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Case Series

Ocular Involvement by Metastatic Breast Cancer: A Case Series and Review of Literature

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ABSTRACT

Ocular metastasis from breast cancer can localize within the extraocular muscles and the orbital fat, bone, conjunctiva and eyelids. Choroid is the primary ocular site for metastatic cancer due to its rich vascular supply and fenestrated choriocapillaries. The most common presenting complaints are visual field defects, blurred vision, and floaters. We present a case series of three patients who were treated for early-stage breast cancer and later presented with ocular metastatic disease either as isolated metastatic lesion or as part of disseminated disease.

Keywords: Breast Cancer, Blurred Vision, Choroid, Ocular Metastasis.

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INTRODUCTION

Breast carcinoma is the most common malignancy in women[1,2,3] and also the most common malignancy causing ocular metastatic disease.[4,5] A long time-lag is often observed between the diagnosis of breast cancer and manifestation of ocular metastasis, reflecting hematogenous spread of the primary tumor and suggesting poor prognosis.[6] The survival of breast cancer patients with orbital metastasis depends largely on the extent of spread to other organs and magnitude of dysfunction. Treatment thereafter becomes palliative with the aim of preserving visual function and preserving quality of life.[7]

CASE 1

A 31-year-old female, initially presented as Stage II-B, left breast cancer, in 2014, which was positive for Estrogen Receptor (ER) and Progesterone Receptor (PR) but negative for Human Epidermal Growth Factor Receptor-2 (her-2 neu). Her family history was notable for breast cancer diagnosed in her maternal aunt. She received neoadjuvant chemotherapy (4 cycles of cyclophosphamide/doxorubicin followed by 12 cycles of paclitaxel) followed by left modified radical mastectomy (MRM), pathology reports showed 4/14 positive lymph nodes and residual invasive ductal cancer Grade-II with negative margins. After MRM, she was offered radiotherapy and started on hormonal therapy (tamoxifen). She was advised to have total abdominal hysterectomy and bilateral salpingo oophorectomy but she declined considering her young age. She was well until she relapsed with metastatic disease (soft tissue, lung and bone) after 3 years which was triple (ER/PR/her-2 neu) positive at the time of relapse. She started chemotherapy docetaxel/trastuzumab/pertuzumab (HERPERDOC) along with zoledronic acid. Unfortunately, she had progressive pulmonary disease after 10 cycles of HERPERDOC. She was then commenced on Ado-trastuzumab emtansine but due to cost and availability issues, she could not receive it. Meanwhile, she started on anastrozole/leuprolide therapy but soon presented to Emergency Department with pain in her left eye along with blurred and washed-out vision. Fundoscopic examination revealed a left eye choroidal mass in the centre and around optic nerve causing exudative retinal detachment and superior choroid infiltration. However, there was no evidence of disease on Magnetic Resonance Imaging (MRI) brain and orbit. Local triamcinolone injections and radiatiotherapy was started on the left eye which led to improvement in her symptoms. Her systemic therapy was then switched to ribociclib and aromatase inhibitors/leuprolide which led to further improvement in her visual symptoms. However, after 2 cycles of ribiciclib/anastrzole, she had a progressive pulmonary disease leading to shortness of breath. She was then started on capecitabine and had a good partial response after 4 cycles as evidenced by Computed Tomography (CT) scan and markers. However, staging CT scan after 7 cycles of capecitabine showed worsening disease with osseous progression, bilateral pleural effusion and new

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metastasis in liver. Unfortunately, she also developed extensive meningeal metastasis, leading to her death at 36 years of age.

