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Case Report

Orbital Metastasis from Breast Cancer: Three Cases and Brief Review of the Literature

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Abstract

Metastatic disease is a relatively rare cause of orbital tumors. While many different types of primary malignancies have been documented, lung and breast cancers are the most prevalent ones among them. Herein, three cases of orbital metastasis from breast cancer are reported. The first patient had no history of primary malignancy, and the initial presentation was orbital metastasis from advanced breast cancer. The second patient had a history of neo-adjuvant chemotherapy, mastectomy, and adjuvant radiotherapy. The recurrence of the disease was diagnosed via symptomatic metastasis to orbit involving the lateral rectus muscle. The third patient had a history of mastectomy, adjuvant radiotherapy, and hormone therapy. Considering that even patients without a diagnosis of primary malignancy may present with orbital metastasis, ophthalmologists' awareness of this issue is critical.

Keywords: Breast cancer, orbital metastasis, orbitotomy

Introduction

Breast cancer is one of the most prevalent malignancies among women. In recent years, with advances in the treatment of breast cancer and an increase in survival rates, metastasis to uncommon sites such as orbit has become more common (1,2). Among all orbital tumors, 1–13% are associated with metastatic illness and almost all are adult population (3,4). Even though it varies among different studies, 15–32% of patients with orbital metastases have no known history of malignancy at the time of diagnosis (5,6). In patients with a history of primary tumor, the time between diagnosis and orbital metastasis is highly variable (4). Kamieniarz et al. (7) reported a case of orbital metastasis diagnosed even 7 years after the primary tumor diagnosis.

Breast carcinoma is one of the most common malignancies that metastasize to orbit. The presence of orbital metastasis is generally associated with poor prognosis as it reflects hematological spread (4,8). Orbital metastasis involving extraocular muscles is an uncommon clinical scenario (9,10). Magnetic resonance imaging (MRI) is helpful for detecting the extent of orbital and extraocular involvement. In general, metastatic lesions seem hypointense on T1-weighted and hyperintense on T2-weighted images (11).

The purpose of this report is to describe three patients with orbital metastasis of breast cancer and to emphasize

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the importance of clinical suspicion and biopsy in diagnosis. The study was conducted in agreement with the tenets of the Helsinki Declaration. The patients were informed about this publication and informed consent was obtained for publishing medical information from each patient.

Case Report

Case 1 – A 48-year-old female was admitted to our clinic due to swelling around her right eye and double vision on her right gaze. She had a history of oral antibiotic use for 1 week with the preliminary diagnosis of preseptal cellulitis. Her medical history was unremarkable. The best corrected visual acuity (BCVA) was bilateral 20/20. She had mild restriction of abduction of the right eye. Intraocular pressures were 12 and 14 mmHg in the right and left eyes, respectively. A firm solid mass was palpated in the right periorbital area. Anterior segment and fundus examinations were within normal limits. Orbital MRI revealed soft tissue infiltrating the entire extraconal and conal distance, involving the episcleral area around the eyeball, and extending toward both palpebral areas and retrobulbar space in the right orbit (Fig. 1). A similar soft tissue that has infiltrated the superior extraconal and conal space was noted in the left orbit. Bilateral diffuse lacrimal gland involvement was also observed. Based on MRI images, an incisional biopsy from the right orbit was performed with the preliminary diagnosis of orbital pseudotumor. Histopathological examination of the specimen revealed metastasis of invasive lobular carcinoma. Thereupon, a systemic investigation was made which revealed a breast imaging-reporting and data system (BI-RADS) 5 lesion in the right breast and BI-RADS 4 lesion in the left breast on mammography. Tru-cut biopsy under ultrasonography guidance concluded as invasive lobular carcinoma. Immunohistochemical examination demonstrated estrogen receptor (ER)-positive breast cancer (Fig. 2). Metastasis was also detected in the bone marrow biopsy performed following the detection of lesions compatible with disseminated sclerotic metastasis showing increased fluorodeoxyglucose (FDG) uptake in the bone structures in the oncological positron emission tomography (PET) examination. Systemic chemotherapy was initiated. The patient is under treatment and regular follow-up for 12 months. No increased FDG uptake in the orbit was observed in the PET scan taken to evaluate the response to treatment.

