

A case of solitary breast metastasis from malignant melanoma of the nasal cavity

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Abstract. Metastatic breast tumors are rare; however, malignant melanoma is one of the primary tumors most commonly reported to metastasize to the breast. Among these, the primary tumors typically associated with metastasis to the breast are cutaneous melanomas. We present, herein, a very rare case of solitary metastasis to the left breast from malignant melanoma of the nasal cavity, which represents less than 1% of all malignant melanomas. The patient, a 78-year-old woman, was treated using a combination of surgery and radiotherapy. In the absence of therapeutic efficacy, disease progression was very rapid. No previous studies have described malignant melanoma of the nasal cavity with solitary breast metastasis. This case report aims to increase awareness of the need to establish treatment strategies based on an understanding of the etiology and pathophysiology.

Introduction

Primary breast cancer is the most common malignancy among females worldwide; however, cancer tumors metastasizing to the breast are fairly rare. The most common cause is spread from a primary cancer in the contralateral breast (1). Other extramammary tumors often metastasizing to the breast include lymphoma, malignant melanoma and lung cancer (2).

Although malignant melanoma involves the skin in the vast majority of cases, lesions affecting the mucosa of the head and neck are rare. Involvement of the nasal cavity is even less common, accounting for less than 1% of all malignant melanomas (3). The clinical features of malignant melanoma of the nasal cavity are non-specific and show poor prognosis due to

local recurrence, nodal involvement and distant metastasis (4). Among malignant melanomas with metastasis to the breast, cutaneous melanomas are the most common (5).

We recently treated a patient with a solitary metastatic breast tumor from a malignant melanoma of the nasal cavity. We present this rare case and discuss the relevant literature herein.

Case report

In November 2010, a 78-year-old female presented to the Department of Otorhinolaryngology at Osaka Medical College Hospital complaining of occasional epistaxis over the course of 6 weeks. Rhinoscopy revealed a brown-black tumor in the left nasal cavity. Head and neck computed tomography (CT) revealed a tumor in the left nasal cavity with invasion to the orbital cavity (Fig. 1A). Biopsy of the tumor led to a histological diagnosis of malignant melanoma. On pathological inspection, a hypervascular, pigmented lesion comprising round to oval-shaped tumor cells was revealed, and a final diagnosis of malignant melanoma was confirmed by immunohistochemical examination for HMB-45, a melanoma marker (Fig. 2A and B). During the investigation of the nasal cavity tumor, the patient had become aware of a growing lump in the upper region of the left breast and was referred to our department in December 2010. Physical examination revealed a well-defined, elastic, soft, immobile tumor in the upper region of the left breast, 4 cm in diameter. Mammography revealed an almost oval-shaped, microlobulated tumor in the left upper breast (Fig. 3). Ultrasonography revealed a heterogeneous mass with unclear margins. Fine needle aspiration cytology from the breast tumor was suggestive of metastatic melanoma, revealing cells similar in character to those of the tumor in the nasal cavity. No evidence of metastasis besides that to the left breast was found on positron emission tomography-CT. Radical resection of both the primary tumor and metastasis was proposed. The patient declined both radical surgery of the nasal cavity, in a maximally invasive operation requiring ophthalmectomy, and palliative surgery including systemic chemotherapy; however, breast surgery was accepted and a left mastectomy with lower axillary lymph node dissection, involving partial resection of the pectoralis major muscle, was performed as

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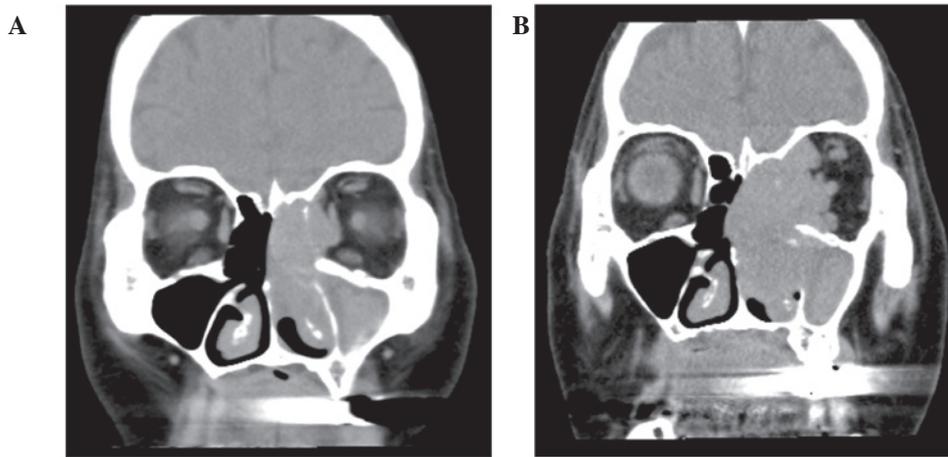


Figure 1. (A) Computed tomography of the head and neck, showing a mass in the left nasal cavity and fluid collection in the paranasal sinus, suggesting paranasal sinusitis. The tumor has invaded to the left orbital cavity. (B) Regrowth of the tumor following shrinkage with heavy ion radiotherapy.

