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Case Report

Melanoma Metastasis to the Left Breast: A Case Report

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Metastatic breast tumors are rare and often misdiagnosed as primary breast cancer. Herein, we present a case of breast metastasis from malignant melanoma. A 46-year-old woman presented to our department with a lump in her left breast. Examination revealed a relatively soft mass measuring 4 cm in diameter in the left breast. A needle biopsy was performed, and immunostaining for S-100, human melanoma black-45, CD56/neural cell adhesion molecule, and Melan-A confirmed a diagnosis of malignant melanoma. The metastasis was confined to the breast and was thus treated by surgery to excise the tumor. Malignant melanoma is a rare disease in the Japanese population and is associated with a poor prognosis because of the risk of early metastasis to multiple organs and lymph nodes. However, when complete resection of distant metastases is feasible, curative resection may be indicated. Herein, we report a case of breast metastasis from malignant melanoma and review previously published case reports on this rare condition.
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Keywords: melanoma, breast neoplasms, prognosis, metastatic breast tumor

Introduction

Malignant melanoma (MM) is the most rapidly increasing cancer worldwide. In Asia, incidence and mortality rates are lower than global averages. Metastatic breast tumor accounts for only 2% of all breast malignancies[1]. Although rare, metastatic breast disease is a diagnostic challenge that requires careful consideration of histological, immunohistochemical, and clinical findings. Herein, we report a case of MM metastasis to the breast. The patient had undergone surgery for MM on her thigh 20 years earlier.

Case Report

A 46-year-old Japanese woman presented with a lump in her left breast that she had noticed 1 week earlier. She had no relevant family history of cancer, including breast, ovarian, pancreatic, and prostate cancers. Her medical history included MM on her left thigh in her twenties, which had been surgically excised. The tumor thickness was 0.8 mm, without ulceration (T1b). A sentinel lymph node biopsy was not performed because there was no enlarged lymph node and tumor thickness was less than 1 mm. During the present physical examination, a relatively soft lump measuring 4 cm was palpated in the upper medial quadrant of her left breast. No skin abnormalities or axillary lymphadenopathy were observed. Laboratory examination showed no significant findings, including LDH.

Diagnostic mammography revealed a high-density mass with finely lobulated margins. This lesion was classified as BI-RADS category 4, indicating a suspected malignancy (**Figure 1**). Breast ultrasonography revealed a 42 × 39 mm oblate spheroid mass exhibiting mixed echogenicity and comprising hyperechoic and hypoechoic ar-

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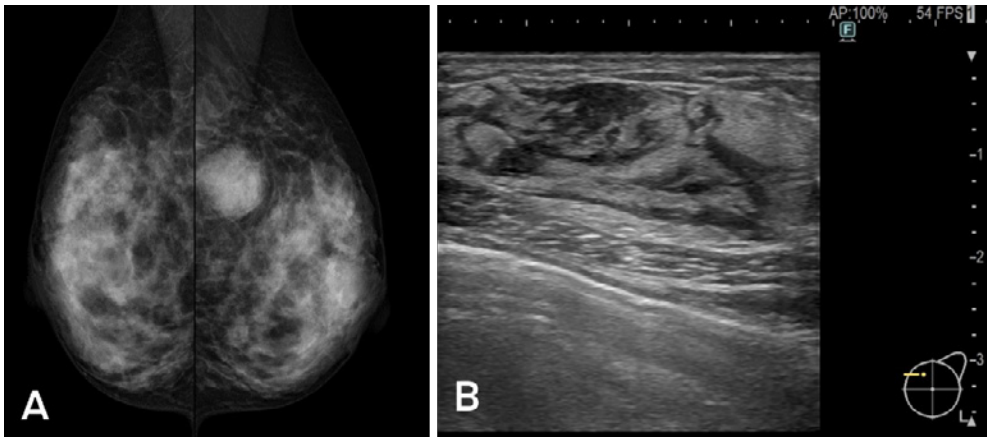

Figure 1 Imaging findings
A: Mammography revealed a high-density tumor in the left breast. B: Ultrasound revealed a 42 × 39 mm oblate spheroid mass.

