

Case Report

Myelomatous Pleural Effusion: A Rare Case Report and Literature Review

Zakaria Maat^a Yousef Taher Hani Al-Asa'd^a Eihab A. Subahi^a
Osama Adil Shafeeq Al-Ameen^a Abdelhaleem Ahmed Elhiday^b

^aDepartment of Medical Education, Hamad Medical Corporation, Doha, Qatar; ^bDepartment of Internal Medicine, Hamad Medical Corporation, Doha, Qatar

Keywords

Myeloma · Plasma cells · Pleural effusion

Abstract

Multiple myeloma (MM) is typically characterized by the neoplastic proliferation of plasma cells producing a monoclonal immunoglobulin. Pleural effusion in MM is uncommon and usually caused by heart failure, pulmonary embolus, and nephrotic syndrome [*Arch Intern Med.* 1978;138(5):727–30; *Chest.* 1994;105(2):622–4]. Here, we report a case of myelomatous pleural effusion as part of the initial presentation of MM in a patient with the IgG-lambda subtype, which is extremely uncommon.

© 2022 The Author(s).
Published by S. Karger AG, Basel

Introduction

Malignant pleural effusion is a relatively rare finding in multiple myeloma (MM) patients, which may be a sign of thoracic involvement, with a frequency of only 6%, and is usually associated with more benign conditions such as nephrotic syndrome, pulmonary embolism, congestive heart failure secondary to amyloidosis, and infection [1–4]. Malignant myeloma cells identified in the cytologic examination of the pleural fluid or by pleural biopsy establish the diagnosis of a myelomatous pleural effusion (MPE) [5]. MPE is extremely uncommon, occurring in less than 1% of cases at the time of the presentation [1, 5, 6]. To date, the majority of studies in the literature have reported experiences with a few cases of MPE and provide a brief literature review [4, 7]. To the best of our knowledge, there have been only a few case series of MPE in the English language literature [8, 9]. In all the reports, the authors concluded

Correspondence to:
Zakaria Maat, zakaria93maat@gmail.com

that MPE in patients with myeloma is often associated with high-risk disease, including deletion 13 chromosomal abnormality, and indicated a poor prognosis despite aggressive local and systemic treatment [2, 4, 8, 9]. Herein, we report a case of a patient who was diagnosed with MPE.

Case Report

A 44-year-old Moroccan male known to have diabetes mellitus who was on oral hypoglycemic agents presented to our hospital with a 3-week history of nonproductive cough and left-sided pleuritic chest pain. He denied fever, hemoptysis, shortness of breath, or palpitation. His review of systems was unremarkable. His vital signs were normal. Lung examination showed reduced breath sounds in the left lower zone. Other systems examination was non-revealing. His labs showed hemoglobin of 8.8 g/dL along with reduced transferrin saturation. Chest X-ray revealed mild to moderate left-sided pleural effusion. At this time, the patient was already on ceftriaxone and azithromycin for possible community-acquired pneumonia. Biochemical laboratory tests showed hypercalcemia, mildly elevated renal indices, low albumin, and normal LDH.

Chest CT showed diffuse destructive lytic bony lesions involving almost all scanned bones including the proximal humeri, clavicles, sternum, scapulae, multiple ribs, and the thoracic spine, involving the bodies and posterior elements. Additionally, multiple left paraspinal soft tissue masses were seen, the largest seen related to the destructive lesion of the T7 vertebral body associated with mild loss of height of T7 vertebral body more on the left side. Moderate left-sided pleural effusion with left lower lobe consolidation/collapse was also noted.

Diagnostic thoracentesis was performed which revealed exudative pleural effusion without evidence of acid-fast bacilli. Cytospin preparation of pleural fluid is cellular and almost stuffed by many plasma cells (scattered and in clusters) on a background of some lymphocytes, a few neutrophils, monocytes/macrophages, and red blood cells. The morphological findings are suggestive of involvement by plasma cell neoplasm including plasma cell myeloma. By this time, other causes of pleural effusion were ruled out; there was no evidence of systemic causes such as heart failure, liver disease, or nephrotic syndrome. Infective effusion was also ruled out; the patient did not have signs or laboratory evidence of infection upon presentation.

