Showa Univ J Med Sci **25**(1), 67～72, March 2013

Case Report

Well-differentiated Papillary Mesothelioma of the Pleura Diagnosed by Video-Assisted Thoracic Surgical Pleural Biopsy : A Case Report

Yuri TOMITA[1)], Makoto NONAKA[1)], Naoya HIMURO[1)],
Daisuke KATAOKA[1)], Masanao NAKASHIMA[2)], Takashi HIROSE[2)],
Miki KUSHIMA[3)] and Mitsutaka KADOKURA[1)]

Abstract : Well-differentiated papillary mesothelioma of the pleura (WDPM-P) is an extremely rare type of mesothelial tumor that is thought to be of low malignant potential. Herein, we report on a case of WDPM-P. A 74-year-old woman was admitted for evaluation of shortness of breath. Pleural effusion was observed in the right thorax. Computed tomography after chest drainage did not reveal any lung or pleural tumors. Abnormally high levels of hyaluronic acid were detected in the pleural effusion. Cytological examination of the effusion revealed Class V findings ; however, it was difficult to distinguish mesothelioma from adenocarcinoma. Because immunological evaluation may have provided more information, video-assisted thoracic surgical pleural biopsy (VATS-PB) was performed. Biopsied frozen specimens were revealed to be mesothelioma, and so localized pleurectomy and partial resection of the diaphragm were performed. Pathological examination established a diagnosis of WDPM-P. Six years postoperatively, the patient is doing well. As demonstrated in the present case, combined VATS-PB and pathological studies are useful for the diagnosis of and determination of surgical indications for pleural malignancies.

Key words : well-differentiated papillary mesothelioma (WDPM), pleural tumor, pleural effusion, thoracoscopy, video-assisted thoracic surgery (VATS)

Introduction

Diffuse malignant mesothelioma (DMM) is one of the most aggressive malignant neoplasms[1)]. It is important to distinguish well-differentiated papillary mesothelioma (WDPM) from DMM because WDPM is an uncommon of type of epithelial tumor thought to be of low malignant potential[2, 3)]. Correlations between asbestos exposure and WDPM have not been established[2, 3)]. The primary clinical symptom in DMM is chest pain, but in WDPM of the pleura (WDPM-P) the primary clinical symptom is dyspnea. Because there are no particular symptoms or a pleural tumor, diagnoses of WDPM-P are difficult and pathological studies, including immunological staining, are warranted. Because of difficulties associated with discriminating small amounts of

[1)] *Division of Chest Surgery, Department of Surgery, Showa University School of Medicine,* 1-5-8 Hatanodai, Shinagawa-ku Tokyo, 142-8666, Japan.
[2)] *Division of Respiratory Medicine, Department of Medicine, Showa University School of Medicine*
[3)] *Department of Diagnostic Pathology, Showa University Hospital*

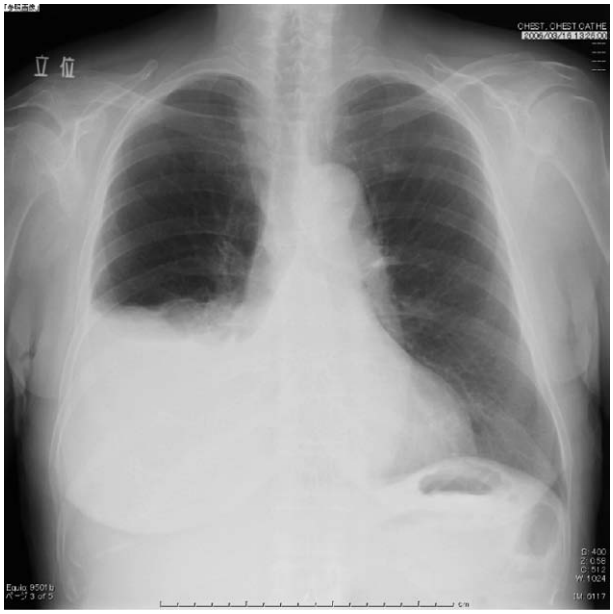

Fig. 1. Chest roentgenogram on admission.
Right pleural effusion is evident.

tissue, it is preferable to perform video-assisted thoracic surgical pleural biopsy (VATS-PB) to obtain a reasonable amount of tissue for analysis. Herein, we report on WDPM-P and the effectiveness of VATS-PB in diagnosing the condition.