Case 2 – A 54-year-old female patient was admitted to our clinic with the complaint of diplopia on the left gaze. Her medical anamnesis indicated a history of neo-adjuvant chemotherapy, mastectomy, and adjuvant radiotherapy for triple-negative metaplastic breast cancer 5 years ago. Ophthalmological examination revealed proptosis and limitation of abduction and elevation in the left eye. BCVA was 20/20 bilaterally. Intraocular pressure was 14 mmHg in both eyes. Anterior and posterior segment examinations were unremarkable. Orbital MRI demonstrated a hypertrophic appearance in the left lateral rectus muscle (Fig. 3). Thyroid function tests, inflammatory, and rheumatologic markers were unremarkable. An incisional biopsy of the lateral rectus muscle was performed under general anesthesia. On histopathological examination of the biopsy specimen, epithelioid-looking tumor cells with necrosis ar-

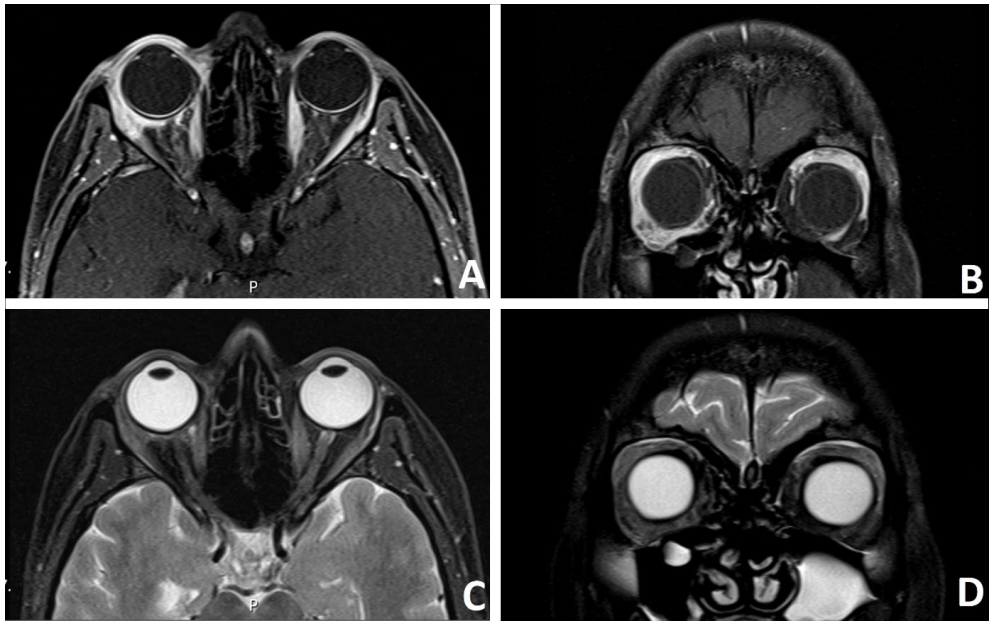

Figure 1. T1-and T2-weighted transverse **(a and c)** and coronal **(b and d)** magnetic resonance imaging (MRI) images of the patient showing bilateral orbital infiltration.

