Case Report

A case of Multiple Myeloma with lung plasmacytoma

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ABSTRACT

Multiple Myeloma (MM) is a malignant proliferation of the plasma cells mainly affecting bone marrow. Most common sites of extramedullary dissemination reported in the literature are skin, liver, kidneys and central nervous system. Multiple Myeloma is rarely associated with lung plasmacytoma. In fact; dissemination of MM in lung is relatively uncommon being described in only 5% of cases and therefore the diagnosis of this entity can be misleading to most clinicians. We report a rare case of lung plasmacytoma with MM in a 65-year-old, smoker, male who presented with shortness of breath and a heterogeneous mass involving the lower left lobe visualized on CT scan. Careful integration of the clinical manifestations with the radiological and pathological data from CT-guided transparietal lung biopsy and bone marrow biopsy led to the diagnosis of Multiple Myeloma with lung plasmacytoma. Given the rarity of this localization, the purpose of this study was to increase knowledge of this disease among pulmonologists, in order to provide more timely diagnosis.

1. Introduction

Multiple myeloma is a malignant monoclonal gammopathy characterized by the clonal proliferation of plasma cells in the bone marrow. This is responsible of osteolytic lesion appearance, bone marrow infiltration, abnormal protein production, installing of immune deficiency. As a result the tumor, its products, and the host response can cause a number of organ dysfunctions and symptoms, including bone pain or fracture, renal failure, susceptibility to infection, anemia, hypercalcemia and occasionally clotting abnormalities, neurologic symptoms and manifestations of hyperviscosity [1]. Uncommonly, proliferation may occur within other tissues in the form of extramedullary plasmacytomas; multiple myeloma is rarely associated with lung plasmacytoma [2,3]. Only 5% of patients with extramedullary plasmacytomas have coexistent multiple myeloma [4]. Here we report a case of multiple myeloma with lung plasmacytoma in a 65 year-old smoker, male.

2. Case report

A 65 year-old male, smoker and occasional alcoholic with a history of left pneumothorax and ischemic heart disease was admitted to our department. The patient presented weakness, significant weight loss, progressive shortness of breath associated to chronic cough and with ongoing hemoptysis over 5 months. Physical examination then found a pale patient with an increasing pulse rate of 120/min and fluctuating oxygen saturation between 91% and 97% on room air. Pulmonary examination revealed dullness and de-
increased breath sounds at the left hemithorax. His chest radiograph showed two dense, heterogeneous and rounded opacities in the left lung without any visible osteolytic lesions [Fig. 1].

First Computerized tomography (CT) of the thorax was performed revealing a peripheral heterogeneous mass (51.3 mm × 63.7mm × 42 mm) involving the lower left lobe in contact with chest wall without focal erosion associated to subpleural nodule with moderate loculated left pleural effusion. A second thoracic CT scan performed within 3 months showed a progression of the lesion (119 mm × 87 mm x 118mm) associated to left pleural masses, nodules and controlateral nodule in the right Fowler. Centrilobular and panlobular emphysema with infracentimetric mediastinal lymph nodes were also seen [Fig. 2].

Pleural fluid was hemorrhagic, exudative, lymphocyte predominant. Smear and culture for mycobacterium tuberculosis were negative. Pleural fluid cytology did not reveal any malignant cells. Laboratory blood investigation showed he had severe yet tolerated anemia with hemoglobin at 7.5 g/dl, total leukocyte count was 8760 cell/mm3, platelets were 364 000 cells/mm3, total serum proteins were 81 mg/dl with serum albumin at 2.4 g/dl. Renal function was normal and no hypercalcemia was found. Serum protein electrophoresis was done and did not reveal any abnormalities. Urinary protein electrophoresis showed a band at the level of total Kappa light chains but without any correspondence with the free light chains.

On bronchoscopic exploration, there was a small bleed coming from the culminal bronchus where we found a flat, smooth and blackish endobronchial formation. We also identified an extra luminal compression of the left Nelson bronchus with no endobronchial growth. A biopsy of the suspected formation was done but the results were inconclusive. Therefore, a CT-guided transpulmonary lung biopsy was performed and revealed unusual mature plasma cell clusters suggestive of plasmacytoma. We completed our investigations with a bone marrow biopsy and the results showed a rich marrow of many megakaryocytes and 12% of plasma cells. No blasts or extra hematopoietic cells have been identified [Fig. 3].

