case report

Metastatic Breast Cancer Presenting As Orbital Mass: A Case Report With Literature Review

Rizwan Shaikh
Khurram Tariq
Suash Sharma
Shou-Ching Tang

Rizwan Shaikh, **Khurram Tariq**, **Suash Sharma**, and **Shou-Ching Tang**, Georgia Regents University Cancer Center, Augusta, GA; and **Shou-Ching Tang**, Tianjin Medical University Cancer Institute and Hospital, Tianjin, Republic of China.

R.Z. and K.T. contributed equally to this work.

Corresponding author: Shou-Ching Tang, MD, PhD, Breast Cancer Multidisciplinary Program, Breast Cancer Interdisciplinary Research Program, Georgia Cancer Center at Augusta University, 1411 Laney Walker Blvd, Augusta, GA; e-mail: stang@augusta.edu

CASE REPORT

A 58-year-old African American female presented to the ophthalmology clinic with a right anterior orbital mass, which was initially suggestive of orbital sarcoidosis. Symptoms included progressively worsening eye pain with pressure headache, orbital tenderness, and decreased vision. The patient first noticed the nodule and drooping of the eyelid 3 months before evaluation and complained of fatigue for approximately 1 year with no accompanying fever, chills, weight loss, or diplopia. The patient's medical history was not significant for any comorbidities, but her family history was significant for breast cancer. Before initial evaluation by ophthalmology, the patient did not have a primary care physician and was not taking any medication, but did have a sulfa allergy that resulted in hives.

On initial presentation, her eye pain and mass was attributed to ocular sarcoidosis. This possibility was further entertained with a chest x-ray that showed midhilar adenopathy and thickening of the minor fissure that was consistent with changes secondary to sarcoidosis. The patient was started on prednisone for presumed orbital sarcoidosis, which was supported by findings of elevated erythrocyte sedimentation rate and angiotensin-converting enzyme. Despite 3 months of steroid therapy, the patient's symptoms persisted, with increasing tightness of the superior orbit, which made the initial sarcoidosis diagnosis unlikely.

Her worsening clinical course was followed by magnetic resonance imaging of the orbits that showed periorbital and preseptal edema bilaterally, with greater severity on the right superior side as a result of asymmetric enhancement. No space-occupying lesions, abscess, or postseptal inflammation were noted. Magnetic resonance imaging of the head was performed and revealed no tumor or acute intracranial process. Differential diagnoses included orbital pseudotumor or IgG4 orbital disease. Approximately 5 months after initial presentation, the patient underwent an orbitotomy with exploration and biopsy of the right inflammatory nodule on the superior orbital rim. Final pathologic diagnosis was infiltrating carcinoma, likely metastasis to the right eye superior orbital mass. There was infiltrating epithelial neoplasm that involved fibroadipose and skeletal muscle tissue, which suggested metastatic infiltrating carcinoma that was estrogen receptor (ER)–positive $> 90\%$ and progesterone receptor (PR) –positive $< 5\%$ (human epidermal growth factor receptor 2 [HER2] ratio, 1.1/1). Overall histologic findings, therefore, were most consistent with an infiltrating carcinoma, likely metastatic, with features that were suggestive of a breast lobular primary, but other unusual local or systemic neoplasia were not excluded. The patient subsequently had staging mammography, computed tomography (CT) scan of thorax with contrast, and bilateral breast ultrasound to evaluate for primary lesion. This was the patient's first mammogram and served as a baseline study. There was a subtle isodense focal asymmetry that measured 13 mm deep to marker, which indicated palpable finding in the right breast and an oval focal equally dense asymmetry in the 9 o'clock position of the left breast. There was no thickening or significant nipple or skin retraction observed. Breast imaging reporting and data system score was 5 and highly suggestive of malignancy. CT scan demonstrated a 1.2-cm right axillary lymph node as well as a 1.3-cm mass-like region of enhancement in the upper outer right breast and a separate region of mild distortion in the lower outer region of the right breast. Breast ultrasonography showed an ill-defined hypoechoic 17-mm mass in the 10 o'clock position of the right breast with additional suggestive ill-defined hypoechoic 10-mm lesion with associated distortion in the 8 o'clock position concerning for satellite lesion. There was a dominant suggestive lymph node in the lower right axillary region that was amenable to ultrasound-guided sampling. Also of note was a nonspecific ill-defined hypoechoic lesion that measured 4 mm in the 5 o'clock position of the left breast

