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Respiratory Medicine Case Reports

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Case report

Massive pleural effusion due to IgG-Kappa subtype multiple myeloma: A case report[☆]Itthiphath Arunsurat^a, Wipa Reechaipichitkul^{a,*}, Apichart So-Ngern^b, Piti Ungareevittaya^c, Nipon Chaisuriya^c, Nattiya Teawtrakul^d, Pailin Ratanawatkul^a, Worawat Chumpangern^a^a Division of Pulmonary, Department of Medicine, Faculty of Medicine, Khon Kaen University, Thailand^b Division of Sleep Medicine, Department of Medicine, Faculty of Medicine, Khon Kaen University, Thailand^c Department of Pathology, Faculty of Medicine, Khon Kaen University, Thailand^d Division of Hematology, Department of Medicine, Faculty of Medicine, Khon Kaen University, Thailand

A B S T R A C T

Multiple myeloma (MM) is a hematologic malignancy of plasma cell origin. Incidence of pleural effusion in multiple myeloma patients is approximately 6%. Myelomatous pleural effusions (MPE) are rare and occur in less than 1% of all MM cases. MPE is associated with advanced diseases, decreased survival time, and poor treatment response.

In our case report, we describe a 59-year old man who presented with MPE at the initial diagnosis of MM. A diagnosis of MPE was reached through pleural fluid cytology and pleural tissue histology. The MPE had good response to initial dexamethasone without local therapy.

1. Introduction

MM is a hematologic malignancy of plasma cell origin. Incidence of pleural effusion in multiple myeloma patients is approximately 6% [1]. We describe an unusual case of MM presented with massive MPE at initial diagnosis. (see Table 1)

2. Case

A 59-year old man was hospitalized for a 1-week progressive paraparesis. He had a back pain without fever or weakness for 2 weeks. One week before admission he developed progressive paraparesis and dyspnea. Bone radiograph showed compression fracture of T₆ vertebral body and multiple osteolytic lesions. Laboratory tests showed anemia, acute kidney injury and hypercalcemia. Chest radiograph showed bilateral pleural effusion. He was referred to Srinagarind Hospital, Khon Kaen university for further investigation.

His medical history was unremarkable. He was a heavy smoker (30-pack-year) and social alcohol drinker. He had history of tuberculosis exposure with his colleague.

On admission, he was afebrile, respiratory rate was 24 times per minute and oxygen saturation was 96% breathing ambient air. He was moderately pale. Trachea was in the midline. Auscultation of the chest

revealed decreased breath sounds with dullness on percussion on both lungs. Neurological examination revealed paraparesis (motor power grade I from V both legs) with diminished deep tendon reflexes without ankle clonus both legs, decreased pinprick sensation below T₆ dermatome, perianal sensation and loose sphincter tone. Ophthalmic, abdomen, lymph nodes, skin, and extremities examinations were unremarkable.

The initial hemoglobin concentration was 7.1 g/dL, and the white blood cell count was $7.2 \times 10^3/\mu\text{L}$, comprised of 75% neutrophils, 19% lymphocytes without increased plasma cells. The platelet count was $305 \times 10^3/\mu\text{L}$. The peripheral blood smear showed rouleaux's formation. The coagulogram showed PT 12.4 seconds (9.5–12.1), PTT 27.2 seconds (27.9–39.4) and INR 1.12. The laboratory chemistry profile showed BUN 55 mg/dL, creatinine 5.5 mg/dL, bicarbonate 16.5 mEq/L, potassium 5.1 mg/dL, calcium 10.3 mg/dL, phosphate 8 mg/dL, globulin 10.3 g/dL, albumin 2.4 g/dL, alkaline phosphatase 80 U/L (30–120).

A chest radiograph showed hemithorax bilateral effusion. A chest CT showed bilateral pleural effusion with pleural thickening, no lung mass or adenopathy were seen (Fig. 1). A whole spine MRI showed pathological compression fracture at T₆ vertebra causing severe compression to spinal cord and exiting nerve root of T₆ and T₇, bilateral paravertebral soft tissue masses at C₅ and C₆ region, no epidural infiltration, and diffuse infiltration at nearly entire vertebra of C-T-L levels.

[☆] This case report was approved by the Human Research Ethics Committee of Khon Kaen University (HE621451).

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<https://doi.org/10.1016/j.rmcr.2019.100984>

Received 13 November 2019; Received in revised form 11 December 2019; Accepted 11 December 2019

Available online 12 December 2019

2213-0071/© 2019 The Authors.