The patient's skull X-Ray also revealed multiple lytic lesions indicating a MM [Fig. 4].

The diagnosis of MM with lung plasmacytoma was then made on the basis of plasma cell infiltration of the bone marrow, lytic bone lesions, and the presence of dystrophic plasma cells in the lung mass. The patient was transferred to the Hematology department for chemotherapy but months later he was unfortunately reported out of sight.

![Fig. 1. Chest radiograph revealing two dense, heterogeneous and rounded opacities in the left lung without any visible osteolytic lesions.](image1)

![Fig. 2. (A)/(B) Computed tomographic scan of the thorax revealing soft tissue mass (119 mm × 87 mm x 118mm) associated to left pleural masses, nodules and controlateral nodule in the right Fowler. Centrilobular and panlobular emphysema with infracentimetric mediastinal lymph nodes.](image2)
3. Discussion

Multiple myeloma is a neoplastic disorder caused by the proliferation of monoclonal plasma cells and production of large amount of monoclonal immunoglobulins. Extramedullary plasmacytoma is a monoclonal proliferation of plasma cells in soft tissues or an organ. It accounts for about 3% of plasma cell malignancies and approximately 80% of which, in the upper respiratory tract (commonly in oropharynx, paranasal sinuses [5,6] and more rarely in the larynx [7]). The relationship between multiple myeloma, solitary plasmacytoma of the bone, and extramedullary plasmacytoma is not well understood.

Extramedullary dissemination of MM involves the spleen, liver, lymph nodes, thyroid, adrenal, ovary, testis, lung, pleura, pericardium, gastrointestinal tract and skin. The classical thoracic manifestation of the disease is involvement of bone of the thoracic cage. Other pulmonary manifestations include consolidation, lung mass, mediastinal lymphadenopathy, interstitial involvement such as reticulonodular pattern and intrapulmonary calcification. However pulmonary parenchyma is an uncommon site of extramedullary involvement in multiple myeloma; only isolated cases with histological proofs have been reported in the literature [6].

In fact the association of multiple myeloma with lung plasmacytoma is extremely rare [2,3]. According to our research only 5% of patients with extramedullary plasmacytomas have coexistent multiple myeloma [4]. In lower airways, plasmacytoma is mainly found in the tracheobronchial tree, hilar structures, and rarely in the lung parenchyma [8,9]. One study described 13 cases of multiple myeloma with different thoracic manifestations, of which six had pneumonia, two had mass lesions, two had multiple nodular lesions, and three had interstitial infiltrates [10]. In Our case the patient had a polylobulated mass lesion associated to homo and contralateral sub-pleural nodules.

Pulmonary manifestations in multiple myeloma as reported by various authors are given in Table 1.

Extramedullary thoracic plasmacytoma is particularly difficult to determine when there is no thoracic vertebral or rib involvement. The radiologic appearance is nonspecific, with findings on a CT scan or MRI mimicking those of primary or metastatic carcinoma, sarcoma, neuroendocrine or neuroectodermal tumour and lymphoma [16,17]. In a study of 958 cases of multiple myeloma, 6% patients presented with an extramedullary plasmacytoma in the lung [18]. In another study, 19 (4.4%) out of 432 patients of multiple
myeloma were identified as having extramedullary disease, common sites being the lymph node, pleura and soft tissues with only 3 cases occurring within the lung parenchyma [19].

Diagnosis of extramedullary dissemination in the lungs can be determined by bronchoalveolar lavage (monoclonal plasma cells are found) or lung biopsy (interstitial infiltrate of plasma cells). Identifying malignant plasma cells in BAL fluid from multiple myeloma patients may be difficult, especially when the plasma cells are mature in appearance or low in number. Diffuse pulmonary myelomatous involvement therefore may be more frequent than has previously been reported. A high index of suspicion is required because infection, hemorrhage, idiopathic pneumonia, edema of the lung, and plasma cell infiltration may have identical radiologic manifestations. Cytological examination of the sputum and BAL fluid and an analysis of cytoplasmic immunoglobulin DNA provide a simpler means of confirming diagnosis and may obviate the more invasive needle biopsy or open lung biopsy. For our patient the diagnosis of MM with lung plasmacytoma was made on the basis of plasma cell infiltration of the bone marrow, lytic bone lesions, and the presence of dystrophic plasma cells in the lung mass following CT-guided transparietal lung biopsy.

