Amelanotic Melanoma Presenting Lymphangitic Carcinomatosis: A Case Report

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Abstract

A 44-year-old man demonstrating cold-like symptoms from the end of August 2013 was referred to us with abnormal shadows on his chest radiograph in September 2013. Clinical examination revealed a painless red-colored mass on the sole of his left foot that had enlarged over the course of one year. The left leg showed marked non-pitting edema that had gradually progressed over a month. A chest CT revealed mediastinal lymphadenopathy and diffuse interstitial septal thickening, and lymphangitic carcinomatosis was suspected. A lung biopsy and left inguinal lymph node biopsy revealed the diagnosis of amelanotic melanoma with lung metastasis.

Key words

Lung metastasis, lymphangitic carcinomatosis, malignant melanoma, amelanotic melanoma

Introduction

As malignant melanoma is generally blackish brown in color, it is recognized as "mole cancer." Patients usually visit a medical institution with a growing mole; however, some individuals have amelanotic melanoma, which may result in a delay in the diagnosis. We encountered a patient who visited a pulmonologist with cold-like symptoms and was diagnosed as having lymphangitic carcinomatosis caused by amelanotic melanoma on the sole of the foot. It is relatively rare for physicians to diagnose lymphangitic carcinomatosis caused by melanoma at the initial clinical examination. Furthermore, amelanotic melanoma is not easily recognized. We herein report our experience with such a case, underscoring the importance of collecting sufficient physical findings, including skin, for making the diagnosis of amelanotic melanoma.

Case

The patient was a 44-year-old man who started to have cold-like symptoms from the end of August 2013, and was found to have abnormal shadows on the chest radiograph at a nearby clinic in September 2013. CT carried out at another hospital for intensive examination revealed mediastinal lymphadenopathy and interstitial septal thickening, and lymphangitic carcinomatosis was suspected. The patient was referred to our hospital and admitted for closer examination. Findings on admission were: height 166 cm, weight 87 kg, consciousness clear, blood pressure 140/88 mmHg, pulse 102/min, arterial oxygen saturation 95% (room air), temperature 35.1°C, respiratory rate 20/min, and performance status (PS) grade 1. A few dry rales could be heard in both lower lung fields on chest auscultation. Examination of the extremities revealed a painless, partially and slightly pigmented erythematous mass on the left sole (Figure 1A). According to the patient, a mass, shown as (b) (Figure

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Figure 1. Skin findings on admission
A painless red mass was observed on the left sole (A). According to the patient, a mass, shown as (b) originally looked like a mass shown as (a), but enlarged over the course of one year (B). The left leg showed marked non-pitting edema that had gradually progressed over the previous month (C).

mulation in the left iliac bone, liver and multiple lymph nodes from the left side of the neck to the inguinal region (Figure 3). Based on the findings, lymphangitic carcinomatosis, hematogenous metastases, and bone and liver metastases were suspected. Based on the clinical course, the lung lesion was suspected to be a metastasis from the mass on the left sole, and the patient underwent transbronchial lung biopsy and an excisional biopsy of the left inguinal lymph node. The lung lesion showed a solid neoplastic focus of oval to polygonal cells with atypical nuclei and eosinophilic cells (Figure 4A). Immunohistochemistry revealed positive staining of the neoplastic cells for HMB-45(+) (Figure 4B) and S-100 (focal+) (Figure 4C), leading to the suspicion of malignant melanoma. A relatively large piece of tissue (20 mm 15 mm 8 mm) was obtained in the excisional biopsy of the left inguinal lymph node, and proliferation of atypical oval cells was observed in the layers from the dermis to fat tissue. The neoplastic cells showed eosinophilic cytoplasm and large nucleoli, as well as melanin pigment in parts (Figure 4D). Immunohistochemistry revealed positive staining of the neoplastic cells for HMB45 (focal+) (Figure 4E) and S-100(+) (Figure 4F), matching the findings of the malignant melanoma; however, there was poor evidence of melanin production. Based on the patient having had the red mass on the left sole for over a year prior to admission and the histopathological findings, the lung lesion was diagnosed as a metastatic lesion from the amelanotic melanoma. Subsequently, the patient’s PS deteriorated to grade 4 with rapid worsening of the respiratory condition, and the patient passed away.