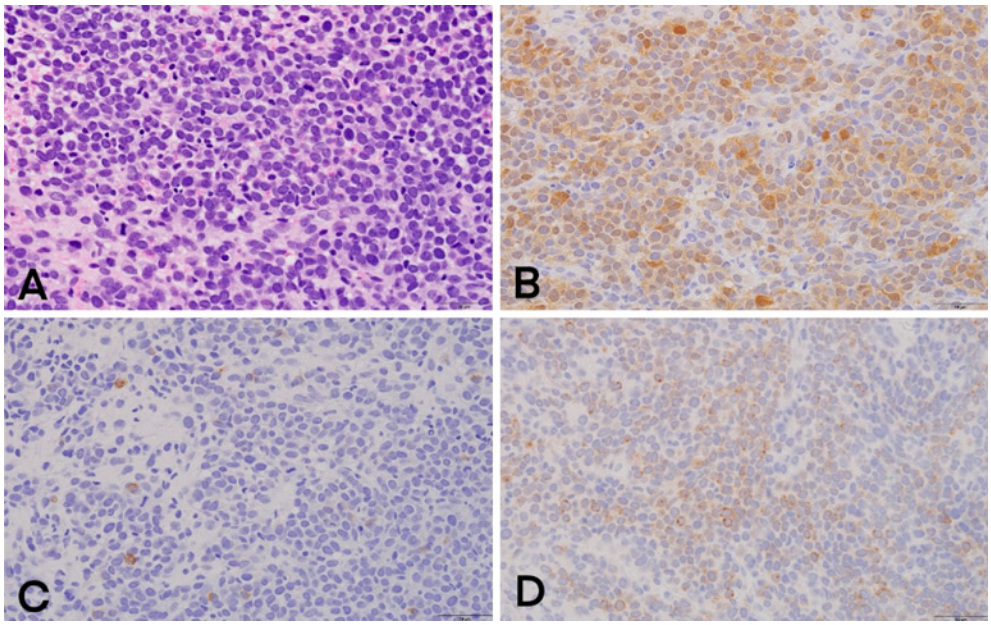

Figure 2 Pathological examination of a core needle biopsy sample
A: Hematoxylin and eosin staining revealed diffuse infiltration of atypical cells with medium-sized, round nuclei. B, C, D: Immunohistochemical staining showed positivity for S-100 (B), HMB-45 (C), and MelanA (D).

eas. Slit-like hypoechoic regions were present in the mass, and it showed an anomalous pattern of vascularity on a color Doppler examination (**Figure 2**). The imaging findings were atypical and did not provide sufficient information to ascertain the histological characteristics of the mass. Therefore, a core needle biopsy was performed to investigate the suspected malignancy and establish a definitive diagnosis.

Histopathological Findings

Hematoxylin and eosin staining revealed diffuse infiltration of atypical cells with medium-sized, round nuclei. Some apoptotic bodies and mitotic figures were observed. The differential diagnosis included poorly differentiated carcinoma, neuroendocrine tumor, lymphoma, and mesenchymal tumor.

Immunohistochemistry

Estrogen receptor and progesterone receptor were both negative, indicating no hormone receptor expression. AE1/AE3 was also negative, suggesting a nonepithelial tumor. Chromogranin A, synaptophysin, insulinoma-

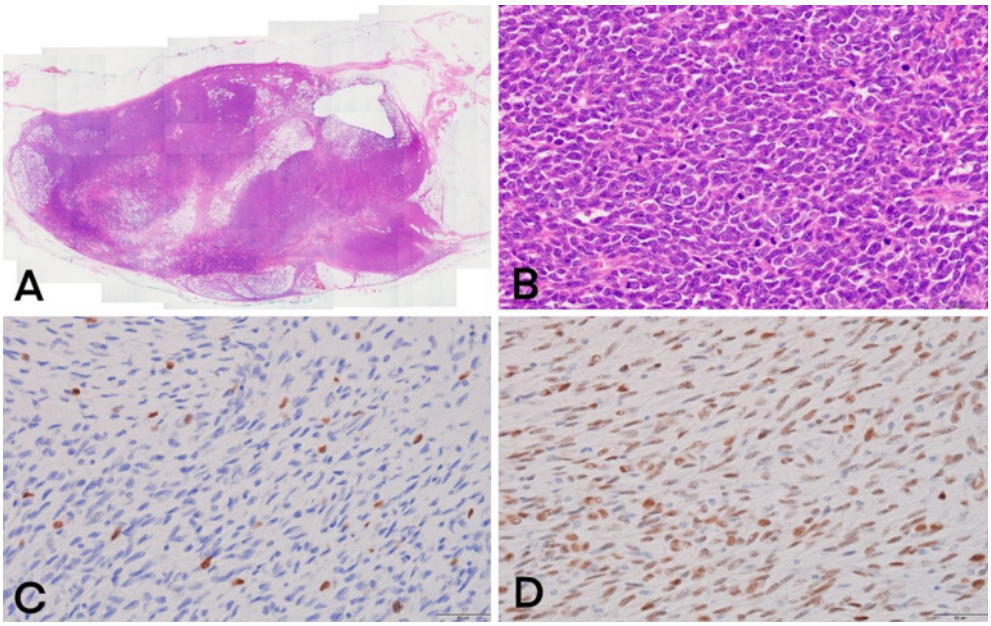

Figure 3 Pathological examination of postoperative specimen
A, B: Postoperative pathological examination with hematoxylin and eosin staining of the tumor. C, D: Immunohistochemical staining showed positivity for SOX-10 (C) and PRAME (D).

associated protein 1 (INSM1), and CD31/INSM1 were all negative, ruling out a neuroendocrine tumor. CD3 and CD20 were both negative, excluding malignant lymphoma and angiosarcoma. The S-100 protein tested positive, and Pmel17 recognized by human melanoma black-45 (HMB-45) was partially positive. CD56/neural cell adhesion molecule (NCAM) was partially positive, and Melan-A was positive, suggesting MM.

