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CASE REPORT

A hematologic condition expressed as a lung disease [version 1; peer review: 2 approved, 1 approved with reservations]

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Abstract

Pleural involvement secondary to Multiple Myeloma is considered a very rare complication. According to the literature only 1% of these patients develop a myelomatous pleural effusion. We present a case of a 39 year old man with multiple myeloma diagnosed six years prior to our evaluation, which developed progressive dyspnea, dry cough and right pleuritic chest pain two weeks prior to admission. On physical examination the patient had decreased breath sounds over the right posterior hemithorax accompanied by dullness to percussion. The chest radiogram was consistent with a right sided pleural effusion. Pleural fluid analysis revealed the presence of abundant abnormal plasma cells. The patient died four weeks after hospitalization. The presence of myelomatous pleural effusion is considered to be a poor prognostic finding, no matter at what disease stage it develops. So far no definite treatment has been shown to improve survival.

Open Peer Review

Approval Status

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Any reports and responses or comments on the article can be found at the end of the article.

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Introduction

Multiple Myeloma (MM) is a malignant neoplasm characterized by abnormal proliferation of plasma cells. The disease is typically manifested by anemia, pathologic fractures, hypercalcemia and renal failure. Pleural involvement in MM is very rare and seldom has been described in the literature. To our knowledge, approximately eighty cases have been mentioned in the largest case series reported. Pleural effusions can be either myelomatous or non-myelomatous, the former being the less common presentation. Most cases of myelomatous pleural effusions are due to IgA MM. We present a case of a patient with a pleural effusion secondary to IgG MM.

Case report

A 39 year old man with hypertension, end-stage renal disease and chronic smoker, diagnosed with MM six years prior to our evaluation, came to our institution complaining of progressive dyspnea, fever, and dry cough of two weeks of evolution. He was treated with a course of oral antibiotics for five days with minor symptom improvement. On admission the patient was found with a temperature of 37.8°C, heart rate was 118/min., respiratory rate was 24 breaths/min., blood pressure was 120/74 mmHg, and oxygen saturation by pulse oximetry was 100% with a venturi-mask at 50% FIO₂. Chest examination revealed multiple bilateral palpable plasmacytomas along the anterior and posterior hemithorax with decreased breath sounds below the right scapular area, and percussion dullness was heard on the right side. Antero-posterior chest radiogram showed a large right side pleural effusion with contralateral shifting of the mediastinal structures and patchy airspace opacities throughout the left lung (Figure 1). Complete blood count revealed pancytopenia with a WBC of $2.8 \times 10^9/l$, Hb of 8.4 g/dl and platelet count of 19×10^9 . Blood chemistry showed a protein of 5.6 g/dl and lactate dehydrogenase of 721 IU/l. Calcium levels were within normal limits. Diagnostic and therapeutic thoracentesis was performed after platelet transfusion and a total of

900 ml of turbid, sero-sanguinous fluid was removed. Pleural fluid analysis was consistent with an exudate and the fluid cytology revealed the presence of abundant atypical plasma cells (Figure 2). Bacteria, fungi and acid fast smear and cultures of the pleural fluid were reported negative. The patient's clinical condition was aggravated by bacteremia, septic shock and respiratory failure requiring mechanical ventilation. The patient was complicated by sepsis and died four weeks after hospitalization.

Discussion

Extra-medullary involvement in MM is considered to be a rare complication of the disease¹. Commonly involved sites are the nasal cavity, lung, pleura, thoracic wall, central nervous system, lymph nodes, spleen, skin and eyes. Involvement of serous cavities such as the pleural cavity, peritoneal cavity, cerebral-spinal space and pericardium is unusual, the pleural cavity being the most common site². Pleural effusions occur in 6% of the patients with multiple myeloma and can be myelomatous or non-myelomatous³⁻⁵. Non-myelomatous pleural effusions can occur secondary to sepsis, pulmonary embolism, chronic renal failure and secondary neoplasm⁶. On the other hand, myelomatous pleural effusions have been described in only in 1% of the patients with MM and the diagnosis is based on the demonstration of monoclonal proteins in the pleural fluid by protein electrophoresis, finding monoclonal plasma cells in the fluid and/or histological examination of the pleura through biopsy^{7,8}. Literature reveals that almost 40% of the cases of myelomatous pleural effusions are due to IgG type⁶.

Multiple treatment regimens have been used including VAD regimen (vincristine, doxorubicin and dexamethasone), prednisolone, melphalan, etoposide, stem cell rescue and pleurodesis without a significant effect on mortality^{6,9}. The use of bortezomib, a protease inhibitor, in refractory multiple myeloma has shown promising

Figure 1. Antero-posterior chest x-ray on admission showing right-sided pleural effusion.

Figure 2. Photomicrograph of pleural fluid showing atypical plasma cells (Giemsa stain x 400).

results. There is a single case of refractory MM and myelomatous pleural effusion treated successfully with intravenous and intrapleural bortezomib^{2,10}.

Conclusion

There has been limited information in the literature regarding pulmonary manifestations of this hematologic malignancy. Pleural effusions can be present as an initial manifestation of the disease or as the disease progresses. As in our case, pleural involvement is associated with poor prognosis and high mortality rate no matter at what disease stage it appears. So far, there are no proven treatment regimens that can halt disease progression. Physicians should be aware of such a fatal complication as it predicts a very poor outcome. For this reason, additional studies towards the development of new treatment strategies should be considered.

Consent

Written informed consent for publication of clinical details and clinical images was obtained from the relative of the patient.

Author contributions

Authors have contributed to the literature review, drafting of the manuscript, revisions of the manuscript and have agreed to the final content.

Competing interests

No competing interests were declared.

Grant information

The author(s) declared that no grants were involved in supporting this work.

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Hermann Einsele

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The response quality following high-dose chemotherapy and autologous stem cell transplantation for multiple myeloma (MM) is clearly correlated with progression-free and probably also overall survival. Thus a major goal of all protocols for the treatment of younger patients with MM is to achieve a chest radiogram (CR). Recent data of the Spanish myeloma study group reveal long-term disease free survival in a subgroup of patients with CR after autologous stem cell transplant (SCT).

Inclusion of novel agents (thalidomide, portezomib or lenalidomide) in the induction regimens prior to stem cell harvest and transplantation has allowed to achieve better remission quality prior to and after autologous SCT and to reduce treatment-related mortality. Recently also protocols containing 2 novel agents have been used to improve induction regimens for patients with multiple myeloma.

In this study the PETHEMA/GEM group has studied and compared 3 induction regimens VTD (2 novel agents), TD and VBMCP/VBAD (an intensive regimen with bortezomib). VTD showed the best equality of remission (CR rate 35% vs 14% with TD and 21% with VBMCP/VBAD/B. Also the PFS after VTD plus autologous SCT was significantly longer when compared two both other induction protocols. Unfortunately 14% of the patients in the VTD arm developed grade 3 and 4 PNP. Thus, future studies should use either bortezomib or proteosome inhibitors with a lower neurotoxicity.

In addition, the VTD regimen in contrast to the GIMEMA study was not able to overcome the poor prognostic impact of high risk cytogenetics. Thus other treatment strategies e.g. allogeneic SCT, novel IMiDs or PI should be evaluated in these high risk MM patients (17p del, 7(4;14)).

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 07 November 2012

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The author has failed to mention if this patient had ever received any chemotherapy previously and if they did what agents were used. Also what was the initial presentation of myeloma in this patient?

The only imaging modality used was a Chest X-ray, it would have been helpful to know if a CT scan was done to evaluate if any pleural based mass was present along with the pleural effusion.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 30 October 2012

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Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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