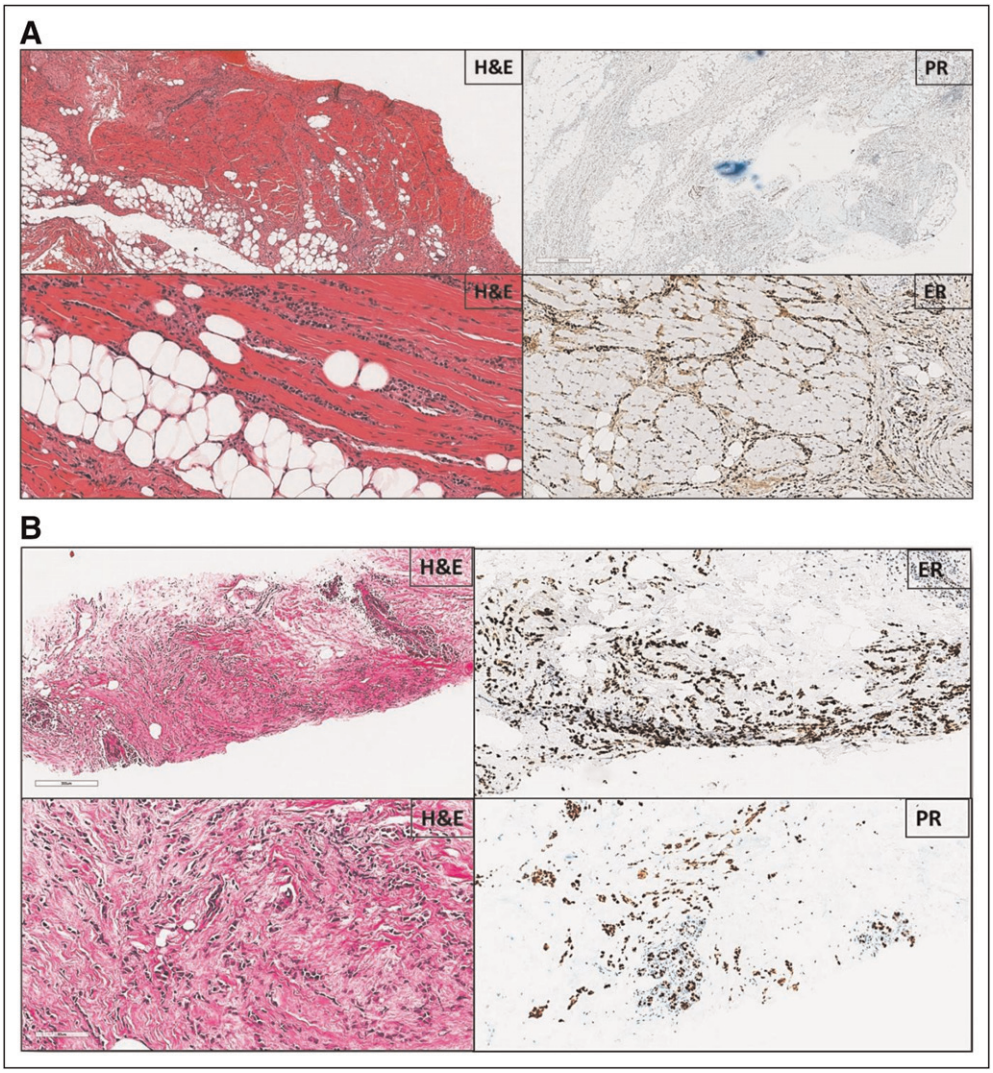

Fig 1. (A) Biopsy specimen of orbit showing metastatic breast carcinoma. Hematoxylin and eosin (H&E) low and high power. Examined section demonstrates an infiltrating epithelial neoplasm that involved fibroadipose and skeletal muscle tissue. Neoplastic cells are present in linear strands, small clusters, and as scattered single cells, without any other differentiation pattern. Neoplastic cells are relatively monotonous, small- to medium-sized polygonal to plasmacytoid cells with variably eccentric, mildly pleomorphic atypical nuclei, small nucleoli, occasional mitosis, and pale-pink cytoplasm. This morphologic picture is diagnostic of metastasis of breast lobular carcinoma—an interpretation supported by diffuse immunopositivity for pankeratin, CK7, estrogen receptor (ER), focally GCDFP-15, and, progesterone receptor (PR). ER (antibody clone: SP1): > 90% of tumor cells show nuclear staining with a strong staining intensity. PRs (antibody clone: 1E2): < 5% of tumor cells show nuclear staining with a moderate staining intensity. (B) Biopsy specimen of breast showing invasive lobular carcinoma. H&E low and high power: Examined sections demonstrate infiltrating epithelial neoplasm. Neoplastic cells are present in linear strands, small clusters, and as scattered single cells, without any other differentiation pattern. Neoplastic cells are relatively monotonous small- to medium-sized polygonal to plasmacytoid cells with variably eccentric, mildly pleomorphic atypical nuclei, small nucleoli, occasional mitosis, and pale-pink cytoplasm.

and mildly prominent left axillary lymph nodes. The following day, the patient had biopsy of the dominant mass in right breast along with right axillary lymph node, which confirmed invasive lobular carcinoma grade II, ER > 90% and PR > 90%, HER2/neu-negative by fluorescence in situ hybridization, with a ratio of 0.9/1. She underwent further staging with CT scan of the chest, abdomen, and pelvis, and bone scans, which revealed multiple mildly enlarged lymph nodes within bilateral subpectoral regions, throughout the mediastinum, and right hilar area: a 1.2-cm right axillary lymph node, a 1.3-cm mass in the right breast, asymmetric thickening of anterior superior bladder