

Solitary pleural myeloma diagnosed by semi-rigid thoracoscopy: A case report and literature review

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Abstract. Multiple myeloma (MM) is characterized by abnormal proliferation of neoplastic plasma cells. Pleural effusion as an initial presentation of this disease is rare, as is true pleural myeloma. We herein present a case of solitary pleural myelomatous lesion in a 70-year-old male patient diagnosed by pleural biopsy via semi-rigid thoracoscopy followed by histopathological examination. Furthermore, a review of the related English literature identified 22 cases of pleural myeloma, only 3 of which were diagnosed by video-assisted thoracoscopy. To the best of our knowledge, this is the first reported case of a solitary pleural myelomatous lesion diagnosed by pleural biopsy via semi-rigid thoracoscopy. Patients with MM with pleural involvement, including the present case, appear to have a short survival despite aggressive treatment. Our patient received chemotherapy with bortezomib, epidriamycin and dexamethasone; however, he deteriorated rapidly after one cycle of chemotherapy and succumbed to the disease 8 weeks after the initial presentation. According to our experience, semi-rigid thoracoscopy is an effective and safe method for obtaining a pleural specimen for histopathological evaluation.

Introduction

Multiple myeloma (MM) is a hematological malignancy that primarily affects elderly individuals. The clinical manifestations of MM, collectively referred to as 'CRAB', include hypercalcemia, renal insufficiency, anaemia and bony lesions, caused by either direct infiltration by neoplastic plasma cells

or deposition of monoclonal immunoglobulins (Ig), particularly light chains. Myelomatous pleural effusion (MPE) is an uncommon manifestation, with only a few cases reported to date (1). Patients with MPE often have advanced-stage disease and poor prognosis, despite aggressive treatment. We herein present a case of MPE diagnosed via semi-rigid thoracoscopy in a patient with IgA- λ MM, and a review of the current literature on clinical manifestations, laboratory examinations and diagnosis of MPE.

Case report

A 70-year-old male patient presented at The First Affiliated Hospital of Wenzhou Medical University (Wenzhou, China) with a 1-week history of cough and exertional dyspnea with no fever, chest pain, purulent sputum and hemoptysis. The patient was a smoker with >20 pack-years, but his medical, social and family history were otherwise unremarkable. On physical examination, the patient appeared pale, with decreased breath sounds and dullness on percussion over the left posterior thorax. The laboratory findings were as follows: White blood cell count, $3.9 \times 10^9/l$ (50.9% neutrophils, 32.7% lymphocytes, and 13.5% monocytes, normal basophils and eosinophils); erythrocyte count, $2.7 \times 10^{12}/l$; hemoglobin, 81 g/l; platelet count, $180 \times 10^9/l$; total protein, 85.5 g/l; albumin, 31.8 g/l; globulin, 53.7 g/l; serum calcium, 3.6 mmol/l [normal limit (NL): 2.1-2.6 mmol/l]; serum creatinine, 180 $\mu\text{mol}/l$ (NL: 44-97 $\mu\text{mol}/l$); urea nitrogen, 8.7 mol/l; C-reactive protein, 30.5 mg/l; lactate dehydrogenase (LDH), 364.0 μ/l ; β_2 -microglobulin, 21.1 $\mu\text{g}/\text{ml}$ (NL: 0.9-2.7 $\mu\text{g}/\text{ml}$); serum κ light chain, 3.4 g/l (NL: 6.3-13.5 g/l); serum λ light chain, 28.3 g/l (NL: 3.1-7.2 g/l); serum IgA, 24.3 g/l; IgM, 153.00 mg/l; IgG, 4.4 g/l; and IgD, 0.43 g/l; the IgE and IgD levels were normal. Carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 and brain natriuretic peptide levels were within normal limits, and the T-SPOT[®] tuberculosis test was negative. Computed tomography (CT) revealed left pleural effusion and atelectasis of the lower lobe of the left lung (Fig. 1). Fiberoptic bronchoscopy revealed no endobronchial lesions. The patient underwent thoracentesis and the pleural fluid was highly cellular, with a nucleated cell count of $1.7 \times 10^9/l$ (42% mononuclear cells), and contained total protein at 46.1 g/l, LDH at 193.0 U/l, adenosine deaminase at 20.0 U/l and CEA