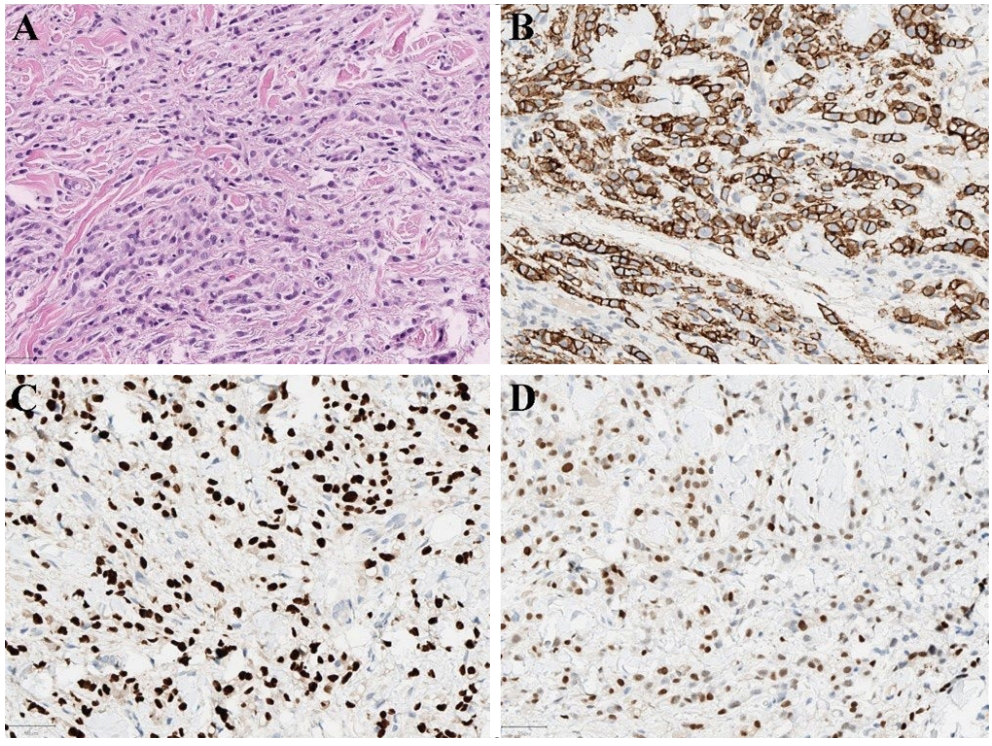

Figure 2. Tumor cells with irregular distribution among collagen bundles (hematoxylin eosin) **(a)**. Immunohistochemical positive staining of E-cadherin **(b)**, GATA-3 **(c)** and estrogen receptor **(d)** in tumor cells.

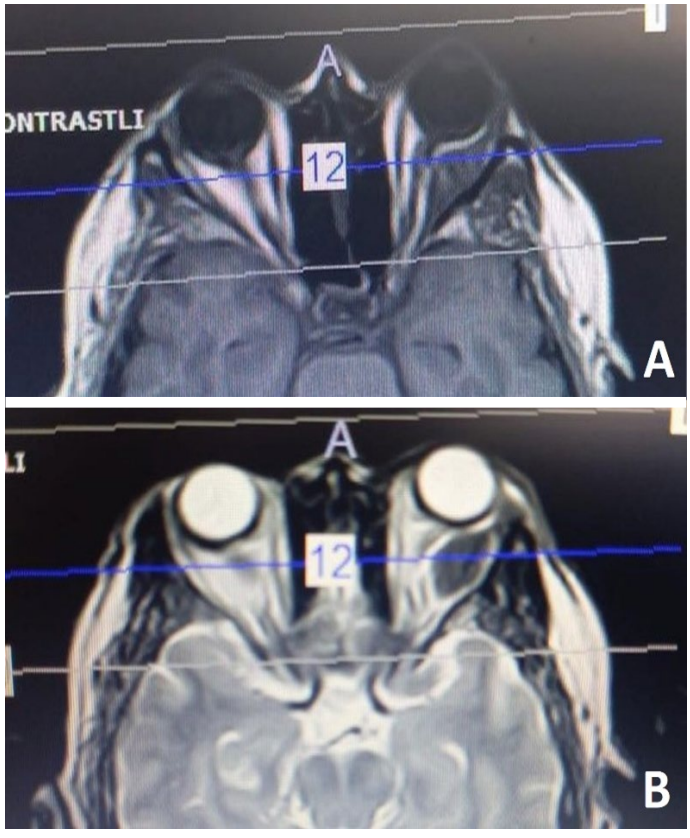

Figure 3. T1-**(a)** and T2-weighted **(b)** MR transverse sections of the patient showing hypertrophic left lateral rectus muscle.

eas were detected. In immunohistochemical examination, ER, progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2/neu) were found to be negative, similar to the primary tumor, whereas cytokeratin staining was found to be positive (Fig. 4). Considering the patient's history of primary malignancy, she was diagnosed with breast carcinoma metastasis. The patient was referred to the medical oncology department due to a recurrence of carcinoma. Despite the resumption of systemic chemotherapy by oncology, the patient passed away from multiple organ failure 6 months after the detection of orbital metastasis.

