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Case Report

Malignant Melanoma of the Lung: Report of Two Cases

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Malignant melanoma (MM) is the most fatal cutaneous neoplasm. Primary MM of the lung is quite rare, and late recurrence of MM is also uncommon. We report 2 cases of pulmonary MM, the first involving primary MM of the lung and the second involving late recurrence 8 years after the initial surgery. Bronchoscopic punch biopsy identified MM in both cases. In the first case, work-up of the patient did not reveal any anomalies other than those in the primary site. In the second case, the patient had a history of thumb amputation for MM 8 years ago. For pulmonary MM, extrapulmonary origin of the tumor must be excluded by detailed examination because melanomas involving the lung are almost always metastatic. Whether the diagnosis is primary or metastatic disease, the potential for recurrence should be considered even in patients with a long disease-free survival.

Key words: malignant melanoma, primary pulmonary melanoma, late recurrence

Introduction

Malignant melanoma (MM) is the most fatal cutaneous neoplasm. Patients with cutaneous melanoma often develop metastasis at other sites on the skin, lymph nodes, or lung.[1)]

Almost every occurrence of MM of the lung is metastatic in origin. Primary MM of the lung is quite rare,[2)] and for its diagnosis, an extrapulmonary origin of the tumor must be excluded by detailed examination of the sites where MM occurs frequently, such as the skin or mucosa.

Late recurrence of MM is also uncommon. Petersen demonstrated that MM patients with a disease-free interval of 5 years or less had a poor prognosis.[3)] On the other hand, Crowley reported that a few patients who had a disease-free interval of 10 or more years had subsequent recurrence.[4)] Therefore, a prolonged disease-free interval of MM cannot be considered a cure.

We report 2 cases of pulmonary MM, the first involving primary MM of the lung and the second involving late recurrence 8 years after the initial surgery.

Case 1

A 58-year-old man with an abnormal shadow on a chest X-ray was referred to Kobe City Medical Center General Hospital for further investigation. Computed tomography (CT) showed a tumor located in the left lower lobe (**Fig. 1**). [^{18}F] fluorine-2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) revealed accumulation at the tumor site (maximum standardized uptake value, 10.9). Bronchoscopic punch biopsy results indicated MM. Subsequent metastatic work-up: brain magnetic resonance imaging (MRI) and endoscopy (upper gastrointestinal scope, colonoscope, and cystoscope) did not uncover any additional abnormalities.

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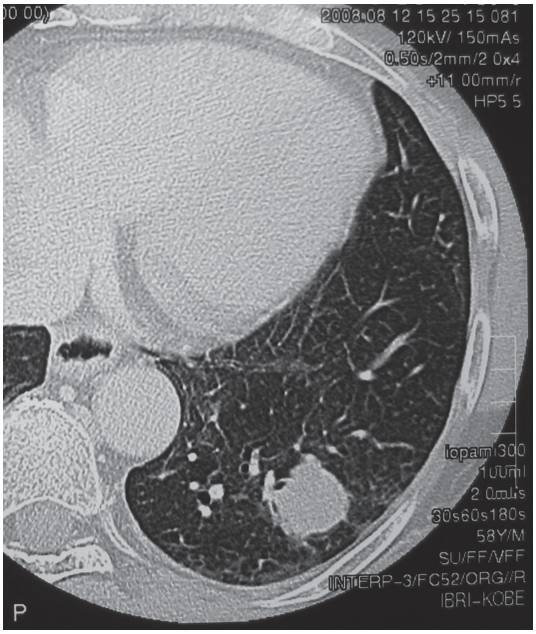

Fig. 1 Case 1: High-resolution CT scan of tumor in the left lower lobe.
CT, computed tomography