Pleural effusion is very rare, occurs in <1% and <100 cases have been reported [20]. The pleural effusion develops at an average of 12 months after the diagnosis. Myelomatous pleural effusion is diagnosed by pleural fluid electrophoresis demonstrating monoclonal protein, demonstration of plasma cell in pleural fluid and histological evidence in pleural biopsy [21,22]. In our case there has been a regression of the pleural effusion therefore other investigation couldn’t be performed.

The differential diagnoses of multiple myeloma are lymphoma, metastatic carcinoma, bone neoplasm and chronic lymphocytic leukemia [17].

After the diagnosis of plasmacytoma, extensive investigation for multiple myeloma is crucial, as the treatment is completely different for both types of plasma cell disorders. The prognosis of patients with pulmonary multiple myeloma is poor and although there have been many advances in the treatment; multiple myeloma remains an incurable disease until now [13]. Regardless of the treatment regimen or initial response to treatment, the disease follows a high relapsing rate in the majority of the patients. Treatment of multiple myeloma depends on patients’ age and prognostic factors. Induction and maintenance therapy are two key steps in the management of newly diagnosed multiple myeloma patients. Induction therapy should initiate immediately following diagnosis and maintenance therapy, a long-term treatment that patients often are given after induction therapy, and (usually) a stem cell transplant [22].

Recently the management of patients with MM has been transformed by introduction of three novel agents: thalidomide, lenalidomide, and bortezomib. According to the 2020 National Comprehensive Cancer Network (NCCN) Multiple Myeloma guidelines, therapy for multiple myeloma should consist of a combination of bortezomib/dexamethasone/lenalidomide or thalidomide as primary induction therapy for autologous stem cell transplant candidates [21,22]. Cyclophosphamide or doxorubicin might also be an alternative. For non-transplant candidates a combination of melphalan/prednisone/lenalidomide or bortezomib is suggested as primary induction therapy [21,22]. The preferred maintenance therapy for autologous stem cell therapy is lenalidomide. Other maintenance options are ixazomib or bortezomib but in certain high-risk cases, bortezomib plus lenalidomide with or without dexamethasone is used. Patients who have a relapse after initial disease control may be treating with any of the agents not already utilized. If the multiple myeloma relapse occurs longer than six months after the initial therapy, then the initial regimen can be used again [21,22]. Recent studies have proved that a monoclonal antibody directed against CD38 called Daratumumab is an effective regimen in patients progressing on lenalidomide maintenance. But additional trials are required to decide the optimal regimen post-lenalidomide maintenance [23].

The latest guidelines by the “International Lymphoma Radiation Oncology Group” present a standardized approach to the use and implementation of definitive Radiation therapy in solitary plasmacytomas [24]. In fact radiation therapy is another effective and optional treatment for localized plasmacytoma in the bone, or in extramedullary (extraosseous) soft tissues. It provides long-term local control in the solitary bone plasmacytomas and is potentially curative in the extramedullary cases [24].
4. Conclusion

It is very important for clinicians to consider multiple myeloma as a differential diagnosis in older patients presenting a bony lesion. Extramedullary dissemination of multiple myeloma in the lung is uncommon and very rare. In most cases MM with lung plasmacytoma manifests in the form of pulmonary nodules. Etiology identification of pulmonary nodules found in patients with multiple myeloma is necessary to ensure adequate and timely therapy. Pulmonary MM is associated with rapid progression of the disease unlike isolated primary pulmonary plasmacytoma that has good prognosis.

Declaration of patient consent

The authors certify that informed consent was obtained. The patient understands that his name and initials will not be published and has given his consent for his images and other clinical information to be reported in the journal.

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Declaration of competing interest

All authors declare no conflicts of interest in relation to the subject matter. We have no financial and personal relationships with other people or organizations that could inappropriately influence (bias) this work.

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