



Primary Pulmonary Malignant Melanoma Presenting as Bilateral Multiple Subsolid Nodules: A Case Report

다수의 양측성 반고형결절들로 발현한 원발성 폐 악성 흑색종: 증례 보고

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Primary pulmonary malignant melanoma is an extremely rare type of melanoma. The radiologic features of primary pulmonary malignant melanoma are nonspecific; however, it almost always presents as a well-demarcated round or lobulated solitary solid nodule or mass. Herein, we report the case of a 78-year-old male with primary pulmonary malignant melanoma that was mistaken for primary pulmonary adenocarcinoma with lepidic growth and was seen as bilateral multiple subsolid nodules on CT.

Index terms Lung Neoplasms; Melanoma; Multiple Pulmonary Nodules; Ground-Glass Opacity

INTRODUCTION

Malignant melanoma (MM) is a malignant tumor of melanocytes. The incidence of MM is increasing rapidly worldwide, with the skin being the most commonly affected site in over 95% of the cases (1). The primary extracutaneous sites of involvement are the ocular, mucosal, gastrointestinal, and genitourinary systems, leptomeninges and lymph nodes (1). Primary pulmonary MM is among the rarest types of melanoma, with only approximately 76 cases in 52 papers having been reported in the literature since 1916 (2). The radiologic features of primary pulmonary MM are yet to be elucidated. More than 80% of primary pulmonary MMs reported were seen as a solitary solid nodule or mass, while only < 20% were multiple or diffuse lesions (2). Herein, we report a case of a 78-year-old male with primary pulmonary MM that was mistaken for primary pulmonary adenocarcinoma with lepidic growth seen as bilateral multiple subsolid

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nodules on CT images.

CASE REPORT

A 78-year-old male was referred to our hospital with a persistent cough for over a month. The patient had a history of smoking for 20 years. The chest radiograph revealed multiple ill-defined nodular opacities in both lungs (Fig. 1A). Contrast-enhanced chest CT images with lung window setting revealed that there were numerous variable-sized ill-defined or well-defined subsolid nodules in both lungs, most of which were part-solid nodules rather than pure ground-glass nodules (Fig. 1B). The relatively smaller nodules were round, while the relatively larger nodules had an irregular or lobulated contour. The maximum diameter of the nodules ranged from < 3 mm to approximately 40 mm. The solid components of some subsolid masses also exhibited a significant contrast enhancement and had air-bronchograms. There were no enlarged hilar or mediastinal lymph nodes. ^{18}F -fluorodeoxyglucose PET/CT revealed multiple intense hypermetabolic nodular lesions in both lungs (maximum standard uptake value: 14.2) (Fig. 1C). There was no other hypermetabolic lesion, indicating this is a primary malignancy. The patient underwent CT-guided transthoracic needle biopsy of the largest subsolid mass in the right lower lobe. There were few tumor cells; however, only brown pigmentation was extensively observed; hence, we suspected MM. Following this, wedge resection was performed in the right upper lobe by video-assisted thoracic surgery. The gross specimen revealed multiple well-demarcated dark brown-colored lesions in the parenchyma of the right upper lobe (Fig. 1D). Histopathological examination of the sections stained with hematoxylin and eosin revealed the invasion of the intact bronchial epithelium by melanoma cells, indicative of MM (Fig. 1D). The tumor showed ovoid cells with brown melanin pigment and frequent mitotic figures (Fig. 1D). Immunohistochemistry revealed that these tumor cells were S-100 protein-positive (Fig. 1D). A thorough physical examination, including cutaneous and mucosal examinations, performed in the operating room to rule out extrapulmonary MM sites revealed a small nevus on the right heel from which a punch biopsy sample was obtained. The pathology was consistent with only atypical melanocytic nevi, not MM. Additionally, endoscopy of both the upper and lower gastrointestinal tracts failed to detect melanoma, and brain MRI, abdomen-pelvic CT, thyroid US, and bone scan were all negative for MM. Since there were no demonstrable MM lesions elsewhere, a diagnosis of primary pulmonary MM was established. Chemotherapy with nivolumab was initiated 3 weeks after the operation. The patient is alive a year after the initial diagnosis.

This retrospective study was approved by the Institutional Review Board of our hospital, and the requirement for informed consent was waived (IRB No. WKH 2021-02-010-001).

DISCUSSION

Pulmonary MM is nearly always metastatic, with a cutaneous origin, and the lung is one of the most common sites for distant metastasis of extrapulmonary MM. Most pulmonary metastases from MM present as a solid nodular pattern, with rare subsolid nodular (3-6) or diffuse infiltrative patterns (7).