CASE 2

A 59-year-old-female presented with locally advanced bilateral breast cancer (ER+/PR-ve/HER2-ve) in July 2009. She was offered neoadjuvant chemotherapy followed by bilateral mastectomy/ axillary lymph node dissection and radiotherapy to both breasts. Extended (10 years) adjuvant hormonal therapy was offered in view of high-risk breast cancer (8/20 lymph nodes positive on histopathology). In November 2018, she presented with dryness and decreased vision in the right eye. On right eye ophthalmological examination, there was marked swelling and decreased movements of extra-ocular muscles with visual acuity reduced to light perception only. MRI of orbit (Figure 1a, b) showed a large heterogeneously enhancing soft tissue lesion (20x23mm) in the right retro-orbital space. The lesion encased the right optic nerve and was inseparable from retro-orbital muscles, causing mass effect on the ipsilateral right globe with resultant proptosis. However, no infiltration of the right globe or intracranial extension of the lesion was seen. Ophthalmologists tried to remove mass but could not do so in its entirety with biopsy of mass confirmed relapsed metastatic triple negative breast cancer. This was recurrence of breast cancer after 10 years of hormonal therapy, reflecting nature and biology of her disease. No systemic disease was found on Positron Emission Tomography (PET) scan. Steroid therapy was started, followed by radiation to right eye retroorbital mass which led to significant improvement in her visual symptoms. Thereafter, she started oral chemotherapy capecitabine.

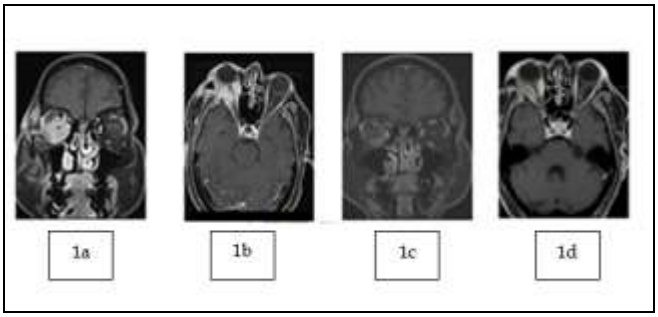

Figure 1a, b: MRI orbit showing a large heterogeneously enhancing right retro-orbital lesion encasing optic nerve without intracranial extension.
Figure 1c, d: MRI orbit showing reduction in size of right intraconal orbital enhancing mass with no intracranial metastatic deposit.

MRI orbit (Figure 1c, d) after 7 cycles of chemotherapy showed reduction in size of right intraconal orbital enhancing lesion. MRI orbit and PET scan after 12 cycles of capecitabine suggested continuing response to chemotherapy. Afterwards, capecitabine was stopped due to poor tolerance (Grade 3 Hand Foot Syndrome). She was then started on exemestane, as her primary tumour was positive for estrogen receptor. Since then, she is doing well and is on active follow up.

CASE 3

A 33-year-old female presented in Medical Oncology clinic in June 2019 with Stage-IIB ER+/PR-ve/HER2-ve breast cancer. She was planned for neo-adjuvant chemotherapy, but was lost to follow up and did not start curative intent treatment. She then returned after 4 months with locally advanced and metastatic breast cancer with nodal, osseous and calvarial metastases. She started chemotherapy AC (cyclophosphamide, doxorubicin) but after 1st cycle of chemotherapy, she developed symptoms of headache, blurred vision, photophobia and diplopia on lateral gaze. Fundoscopic examination and cerebrospinal fluid studies were normal. MRI brain and orbit (Figure 2a, b) showed very subtle abnormal signal and diffusion restriction involving the right intraconal compartment inferior to the optic nerve concerning for intraconal/perineural metastases, however, there was no abnormal meningeal enhancement.