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Abbreviations: MM, multiple myeloma; MPE, myelomatous pleural effusion; NL, normal limit; CT, computed tomography; VATS, video-assisted thoracoscopy

Key words: multiple myeloma, plasma cells, pleural effusion, thoracoscopy

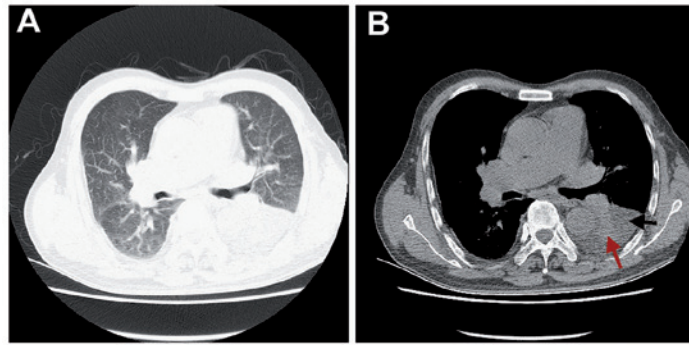


Figure 1. Computed tomography scans of the chest. (A) Lung window and (B) mediastinal window showing left pleural effusion (black arrow) and compressive atelectasis of the lung (red arrow).

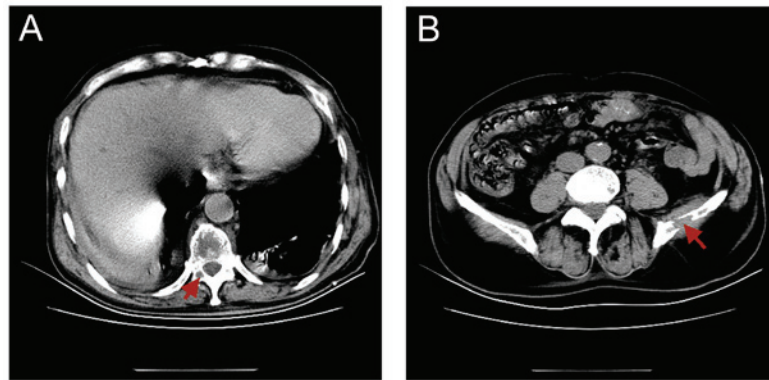


Figure 2. Abdominal computed tomography scans showing lytic lesions of (A) of a thoracic vertebra and (B) the innominate bone (arrows).

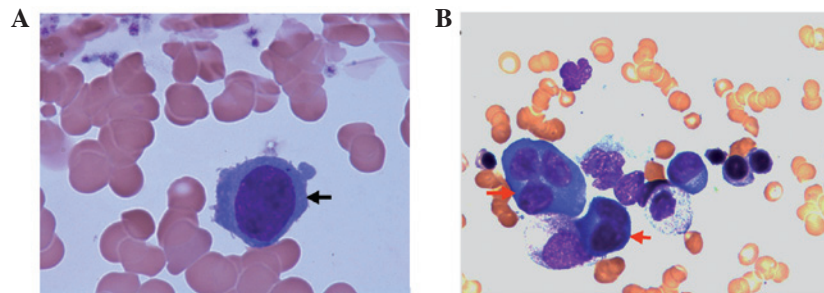


Figure 3. Cytology of the bone marrow. (A) Normal plasma cell (arrow). (B) Malignant plasma cells were detected in the bone marrow, characterized by large, eccentrically placed, pleomorphic nuclei with prominent nucleoli (arrows). Wright-Giemsa stain; magnification, x400.