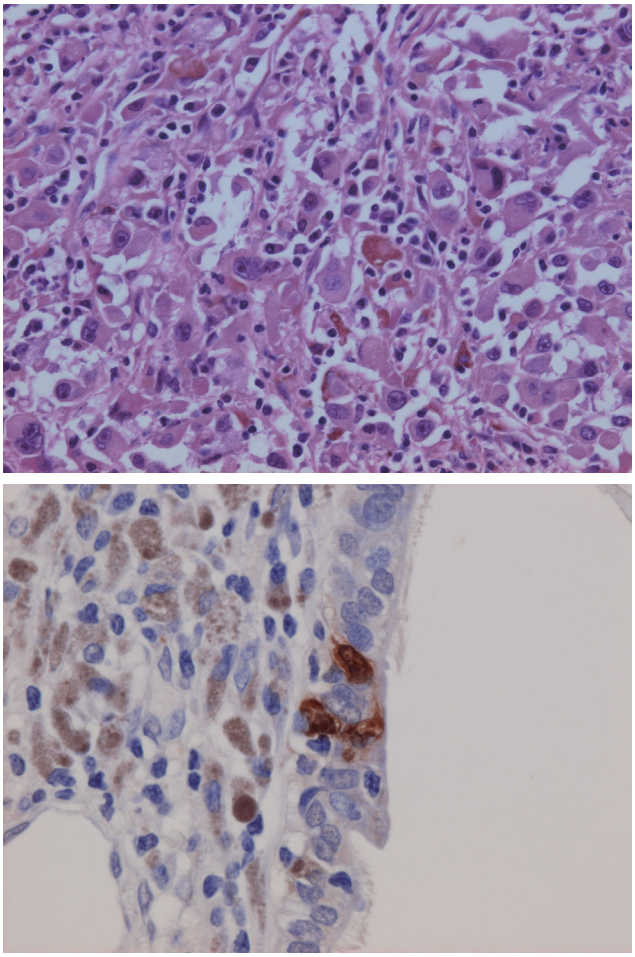

Fig. 2 Case 1: Histopathological features. Features were compatible with those of primary pulmonary MM. **A**, hematoxylin and eosin stain; **B**, S-100 immunohistochemical stain.
MM, malignant melanoma

Opthalmic, skin, oral, and rhinal examinations by specialists did not find any extrapulmonary disease.

A video-assisted lobectomy with mediastinal lymph node dissection was carried out. The tumor was 23 × 20 × 28 mm, and its histological examination revealed features of MM with predominantly epithelioid cells, junctional change, and mitotic activity (**Fig. 2A**). Immunohistochemical stains were strongly positive for antibodies to S-100 protein (**Fig. 2B**) and negative for human melanoma black-45 and cytokeratin. There were no lymph node metastases. These findings were compatible with those of primary MM of the lung.

The patient was started on adjuvant chemotherapy with dacarbazine. A follow-up brain MRI after the patient had received 2 cycles of chemotherapy showed a metastatic lesion in the left frontal lobe. The patient had radiosurgery for the brain metastasis concurrent with chemotherapy. However, the lesion continued to grow and was removed surgically. Seven days after a craniotomy (and 6 months after lung lobectomy), the patient died from acute pulmonary thromboembolism. According to the wishes of the family, we did not perform an autopsy.

Case 2

A 69-year-old woman with a 8-year history of right-thumb amputation for MM presented with bloody sputum and an abnormal shadow on the chest X-ray and was admitted to the hospital. The CT showed a tumor located in the right upper lobe (**Fig. 3**). Transbronchial biopsy lead to a histological diagnosis of MM. Subsequent work-up including brain MRI and bone scintigraphy failed to find additional abnormalities. A right upper lobectomy with mediastinal dissection was preformed. The tumor was 40 × 36 mm. Histological examination of the tumor revealed MM with predominantly epithelioid tumor cells. We did not detect metastases to the lymph node though the tumor seemed to have metastasized from the initial lesion of the right thumb.

A month after the operation, a follow-up FDG-PET revealed accumulation at mediastinal lymph nodes; this

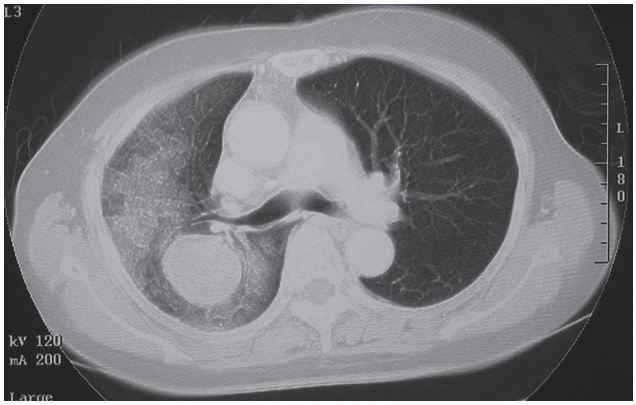

Fig. 3 Case 2: High-resolution CT scan of tumor in the left lower lobe.
CT, computed tomography

was thought to indicate recurrence. Dacarbazine chemotherapy was administered to the patient. Two months later, the CT showed a metastatic lesion in the liver and the patient was started on transcatheter arterial embolization (TAE). Two months after the TAE (and 4 months after lung lobectomy), brain MRI and body CT showed multiple metastases of the brain, skin, and lung. She died of massive hemoptysis six months after the operation.