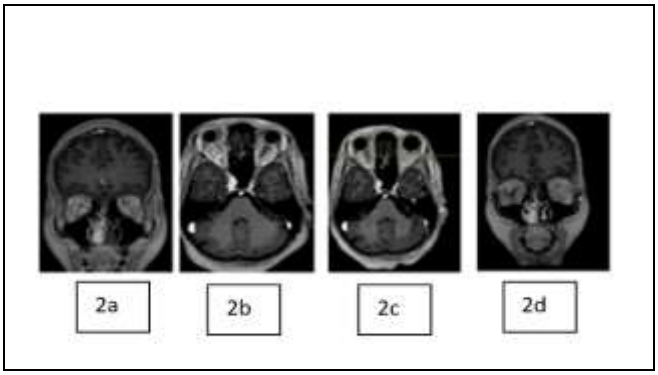

Figure 2a, b: MRI brain and orbit showing osseous metastatic deposits involving the skull bones along with subtle abnormal signal and diffusion restriction involving the right intraconal component inferior to the optic nerve.
Figure 2c, d: MRI brain and orbit showing interval treatment response in previously demonstrated ill-defined enhancing thickening along the right optic nerve. Residual non-enhancing fat stranding is still appreciable with no internal diffusion restriction.

Steroid therapy was started followed by palliative radiotherapy to brain and right intraconal

metastases. Her headache, visual problem and dizziness started to settle down. She then went on to receive 6 cycles of AC chemotherapy. Interim staging CT scan and MRI brain (Figure 2c, d) showed good treatment response. She was then switched to capecitabine. Currently she is receiving capecitabine and zoledronic acid uneventfully and has been doing well.

DISCUSSION

Metastatic spread to the eye is rare and hematogenous, as eye does not have a well-defined lymphatic system.[7] In women, breast cancer is the most common primary tumor metastasizing to the orbit.[8] The incidence of orbital metastasis from breast cancer varies from 5-30% but the potential pathogenesis of this association is unknown as it is considered that certain tissue–specific characteristics of orbital microenvironment play a role in this metastatic phenomenon.[8] Possible risk factors include hormonal, genetic and environmental factors along with female gender, obesity, liver cirrhosis and breast cancer gene (BRCA) 2 mutation.[9] Breast cancer can metastasize to any ocular structure; however the uveal tract is most likely to be affected due to its rich vascular supply.[10] Choroidal metastasis accounts for 90% of the metastatic lesions, while ciliary body and iris are involved in 10% of cases.[11] The first case of choroidal metastasis was documented by Perl,[12] in which the metastatic foci typically appear as creamy yellow plaque-like subretinal lesions.[13] CT and/or MRI are important diagnostic modalities with confirmation done by histopathology after surgical resection or biopsy as metastatic spread to other organs like liver, lungs and bone usually precedes orbital metastasis, however, ocular metastasis is seldom the initial presentation of metastatic disease.[14-16] The goals of management of ocular metastatic lesions include restraining the growth of the metastatic lesion, preserving visual function and improving quality of life of patients.[7] Treatment intent becomes palliative, since presence of ocular metastasis points towards hematogenous spread of the disease, even if there is no evidence of other organs involvement as no specific treatment guidelines are available so far for the treatment of metastatic ocular involvement by breast carcinoma: laser treatment, external beam radiation therapy (EBRT), surgery, systemic endocrine and chemotherapy and anti-vascular endothelial growth factor (VEGF) therapy all have been tried with variable outcomes in literature,[1] in addition, surgery can be useful in ameliorating patients' signs and symptoms particularly in case of solitary lesion where metastatic lesion can be totally excised.[17] Prognosis of breast cancer patients with ocular metastasis is poor; survival ranges from 1 to 116 months[18] with a mean of 31 months with survival outcome largely defined by other organs metastasis and degree of dysfunction.

CONCLUSION

The development of ocular metastasis presents an important and challenging scenario in breast cancer patients. Patients' clinical presentation, including blurred vision, visual field defect, double vision and/or proptosis, should draw suspicion of malignancy and it should warrant further ophthalmological evaluation, particularly in breast cancer patients.

Patients' Consent

The study was given exemption from patients' written/informed consent by Institutional Ethical Review Board.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

JI & FS: Data acquisition, data analysis, critical review, approval of the final version to be published.

AA & NK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

SAMH, MA & NS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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