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Table 1

Laboratory tests	At admission	3 weeks later
Serum creatinine (mg/dL)	5.5	0.74
Serum calcium (mg/dL)	10.3	8.2
Serum globulin (g/dL)	10.3	3.9
Hb (g/dL)	7.1	7.3 ^a

^a 1 unit of leukocyte poor red blood cell was transfused during admission.

Diagnostic thoracentesis produced clear and colorless fluid with feature suggestive of a lymphocytic (38%) exudate (total protein 5.3 g/dL, LDH 463 U/L, sugar 159 mg/dL, ADA 12.3). Cytological analysis of the pleural fluid showed abnormal plasma cells. Pleural biopsy revealed myeloma with Kappa-light chain restriction (immunohistochemistry showed positive for CD138 and Kappa but negative for Lambda) (Figs. 2 and 3).

Diagnostic bronchoscopy was performed, bronchial wash for mycobacterial culture, fungal culture, and Xpert MTB/RIF assay were negative.

Serum protein electrophoresis demonstrated monoclonal gammopathy, and the immunofixation test showed IgG-Kappa monoclonal gammopathy (IgG >6938 mg/dL (1541–2315), IgA 57.10 mg/dL (230–329), Kappa free light chain 164.40 mg/L, Lambda free light chain 12.64 mg/L, Kappa/Lambda ratio 13.2). B₂-microglobulin was 32.28 mg/L. The cytogenetic tests for multiple myeloma was not available at our center.

Bone marrow aspiration and biopsy showed monotypic plasma cell population with Kappa light chain restriction (immunohistochemistry showed positive for CD138 and Kappa but negative for Lambda) (Fig. 4).

The final diagnosis was MM with bilateral MPE and T₆-spinal cord compression, International staging system (ISS) III (Durie-Salmon stage IIIB).

Dexamethasone 40 mg. per day was started as initial therapy. T₆-laminectomy was performed, the intraoperative findings were greyish tumors in laminar and pedicle cortex. The spinal tissue revealed myeloma with Kappa-light chain restriction (immunohistochemistry showed positive for CD138 and Kappa but negative for Lambda).

After the operation, the motor power of legs was improved to grade IV from V. Chest radiograph after 1-week of dexamethasone showed resolution of pleural effusion (Fig. 5). Serum creatinine and calcium

were within normal limits. After three weeks of admission, he was discharged. The patient was treated with VCD regimen (Bortezomib, cyclophosphamide and dexamethasone) at outpatient department.

3. Discussion

The common causes of pleural effusion in MM are congestive heart failure due to amyloidosis, chronic renal failure, hypoalbuminemia, pulmonary embolism and infection [1]. MPE are rare and occur in less than 1% of all MM cases [1] while myelomatous peritoneal and pericardial effusion are extremely rare [2]. The first case of MPE was reported in 1994 by Rodriguez et al. [3]. They suggested a diagnostic criterion for MPE which composes of three parameters: 1) demonstration of monoclonal protein in pleural fluid electrophoresis; 2) detection of atypical plasma cell in the pleural fluid; and 3) histological confirmation with a pleural biopsy or autopsy [3].

A systemic review in characteristics of 153 patients with MPE was reported in 2018 by Riveiro et al. [4]. The median age was 62 years and male predominant (1.7:1). The most common symptoms were dyspnea and bone pain, and the most common abnormal laboratory test results were anemia and renal failure [5]. Few patients have MPE at first diagnosis of MM [1,5,6]. MPE was predominantly unilateral (63.9%) and more than two-third of hemithorax (54.5%) [5].

In most cases of MPE, the pleural fluid profile is lymphocytic (78.6%) exudate (97.4%) [4]. The most common subtype in a study of 23 patients with MPE by Zhong et al. was IgA- Kappa (39%), followed by Lambda-light chain (26%), IgG- Kappa (13%), non-secrete (13%) and Kappa-light chain MM (9%) [5]. However, in a study of 30 patients with MPE by HJ Kim et al., the most common subtype was Light chain (30%), followed by IgG (26%), IgA (23%), IgD (16%) and non-secretory myeloma [11].

MPE is associated with advanced diseases (International staging system (ISS) >I) [5,6,11]. The reported median survival time of MM with MPE is lower than the median survival of 29 months observed in MM ISS III [6–8,11]. In a study of HJ Kim et al., early onset of MPE was associated with shorter median overall survival (2.8 vs. 26 months from initial diagnosis of MM) [11]. Moreover, MPE is associated with poorer treatment response. Bortezomib-based therapy combines with local therapy (thoracentesis, chest drainage or pleurodesis) can achieved the best response in MPE patients [4,9,10]. In a study of HJ Kim et al. (based



Fig. 1. Bilateral pleural effusion with pleural thickening.

