

CASE REPORT

Rapidly progressing metastatic malignant melanoma mimicking primary pleural tumor: A case report

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Email: tatyoshi@ncc.go.jp**Abstract**

Malignant melanoma is the most aggressive skin cancer that originates from melanocytes. Primary or metastatic pleural melanoma shares clinical and imaging characteristics with primary pleural tumors, such as pleural mesothelioma. Identification of the primary site can be challenging to distinguish between primary and secondary melanomas. We report a case of a 46-year-old woman with metastatic, rapidly progressing pleural melanoma mimicking primary pleural tumor. The metastatic pleural tumor from a primary cutaneous melanoma was diagnosed by reevaluating a previous surgical specimen. When evaluating patients with pleural melanoma, the primary site should be reevaluated to distinguish between primary and secondary melanomas.

KEYWORDS

BRAF V600E, cutaneous malignant melanoma, metastatic pleural tumor

INTRODUCTION

Malignant melanoma is the most aggressive skin cancer that originates from melanocytes. It is primarily located in the skin, but can also affect the eyes, ears, mouth, gastrointestinal tract, genital mucosa, and leptomeninges.¹ The cutaneous or ocular form is the most common form of melanoma. The lungs are common metastatic sites of cutaneous melanoma, whereas primary pulmonary or pleural melanomas and pleural metastases are rare.² Chen et al.³ reported that among 130 patients with thoracic metastasis from melanoma, only three (2%) had malignant pleural effusion. Additionally, pleural melanoma is often misdiagnosed as other types of primary pleural cancers. Therefore, it is important to distinguish primary and metastatic pleural melanomas from other primary pleural cancers. We report a case of metastatic, rapidly progressing pleural melanoma mimicking primary pleural tumor, diagnosed by reevaluating a previous surgical specimen.

CASE REPORT

A 46-year-old woman presented with dyspnea and cough that gradually worsened over several months. Chest

computed tomography revealed a large right-sided pleural tumor with heterogeneous contrast enhancement and massive pleural effusion. The tumor invaded the superior vena cava across the pericardium, and the mediastinum shifted to the left (Figure 1, left). The patient was transferred to our hospital for diagnosis and treatment. Endobronchial ultrasound-guided transbronchial needle aspiration was performed from the tracheal bifurcation using 22-gauge needle, leading to a histological diagnosis of melanoma (Figure 2(a)). The patient had undergone surgery for an 8-mm skin mass in the preauricular region 3 years ago at another hospital and had been diagnosed with atypical melanocytic proliferation, not melanoma, at the time of surgery. We retrospectively reviewed the surgical specimen and identified a melanoma (Figure 2(b)). Therefore, the patient was diagnosed with a metastatic pleural tumor from a primary cutaneous melanoma. She received nivolumab (1 mg/kg body weight) and ipilimumab (3 mg/kg) because of the rapid tumor progression and massive pleural effusion. However, the tumor rapidly progressed and filled the right chest cavity (Figure 1, middle). The patient's treatment was switched to dabrafenib (300 mg/day) and trametinib (2 mg/day) because the tumor was positive for *BRAF* V600E mutation.