Serum protein electrophoresis showed low albumin, and there was a monoclonal band typed and proved to be IgG lambda. The size of the band is about 99.8 g/L. There was electrophoretic evidence of hypogammaglobulinemia. 24-h urine Bence-Jones protein was high (1.39 g/24 h, lab normal reference range: 0.03–0.15 g/24 h). The kappa/lambda ratio was found to be low at 0.1 (lab normal reference range: 0.26–1.65). Serum IgG was high 95.98 g/L (lab normal reference range: 7–16 g/L), and B-2 Microglobulin was high 13.1 mg/L (lab normal reference range: 0.8–2.4 mg/L).

Spine MRI revealed diffuse enhancing marrow lesions demonstrated throughout the whole spine, pelvis, and hips with nodular left paraspinal masses. Bone marrow aspirate was hemodilute with approximately 8% plasma cells and <1% blasts. Bone marrow biopsies showed hypercellular marrow with variable cellularity ranging from 65 to 95% with diffuse and interstitial infiltration with plasma cells. The infiltration is estimated at 65% of cellularity. The plasma cells express CD138 with lambda light chain restriction. There is an increase in the reticulin fibers in the diffusely infiltrated areas. Flow cytometry analysis shows a population of monotypic plasma cells comprising 8% and expressing CD38 and 138 with cytoplasmic lambda light chain restriction and aberrant expression of CD56 and CD117. Interphase fluorescence in situ hybridization evaluation was performed on interphase nuclei cells from the

Table 1. Interphase fluorescence in situ hybridization (iFISH)

Probe	Chromosome location	FISH results	ISCN nomenclature
RB1/CEP10	13q14	Abnormal	Nuc ish(CEP10 × 2, RB1 × 1)[15/200]
TP53/CEP17	17p13.1/17p11.1-q11.1	Normal	Nuc ish(CEP17, TP53) × 2[279/300]
IGH	14q32	Abnormal	Nuc ish(5'IGH × 2, 3'IGH × 1) (5'IGH con 3'IGH × 1)[14/200]

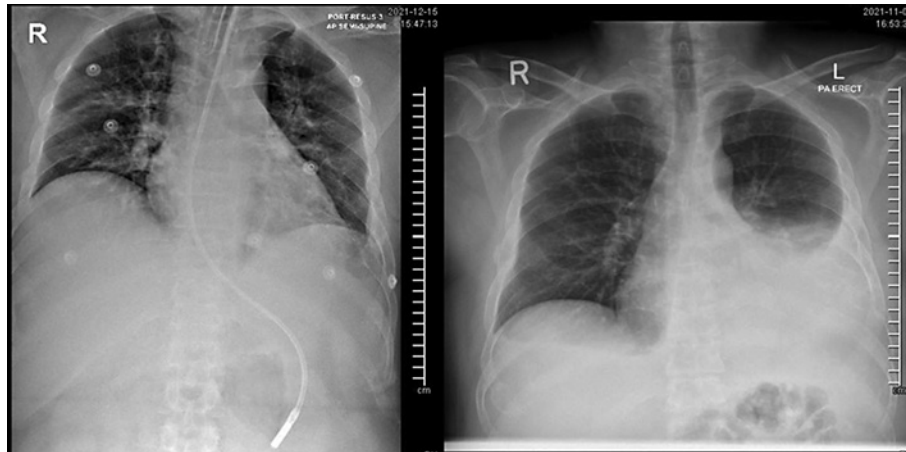


Fig. 1. Chest X-ray before (right) and after (left) 2 months of chemotherapy.

bone marrow (Table 1). RB1/CEP10, TP53/CEP17, and IGH probes were used. The analysis revealed an abnormal hybridization signal pattern with deletion of RB1 probe on 13q14 and loss of 3' of IGH probe in ~7% of the cells analyzed. These findings were consistent with bone marrow involvement by plasma cell myeloma. FISH cytogenetics such as t 4:14, del p53, and t 14:16 was not done. Based on the R-ISS classification, our patient has stage II disease.

The patient received bortezomib/lenalidomide/dexamethasone (VRD regimen) along with daratumumab, achieving resolution of the pleural effusion after 2 months from starting therapy (Fig. 1). By this time, the patient presented with confusion and fever; a diagnosis of bacterial meningitis was made and required intensive care hospitalization, but unfortunately, he passed away.

