

[CASE REPORT]

Primary Pleural Melanoma: A Case Report and Literature Review

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Abstract:

Primary pleural melanoma is an extremely rare neoplasm, and to the best of our knowledge, there have been only 8 case reports of this condition in the English literature. We herein report a rare case in which the cytological and immunocytochemical analyses of pleural fluid and ultrasonography (US)-guided biopsy of a pleural lesion were useful for the diagnosis primary pleural melanoma. This case highlights the importance of careful physical examinations, cytomorphologic and immunocytochemical analyses of pleural fluid, as well as the utility of US-guided biopsy of the pleural lesions in the diagnosis of primary pleural melanoma.

Key words: pleura, melanoma, ultrasonography-guided biopsy

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Introduction

Primary pleural melanoma is an extremely rare neoplasm. To the best of our knowledge, there have been only 8 case reports on this condition in the English literature (1-10). It is difficult to distinguish whether a pleural melanoma is primary or metastatic. Wilson proposed clinical criteria for the diagnosis of primary pulmonary melanoma (9), and it is thought to be relevant for the diagnosis of primary pleural melanoma.

We herein report a rare case in which the cytological and immunocytochemical analyses of pleural fluid and ultrasonography-guided biopsy of pleural lesions were useful for the diagnosis of primary pleural melanoma. We also present a literature review of reported cases of primary pleural melanoma.

Case Report

An 83-year-old Japanese man presented with left-sided chest pain and dyspnea, which had lasted for a few hours.

He had a history of old myocardial infarction, paroxysmal atrial fibrillation, hyperlipidemia, hearing loss, and corneal transplantation in both eyes for corneal leukoma. He drank alcoholic beverages occasionally and was a non-smoker. His initial vital signs were unremarkable. There was no lymphadenopathy, hepatosplenomegaly, or edema. Decreased breath sounds and dullness were present at the base of the left lung. A cardiovascular examination was normal. Laboratory test values, including values reflecting the liver, renal, and thyroid function, were unremarkable. The patient's serum albumin and brain natriuretic peptide levels were within the normal limits. Chest radiography showed a large amount of pleural effusion in the left hemi-thorax, and chest computed tomography (CT) showed multiple nodular pleural thickening with pleural effusion in the left hemithorax (Fig. 1). Thoracentesis revealed bloody pleural effusion. Cytology of the pleural fluid revealed loosely aggregated large malignant cells, which had large eccentric nuclei and granular cytoplasmic melanin pigment. Immunocytochemistry revealed that the malignant cells were positive for S-100 and human melanoma black-45 (HMB-45), and negative for calretinin, D2-40, desmin, epithelial membrane antigen (EMA), thyroid

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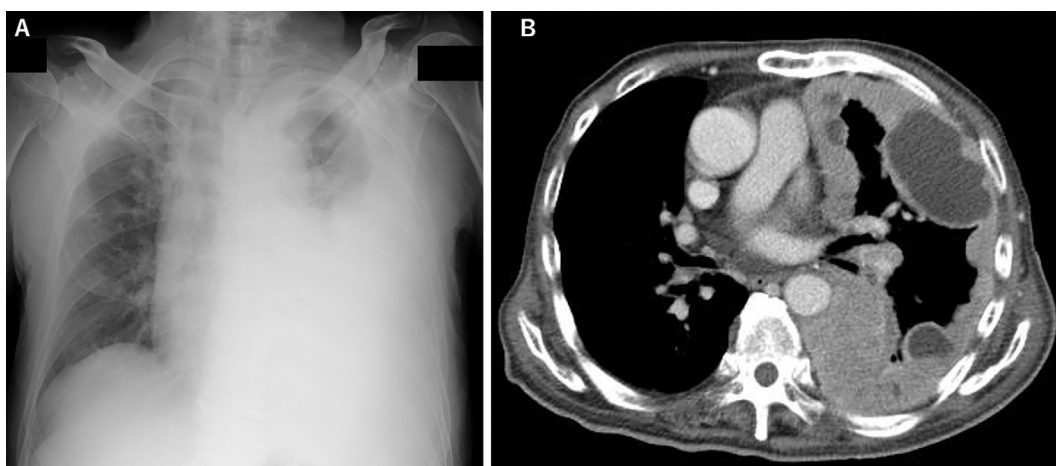


Figure 1. Chest X-ray (A) and Chest-CT (B) at the time of admission.