Case Report

A 74-year-old woman visited our hospital because of shortness of breath. She had no history of exposure to asbestos. The patient was admitted for the evaluation of pleural effusion in the right thorax, found on chest roentgenogram (Fig. 1). Following chest drainage, hyaluronic acid concentrations in the pleural effusion were determined to be higher than normal (63,600 ng/mL). Cytological examination of the effusion revealed Class V findings suggestive of mesothelioma, but it was difficult to distinguish the condition from adenocarcinoma. Lung and pleural tumors were not observed on chest computed tomography (CT) after chest drainage.

We elected to use VATS-PB to aid in the diagnosis of our patient's pleural disease. During the procedure, some localized myxomatous small white nodules with a papillary configuration were observed on the surface of the parietal pleura and diaphragm (Fig. 2). No pleural plaques were evident. Although malignant pleural mesothelioma was not suspected at the time of surgical observation, these biopsied frozen specimens were determined pathologically to be malignant mesothelioma. Because the patient had coexisting conditions (i.e. chronic heart failure, diabetes mellitus, and hyperlipidemia), an extrapleural pneumonectomy was thought to be unsuitable. Therefore, localized pleurectomy and partial resection of the diaphragm were performed. Direct suturing of the diaphragm was possible. The mean size of each tumor was 5 mm.

According to the final pathological diagnosis of WDPM-P, there was a focally well-

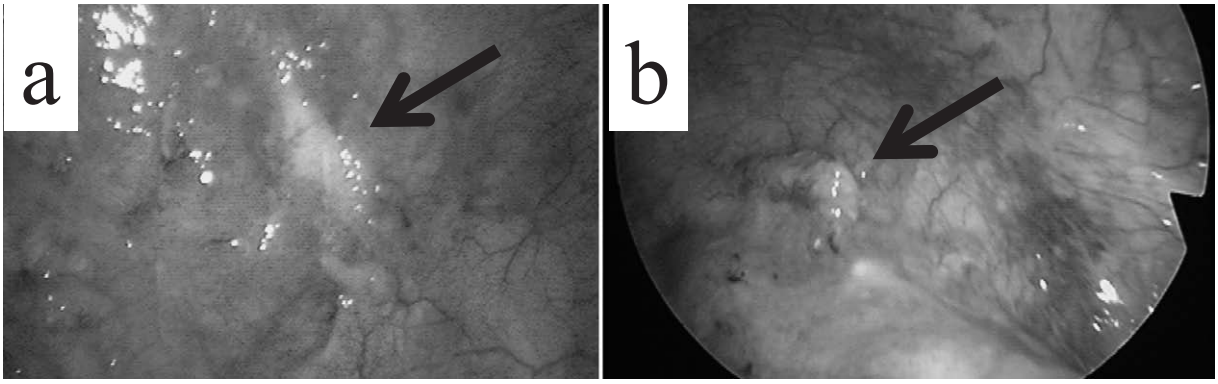

Fig. 2. Intrathoracic findings.
Localized myxomatous small white nodules (arrows) are observed on (a) the surface of the parietal pleura and (b) the surface of the diaphragm.