Discussion

MM affects the bone marrow generally, and the most common presentations of MM patients include anemia, bone pain, and elevated creatinine [10]. Extramedullary disease is less common and usually predicts a poorer prognosis [11]. One of these manifestations is pleural effusion which is uncommon and happens in approximately 6% of the patients. Most frequently, the causes of the effusion are infections due to associated hypogammaglobulinemia or bone marrow suppression caused by treatment, heart failure due to hyperviscosity or amyloidosis, renal failure, pulmonary embolism, and hypoalbuminemia [12]. However, MPE is far less common and happens in less than 1% of MM patients [1].

Identification of MPE is mainly based on cytological analysis and immunohistochemistry. Pleural biopsy, if done, can also help in identifying this type of effusion. In our case, the patient

was diagnosed with MPE based on cytospin preparation of pleural fluid, and due to high clinical suspicion, we proceeded with MM workup based on these findings. However, CD138 testing of cells in the pleural fluid was not done.

Although the most common type of MM is IgG kappa, it is not the most common type found in patients with MPE. Reports varied widely in the frequency of different types of MM in patients with MPE, and the IgA type appears to be the most common in most reports. In one study, it was reported that IgA disease is found in up to 80% of the cases [13], and others reported the IgA kappa type presenting in 39%, followed by the lambda light chain type at 26%, IgG kappa at 13%, nonsecretory 13%, and then kappa light chain MM 9% in a study of 23 patients [14]. A higher incidence of the IgD type with MPE was also reported, reaching 16% in a study of 30 patients [15] and 31.6% in a study of 19 patients [9].

Pathogenesis is still not well defined, and plausible mechanisms of MPE include invasion from adjacent skeletal lesions, extension from chest wall plasmacytomas, tumor infiltration of the pleura, and mediastinal lymph node involvement causing lymphatic obstruction [16]. Management of MPE includes local management of the pleural effusion such as therapeutic thoracentesis or pleurodesis and chemotherapy of MM. Identifying MPE is essential as it has both prognostic and therapeutic considerations. Till now, there is no unified approach for MPE management. Multiple case studies reported different approaches to treatment with variable outcomes. However, a literature review done by Yanamandra et al. [17] showed that outcomes in patients who developed MPE were poor with 90.9% mortality and median survival of 2.47 months. In one case report, a trial of intrapleural treatment was done, and the patient received bortezomib, doxorubicin, and dexamethasone, and 2 days after the treatment, the bortezomib dose was divided in half into intravenous and intrapleural; the patient became thoracentesis-independent, and a repeat CT scan confirmed significant regression of pleural effusion. Reporters claim that increased intrapleural concentration of bortezomib as a result of local administration might represent a possible major factor responsible for the rapid remission of MPE [18]. In another case report, a patient with massive right MPE received 4 courses of the VRD regimen as induction therapy, and partial response was achieved, after that daratumumab was given in 2 courses of the daratumumab, lenalidomide, and dexamethasone regimen, after which the pleural effusion completely resolved [19]. Compared to our case, we used VRD and daratumumab from the beginning, achieving a similar response in regards to pleural effusion resolution. Our patient responded to the regimen with regard to pleural effusion as evidenced by a chest X-ray after 2 months. However, traditional myeloma response could not be appreciated since the patient developed bacterial meningitis and clinically deteriorated and died consequently. Further studies are needed to better understand the pathogenesis of MPE and MM in general, which will hopefully shed light on better treatment options.

Conclusion

Despite being rare, MPE at initial presentation usually indicates a high disease burden and can indicate a poorer prognosis.

Statement of Ethics

Written informed consent was obtained from the patient's next of kin for publication of the details of their medical case and any accompanying images. This article was approved by Hamad Medical Corporation Medical Research Center, approval number (MRC-04-22-061)

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

The publication of this manuscript was supported by the Internal Medicine residency program, Hamad Medical Corporation (HMC).