Unlike metastatic involvement, primary pulmonary MM is extremely rare. There are only 76 cases in 52 papers that have been reported in the literature since 1916 (2), with the anatomical site of the primary pulmonary MM showing a slight predilection for the left lung,

Fig. 1. Primary pulmonary malignant melanoma in a 78-year-old male.

A. The chest radiograph reveals multiple ill-defined nodular opacities in both lungs.

B. Contrast-enhanced axial and coronal chest CT images with lung window setting show numerous variable-sized, ill-defined or well-defined subsolid nodules in both lungs, most of which are part-solid nodules rather than pure ground-glass nodules. Some subsolid masses show an irregular or lobulated contour with air-bronchograms in the right upper lobe and right lower lobe (arrows).

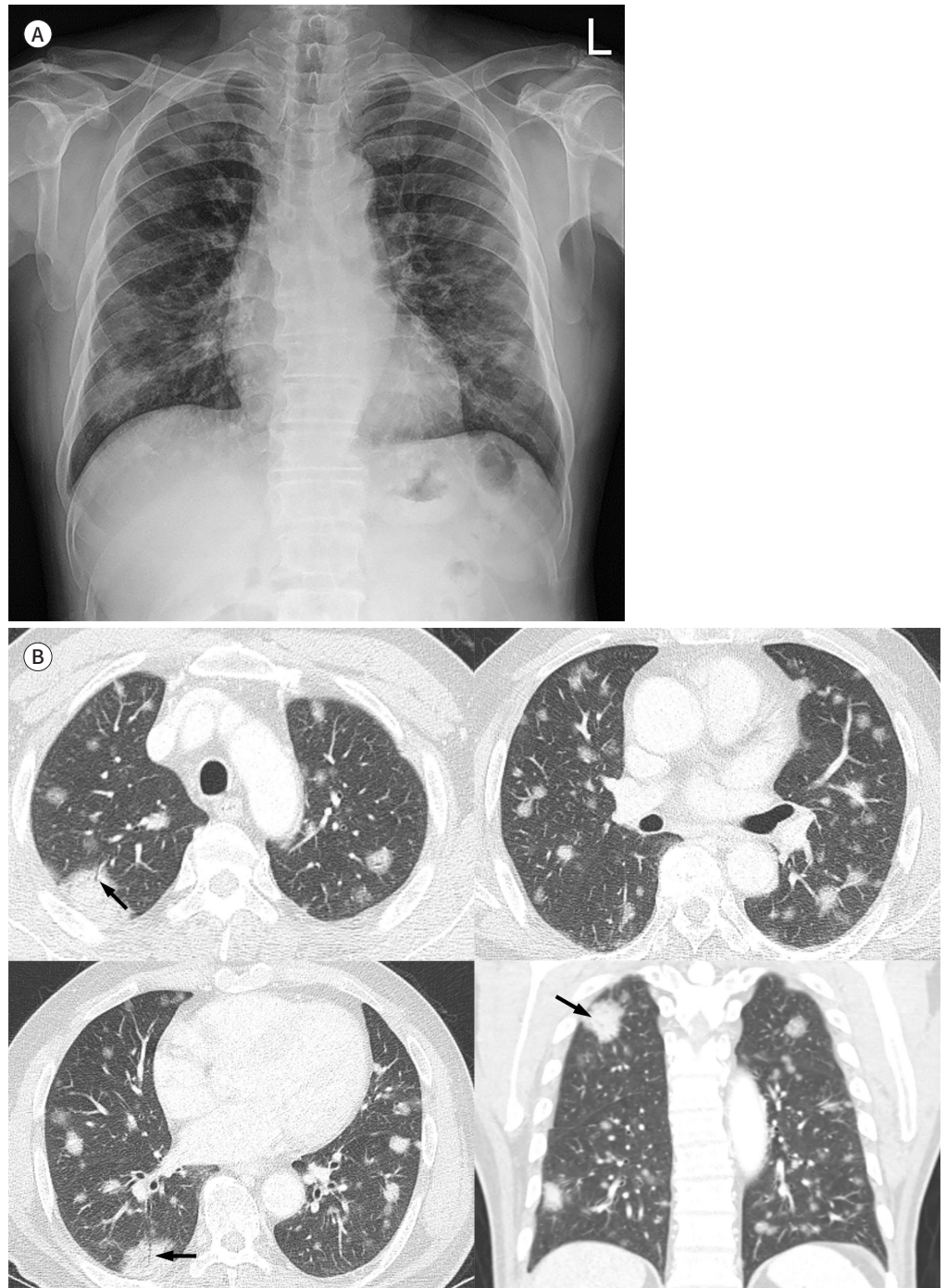
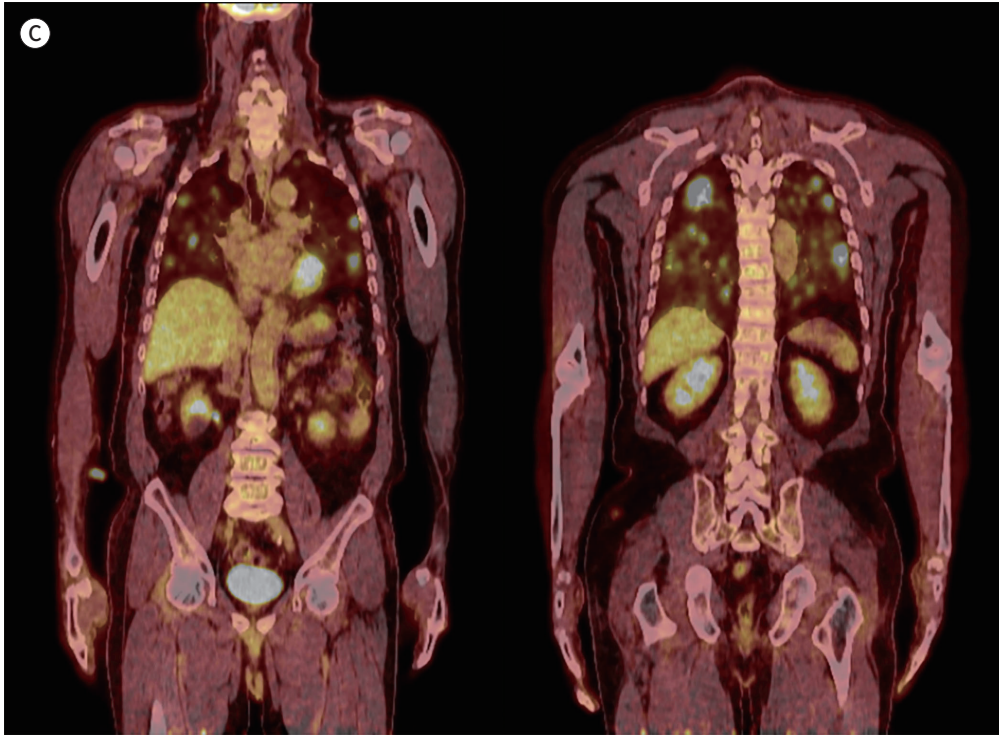