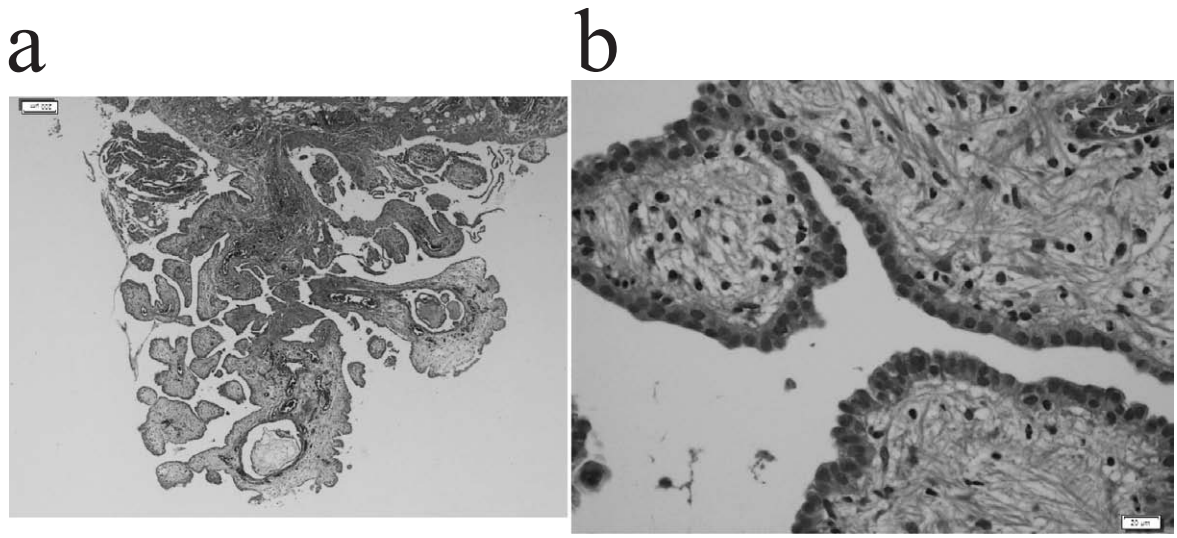

Fig. 3. Pathological findings.
(a) Papillary structures of the pleura with fibrous connective tissue cores. (b) The papillae are lined with a single layer of uniform mesothelial cells.

differentiated papillary structure consisting of fibrous papillary cores lined by a single layer of cuboidal mesothelial cells (Fig. 3). Tumor cells demonstrated minimal atypia. Anaplastic features and mitoses were not observed. There was no invasive growth to the stroma. Immunohistochemical investigation revealed that the tumor cells were positive for the mesothelioma marker HBME-1 (Fig. 4) and calretinin, but were negative for carcinoembryonic antigen (CEA) and Ber-EP4.

Because postoperative pleural effusion cytology showed a few suspicious cells, the patient underwent adjuvant chemotherapy (CDDP 60 mg/m^2, pemetrexed 500 mg/m^2, four courses). Six years after surgery the patient is alive without any pleural effusion or evidence of recurrence (Fig. 5).

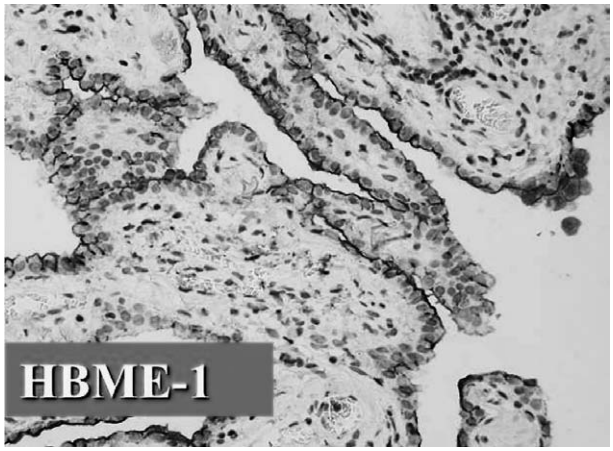

Fig. 4. Pathological findings showing that the sample was positive for the mesothelioma marker HBME-1.

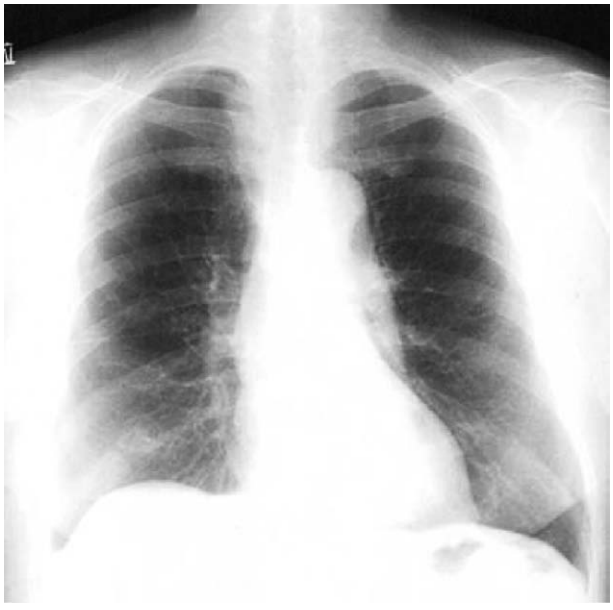

Fig. 5. Chest roentgenogram after surgery and chemotherapy.
There is no evidence of pleural effusion or a tumor.

Discussion

The number of patients with DMM is increasing, and the prognosis of DMM is poor, with an overall median survival of 8～12 months after diagnosis and no satisfactory treatment[1)]. In contrast, WDPM-P is an exceedingly rare subtype of epithelial mesothelioma of uncertain malignant potential that grows slowly and is associated with prolonged survival[2, 3)]. WDPM-P has been reported in both men and women without a history of asbestos exposure[2, 3)]. Indeed, our patient did not have any history of asbestos exposure and there were no pleural plaques found.

