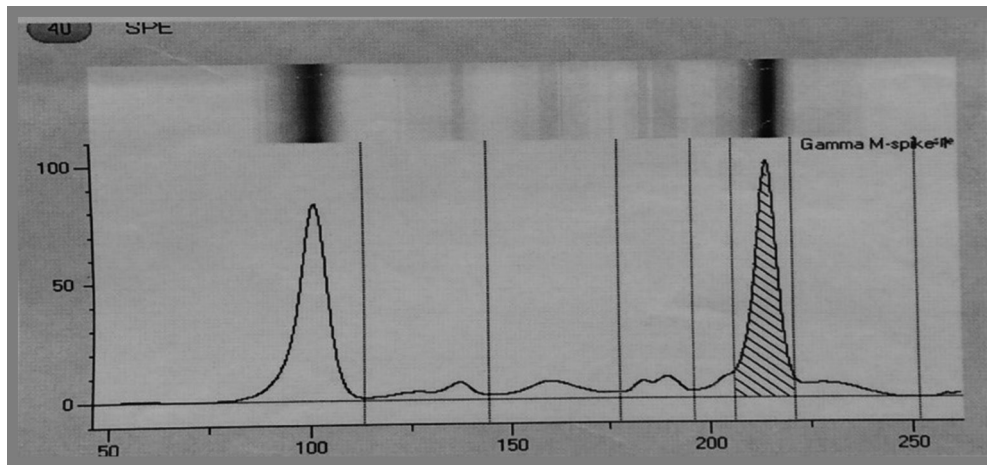


Figure 4: Plasma Protein electrophoresis showing M spike and increased gamma globulin levels

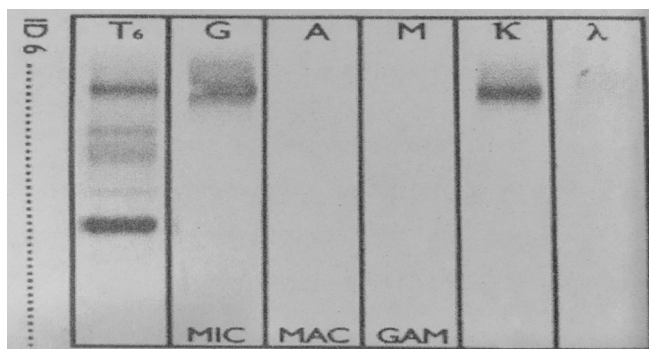


Figure 5: Increased kappa free chains and increased kappa/lambda ratio



Figure 7: Computed tomography chest after four cycles of chemotherapy

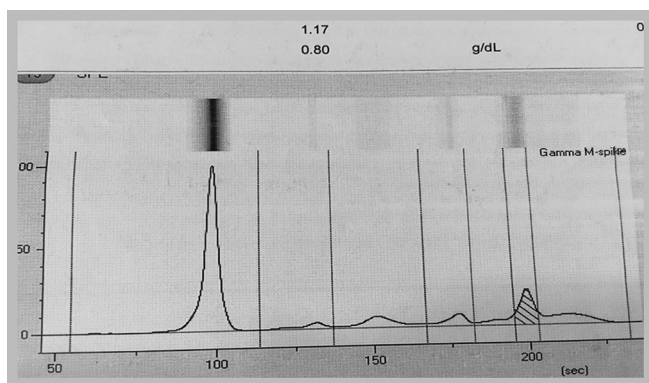


Figure 6: Plasma protein electrophoresis showing a decrease in M spike level and gamma globulin level after four cycles of chemotherapy

The mean overall duration of survival after being diagnosed with MM is 33 months with considerable individual variation.^[9] Negative prognostic indicators include older age, a previously diagnosed plasma cell disorder, and key laboratory findings.^[10] Laboratory findings indicating a worse prognosis include elevated β -2 microglobulin, serum albumin, and C-reactive protein. The BM cytogenetics can also be used to help determine prognosis up on diagnosis.^[11]

Lung involvement and pulmonary infiltrates are not common in a case of MM. Most of the time, we suspect lung infection. MM should be taken into consideration in the differential diagnosis of pulmonary infiltration in patients with MM. The possibility of myelomatous pulmonary infiltrates should be suspected in the absence of fever, failure to respond to antibiotics, and resolution to myeloma treatment. Analysis of BAL fluid and lung biopsy for the presence of plasma cells and IHC provides a means of establishing the diagnosis. Pulmonary involvement indicates aggressive nature of the disease. Treatment of MM along with supportive care should be started at the earliest in these cases.

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