

CASE REPORT

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Orbital Metastasis of Breast Carcinoma

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Abstract: We report a case of orbital metastasis in a previously diagnosed metastatic breast cancer in a 46-year old woman presenting with diplopia and proptosis of her left eye bulb. An orbital computed-tomography (CT) and a magnetic resonance imaging (MRI) both revealed an intra-orbital extra-bulbar mass of 1.5×3 cm in size, in the left orbit. The patient had been diagnosed with stage IV breast cancer 4 years before. She had received chemotherapy with docetaxel and was on hormone therapy at the time of presentation of her eye symptoms. Current treatment included systemic combination therapy with docetaxel and capecitabine as well as local irradiation with stereotactic radiosurgery (cyberknife). There was a gradual improvement of local symptoms and signs. The metastatic involvement of the orbit in malignant tumors is a rarely diagnosed condition. Breast cancer accounts for the majority of these cases. The appearance of eye symptoms in patients with a history of cancer should always be investigated with a consideration of ocular metastatic disease.

Keywords: orbital metastases, breast cancer, orbit

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Introduction

Breast cancer can metastasize to many sites, but the orbit is an infrequent location and a comparatively rare site of distribution among the ocular area structures. Longer survival of patients with metastatic disease as well as advances in diagnostic imaging may explain the increasing frequency of ocular involvement¹ that occurs in up to one third of breast cancer patients.² Bone metastases as a sole metastatic site in breast cancer portend a good prognosis as opposed to visceral disease and are seen frequently in the ER/PR (+) Her2/Neu (-) subset of the disease. Nevertheless, they may present a particular clinical problem if they are neighboring sensitive structures such as the spine or the eye, as in this case, and may need urgent treatment to preserve patient's quality of life and function.

Case Report

A 46-year old woman, with a history of a grade 2, hormone receptor-positive, HER2-negative ductal adenocarcinoma of the left breast, presented with diplopia, exophthalmos, decreased visual acuity and pain in her left eye.

Initial diagnosis was made 4 years previously, when the patient suffered a pathologic right femor fracture. Clinical examination revealed skin retraction and an estimated 4 × 5 cm palpable mass in the left breast. The area of the right femor was treated with one dose of analgesic external-beam radiotherapy. Patient subsequently underwent a lumpectomy. A total hip arthroplasty was performed a few days later. Breast carcinoma metastatic to the right femoral bone was confirmed histopathologically. Staging CTs of thorax and abdomen and a bone scan were negative for other metastatic lesions.

Preoperatively elevated serum CA 19-9 and CA 15-3 levels immediately normalized after surgery and the patient was started on docetaxel at 30 mg/m² weekly for 12 weeks followed by hormonal therapy, consisting of goserelin and tamoxifen, as well as zoledronic acid. Further metastatic bone lesions developed in the spine and the patient received analgesic radiotherapy (30Gy) to the lumbar spine. Due to progression of bone disease hormonal therapy was switched to anastrozole and then to letrozole.

Four years after the initial diagnosis, the patient presented with diplopia to all gaze directions, exophthalmos and bulb proptosis. Ophthalmologic examination

revealed reduced visual acuity to 4/10 in left eye. A CT and MRI of the orbits and head were performed, both showing a solid, intra-orbital, extra-bulbar, 1.5 × 3 cm mass, occupying the inferior quadrant of the left orbit (Figs. 1–3). Concomitant serum tumor markers elevation together with the imaging findings, were most compatible with metastatic disease in the orbit. A combined chemotherapy treatment with docetaxel 75 mg/m² intravenously on day 1 and capecitabine 1000 mg/m² per os twice daily for 14 out of every 21 days was started. Additionally, the orbital mass was irradiated with the use of a cyberknife image-guided stereotactic radiosurgery system in one session, with a total dose of 1700 cGy being delivered to the tumor with 6MV photons. Eye symptoms resolved almost completely during the following weeks, while there was also a gradual decrease in serum tumor marker levels. An orbital CT was performed 7 months after diagnosis of orbital involvement and disclosed regression of the tumor, measuring 0.6 cm by 1.7 cm (Fig. 4). The patient remains free from ocular symptoms 18 months after stereotactic treatment.

Discussion

We describe a case of orbital metastasis presenting as a relapse of a known, previously treated, metastatic breast carcinoma.

Orbital metastases represent a small but increasing percentage of all orbital tumors, reported in different case studies and series to have an incidence of 1% to 13%. Breast cancer is by far the most common primary site, accounting for 28.5%–58.8% of cases of orbital metastases, followed by lung, prostate, gastrointestinal,

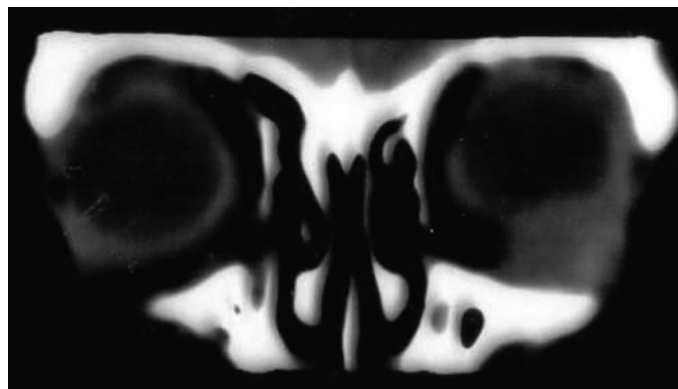


Figure 1. Orbital CT of the patient before treatment for orbital metastasis showing a soft-tissue mass inferior the left bulb.