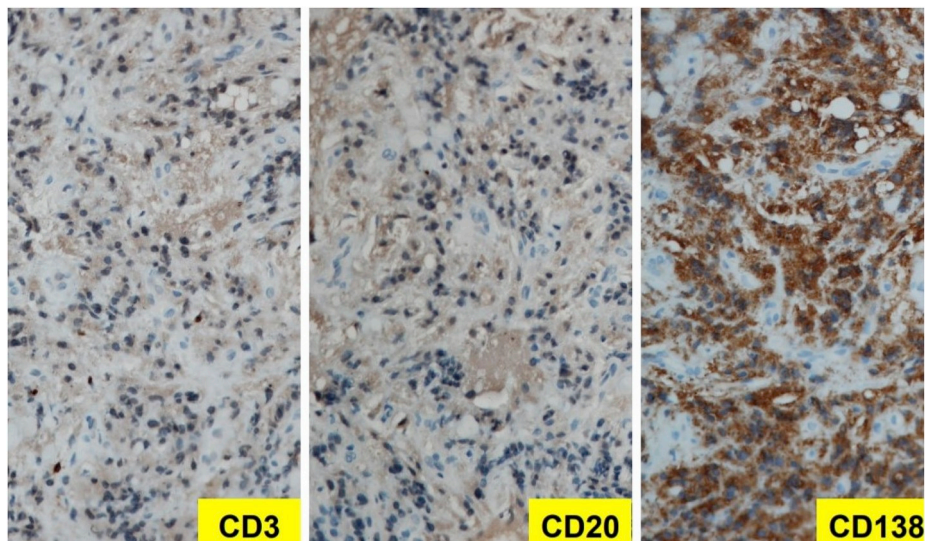


Fig. 2. Immunohistochemistry stain of pleural tissues showed CD138-positive cells.

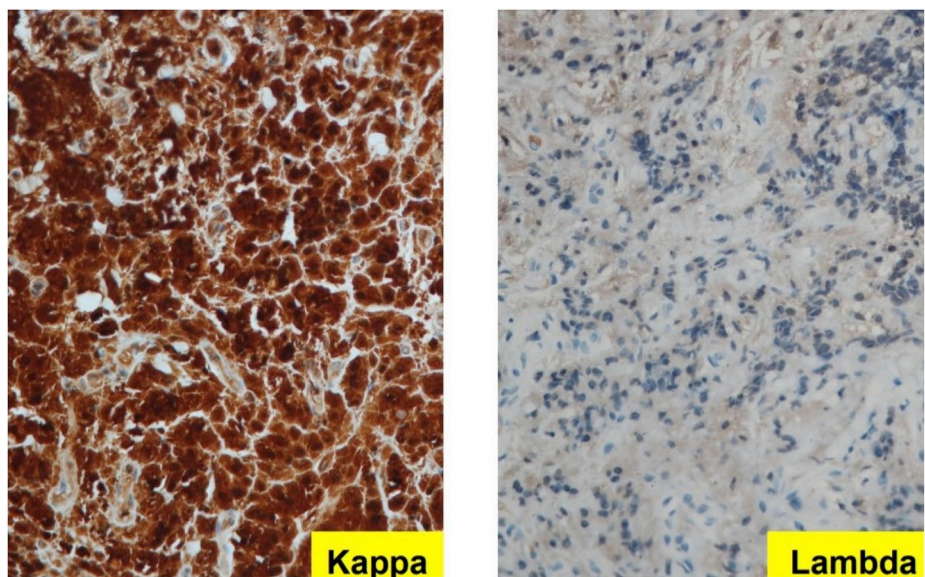


Fig. 3. Immunoglobulin stain of pleural tissue showed Kappa-light chain restriction.

on Vincristine, Adriamycin, Dexamethasone regimen), MPE disappeared in a 58% of patient who received chemotherapy, which median response duration (defined as days from disappearance to relapse of MPE) was 123 days, compared with 5.7 month in a study of Zhong et al. (based on Bortezomib regimen) [5,11]. The data of Autologous stem cell transplant (ASCT) in MM with MPE is limit due to shortened survival of these patients. In one study of high-risk MM with MPE based on complex karyotypic abnormalities, small number of patients receiving ASCT after high dose chemotherapy did not show clear survival benefit [16].