at 1.5 $\mu\text{g/l}$; thus, the effusion was considered as exudative according to the Light criteria (2). Malignant cells were not found in the pleural fluid. Immune fixation electrophoresis of the blood revealed IgA- λ -type monoclonal immunoglobulin. The patient underwent bone marrow aspiration twice. The first bone marrow biopsy showed no significant abnormalities (Fig. 3A), while the second revealed a mildly hypercellular marrow with 13% plasma cells (Fig. 3B). Semi-rigid thoracoscopy was performed, which revealed a solitary pleural nodule sized $\sim 1 \times 0.8$ cm on the parietal pleura (Fig. 4). Histopathological evaluation of the biopsied nodule revealed sheets of neoplastic plasma cells, which were positive for CD38 and multiple myeloma oncogene 1 (MUM1), with λ light chain restriction and a Ki-67 index of 50% (Fig. 5). The patient was diagnosed with IgA- λ -type MM with pleural involvement, based on the

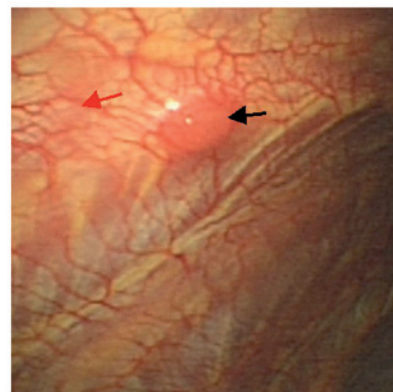


Figure 4. View of the left pleura on semi-rigid thoracoscopy, showing a solitary nodule on the parietal pleural surface (black arrow) and pleural congestion (red arrow).

