CASE REPORT

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Metastasizing breast carcinoma to middle cranial fossa with extensive hyperostosis which occurred 8.5 years after the initial treatment

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ABSTRACT

Introduction: Breast cancer is the second most common primary tumor with brain metastases. Breast cancer metastasizing to the neurocranium can include the skull, dura, or parenchyma of the brain. Skull metastases were most often found in the breast, typically presenting as osteolytic.

Case Presentation: A 53-year-old woman with a history of breast cancer surgery 8.5 years before she had a headache, nausea, and right visual disturbance. Neuroimaging studies have identified a large tumor in the anterior part of the right middle cranial fossa associated with severe hyperostosis of the underlying bones. Intraoperative exposure revealed that the primary tumor site was dura mater of the middle cranial fossa. The tumor has been histologically diagnosed as metastatic breast carcinoma with sphenoid bone invasion.

Conclusion: Dural breast cancer metastasis may pose this uncommon characteristic of severe hyperostosis, which should be considered in primary skull tumor differential diagnosis.

Keywords: Hyperostosis, Brain metastasis, Breast cancer, skull base tumor

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INTRODUCTION

Breast cancer is the second most common primary tumor with brain metastases.1 The risk of developing brain metastasis has been reported to range from 10 to 16% among living advanced breast cancer patients.2,3 Breast cancer metastasizing into the neurocranium may involve the skull, the dura, or the brain parenchyma. Skull metastases were most commonly from breast, lung, prostate and thyroid, which typically appeared as osteolytic.4 We here present a case of breast cancer metastasis in middle cranial fossa with extensive hyperostosis of skull base which occurred 8.5 years after the initial treatment.

CASE REPORT

A 53-year-old female was diagnosed with right breast carcinoma and underwent a mastectomy and axillary lymph nodes dissection in 2007. Histologically the tumor was invasive ductal carcinoma with features of histological grade 2 and nuclear grade 2. The tumor was estrogen receptor-positive, progesterone receptor-positive, and HER2 negative. She underwent four courses of ECF (epirubicin, cisplatin, and fluorouracil combination) therapy and four courses of docetaxel treatment. She had been in good control of cancer with hormonal therapy using estrogen receptor blocker, tamoxifen, for the following 32months then with exemestane thereafter.

At 8.5 years after the initial diagnosis she complained of headache, nausea, and right visual disturbance. A breast oncologist following-up her found her blood carcinoembryonic antigen (CEA) level was elevated, 11.2 ng/mL. Fluorodeoxyglucose (FDG)-positron emission tomography (PET)-scan for ruling out of systemic metastasis revealed an abnormal accumulation of the tracer at the right anterior temporal region (Figure 1). She was referred to our department. Neuro-ophthalmologic examination showed a right optic atrophy and visual disturbance (visus: 20/200). Computed tomography (CT) scan showed a round hyperdense tumor in the anterior part of right middle cranial fossa with extensive hyperostosis involving petrous, sphenoidal and ethmoidal bones (Figure 2).

On T1 weighted-magnetic resonance imaging (T1W-MRI), the tumor was iso-intense (Figure 3a) and iso-hypointense (Figure 3b) on T2W-MRI. The T2 hyper intensity rim posterior to the tumor suggests the extra-axial, dural origin, nature of the

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tumor. The tumor was homogeneously enhanced on gadolinium contrast MRI and tumor tissue extended up to the right ethmoid sinus (Figure 3c,d).

Under the preoperative diagnosis of metastatic breast cancer or meningioma, she underwent right fronto-temporal craniotomy for tumor removal. Tumor tissue was strongly attached to the dura mater and soft in consistency. Although adhesion to the brain surface was severe, the tumor was separated from anterior temporal lobe with partial resection of the softened brain cortex adjacent to the tumor. The subtotal removal of the tumor was accomplished except for the part of tumor tissue surrounding the right optic nerve and internal carotid artery (Figure 4). Moreover, the bony specimen from greater wing of sphenoid bone was served for the pathologic study.

The Histopathological finding of the resected tumor tissue was compatible with primary breast cancer (Figure 4a). Involved bony tissue showed focal infiltration of cancer cells (Figure 4b). Estrogen receptor stain, progesterone receptor stain, and human epidermal growth factor receptor 2 (HER2) stain showed similar features to her previously resected breast cancer (Figure 4c,d,e). The MIB-1 index was 20% (Figure 4f).

Postoperatively, the patient was alert and developed transient right ptosis and mild hemiparesis which recovered in a month. Her postoperative MRI showed a subtotal removal and a residual tumor tissue around right internal carotid artery (Figure 45). Then she had 50Gy of extended local radiation. Postoperative FDG-PET scan showed no other metastatic lesions. Her blood CEA level has returned normal, 3.0-3.8 ng/mL. She has been in good daily activity for the last ten months after the craniotomy under a monthly intramuscular injection of fulvestrant 500 mg, a selective estrogen receptor down regulator.