wall possibly representing cystitis, a 5-mm right upper lobe pulmonary nodule, and a 4-mm left upper lobe pulmonary nodule. Bone scan showed increased radiotracer activity in the left 2nd and 6th rib suggestive of osseous metastasis. The patient was referred to the medical oncology clinic for management of metastatic breast cancer. Upon evaluation by hematology-oncology, the patient was doing well clinically without many symptoms. Other than irritation from her right eye, toothache, and reduced energy, she denied any recent change in appetite or weight loss and, in fact, she had weight gain from use of steroids. There was no rib pain or vision change, and she was sleeping well. There was no fever, chills, nausea, vomiting, diarrhea, constipation, hematuria, productive cough, chest pain, or night sweats. She had a performance status of 0. The patient was given her diagnosis of biopsy-proven metastatic right breast cancer involving right axillary lymph node, right orbital region, rib lesion, and possible lung nodules. Biopsy of her orbital mass and breast mass confirmed ER-/PR-positive and HER2-/neu-negative metastatic breast cancer (Fig 1A and 1B).

After discussing options for surgery, radiation, and systemic therapies, the patient was offered

This morphologic picture is diagnostic of invasive lobular carcinoma—an interpretation supported by immunohistochemistry. The Nottingham grade 2 assessment was given on the basis of the numerical assessment score of 3 for tubule formation, 2 for pleomorphism, and 1 for mitosis, for a total score of 6. Neither DCIS, nor LCIS were noted in the specimen. ERs (antibody clone: SP1): > 90% of tumor cells show nuclear staining with a strong staining intensity. PRs (antibody clone: 1E2): > 90% of tumor cells show nuclear staining with a strong staining intensity.

palliative chemotherapy to control the disease and to improve quality of life. The patient was informed about the standard single and sequential chemotherapies, such as taxanes, and our ongoing phase III clinical trial of docetaxel with or without 1-methyl-D-tryptophan (indoximod). Indoximod inhibits indoleamine-2,3-dioxygenase to reduce antitumor tolerance. The patient showed interest and was enrolled in the indoximod clinical trial.