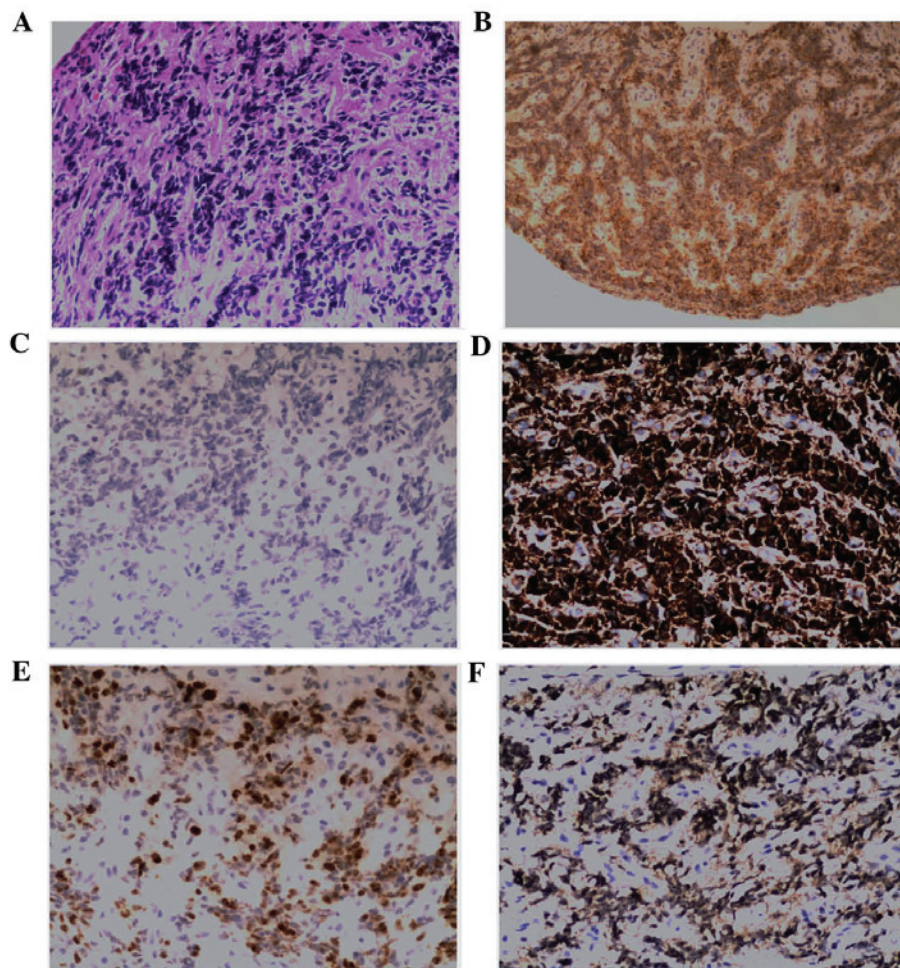


Figure 5. Histopathology and immunohistochemistry images of the pleural biopsy specimen (magnification, x200). (A) Hematoxylin and eosin staining revealed abnormal proliferation of plasma cells. The immunohistochemical staining results were as follows: (B) CD38⁺, (C) κ , (D) λ ⁺, (E) Ki-67⁺ (>50%) and (F) multiple myeloma oncogene 1 (MUM1)⁺. Positive staining for CD38 is characteristic for malignant plasma cell disease. The myeloma-specific oncogene MUM1 is a key regulator of several steps in lymphoid, myeloid and dendritic cell differentiation and maturation. κ and λ , light chains in multiple myeloma.

clinical manifestations, laboratory examinations, radiographic findings and the results of bone marrow and pleural biopsies. The patient received chemotherapy with bortezomib, epirubicin, melphalan and dexamethasone; however, he deteriorated rapidly after one cycle of chemotherapy and succumbed to the disease 8 weeks after the initial presentation.

Written informed consent was obtained from the patient regarding the publication of this case report and any accompanying images.

Discussion

As a hematopoietic malignancy, MM primarily affects the bone marrow, but may also involve extramedullary tissue. The characteristic clinical manifestations of MM, collectively referred to as 'CRAB', include hypercalcemia, renal failure, anemia and bone lesions. MPE is an uncommon manifestation, occurring in ~6% of patients with MM (1). Our patient presented with the typical 'CRAB' signs and symptoms in addition to a pleural myelomatous lesion. The possible etiological factors for pleural effusion include congestive heart failure secondary to amyloidosis, chronic renal failure, nephritic syndrome secondary to renal tubular infiltration

with paraprotein and development of glomerular damage, direct infiltration of pleural fluid from adjacent tissues, hypoalbuminemia, pulmonary embolism, secondary neoplasm, lymphatic drainage obstruction by tumor infiltration, infection and pleural myelomatous involvement (3). It has been reported that 80% of MPE cases are related to IgA MM (4); our patient was also IgA type. In the present case, the unilateral exudative effusion was mainly attributed to a localized pleural myelomatous lesion. Chemotherapy is the mainstay of therapy for pleural myeloma, despite the low response rate and short survival time.

An English literature search for related studies between 1990 and 2015 was conducted through PubMed, using the search criteria ('pleural effusion' and 'multiple myeloma') or 'myelomatous pleural effusions', which yielded 152 candidate articles. Based on the inclusion criteria (pleural myelomatous involvement confirmed by cytological analysis of pleural effusion or histopathological evaluation of pleural biopsy specimens), a total of 22 cases were included in the final review and analysis. The patient characteristics, including general information, laboratory test results, diagnostic methods and clinical outcomes, were retrospectively reviewed and are summarized in Table I. The patient age ranged from 40 to 83 years, with

Table I. Reported cases of pleural myeloma.