DISCUSSION

Breast cancer in females is the leading cause of skull metastases. Cumulative incidence of brain metastasis was 5 per cent at five years in patients with breast carcinoma. Brain metastasis from breast cancer has been suggested to occur more commonly in younger people, those with larger tumors or higher nuclear grade, in some subtypes such as estrogen-receptor (ER)-negative, triple negative, HER2 over expressive tumors and those with nodal metastasis. Metastasis tends to occur a few years after breast cancer is detected, but metastasis is not rare at five or ten years after diagnosis. Recent development in breast cancer diagnosis through hormonal and biological therapy has extended free progression survival. Yet patients with ER-positive / HER2-negative breast cancer, like ours, have a lower chance of brain metastasis relative to patients with triple-negative or HER2-positive phenotype, yet subsequently develop brain metastasis during the disease.

In our case, due to the presence of T2 hyperintensity rim indicating CSF space in

Figure 1. Axial fluorodeoxyglucose (FDG)-positron emission tomography (PET)-scans a, b. Hyperaccumulation of tracer was seen in the anterior part of the middle cranial fossa (arrows).

Figure 2. Axial and coronal computed tomography (CT) scans a, b. Slight hyper-density tumor was seen behind the sphenoid wing (arrows) c, d. Bone density images showed a marked hyperostosis in the sphenoid, ethmoid, and petrous bones (encircled).
the tumor-brain interface and intraoperative inseparability of the tumor from the dura mater, we suppose that the metastasis to middle cranial fossa is primarily involved in dura mater of middle cranial fossa. 70 per cent of cases showed skull extension in a sequence of intracranial dural metastases. In our report, the specimen from the bone with extensive hyperostosis was found to have tumor cell infiltration also. Skull metastases from breast cancer typically appear as large, osteolytic, hypervascular lesions. Tumors produce many factors that stimulate osteolysis: parathyroid hormone-related protein (PTHrP), interleukin (IL)-11, IL-8, IL-6, and receptor activator of nuclear factor-κB ligand.

We reporting in our case, the osteoblastic changes in underlying skull base was so extensive. Commonly prostate cancer has a propensity to metastasize to the bone with hyperostosis, which classified as osteoblastic change. The mechanisms responsible for osteoblastic growth in the bone are complex and include osteoclast and osteoblast tumor stimulation, as well as bone microenvironment response. Growth factors originating from tumor cells, including such platelet-derived growth hormone, insulin-like growth factors, adrenomedullin, and vasoactive peptide endothelin-1, have also been involved in osteoblast bone metastases. Pathomechanism of extensive skull hyperostosis metastasized by breast cancer should be analyzed in the light of these molecular histories, personal hormonal status and history of therapy.

In addition to rare cases of skull base metastases, there are also primary skull tumors correlated with hyperostoses such as osteoma, chondrosarcoma, chordoma, and fibrous dysplasia. Nonetheless, the most common primary intracranial neoplasm inducing hyperostosis is meningioma and hyperostosis is shown in 25-49 per cent of meningiomas. In fact, the likelihood of meningioma as a preoperative diagnosis could not be dismissed. Nevertheless, increased CEA and acute development of visual problems accepted breast cancer metastases as a key preoperative diagnosis.

The first treatment chosen for our patient was surgical removal. A single brain lesion, lack of systemic metastatic lesion, and surgical accessibility of brain lesions led to a decision on operative procedure. The goal of the procedure was to create a definitive diagnosis and to reduce the mass effect. In addition, we gave her 50-grey extended local radiation for residual tumors and tumor beds since, as is documented, radiotherapy is an independent beneficial factor for sustained survival in cases of
She is currently undergoing a new type of hormonal therapy, fulvestrant 500 mg, for the E2R positive breast cancer. Treatment options for patients who experience disease progression after nonsteroidal aromatase inhibitors therapy are limited. However, a randomized trial of fulvestrant 250 mg versus fulvestrant 500 mg in patients with endocrine progression of disease showed a substantial increase in median progression free survival (5.5 vs. 6.5 months) in the fulvestrant 500 mg group.

To the best of our knowledge, this is the first report of metastasizing breast carcinoma to dura mater of middle cranial fossa causing such an extensive hyperostosis. Dural metastasis of breast cancer may present with this unusual feature which should be considered in differential diagnosis of primary skull tumor like meningioma.

**CONFLICTS OF INTEREST**

There are no conflicts of interest.

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**AUTHORS’ CONTRIBUTIONS**

Mohammad Ali Akbar is the main author and was in charge of writing, editing and finalizing the script. Muhammad Kamil, F M Moinuddin, Shingo Fujio, Hirofumi Hirano, and Takuihiro Higashi contributed to the construction of the case presentation, the formulation of the idea, and the case presentation script. Junko Kawano, Ikumi Kitazono have contributed to the case presentation and the quest for literature. Arie Ibrahim, Yuriz Bakhtiar, Thohar Arifin, Zainal Mustaqim and Kazunori Arita conducted a literature search and reviewed the final text.

**REFERENCES**


**Figure 5.** Postoperative gadolinium-enhanced MRIs
Axial (a) and coronal (b) images showed subtotal removal of the tumor and a residue near the right internal carotid artery and optic nerve (arrows).