Positron emission tomography/computed tomography showed moderate F-18 fluorodeoxyglucose accumulation in the subcutaneous tissue of the left breast. No significant uptake was observed in the left thigh or other areas where the MM had previously been surgically excised.

Postoperative Histopathological Findings

The mass was excised at the same hospital where the patient had previously undergone surgery for MM of the left thigh. Microscopic findings revealed that the tumor morphology closely resembled its appearance on ultrasonography (**Figure 3**). The tumor was composed mainly of round cells with large nuclei and contained some spindle-shaped cells. Melanin was not prominent. A few cells tested positive for neuroendocrine markers such as CD56 and NCAM. Sry-related HMG-Box gene 10 (SOX-10) and preferentially expressed antigen in melanoma (PRAME) staining were both positive, suggesting MM. The horizonal resection margin was almost 2 cm. The tumor was in the breast and close to the pectorals major, so the vertical margin was less than 1 cm; however, as much tissue as possible was removed. The patient's postoperative recovery was uneventful, and she was discharged in good condition. However, 5 months after surgery, a suspected recurrent breast tumor was detected at the resection margin, and subsequent resection confirmed MM recurrence. No adjuvant therapy was performed after the first resection of the breast metastatic tumor because the physician responsible considered it unnecessary, as it was a very late recurrence and the resection margin for the tumor was negative. After the second breast surgery, combination therapy comprising BRAF inhibitor and MEK inhibitor as adjuvant therapy was administered because of the presence of the BRAF V600E genetic mutation.

Informed Consent

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Discussion

Metastatic breast tumors are rare, accounting for only approximately 2% of all malignant breast tumors[1]. This low prevalence often makes these tumors difficult to diagnose, and they are frequently misdiagnosed as primary breast cancer on initial presentation. Among metastatic malignant tumors of the breast, MM is the most com-

mon, accounting for 30%–40% of cases. The incidence of MM among Asians is low, at approximately 1.7 cases per 100,000 individuals; thus, a detailed patient history is crucial for accurate diagnosis[2].

A search for case reports of breast metastasis from MM in Japan revealed a total of four cases, which increased to seven when data from conference proceedings were included[3–5]. The median age of the four patients (three women and one man) was 57 (49–76) years. The interval between the initial MM diagnosis and subsequent breast metastasis varied: two patients developed recurrence within 5 years and two had very late recurrences (after > 20 years). All previous patients had internal masses without skin lesions, but the present case was particularly difficult to diagnose because melanin was absent and black tissue was not visible through the skin. When breast metastasis occurs within 5 years of an initial melanoma diagnosis, clinical diagnosis of metastatic breast tumor is straightforward. However, in cases of late recurrence or when the initial presentation is a breast mass, primary breast cancer is often suspected initially.

In a study by Zhou et al.[6] of 238 cases of metastatic malignant breast tumors from 2005 to 2015, the vast majority (94%) were unilateral, and 33 (14%) were metastases to the ipsilateral axillary lymph node. In 39 cases (16%), the breast tumor was the initial manifestation, and primary breast cancer was often suspected[6]. Similarly, in our case, MM was not initially suspected, and definitive diagnosis was reached only after immunohistochemical analysis.

Arora et al.[7] studied 15 patients (median age: 38 years) with breast metastases from MM: 14 were premenopausal and 80% had a primary melanoma located on the trunk or upper limbs. Cases of breast metastasis from MM in Japan do not exhibit a specific trend regarding age or primary site of melanoma[3–5]. Further accumulation of such cases is needed to enhance our understanding.

MM is characterized by cancerous transformation of melanocytes. At diagnosis, 20% of cases have lymph node metastases and 9% have distant metastases. The 5-year survival rate for stage I/II disease is 85%–99%, but this rate declines significantly to 70% for stage IIIC, which involves distant metastases. In Japan, early detection and timely treatment of MM remain significant challenges[8].

Ravdel et al.[9] reported that median survival for patients with breast metastases from MM was 12.9 months. Many patients with breast metastases also have multiple distant metastases at the time of diagnosis, resulting in a poor prognosis[9]. Most patients with distant metastases present with multiple metastatic sites, often precluding surgical intervention. However, when completely resectable distant metastases are discovered after primary tumor surgery, some patients experienced long-term survival without new lesions after resection[10–12]. Among the four cases of breast metastasis from MM reported in Japan, two were preoperatively diagnosed with metastatic melanoma and both were treated by partial mastectomy[3–5]. In the present case, MM was diagnosed preoperatively, and because no other distant metastases were observed at the time of this extremely late recurrence (20 years after the primary surgery), the tumor was resected. However, the patient experienced local recurrence 5 months later. After another tumor resection, adjuvant therapy with BRAF and MEK inhibitors was planned. As the number of treatment options continues to increase, the additional reported cases will enhance our understanding and management of this condition.

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