Case Report

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Diffuse Interstitial Infiltrative Lung Metastasis of Malignant Melanoma: a Case Report

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A diffuse interstitial infiltrative pattern of lung metastasis in a patient with malignant melanoma is rare and can be confused with benign conditions such as pulmonary edema or drug-induced pneumonitis. We experienced a case of diffuse interstitial infiltrative lung metastasis in malignant melanoma in a 37-year-old man. This case was confirmed by a transbronchial lung biopsy. We herein describe the findings on CT and positron emission tomography scan.
Index terms: *Malignant melanoma; Lung; Metastasis; Interstitial disease*

INTRODUCTION

Lung metastasis of malignant melanoma usually appears as solitary or multiple discrete pulmonary nodules. A diffuse interstitial infiltrative pattern is rare and can be misdiagnosed as more commonly accompanying conditions including pulmonary edema or drug-induced pneumonitis. We experienced a 37-year-old man with diffuse interstitial infiltrative lung metastasis of malignant melanoma and report findings of computed tomography (CT) and fluorine 18 fluorodeoxyglucose (FDG) positron emission tomography (PET).

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CASE REPORT

A 37-year-old man underwent a tumor excision from the skin of his lower back which was diagnosed as Clark's level IV malignant melanoma with a depth of 12 mm and lymphatic permeation. An examination performed five months later did not show any evidence of tumor recurrence or metastasis. One year later, a follow-up fluorine 18 FDG PET examination demonstrated multiple metastatic lymph nodes in the retroperitoneum, right inguinal area, right axilla, and right chest wall. Although immunotherapy using dendritic cell was started, metastatic lymph nodes showed an increase in the size and number of tumors at the six month follow-up PET/CT.

Two months later, the patient was presented at our institution with dry cough for one month. Chest radiograph (Fig. 1A) demonstrated diffuse reticulonodular opacities in both lungs and a small amount of pleural effusions. Chest computed tomography (CT) scan (Fig. 1B) demonstrated intralobular interstitial thickenings and areas of ground-glass opacity with bilateral pleural effusions. Our first diagnostic impression was pulmonary edema, and interstitial lung disease. Pulmonary hemorrhage was also considered in differential diagnoses. The laboratory tests, however,

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including CBC hemoglobin level and antinuclear antibody level were normal except for widening of the alveolar-arterial oxygen gradients (38.6 mmHg). The cytology and bacterial culture of the sputum were negative. Cardiac function was also normal on echocardiography. A follow-up FDG PET-CT scan was performed 1 month later and