Case 3 – A 45-year-old female with a history of ER-positive, PR, and HER2/neu negative invasive lobular carcinoma was referred to our clinic for right-sided exophthalmos for 3 weeks. Her medical history revealed breast cancer diagnosed 4 years ago. The treatment history of the patient included a total mastectomy, axillary lymph node dissection, chemotherapy, radiotherapy, and hormone therapy. After the recurrence of the disease a year ago, chemotherapy and abemaciclib treatments were initiated. An ophthalmological examination revealed proptosis in the right eye. BCVA was bilateral 20/20. There was no sign of optic nerve dysfunction on ophthalmological examination. No limitation in eye movements was detected. Intraocular pressures were 19

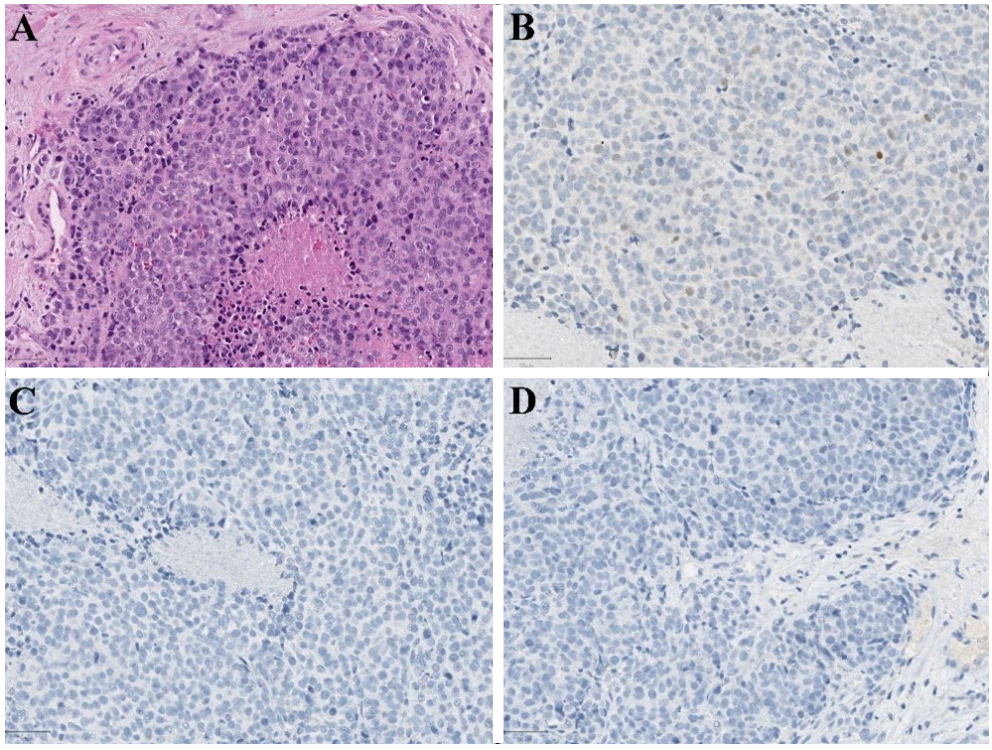

Figure 4. Necrotic tumor cell group consisting of undifferentiated cells with prominent nucleoli and epithelioid appearance (hematoxylin eosin) **(a)**. Immunohistochemical focal and weak staining of GATA-3 **(b)**, negative staining of estrogen receptor **(c)**, and PR **(d)** in tumor cells

and16 mmHg in the right eye and the left eye, respectively. Examinations of the anterior and posterior segments were normal. Since the patient had a history of malignancy, an orbital MRI was performed which demonstrated an infiltrative soft-tissue mass diffusely surrounding half of the intraorbital segment of the optic nerve in the right orbit (Fig. 5). In addition, there were multifocal similar soft-tissue lesions in the inferior palpebral region and its adjacent medial anterior part of the orbit. On MRI findings, an incisional biopsy through anterior orbitotomy was performed. The histopathological analysis supported the metastases of breast cancer. Immunohistochemical staining revealed ER positivity (Fig. 6). No malignant cell was detected in the lumbar puncture (LP) performed to rule out cranial leptomeningeal carcinomatosis. The systemic chemotherapy regimen was arranged by medical oncology. The patient is on follow-up and no additional ophthalmological symptoms developed for 6 months.