Author Contributions

Case identification and eligibility assessment: Zakaria Maat. Critical review of the manuscript and revisions: Abdelhaleem Ahmed Elhiday. Initial manuscript writing: Zakaria Maat, Osama Adil Shafeeq Al-Ameen, Yousef Taher Hani Al-Asa'd, and Eihab A. Subahi. Literature review: all the authors. Review and approval of the final manuscript: all the authors.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

- 1 Kintzer JS, Rosenow EC, Kyle RA. Thoracic and pulmonary abnormalities in multiple myeloma. A review of 958 cases. *Arch Intern Med*. 1978;138(5):727–30.
- 2 Rodriguez JN, Pereira A, Martinez JC, Conde J, Pujol E. Pleural effusion in multiple myeloma. *Chest*. 1994; 105(2):622–4.
- 3 Alexandrakis MG, Passam FH, Kyriakou DS, Bouros D. Pleural effusions in hematologic malignancies. *Chest*. 2004;125(4):1546–55.
- 4 Meoli A, Willisie S, Fiorella R. Myelomatous pleural effusion. *South Med J*. 1997;90(1):65–8.
- 5 Usköl BT, Türker H, Emre Turan F, Unal Bayraktar O, Melikoğlu A, Tahaoğlu C, et al. Pleural effusion as the first sign of multiple myeloma. *Tüberk Toraks*. 2008;56(4):439–42.
- 6 Chen H, Li P, Xie Y, Jin M. Cytology and clinical features of myelomatous pleural effusion: three case reports and a review of the literature. *Diagn Cytopathol*. 2018 Jul;46(7):604–9.
- 7 Kim YJ, Kim SJ, Min K, Kim HY, Kim HJ, Lee YK, et al. Multiple myeloma with myelomatous pleural effusion: a case report and review of the literature. *Acta Haematol*. 2008;120(2):108–11.
- 8 Kamble R, Wilson CS, Fassas A, Desikan R, Siegel DS, Tricot G, et al. Malignant pleural effusion of multiple myeloma: prognostic factors and outcome. *Leuk Lymphoma*. 2005 Aug;46(8):1137–42.
- 9 Cho YU, Chi HS, Park CJ, Jang S, Seo EJ, Suh C. Myelomatous pleural effusion: a case series in a single institution and literature review. *Korean J Lab Med*. 2011 Oct;31(4):225–30.
- 10 Kyle RA, Gertz MA, Witzig TE, Lust JA, Lacy MQ, Dispenzieri A, et al. Review of 1,027 patients with newly diagnosed multiple myeloma. *Mayo Clin Proc*. 2003 Jan;78(1):21–33.
- 11 Alkan O, Tiryaki TO, Kalayoglu-Besisik S. Myelomatous pleural effusion: a rare involvement in myeloma. *J Med Cases*. 2020;11(3):55–6.
- 12 Ghorbel IB, Feki NB, Lamoum M, Hamzaoui A, Khanfir M, Salem TB, et al. Pleural myelomatous involvement in multiple myeloma: five cases. *Ann Saudi Med*. 2015 Jul–Aug;35(4):327–30.
- 13 Shirdel A, Attaran D, Ghobadi H, Ghiasi T. Myelomatous pleural effusion. *TANAFFOS Respiration*. 2007;6(2 spiraling):68–72.
- 14 Zhong Y, Zhang J, Wang H. Myelomatous pleural effusion involvement in 23 patients with multiple myeloma: a single-center clinical analysis. *Thorac cancer*. 2015 May;6(3):359–62.
- 15 Kim HJ, Choi DR, Yun G-W, Park E, Kim SJ, Lee YK, et al. Myelomatous pleural effusion of multiple myeloma: characteristics and outcome. *Blood*. 2009 Nov 20;114(22):3874.
- 16 Lang KJ, Lidder S, Aitchison R. Massive pleural effusion due to IgG multiple myeloma. *Hematol Rev*. 2009 Jul; 1(2):18.

- 17 Yanamandra U, Deo P, Sahu KK, Nampoothiri RV, Gupta N, Prabhakaran A, et al. Clinicopathological profile of myelomatous pleural effusion: single-center real-world experience and review of literature. [Clin Lymphoma Myeloma Leuk](#). 2019 Mar;19(3):183–9.e1.
- 18 Klanova M, Klener P, Trneny M, Straub J, Spicka I. Intrapleural bortezomib for the therapy of myelomatous pleural effusion: a case report. [Case Reports Immunol](#). 2012;2012:978479.
- 19 Wada A, Yasumura S, Kajikawa S, Murakami J, Sato T. Successful treatment of myelomatous pleural effusion with daratumumab administration before autologous peripheral stem cell transplantation. [Rinsho Ketsueki](#). 2020;61(8):879–84.