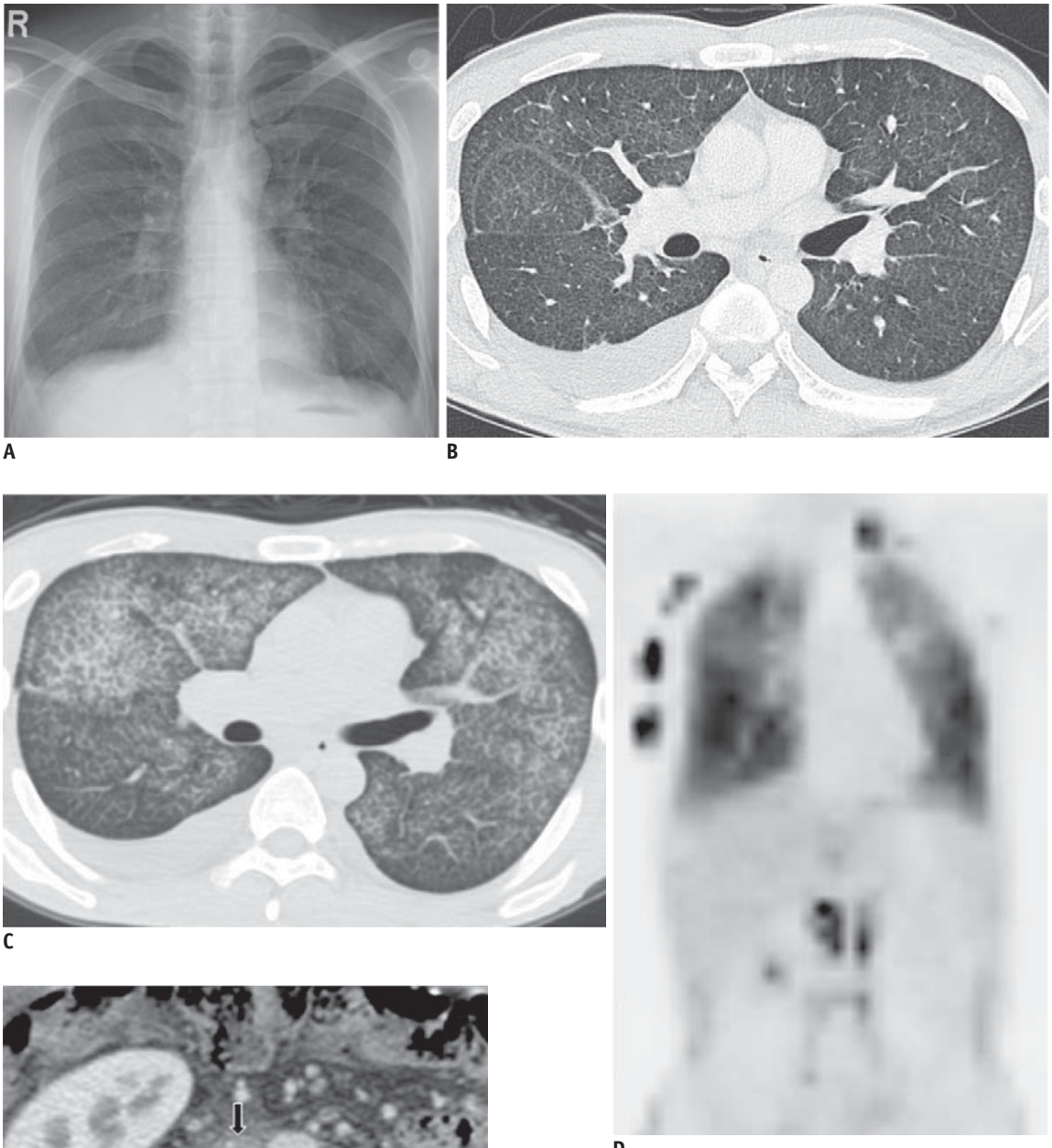

Fig. 1. 38-year-old man with diffuse interstitial infiltrative lung metastasis of malignont melanoma.
A. Chest radiograph shows diffuse reticulonodular opacities in both of lungs with bilateral pleural effusions. **B.** Chest CT image (lung window) demonstrates intralobular interstitial thickenings and areas of ground-glass opacity with bilateral pleural effusions. **C-E.** Follow-up FDG PET/CT scan two months later shows extensive intralobular interstitial thickenings and diffuse areas of ground-glass opacity with bilateral pleural effusions on contrast-enhanced CT image (lung window) (**C**) and diffusely increased FDG uptake in both lungs with metastatic LNs in right chest wall, left neck, and retroperitoneum on PET image (**D**) CT image shows irregular narrowing of inferior vena cava (white arrow), suggesting invasion of inferior vena cava by metastatic aortocaval lymph node (black arrow) (**E**).

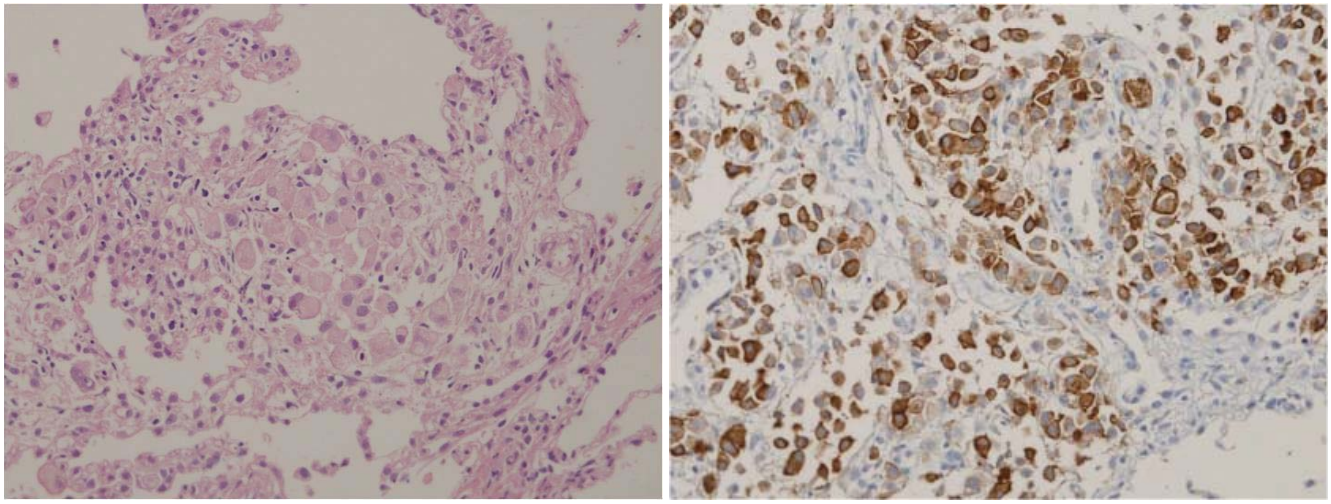

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Fig. 1. 38-year-old man with diffuse interstitial infiltrative lung metastasis of malignont melanoma.
F. Photomicrographs of histologic specimens show that tumor cells predominantly infiltrates in alveolar capillaries and interstitium. Tumor cells are round to oval in shape with enlarged nuclei and plump cytoplasm. **G.** Immunohistochemical stain for HMB-45 is positive for tumor cells.