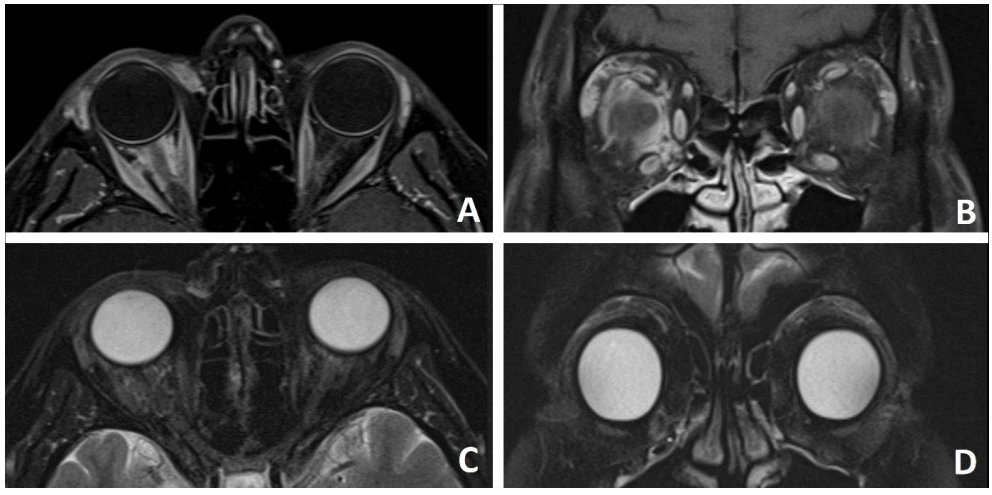

Figure 5. T1-and T2-weighted transverse **(a and c)** and coronal **(b and d)** magnetic resonance imaging images of the patient demonstrating infiltrative soft tissue in the right orbit.