Fig. 1. Primary pulmonary malignant melanoma in a 78-year-old male.

C. ^{18}F -fluorodeoxyglucose PET/CT image reveals multiple intense hypermetabolic nodular lesions in both lungs (maximum standardized uptake value 14.2). There are no other hypermetabolic lesions, indicating that this is a primary malignancy.

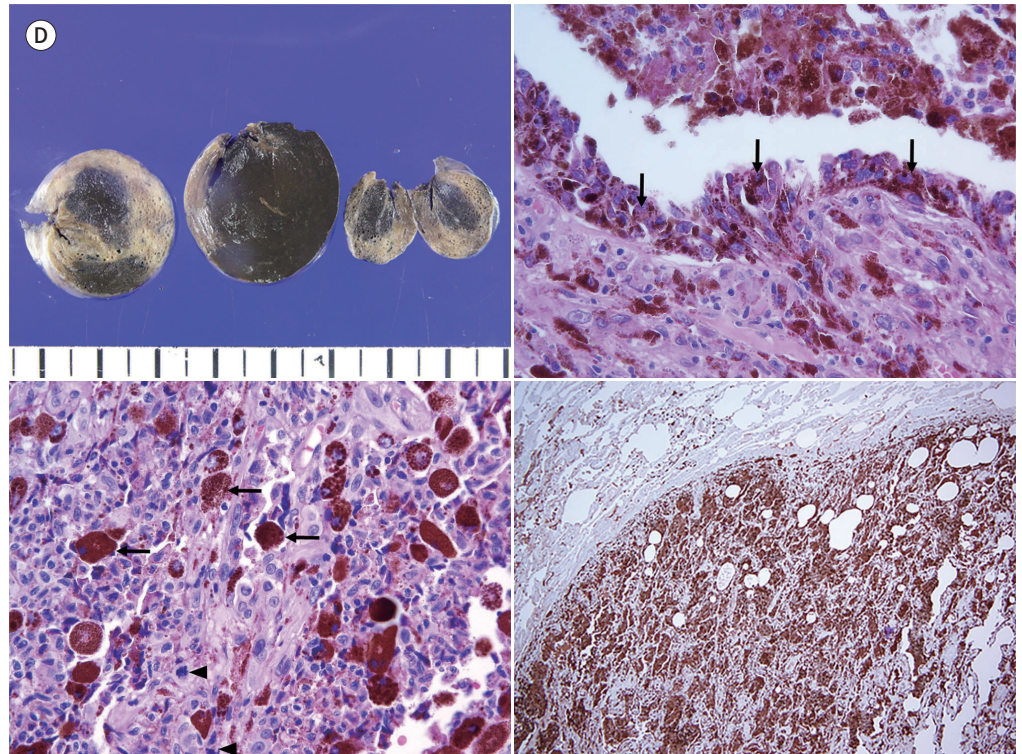


lower lobes, and the central areas. The median age of the patients at diagnosis was 60 years, and 64.4% of the patients were males. Regarding the radiological features of primary pulmonary MMs, more than 80% of the cases presented with a solitary solid nodule or mass, while only < 20% presented with multiple or diffuse lesions (2). Moreover, there were only two cases of primary pulmonary MM presenting with a subsolid ground-glass opacity or consolidation (8, 9). Feng et al. (8) reported pulmonary MM in the form of two discrete nodules with a surrounding paving pattern in the right upper lobe and left lower lobe. Filippini et al. (9) also reported primary pulmonary MM presenting as a mixed ground-glass opacity and consolidation in the right upper lobe and right lower lobe. However, the present case differs from these two previous cases in that the main radiologic finding was bilateral multiple variable-sized subsolid nodules.

The formation of MM starts with junctional changes in MM cells just below the bronchial epithelium, followed by the invasion of the bronchial epithelium by melanoma cells and apparent melanoma formation below the epithelium (9). We hypothesize that the MM cells present in the bronchial epithelium or subepithelium were observed as subsolid ground-glass opacity lesions on the CT scan. In addition, some studies have described the morphological differences between the subsolid and solid patterns seen on chest CT (3, 4). A subsolid nodular pattern reflects the replacement growth pattern of tumor cells just beneath the alveolar epithelium with partial effacement of the alveolar architecture, suggesting early-stage tumor (4). On the other hand, in the solid pattern, the local spread of the neoplastic cells leads to complete

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D. Gross pathological image shows multiple well-demarcated dark brown-colored lesions in the parenchyma of the right upper lobe (left upper panel). Histopathological examination shows the invasion of the intact bronchial epithelium by melanoma cells (arrows) (H&E stain, $\times 400$) (right upper panel). The tumor shows ovoid cells with brown melanin pigments (arrows) and frequent mitotic figures (arrowheads) (H&E stain, $\times 400$) (left lower panel). Immunohistochemical stain for S-100 ($\times 40$) is positive for the tumor cells (right lower panel). H&E = hematoxylin and eosin



effacement of the alveolar space, suggesting late-stage tumor (4).

When we found multiple subsolid nodules and masses on CT images, we interpreted them as primary lung adenocarcinoma with lepidic growth. Most primary lung malignancies manifesting as subsolid nodules have been proven to be adenocarcinoma in situ or minimally invasive or invasive adenocarcinoma with predominant lepidic growth (10). In addition, it can be seen in lymphoma or a lymphoproliferative disorder, but rarely in metastasis. It has been reported that subsolid pulmonary metastases from MM typically grow faster than primary lung cancer and have a significantly shorter doubling time; in three cases of pulmonary metastasis of MM with subsolid nodules, the doubling times reported were 27, 47, and 230 days (4-6), whereas in 22 cases of adenocarcinoma showing ground-glass opacities, the doubling time was, on average, 728.5 days (range, 259–2196 days) (10). These studies target the subsolid nodules of the pulmonary metastases of MM. However, the growth rate is thought to be helpful in the differential diagnosis of primary pulmonary MM that presents as subsolid nodules.

In conclusion, this is an unusual case report of primary pulmonary MM appearing as bilateral multiple subsolid nodules on chest CT images. Primary pulmonary MM, which presents as subsolid nodules, could be included in the differential diagnosis of subsolid pulmonary

nodules as a rare possibility after primary lung malignancy has been ruled out, especially when the subsolid nodules grow rapidly.

Author Contributions

Conceptualization, all authors; investigation, all authors; writing—original draft, all authors; and writing—review & editing, all authors.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

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다수의 양측성 반고형결절들로 발현한 원발성 폐 악성 흑색종: 증례 보고

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원발성 폐 악성 흑색종은 흑색종 중에서 굉장히 드문 유형이다. 원발성 폐 악성 흑색종의 방사선학적 소견은 비특이적이거나 거의 항상 경계가 좋은 등근 혹은 소엽상의 결절 혹은 종괴로 나타난다. 이에 저자들은 전산화단층촬영에서 다수의 양측성 반고형결절로 보여 레피딕 성장을 하는 원발성 폐선암으로 오인되었던 원발성 폐 악성 흑색종 환자 1예를 보고하고자 한다.

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