Discussion
Malignant melanoma is a highly life-threatening tumor that develops from melanocytes, with melanin-producing capability. Melanomas in which no pigmentation is observed macroscopically, referred to as amelanotic melanomas, are relatively rare and undifferentiated tumors, accounting for approximately 2% of all malignant melanomas\(^1\). Although amelanotic melanomas generally appear white to red in color due to the absence of macroscopically visible melanin pigment, slight or partial pigmentation is detectable in many cases\(^2\). Histopathological findings vary; some tumors show no deposition of melanin pigment, while others show slight deposition\(^3\). In the present case, partial pigmentation was observed. However, because we performed an excisional biopsy of the lymph node instead of a direct biopsy of the neoplas-
tic lesion, this partial pigmentation was not sufficiently evaluated. Based on the patient’s self-report that no pigmentation was initially noted, as well as the histopathological findings of the lymph node excisional biopsy, amelanotic melanoma was diagnosed in this case.

Patients with malignant melanoma have a poor prognosis, as this tumor has a propensity to metastasize hematogenously via the lymphatic route to distant sites from a very early stage. It is reported that, due to the reduced melanin-producing capability, amelanotic melanomas show a low degree of differentiation and a high proliferation capacity compared to pigmented malignant melanomas. The absence of pigmentation often results in a delay in detailed examination and treatment for the malignant disease; the treatment tends to start after the disease has progressed to a relatively advanced stage. The five-year survival rate in pigmented malignant melanoma patients with lymph node metastasis is 42%, whereas that in amelanotic melanoma patients with lymph node metastasis is a significantly lower 15%.

The most frequently reported sites of metastasis are the skin and lymph nodes, followed by the lungs. With regards to lung metastasis, Harpole et al. reported that lung metastasis was found in 945 (12%) of their 7564 patients with malignant melanoma. It is said that metastases from malignant melanoma can occur even 10 years or more after the initial onset, emphasizing the need for caution; there is one report of a patient who developed lung metastasis 27 years after the initial diagnosis. According to a past report, metastatic foci observed in the lung on chest imaging were visualized as solitary nodules in 14 patients, multiple nodules in 41 patients, miliary nodules in 8 patients, and lymphangitic carcinomatosis in 5 patients; among these, multiple nodular shadows are reported to be the most frequent. The patient reported here had first noted the skin lesion one year prior to his hospital admission, and it was considered that this lesion had metastasized to the inguinal, abdominal, and mediastinal lymph nodes via the lymphatic route, resulting in lymphangitic carcinomatosis. We consider that the lymphatic edema in the left foot was also associated with such lymphatic spread of the cancer, and hematogenous metastasis.
Figure 3. 18FDG-PET imaging findings on admission

18FDG-PET images at the levels of neck (A), tracheal carina (B), inferior pulmonary veins (C), liver (D), pelvic cavity (E), and inguinal regions (F) showed accumulation in left iliac bone, liver and multiple lymph nodes from the left side of the neck to the inguinal region.

occurred at the same time, producing nodular shadows in the lung fields.

As to available treatments for malignant melanoma with metastasis, monotherapy with a BRAF inhibitor, which targets the BRAF V600E mutation observed in approximately half of patients with malignant melanoma, has achieved response rates exceeding 50%. Unfortunately, we were unable to conduct either the genetic test or administer treatment because the patient’s PS had deteriorated to grade 4 by the time the histological diagnosis was made.

Malignant melanoma is usually characterized by a blackish brown color, like the color of moles in general. However, some individuals have amelanotic melanoma, which may result in a delay in the diagnosis. In the present case, examination of cold-like symptoms by a pulmonologist led to the discovery of amelanotic melanoma. Even for pulmonologists who frequently deal with lymphangitic carcinomatosis, it is relatively rare to experience cases with this disease caused by malignant melanoma. Our present case highlights the importance of thorough investigation of the patient’s history and physical examination.

References

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