DISCUSSION

Increasing incidence of ocular involvement is attributed to longer survival of patients with metastatic disease and advancements in diagnostic imaging. Many cases of orbital mass are found in patients who have been previously diagnosed with breast cancer, although the initial finding in undetected primary cancer is staggering, accounting for up to 25% of cases.[1] The majority of ocular and orbital metastasis is a primary result of breast lesions. Of those patients who are affected, 12% to 31% will be newly diagnosed cancer cases. In cases in which the orbit is the main suspected area of distant metastases, the likelihood of additional systemic involvement remains high. There is an increasing number of orbital metastasis, with an incidence of 1% to 13%. Of all cancers that affect the orbit, breast cancer is the primary source in 28.5% to 58.8% of cases. Other primary cancers that affect the orbit include non–small-cell lung, prostate, GI (esophageal), kidney, and skin (melanoma). Conversely, the orbit is an uncommon place for breast cancer metastasis and site of initial presentation. Of 12% to 31% patients affected, eye metastasis is the first indication of malignancy or metastatic spread. Symptoms of orbital metastasis include diplopia, blurry vision, decrease in visual acuity, eye pain, inflammation and redness of the eye and/or periorbital structures, conjunctival or scleral injection, loss of eye motility, palpebral ptosis, visible mass, displacement or proptosis of the globe, orbital bone involvement, and/or chemosis.[2,3]

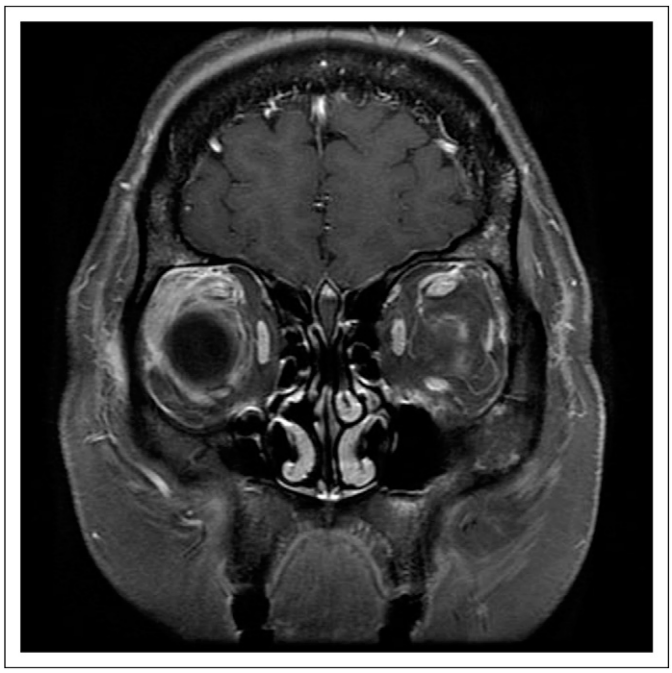

Fig 2. Postcontrast fat-saturated T1 gated magnetic resonance imaging scan of the head. Metastatic orbital lesion infiltrates the orbital fat and disrupts extraocular musculature.

Treatment is usually palliative once diagnosis of metastatic breast cancer is made and is prescribed for symptom relief and improvement of orbital function.[2] The hematogenous seeding of cancer to the orbit reflects systemic disease that has likely spread to other sites.[1] Main interventions are the use of systemic chemotherapy or hormone therapy, depending on receptor testing of lesion, with or without local radiation or surgical resection.[4] Radiotherapy has an objective response rate up to 79%, and in 80% of cases it restores vision but does risk cataract formation and radiation retinopathy.[2] It can be used in patients with such symptoms as persistent pain and bony destructions, though with little effect on vision improvement.

Surgery is recommended only for establishing a diagnosis or for palliation in the setting of extensive local involvement. Extensive orbital surgery is not curative and has high ocular morbidity. Enucleation or other radical measures are futile in terms of progression or survival and should only be used in treatment of intractable pain or unmanageable local hygiene as a result of tumor burden. Chemotherapy followed by hormone therapy in hormone-sensitive tumors is indicated in progressive systemic disease in the setting of orbital metastasis in patients with good performance status.[1] Patients with bony involvement of the orbit and other sites should be offered bone-modulating agents, such as bisphosphonates or denosomab.

In conclusion, we present a unique case of orbital mass as the presenting feature of ER-positive, HER2-positive metastatic breast cancer (Fig 2). We shed light on the paucity of available guidelines for treatment of this disease. It will be interesting to collect additional cases to analyze genomic changes to identify specific genes that are involved in organ-specific involvement of metastasized tumor cells. This may help to develop targeted

therapy for patients with metastatic breast cancer with specific organ involvement. In addition, in cases in which metastatic breast cancer does not express ER, PR, or HER2, novel tissue microarrays using mRNA, micoRNA, and proteins are being validated to identify the breast tissue origins.[5-9]

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