Currently, cytogenetic risk stratification are the power prognostic factors in MM. Patients with t (14; 14), t (14; 16), t (14; 20), del17p13, or gain 1q by FISH account for 25% in MM and have shortened median survival with standard therapy [12,13]. A case report of early onset MPE with IgG-Kappa showed rapid reaccumulation of MPE within one week after starting VCD regimen, and was controlled with Bortezomib, Daratumumab, and dexamethasone regimen. The cytogenetic and fluorescence in situ hybridization (FISH) studies showed a gain of chromosome 9 and 13q/14 (RB1) deletions [14].

It is interesting to note that in our case, bilateral MPE was presented

at the first diagnosis of MM, as well as acute kidney injury, anemia, hypercalcemia and pathological fractures, which was an advanced stage of MM (ISS III). The MPE was diagnosed by detection of atypical plasma cell in the pleural fluid with immune-histological confirmation in pleural tissue. The monoclonal protein subtype of our case was IgG-Kappa, but he had good response to initial dexamethasone without local therapy, such as drainage, or pleurodesis. We hypothesize that our case may have favorable cytogenetic characterizations such as hyperdiploidy. In term of specific hyperdiploidies affecting prognosis, trisomy 3 and/or 5 significantly improve overall survival [15]. However, cytogenetic analysis was limitation in our case.

4. Conclusion

MPE is a rare clinical manifestation of MM and associates with advanced diseases and poor outcome. Our case was unusual case of MPE which was the first presentation of MM and had good response to initial dexamethasone without local therapy. It is interesting to conduct the further study of cytogenetic subtype of MPE and their treatment

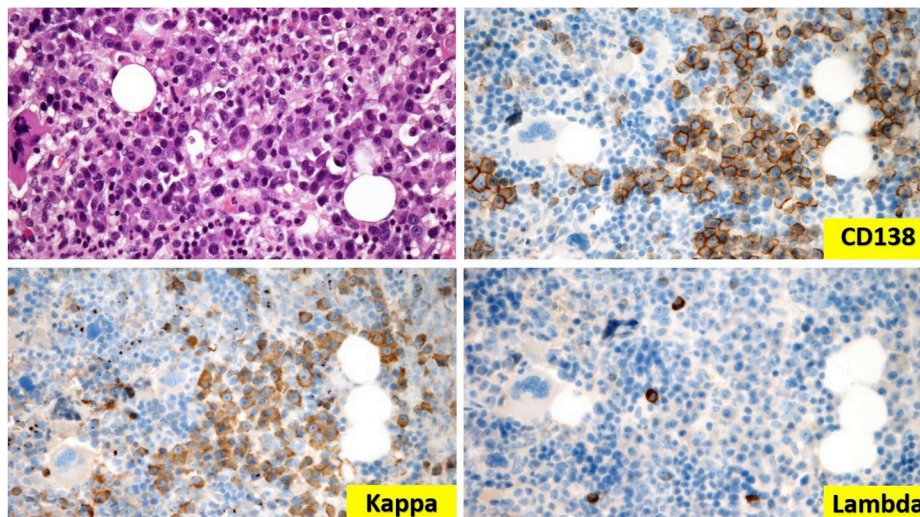


Fig. 4. Bone marrow biopsy showed monotypic plasma cell population with Kappa light chain restriction (immunohistochemistry showed positive for CD138 and Kappa but negative for Lambda).

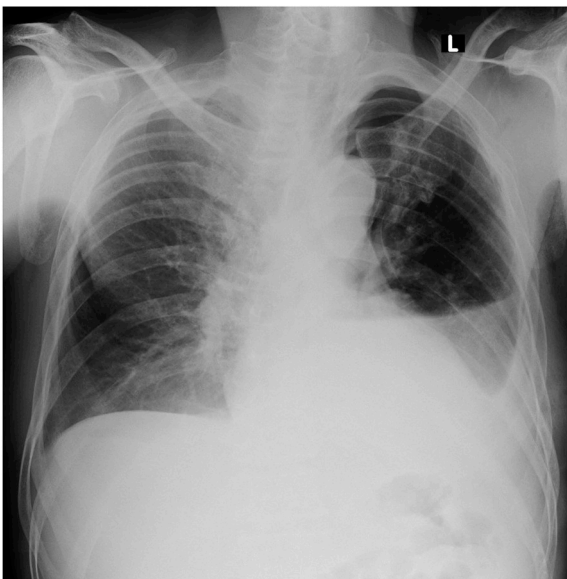


Fig. 5. Chest radiograph after start dexamethasone.

responsiveness.

Declaration of competing interest

The authors of this case report have no conflict of interest.

Acknowledgements

The authors are grateful to the Faculty of Medicine, Khon Kaen University for the support and Professor James Arthur Will for assistance with the English-language presentation.

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