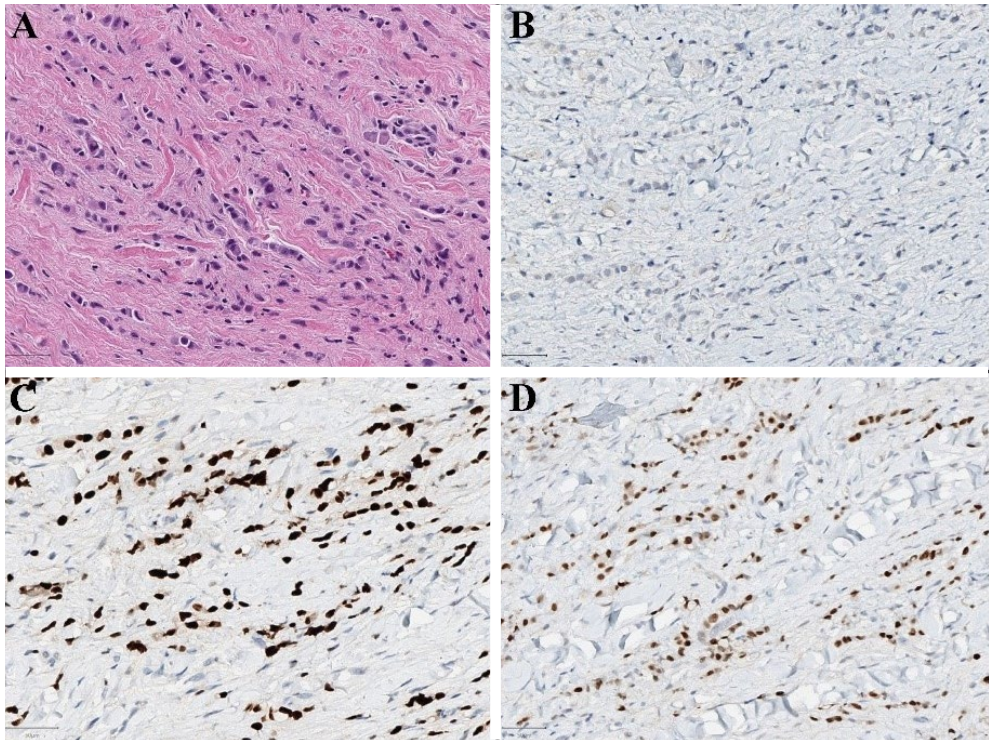

Figure 6. Discohesive tumor cells arranged in single files, cords, and single cells (hematoxylin eosin) **(a)**. Immunohistochemical negative staining of E-cadherin **(b)**, positive staining of GATA-3 **(c)** and estrogen receptor **(d)** in tumor cells

Discussion

Metastatic disease is a rare cause of orbital tumors. Among metastatic tumors of the orbit breast cancer is one of the most frequent ones (4). This predisposition may be related to estrogen produced by periorbital fat tissue (12). As lymphatic drainage of the orbit is limited, the presence of orbital metastasis of breast cancer points out hematological spread (13).

Symptoms of orbital metastasis are similar to other orbital disorders and consist of visual disturbance, restriction of ocular mobility, diplopia, proptosis, pain, and periorbital swelling (14). The chief complaint in two of the cases was diplopia.

It should be kept in mind that patients without a primary malignancy diagnosis may present with metastatic disease as their initial clinical presentation (5,6). As in the first case, although the patient had stage 4 invasive lobular carcinoma accompanied by bone marrow metastasis, the patient was diagnosed through orbital involvement. On the other hand, as in the second and third cases, patients may develop a relapse of their malignancies thorough orbital metastasis years after the initial diagnosis of carcinoma. Vlachostergios et al. (11) reported a 4.5–6.5 years delay between the initial diagnosis and orbital metastatic disease. Metastatic disease should be kept in mind in patients with orbital symptoms and histopathological examination should not be delayed when necessary.

The diagnostic approach should begin with clinical suspicion and imaging. MRI is generally preferred due to its superiority in imaging soft tissues. It also guides the surgeon in the planning of the biopsy. Histopathological confirmation by biopsy is the gold standard for definitive diagnosis of metastasis (4).

Although orbital metastases can be found in any anatomical location, they generally tend to be located in the anterior orbit (4). Due to their mobile nature, extraocular muscle involvement by breast cancer metastasis is infrequently encountered in clinical practice (9). However, ocular motility limitation in any patient with a history of malignancy should suggest the possibility of metastatic invasion. In addition, leptomeningeal carcinomatosis and optic nerve metastasis can also be encountered rarely in the course of metastatic breast carcinoma (15). In case of clinical suspicion, neuroimaging and LP should be performed as in the third case.

There are limited data in the literature about the histological types of breast cancer that metastasize to the orbit. In a retrospective analysis of 28 cases, 14 patients had ductal, 13 patients had lobular, and one patient had micropapillary histology (12). Metaplastic breast cancer is a rare malignancy that accounts for less than 1% of all types of breast carcinoma. It is known to be associated with poor prognosis and most commonly causes lung and bone metastasis (16). To the best of our knowledge, there is no previous report of

metaplastic breast cancer that metastasizes to the orbit.

Treatment modalities of orbital metastasis include systemic chemotherapeutic regimens and hormone therapy for systemic control of malignancy, and when needed local interventions such as external beam radiotherapy to improve the patient's visual function and quality of life (4,12). In the present cases, local treatment modalities were not preferred because the patients had no symptoms other than diplopia.

Conclusion

In patients with proptosis and ocular motility deficit, orbital metastasis should be kept in mind whether or not there is a previous history of malignancy. Histopathological analysis is a must to provide a final diagnosis. Ophthalmologists play an important role in the detection of metastatic carcinoma even before the diagnosis of primary malignancy.

Disclosures

Informed consent: Written informed consent was obtained from the patients for the publication of the case report and the accompanying images.

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