First author (Refs.)	Year	Age/gender	Ig type	EMI	Osteolysis	Pathology	Thoracoscopy	Survival ^a (months)
Jiang (5)	2015	78/ND	IgD	No	Yes	CPE	No	ND
Suwatanapongched (6)	2014	76/M	IgG- λ	No	Yes	CPE	No	1
Zhang (7)	2014	53/M	IgG- κ	No	No	Pleural biopsy	VATS	ND
Xu (8)	2013	45/M	Negative	No	Yes	Pleural biopsy	No	12
Chim (9)	2013	56/M	IgG- λ	No	No	ND	No	5
Oudart (3)	2012	62/F	IgG- κ	ND	ND	CPE	No	ND
Klanova (10)	2012	43/F	IgG- κ	Yes ^b	Yes	CPE	No	12
Keklik (11)	2012	52/M	IgG- κ	No	Yes	CPE	No	ND
Al-Farsi (12)	2010	56/M	IgG- κ	No	Yes	CPE	No	6
Huang (13)	2010	67/F	IgA- λ	NG	ND	CPE	No	ND
Malhotra (14)	2010	50/M	ND	NG	ND	CPE	No	2
Ghoshal (15)	2010	61/F	ND	NG	Yes	Pleural biopsy	No	ND
Nakazato (16)	2009	74/M	IgG- κ	Yes ^b	Yes	CPE	No	8
Neuman (17)	2009	47/M	ND	ND	Yes	CPE	No	ND
Chang (18)	2009	83/F	IgD- λ	ND	No	CPE	No	2
Yokoyama (19)	2008	58/M	IgD	Yes ^b	NG	Pleural biopsy	No	3
Kim (20)	2008	76/F	IgA- λ	ND	Yes	CPE	No	1
Dhingra (21)	2007	40/M	IgG	ND	Yes	CPE	No	ND
Inoue (22)	2005	51/F	IgG- λ	Yes ^b	ND	Pleural biopsy	VATS	10
Kim (23)	2000	61/F	IgG- λ	ND	ND	Pleural biopsy	No	ND
Rodríguez (4)	1994	51/M	IgA- κ	ND	Yes	CPE	No	11
Makino (24)	1992	73/F	IgG	ND	No	CPE	No	ND
Present case	2015	70/M	IgA- λ	ND	Yes	Pleural biopsy	SRTS	8

^aAfter presentation with pleural effusion. ^bLymphadenopathy. EMI, extramedullary involvement; ND, not defined; CPE, cytology of pleural effusion; M, male; F, female; PM, pleural myeloma; PE, pleural effusion; VATS, video-assisted thoracoscopy sampling; Ig, immunoglobulin; SRTS, semi-rigid thoracoscopy.

a mean of 60 years and a slight male predominance. The diagnosis was made by cytological analysis of the pleural effusion in 15 cases; pleural biopsy specimens were examined in 7 patients, including 3 undergoing video-assisted thoracoscopy sampling (VATS) and 1 undergoing semi-rigid thoracoscopy (present case). The diagnostic method for pleural myeloma was not specified in the remaining case. All patients with pleural involvement had a short survival (ranging from 4 weeks to 12 months) after presentation with pleural effusion. The literature review revealed that MM with pleural involvement most commonly affects older (≥ 50 years) and elderly patients (≥ 65 years) and is associated with a poor prognosis.

In the previously reported cases reviewed herein, pleural myeloma was identified by pleural effusion cytology or/and histological examination of pleural biopsy specimens, despite the advantages of thoracoscopy, or open and multiple-site biopsy. However, a localized pleural myelomatous lesion is difficult to detect on CT or ultrasonography, which hampers image-guided direct biopsy of the lesion. With the advances in thoracoscopic techniques, open and multiple-site pleural biopsy may be performed by VATS or semi-rigid thoracoscopy. These procedures may improve the diagnostic rate in patients with pleural lesions of unknown etiology. However, thoracoscopy is rarely considered as a feasible option for

identifying the etiology of pleural effusion in patients with MM. In selected patients, semi-rigid thoracoscopy may be superior to VATS in terms of safety and cost-effectiveness. As semi-rigid thoracoscopy may be successfully performed under local anesthesia and intravenous sedation, the majority of patients with mild or moderate cardiopulmonary dysfunction may safely undergo this procedure, while they would not be eligible for VATS due to the risks associated with general anesthesia. Our patient underwent semi-rigid thoracoscopy with biopsy of a small solitary nodule on the left parietal pleura, which was diagnosed as a myelomatous lesion. To the best of our knowledge, this was the first report of a solitary pleural myelomatous lesion diagnosed by pleural biopsy via semi-rigid thoracoscopy. Semi-rigid thoracoscopy may be successfully performed by pulmonologists under local anesthesia. The procedure appears to be safer, more cost-effective and comfortable for patients compared with VATS.

In summary, we reported a case of solitary pleural myelomatous nodule diagnosed by semi-rigid thoracoscopy and pleural histopathology. Although MPE is uncommon, MM should be considered in patients with pleural effusion of unknown etiology. Semi-rigid thoracoscopy appears to be a feasible option for diagnosing pleural myeloma in the era of precision medicine.

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