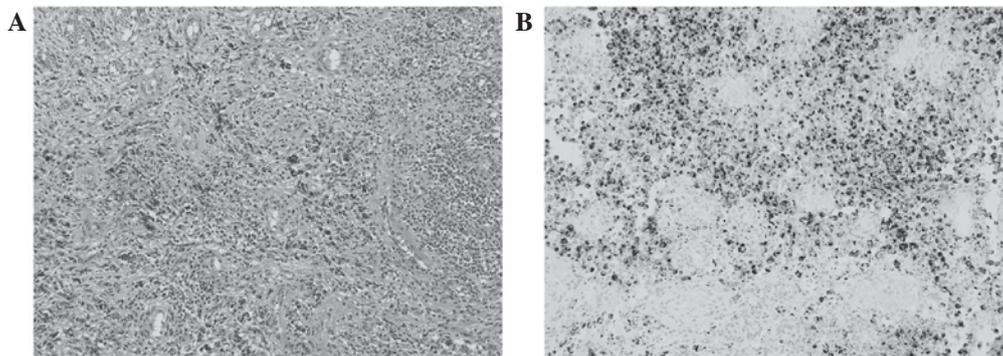


Figure 2. Malignant melanoma. (A) Infiltrating neoplastic cells containing brown melanin pigment. Abundant angiogenesis is evident within the submucosa of the nasal cavity. H&E; magnification, x100. (B) High-intensity positive immunostaining for HMB-45 within tumor cells (magnification, x100). H&E, hematoxylin and eosin.

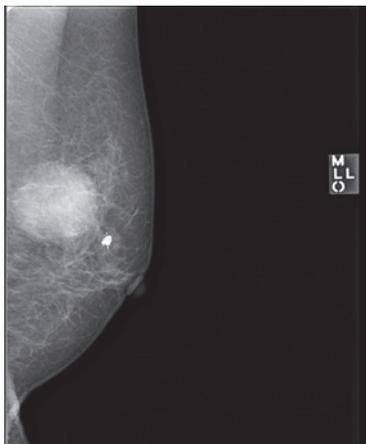


Figure 3. Mammography showing an almost oval-shaped, microlobulated tumor, assessed as a suspicious abnormality.

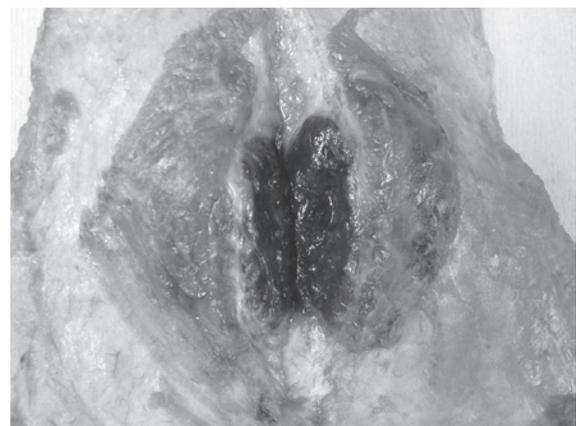


Figure 4. Macroscopic evaluation of the resected breast, revealing a brown-black tumor with a soft consistency.

a result of suspected muscle invasion (Fig. 4). Although the dissected axillary lymph nodes were swollen, no metastasis of malignant melanoma was apparent under microscopy. For treatment of the primary site, heavy ion radiotherapy was performed in accordance with the wishes of the patient.

The tumor initially reduced in size by 30% over a 2-month period; however, it showed regrowth during the month of radiotherapy (Fig. 1B). The disease subsequently progressed very rapidly. Anticancer therapy was eventually suspended 3 months after the initial radiotherapy and only palliative

care was administered. Finally, the patient was admitted into a hospice in August 2011.