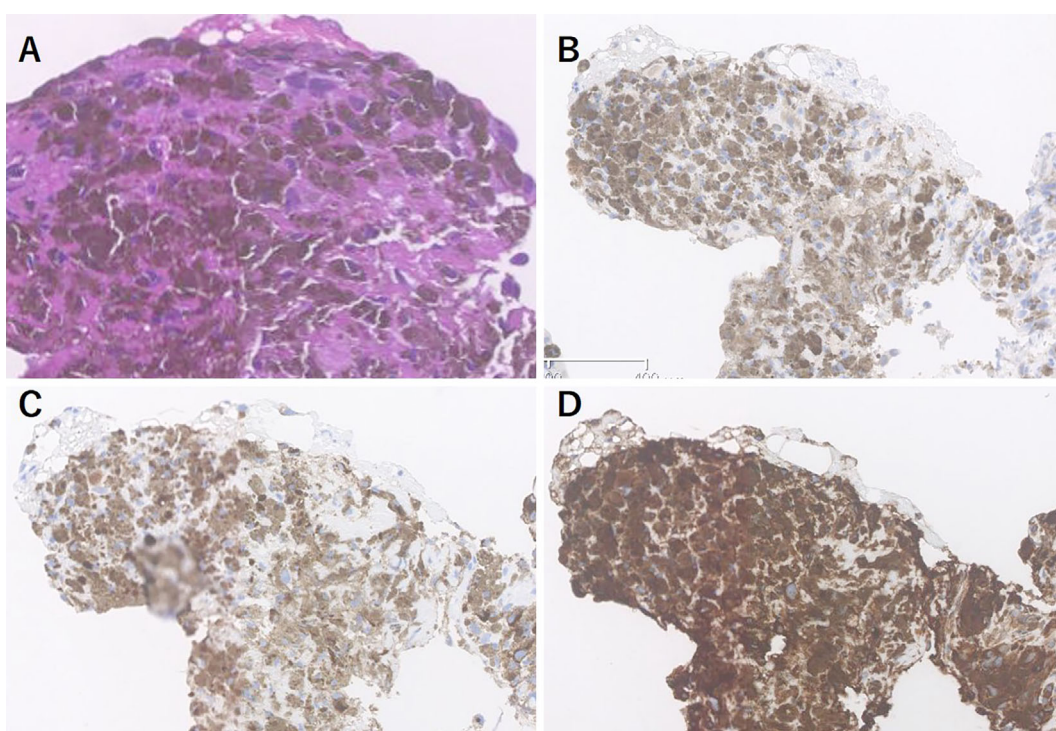


Figure 2. A specimen of the pleural lesion obtained by ultrasonography-guided biopsy. Hematoxylin and Eosin staining (A) revealed the aggregation of large malignant cells, which had large eccentric nuclei and granular cytoplasmic melanin pigment. Immunocytochemical staining was positive for the expression of S-100 (B), human melanoma black-45 (HMB-45) (C), and vimentin (D).

transcription factor 1 (TTF-1), and Napsin A, which further supported the diagnosis of melanoma (Fig. 2). Ultrasonography (US)-guided transthoracic biopsy of the pleural lesion was performed, and both histological and immunohistochemical examinations confirmed the diagnosis (Fig. 2). Detailed physical examinations of the patient failed to reveal any site of primary melanoma in the skin, eyes, oral cavity, genital or anal regions.

The patient received chemical pleurodesis using OK-432 for the relief of dyspnea due to massive pleural effusion. Thereafter, he declined any further treatment, and died of respiratory failure at 1 month after the diagnosis. The

autopsy revealed a muddy black-colored tumor that had widely disseminated in the left thoracic cavity (Fig. 3). The tumor was mainly located in the left visceral pleura and invaded the left lung tissue. Moreover, the tumor also disseminated to the left parietal pleura, diaphragm, peritoneum and mesenterium. No primary site was found at any location, including the skin and other mucous membranes. Based on these findings, the patient was diagnosed with primary pleural melanoma. Unfortunately, at the time of the diagnosis of this patient, there were no commercially available tests for the assessment of the BRAF mutation and programmed death-ligand (PD-L1) expression status; thus, we could not

obtain these results.

Discussion

Melanoma develops by malignant transformation of melanocytes and commonly originates from the skin. It also less commonly originates from the retina, digestive tract, liver, upper respiratory tract, lung, urethra and prostate (10-15). Although pleural metastasis from cutaneous melanoma is relatively common, primary pleural melanoma is extremely rare. To the best of our knowledge, there have only been 8 case reports of this condition (Table) (1-8).

Chronic stress, such as ultraviolet ray and white race are known risk factors for melanoma. Jeremy and Earle observed a 5% increase in the risk of developing melanoma in patients with sizable congenital nevi (16). Olsen et al. reported that individuals exhibiting 25 or more of typical congenital skin nevi or 1 or more atypical skin nevi may be at high risk of melanoma (17). Our patient did not have multiple or atypical nevi. In spite of the unclear pathogenesis of primary pleural melanoma, several hypotheses have been proposed (16, 17): (1) growth from pigment blast cells, (2)

growth from multipotent stem cells, (3) squamous metaplasia, (4) growth from aberrant skin nevus cells in the pleura which transfer along the lymphogenous pathway, and (5) disappearance of the primary tumor after metastasis in the pleura.