A clinical diagnosis of WDPM-P is very difficult to make because it has no characteristic clinical or radiological features. In the present case, the patient's subjective symptom was dyspnea without chest pain ; chest CT revealed pleural effusion with no pleural thickening or nodules.

A diagnosis of mesothelioma is made on the basis of morphological appearance, including invasion of adipose and connective tissue. However, in the present case, no invasion of these tissues was evident. Generally, a definitive diagnosis of mesothelioma is made pathologically and immunohistochemically, but the tiny amounts retrieved by needle biopsy can only reveal mesothelial proliferation on the pleural surface. In the absence of invasion, one should not diagnose mesothelioma[4, 5]. Well-oriented biopsies and larger samples for testing are needed for an accurate diagnosis. Thus, surgical resection for biopsy is preferable[2].

Intraoperative findings of WDPM-P most often indicate involvement of the parietal pleura, either as a solitary mass or multiple lesions of various sizes, with firm gray-white lesions, as in the present case[6].

Adenocarcinomas can be differentiated from WDPM-P on the basis of immunostaining for CEA, Ber-EP4, and calretinin. Specifically, WDPM-P is positive for HBME-1, calretinin and p53, but is negative for CEA and Ber-EP4. It has been suggested that serum CA-125 is a useful marker for monitoring WDPM-P[3].

There are no standard treatments for WDPM-P. Some studies report the use of surgical resection, immunotherapy, chemotherapy, and radiotherapy for the treatment of WDPM-P, although there are no publications regarding the outcomes of chemotherapy or radiotherapy trials[7-9]. In the present case, adjuvant chemotherapy with CDDP and pemetrexed was applied because postoperative pleural effusion cytology revealed suspicious cells. Following this treatment, there is no evidence of recurrence 6 years after surgery. However, further postoperative observation of the patient is warranted.

In conclusion, we encountered a very rare case of WDPM-P. This disease is a particular type of mesothelioma and patients with WDPM-P can have prolonged survival. Thus, it is important to distinguish WDPM-P from DMM and/or other lung carcinomas. Here, small amounts of tissue made it difficult to diagnose any type of mesothelioma, so we performed VATS-PB to obtain a reasonable amount of tissue for analysis, which enabled us to make a correct diagnosis.

References

1) Rice D, Rusch V, Pass H, *et al*. Recommendations for uniform definitions of surgical techniques for malignant pleural mesothelioma: a consensus report of the International Association for the Study of Lung Cancer International Staging Committee and the International Mesothelioma Interest Group. *J Thorac Oncol*. 2011;**6**:1304-1312.

2) Galateau-Salle F, Vignaud JM, Burke L, *et al*. Well-differentiated papillary mesothelioma of the pleura: a series of 24 cases. *Am J Surg Pathol*. 2004;**28**:534-540.

3) Kao S, Mahon K, Lin B, *et al*. Pleural well-differentiated papillary mesothelioma: a case report. *J Thorac Oncol*. 2009;**4**:920-922.

4) Churg A, Colby TV, Cagle P, *et al*. The separation of benign and malignant mesothelial proliferations. *Am J Surg Pathol*. 2000;**24**:1183-1200.

5) Butnor KJ, Sporn TA, Hammar SP, *et al*. Well-differentiated papillary mesothelioma. *Am J Surg Pathol*. 2001;**25**:1304–1309.
6) Hoekstra AV, Riben MW, Frumovitz M, *et al*. Well-differentiated papillary mesothelioma of the peritoneum: a pathological analysis and review of the literature. *Gynecol Oncol*. 2005;**98**:161–167.
7) Daya D, McCaughey WT. Well-differentiated papillary mesothelioma of the peritoneum. A clinicopathologic study of 22 cases. *Cancer*. 1990;**65**:292–296.
8) Treasure T, Waller D, Tan C, *et al*. The mesothelioma and radical surgery randomized controlled trial: the Mars feasibility study. *J Thorac Oncol*. 2009;**4**:1254–1258.
9) Malpica A, Sant'Ambrogio S, Deavers MT, *et al*. Well-differentiated papillary mesothelioma of the female peritoneum: a clinicopathologic study of 26 cases. *Am J Surg Pathol*. 2012;**36**:117–127.

[Received December 15, 2012 : Accepted December 25, 2012]