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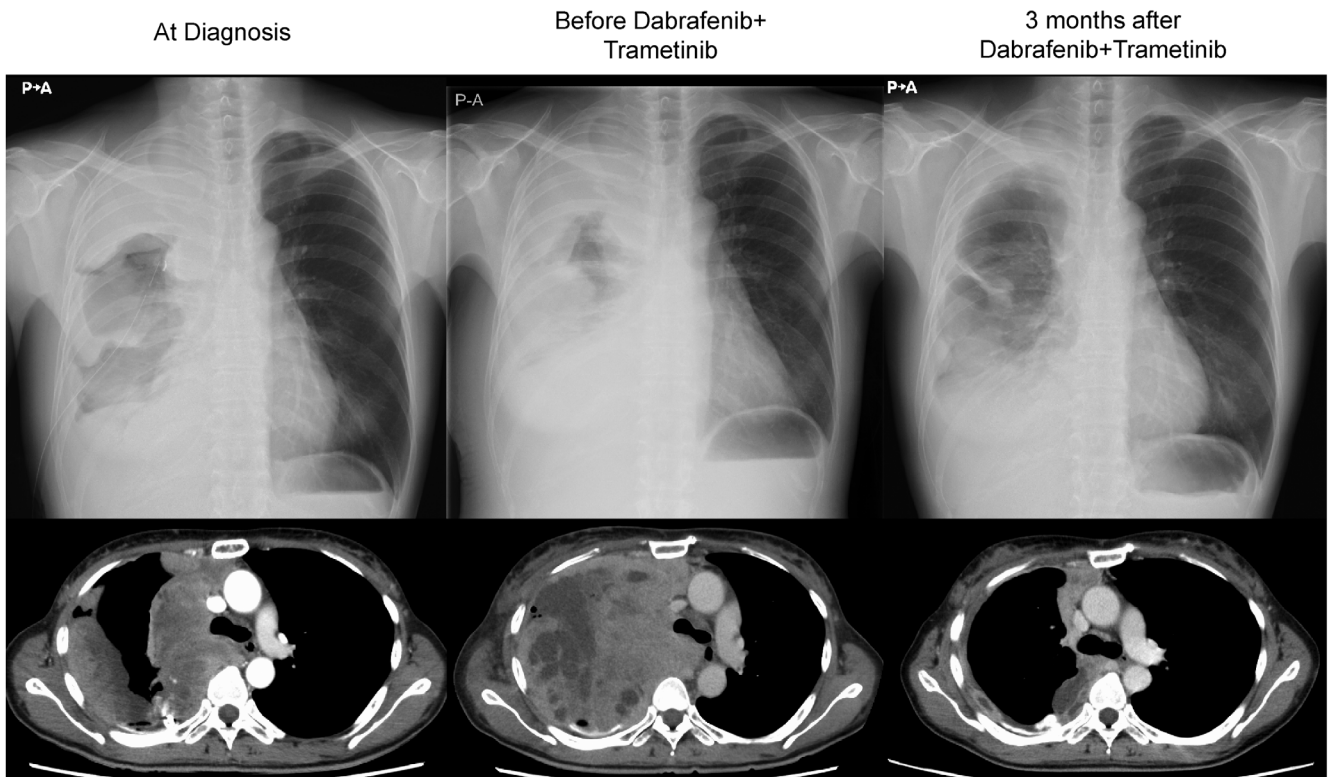


FIGURE 1 Chest radiography and computed tomography at the time of diagnosis (left), before (middle), and 3 months after dabrafenib (300 mg/day) and trametinib (2 mg/day) treatment

The pleural tumor partially responded to treatment (Figure 1, right), but progressed 5 months after the initiation of dabrafenib and trametinib.

DISCUSSION

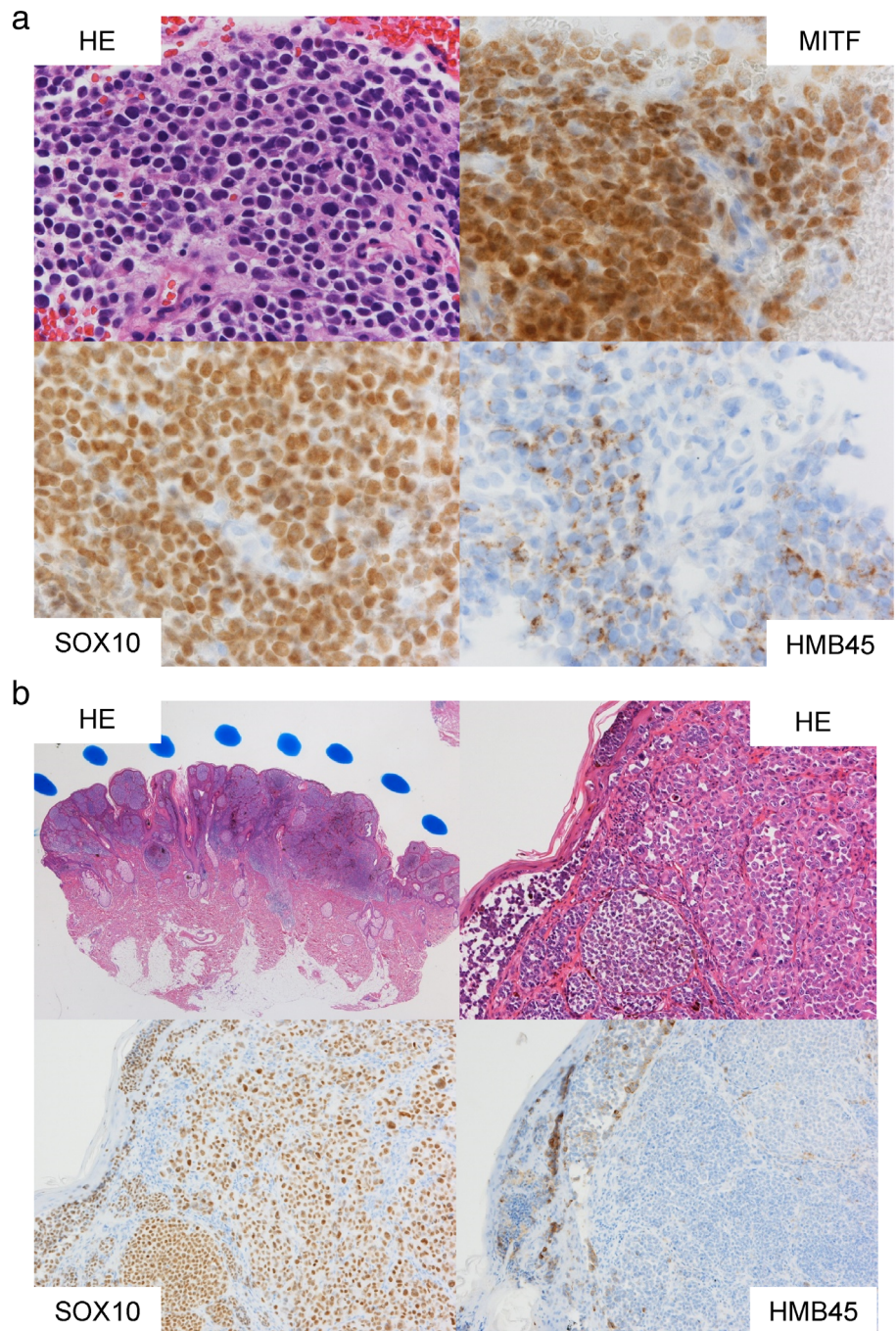
Primary or metastatic pleural melanoma shares clinical and imaging characteristics with primary pleural tumors, such as pleural mesothelioma. To diagnose primary pleural melanoma, three basic clinical criteria should be considered: (i) no previously removed skin tumor, unless the pathological examination revealed no malignancy and the availability of slides for reevaluation; (ii) a solitary tumor in the surgical specimen from the pleura; and (iii) no demonstrable melanoma in other locations at the time of surgery.^{4–6} Reevaluating the primary site is essential to distinguish primary from secondary melanomas.⁷ In this case, only pleural tumors were observed on a computed tomography scan. The surgical specimen of the skin mass from 3 years ago was reevaluated, and the pleural tumor was diagnosed as a metastasis from the cutaneous melanoma.