Among the 9 reported cases of primary pleural melanoma, including our case, the main symptoms were dyspnea (n=8), chest pain (n=4), and cough (n=3). All cases showed moderate to a massive pleural effusion, the gross appearance of which was hemorrhagic or black. On the other hand, Chen et al. reported that pleural effusion was not common in patients with metastatic pleural melanoma (18, 19). This difference between primary and metastatic pleural melanoma may be useful for differentiation. The color of the pleural fluid is an essential clue to diagnosing this condition. Other reported causes of black pleural effusion include *Aspergillus niger* pleuritis, *Rhizopus oryzae* pleuritis, pancreatic pleural effusion, and hemothorax (20). In our patient, cytological and immunohistochemical examinations of the pleural fluid triggered the suspicion of melanoma, and a definitive diagnosis was made based on the US-guided biopsy findings. To the best of our knowledge, this is the first case of primary pleural melanoma diagnosed by US-guided biopsy. The following methods are used to obtain biopsy specimens of pleural lesions: percutaneous pleural biopsy with Cope and Abrams needles, CT-guided biopsy, thoracoscopic biopsy, and thoracotomy. There have been no studies about the diagnostic accuracy of these methods for primary pleural melanoma because of its rarity. In malignant mesothelioma, which is the most frequent primary pleural malignancy, thoracoscopic biopsy has been reported as the standard method for obtaining specimens for a histological diagnosis, the accuracy of which is >95% (21, 22). In patients with a poor performance status or relatively large lesions, CT-guided biopsy is suggested because of its lower complication rate and favorable diagnostic accuracy (23). In comparison to CT-guided biopsy, US-guided biopsy has been reported to have the following advantages: a lower complication rate, lower cost, shorter procedure time, and lower radiation exposure (24, 25). Our patient was elderly with a poor PS and

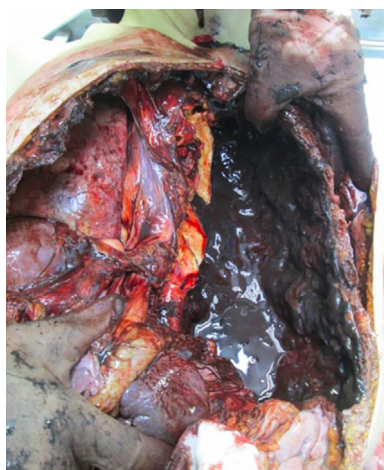


Figure 3. Autopsy revealed a muddily black-colored tumor widely disseminated in the left thoracic cavity.

Table. Treatment and Prognosis of the Previously Reported Case Reports and Our Patient.

Reference	Age	Sex	Treatment	Prognosis
[1]	49	M	Adriamycin	10 months
[2]	61	M	The patient refused treatment.	Not available
[3]	50	M	Chemical pleurodesis Dacarbazine + Cisplatin + Vincristine	Not available (at least 7 months)
[4]	49	M	None	2.5 months
[5]	46	M	Chemical pleurodesis Dacarbazine + Cisplatin + Vincristine	Not available (at least 7 months)
[6]	36	F	The patient refused treatment.	1 month
[7]	61	M	Dacarbazine + Cisplatin + Interferon- α 2b	2 months
[8]	40	M	The patient refused treatment.	1 month
Present Case	83	M	Chemical pleurodesis The patient refused treatment.	1 month

had large lesions. Thus, we chose to perform US-guided biopsy and were able to obtain a diagnosis without complications.

There are no established diagnostic criteria for primary pleural melanoma. Jensen and Egedorf proposed the following six clinical diagnostic criteria for primary pulmonary melanoma (not primary pleural melanoma): (1) no previously removed pigmented skin tumors, (2) no removed ocular tumors, (3) a solitary tumor in the surgical specimen, (4) tumor morphology compatible with a primary tumor, (5) no demonstrable melanoma in other organs at the time of operation, and (6) autopsy without primary melanomas being demonstrated elsewhere (20). These criteria are considered appropriate for the diagnosis of primary pleural melanoma. In our patient, the autopsy revealed no primary site other than the left pleural cavity, where the disease extent was most severe. We thought that he met 5 of the 6 items of the diagnostic criteria, with the exception being “(3) a solitary tumor in the surgical specimen”. Since it was impossible to meet the sixth criterion before death (“autopsy without primary melanomas being demonstrated elsewhere”), we believe our patient was definitively diagnosed while he was alive.

The treatment options for primary pleural melanoma include surgery, radiotherapy, and chemotherapy (e.g., adriamycin, and cisplatin plus dacarbazine). However, despite these various treatment options, the prognosis is poor. In fact, 5 of the 8 reported cases of primary pleural melanoma died within 1 year of the diagnosis (1-8) (Table). In recent years, molecularly targeted drugs and immune checkpoint inhibitors have been introduced in chemotherapy for malignant melanoma and are associated with better treatment outcomes. Thus, the benefit of these new drugs may be produced in primary pleural melanoma in the future.

Conclusion

We experienced a rare case of primary pleural melanoma. This case highlights the importance of careful physical examinations, and cytomorphologic and immunocytochemical analyses of pleural fluid, as well as the utility of US-guided biopsy of the pleural lesions in the diagnosis of primary pleural melanoma.

The authors state that they have no Conflict of Interest (COI).

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