Discussion

The clinically observed incidence of metastatic breast tumors was 0.5-1.2% in all breast neoplasms and 6% in an autopsy series (6). Georgiannos *et al* reviewed the clinical data for secondary tumors in the breast, revealing a frequency of 3.2%, with the majority representing metastasis from a contralateral breast cancer (7).

Characteristics of metastatic breast tumors usually include presence in the superficial tissues and well-defined multinodular masses in the upper outer quadrant of the breast. The absence of calcification on radiological examination, such as mammography, is an additional suggestive feature (8). In the present case, a single breast tumor was present in the upper middle quadrant of the deeper mammary gland, therefore differentiation from primary breast neoplasm was required.

Malignant melanomas account for only 2-8% of all cancers arising in the nasal cavity, and mucosal melanoma of the nasal cavity is rarely encountered (<1% of all malignant melanomas) (9). Given the rarity of this disease, no universally accepted staging system has been devised. The most fundamental treatment is wide resection of the primary site. Radiotherapy combined with surgery is recommended in cases of local recurrence or incomplete lesion removal; however, the majority of cases are resistant to radiotherapy, as in the present case. In addition, few standard systemic chemotherapies are regarded as effective. This disease is aggressive and distant metastases to the liver, lungs and brain, and regional metastases to subcutaneous tissues are the major causes of mortality in the majority of cases (10). In our institute, the 5-year survival rate for malignant melanoma of the nasal cavity is 36%. In addition, the 2-year survival rate of patients with distant metastases is only 13%, compared to 100% in the absence of distant metastases. Early detection and diagnosis with appropriate treatment should therefore be emphasized.

Metastases from cutaneous malignant melanoma represent the majority of cases of melanoma involving the breast with the most common primary sites associated with breast involvement on the arms and trunk (5). The mechanism of breast involvement in these cutaneous malignant melanomas may involve direct lymphatic and/or vascular drainage routes from the primary site to the breast. In the present case, breast metastasis was suggested to have occurred hematogenously, given that the primary tumor showed a rich blood supply and no axillary lymph node involvement was detected. As another mechanism, a hormonally-based association with the progression of melanoma has been suspected. Although the influence of estrogen in the development and progression of melanoma has been controversial, epidemiological evidence implicating estrogens in the etiology of melanoma has been accumulating (11). Estrogen receptors have been detected in certain melanoma cells, although at low levels and infrequently (12). The peak incidence age of melanoma among females coincides with the perimenopausal age. In a review of 15 patients with breast metastasis from cutaneous melanomas, the majority of patients (93%) were premenopausal women with

a mean age of 39 years (5). In another retrospective review of 27 patients with mammary metastasis from malignant melanoma, including cutaneous melanoma, 70% of patients were premenopausal (13).

In terms of the treatment for metastatic melanoma, insufficient results have been obtained using systemic chemotherapies, with response rates below 20% (14). The epidemiological and clinical evidence of melanoma potentially being an estrogen-dependent tumor suggests the possible efficacy of adding hormonal therapy to chemotherapy; however, single-agent hormonal therapy is minimally active. A preliminary report in which a high response rate was acquired using chemotherapy concurrent with tamoxifen has attracted attention (15). In addition, in a case series on malignant melanomas of the nasal cavity, 3 patients without distant metastases who responded to tamoxifen concurrent with chemotherapy were reported in 1997 (16). While a meta-analysis of randomized controlled trials did not demonstrate any significant improvement in the overall response rate, complete response rate or survival rate when tamoxifen was administered along with chemotherapy regimens for patients with metastatic melanoma; overall response rates tended to favor the combined regimens (17). In previous clinical trials and practices, tamoxifen, which was originally used as a target therapy to treat estrogen receptor-positive breast cancer patients, has been administered irrespective of the estrogen receptor status of tumor cells, therefore estrogen receptor-negative cases would have received no benefit from this hormonal therapy. In the present case, immunohistochemical staining for estrogen receptors yielded negative results (data not shown); however, hormonal therapy may be an option for patients with estrogen receptor-positive tumor cells, as this therapy is less toxic than chemo- or radiotherapy.

To the best of our knowledge, no previous reports in the English literature have described malignant melanoma of the nasal cavity with solitary breast metastasis. This case was unusual not only in that the primary site was the nasal cavity, but also because the solitary metastasis to the breast occurred in a postmenopausal woman. At present, radical surgery remains the only fundamental therapy; however, the establishment of treatment strategies based on a comprehensive understanding of both etiology and pathophysiology is needed for rare cases such as this.

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