Several treatments, including the immunotherapy combination of nivolumab plus ipilimumab, and targeted therapy combinations with the BRAF/MEK inhibitor such as dabrafenib plus trametinib, have been introduced over the

past decade. These regimens have dramatically improved outcomes in patients with cutaneous melanoma, especially those with *BRAF* V600-mutant disease, which constitutes ~50% of metastatic cutaneous melanoma cases.^{8,9} A matching-adjusted indirect comparison demonstrated more favorable overall survival and progression-free survival benefits among patients with *BRAF*-mutant melanoma treated with nivolumab plus ipilimumab, compared with those treated with targeted therapy combinations, such as dabrafenib plus trametinib.¹⁰ On the other hand, the BRAF/MEK inhibitors may be preferred in patients with rapidly progressing disease and/or symptoms, because BRAF/MEK inhibitors have a shorter time to response compared with checkpoint immunotherapies. In our patient, we selected nivolumab plus ipilimumab because *BRAF* V600E immunohistochemistry was negative, but nivolumab plus ipilimumab failed to elicit a response. Meanwhile, we changed to dabrafenib plus trametinib after *BRAF* V600E mutation confirmed by sequencing, and dabrafenib plus trametinib achieved a good response.^{11,12}

In conclusion, we have presented a case of rapidly progressing metastatic pleural melanoma, diagnosed by reevaluating a previous surgical specimen. Pleural metastasis alone from cutaneous melanoma is a rare and ill-defined condition.¹³ When evaluating patients with pleural melanoma, the primary site should be reevaluated to distinguish between primary and secondary melanomas.

FIGURE 2 Pathological results of (a) the specimen obtained from endobronchial ultrasound-guided transbronchial needle aspiration and (b) surgical specimen of skin (hematoxylin and eosin [HE] and immunohistochemical results [MITF, SOX10, and HMB-45, respectively])



CONFLICT OF INTEREST

T.Y. has received grants and personal fees from AstraZeneca, Bristol-Myers Squibb, grants from AbbVie, MSD, Ono Pharmaceutical, Takeda Pharmaceutical, and personal fees from Chugai, Novartis. Y.Y. has received personal fees from Archer, AstraZeneca, Chugai, Dako-Agilent, MSD, Novartis, Pfizer, Thermo-Fisher Science, and Ventana-Roche. C.O. has received grants and personal fees from AstraZeneca, Bristol-Myers Squibb, Chugai, Eli Lilly, Janssen Pharma, Kyorin, MSD, Nippon Kayaku, Novartis, Ono Pharmaceutical, Pfizer, Taiho Pharmaceutical, Takeda Pharmaceutical, grants from Kissei, and personal fees from

Boehringer Ingelheim, Celtrion. The remaining authors declare no competing interests.

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