the intralobular interstitial thickenings and ground-glass opacity with bilateral pleural effusions were found to have been aggravated on CT images (Fig. 1C). Progression of metastases to lymph nodes and skin were also noted, with the presence of irregular narrowing of the inferior vena cava (IVC), suggesting the invasion of the IVC by metastatic aortocaval lymph nodes (Fig. 1E).

The corresponding PET images showed diffuse markedly increased FDG uptake in both lungs, which suggested the possibility of tumor involvement (Fig. 1D). A transbronchial bronchoscopic lung biopsy (TBLB) was performed to obtain a more definite diagnosis. The pathological findings demonstrated extensively infiltrated melanoma cells in capillaries and alveolar interstitium (Fig. 1F, G). The patient developed pulmonary and circulatory failure and eventually expired one month after undergoing the lung biopsy.

DISCUSSION

A malignant melanoma can metastasize anywhere in the body with the lungs being one of the most common sites for distant metastasis with an incidence of 70–82% (1). Most pulmonary metastases exhibit multiple discrete nodules. Diffuse interstitial infiltrative metastasis is a rare pattern and only a few cases have been reported as a miliary or lymphangitic pattern on a chest radiograph (2–4). Chen et al. (4) reported miliary pattern metastases in only two (1.5%) of 130 cases with metastatic melanomas of the lungs. Dwyer et al. (3) also found a diffuse metastatic pattern in two (2.4%) of 84 patients with lung metastases of melanomas with a histologic evaluation of diffuse pulmonary metastases demonstrating disseminated tumor emboli in the capillaries within the alveolar septa, which provided evidence of hematogenous metastases. They postulated the mechanism of septal thickening was the result of direct growth of the embolic tumor cells into the septa rather than retrograde lymphangitic spread from obstruction. Our case also demonstrated extensive malignant melanoma cells in the alveolar capillaries, which showed a diffuse interstitial infiltrative pattern of hematogenous dissemination.

The alveolar septal thickening by tumor cells can cause a defect in diffusion from the alveolus to the capillary, which is manifested as a widening of alveolar-arterial oxygen gradient. This may also account for the rapidly progressing impairment of pulmonary function and poor prognosis. Our patient showed an alveolar-arterial oxygen gradient of 38.6 mmHg (normal, < 10 mmHg) and expired only three months after development of lung metastasis. The previous studies showed that patients with diffuse interstitial infiltrative lung metastases showed poorer prognoses than patients with a solitary or multiple discrete nodule patterns. A multiple discrete pattern had a mean survival of survival of 4 weeks–4.5 months, while the solitary pattern had a survival rate of 50.7 or 30.9 months, respectively (2–4).

Dwyer et al. (3) suggested that sudden diffuse interstitial infiltrative metastases reflect a period during which the lung is at an extremely high risk for intensive embolic

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showers because in most cases, only a tiny percentage of embolic tumor cells can successfully colonize, which may account for the usual discrete nodule patterns. In the case presented in this study, although histologic confirmation was not done, it was suspected that metastatic lymph nodes in the retroperitoneum invaded the inferior vena cava on CT images and could be the source of intense hematogenous metastases.

To our knowledge, this is the first report of CT and FDG PET scan findings of diffuse interstitial infiltrative lung metastases of malignant melanoma. The diffuse alveolar septal thickenings presented as ground-glass opacity with intralobular septal thickening on CT images. The thickening of interlobular septa and axial interstitium was not prominent unlike lymphangitic metastasis. These findings could also be observed in pulmonary edema or drug-especially chemotherapeutic agent-induced pneumonitis (5). If a markedly increased FDG uptake rate was present in the corresponding lung field is demonstrated as our case, pulmonary edema can be ruled out, but both diffuse interstitial infiltrative metastasis and drug-induced pneumonitis can show increased FDG uptake on PET. The clinical information, whether or not chemotherapy was performed, or whether the progression status of primary or metastatic tumor would help in the differential diagnosis, is not definite. In the setting of progressive tumor metastasis, if diffuse interstitial thickening in the lung has developed on CT scan, especially if the invasion of a large vessel is suspected, the possibility of an intense embolic shower should be suggested and a liver biopsy be recommended for a definite diagnosis.

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