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

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Received January 26, 2016; Accepted August 1, 2016

DOI: 10.3892/mco.2016.1000

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, epiadriamycin 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.

Case report

A 70-year-old male patient presented at The First Affiliated Hospital of Wenzhou Medical University (Wenzhou, China) with a 3-month history of cough and exertional dyspnea without fever, chest pain, purulent sputum and hemoptysis. The patient was a smoker with >20 pack-years, but his medical 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, 3.9x10³/³ (50.9% neutrophils, 32.7% lymphocytes, and 13.5% monocytes, normal basophils and eosinophils); erythrocyte count, 2.7x10¹²/l; hemoglobin, 81 g/l; platelet count, 180x10³/³; 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 µmol/l (NL: 44-97 µmol/l); urea nitrogen, 8.7 mol/l; C-reactive protein, 30.5 mg/l; lactate dehydrogenase (LDH), 364.0 µ/l; β2-microglobulin, 21.1 µg/ml (NL: 0.9-2.7 µg/ml); serum λ 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, 150.00 mg/l; IgG, 4.4 g/l; and IgM, 0.43 g/l; the IgE and IgD levels were normal. Carcinoma embryonic 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 1.7x10³/³ (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
at 1.5 µg/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 biopsy 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 ~1x0.8 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
clinical manifestations, laboratory examinations, radiographic findings and the results of bone marrow and pleural biopsies. The patient received chemotherapy with bortezomib, epiradimycin 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 | Survivala (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                |
| Klama (10)           | 2012 | 43/F       | IgG-κ   | Yes | Yes        | CPE       | No           | 12                |
| Keklik (11)          | 2012 | 52/M       | IgG-κ   | Yes | 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 | 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 | Yes        | 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 | Yes        | ND        | Pleural biopsy | VATS | 10                |
| Kim (23)             | 2000 | 61/F       | IgG-λ   | ND  | ND         | Pleural biopsy | No  | ND                |
| Rodriguez (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/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 thorascopic 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 pathology. Semi-rigid thoracoscopy appears to be a feasible option for diagnosing pleural myeloma in the era of precision medicine.
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