Discussion

Melanoma is a malignant neoplasm of melanocytes, and more than 90% of the reported cases are cutaneous in origin.[5] Melanomas involving the lung are almost always metastatic, and it is extremely rare to find a true primary lesion.[2] Metastasis from an occult primary lesion must be excluded by proposed criteria.[2, 6, 7] Fewer than 60 such cases have been documented in the English literature. Late recurrence of MM is also infrequent, although it appears to be a growing problem. We report 2 cases, the first involving primary melanoma of the lung and the second involving late recurrence 8 years after the initial surgery.

A diagnosis of primary MM of the lung is proposed when patients meet the following clinical and pathological criteria.[2, 6, 7]

Clinical criteria

- · No history suggestive of a previous melanoma
- · No demonstrable melanoma in any other organ at the time of surgery
- · A solitary tumor in the surgical specimen from the lung
- · Tumor morphology compatible with that of a primary tumor
- · No evidence at autopsy of a primary melanoma elsewhere

Pathological criteria

- · Obvious melanoma cells confirmed by immunohistochemical staining for S-100 and HMB-45, and possibly by electron microscopy
- · Evidence of junctional change
- · "Nesting" of cells beneath the bronchial epithelium
- · Invasion of the intact (i.e. nonulcerated) bronchial epithelium by melanoma cells

Although an autopsy could not be performed in Case 1, the patient was considered to have a primary MM of the lung because the detailed examinations excluded an extrapulmonary origin of the tumor.

Pathological features in Case 1 were compatible with those that have been suggested above. However, several studies have demonstrated these pathological features were probably not specific to those of primary MM of the lung. An intraepithelial growth of melanoma metastatic to the lung has been documented previously.[8] De Wilt reported that distinguishing primary from metastatic pulmonary melanoma was best performed based on clinical behavior, particularly the pattern of spread, rather than on histopathological criteria.[9]

The pathogenesis of primary MM of the lung is not understood. However, several hypotheses that attempt to explain how primary malignant melanoma can develop in the lung are widely accepted. One hypothesis suggests that tumors arise from melanocytes that have migrated along with the primordial tubular respiratory tract during embryogenesis, and are also present in the esophagus and pharynx.[7, 10, 11] Another hypothesis suggests that epithelial cells undergo metaplastic transformation into melanocytes because squamous metaplasia is occasionally observed in melanoma-affected epithelium.[12] It has also been proposed that neuroendocrine (Kultschitzky) precursor cells have the potential to undergo melanocytic differentiation. Both cell types are histogenetically related and of neural crest origin.[13]

Late recurrence of MM is infrequent, with a reported incidence of 2.4%.[4] Moreover, Crowley demonstrated that 25% of patients with a disease-free interval of 10 or more years had subsequent recurrence.[4] Thus, a prolonged disease-free interval of MM cannot be considered a cure. In clinical practice, patients treated for MM should be followed, considering the

potential for recurrence even if they have a long disease-free interval. Patients with a suspected lesion need prompt evaluation and treatment.

Irrespective of the length of the disease-free interval (short or long), both patients had a poor prognosis after pulmonary surgery, although the treatment of choice for primary/metastatic MM of the lung was radical surgical excision. Several studies have demonstrated better prognosis for surgically resected patients than that for nonsurgically treated patients. In a study by de Wilt, the 5-year actuarial survival rate was 42% for patients with isolated pulmonary melanoma and no known primary tumor.[9] Harpole reported that the 5-year actuarial survival rate was 20% for selected patients with solitary pulmonary metastasis undergoing resection.[14] Although MM is a fatal neoplasm, further investigation is needed for understanding long-term prognosis and treatment.

We reported rare 2 cases of MM. If a patient has pulmonary MM, an extrapulmonary origin of the tumor has to be excluded by detailed examination because melanomas involving the lung are almost always metastatic. In addition, irrespective of whether the diagnosis is primary or metastatic disease, physicians should always consider the potential for recurrence in any patient with MM, even in those with a long disease-free survival.

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