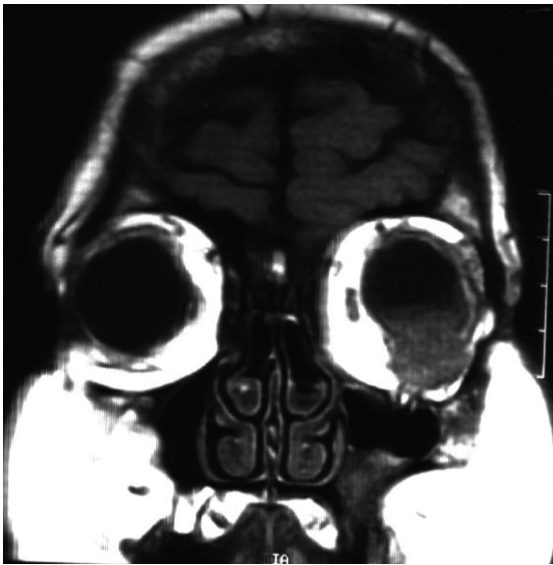


Figure 2. Orbital MRI of the patient before treatment for orbital metastasis showing a T1-weighted orbital tumor, hypointense compared to fat.

kidney and skin (melanoma) cancers.¹⁻⁵ Unilateral disease is the usual presentation while intra-orbital anatomical distribution involves predominantly the lateral and superior quadrants.¹ Orbital metastatic lesions usually present in patients with established diagnosis of disseminated cancer and there is a long medial time interval of 4.5–6.5 years from diagnosis for breast carcinoma. The longest intervals from the diagnosis of primary breast cancer to the presentation



Figure 3. Orbital MRI of the patient before treatment for orbital metastasis showing a T2-weighted orbital tumor, hyperintense compared to fat.

of orbital metastasis are 25 and 28 years respectively.^{6,7} However, in up to 25% of cases, orbital metastasis is the initial finding of a previously undetected primary cancer.^{1,8-12}

Due to a tissue-specific preference of breast cancer to extra-ocular muscle and surrounding orbital fat, diplopia resulting from mobility deficits is a prevalent symptom. Other common symptoms and signs include proptosis, eyelid swelling or visible mass, pain, palpebral ptosis, bulb divergence and blurred vision, caused by infiltration or compression. Enophthalmos is a less common but distinctive sign of orbital infiltration by scirrhous breast adenocarcinoma.^{1,5,13,14} In a recently reported case, orbital metastasis presented as neurotrophic keratitis.¹⁵

Definite diagnosis of an orbital lesion requires an orbital biopsy (either FNA or open biopsy). However, in patients with known metastatic cancer, as in our case, the latter may be avoided if there is a strong clinical and imaging suspicion for metastatic disease. It should only be done in patients with no known previous history of cancer and in patients in whom the orbit is the only site of suspected metastasis in whom having a definite diagnosis would change the overall management of the patient.¹ Metastatic lesions to the orbit usually present as irregularly shaped masses on non-contrast CT which are isodense to muscle. With contrast injection, they show slight enhancement. Orbital bony wall involvement is also a common finding, especially in prostate cancer. On MRI, metastatic disease is usually hypointense to fat on T1-weighted images (T1WI) and hyperintense to fat on T2WI.

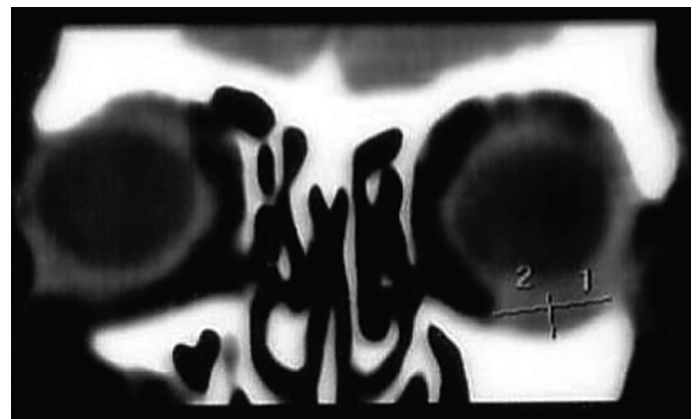


Figure 4. Orbital CT of the patient 7 months after initiation of treatment for orbital metastasis: tumor now measuring 1.7 × 0.6 cm.

Table 1. Summary of case reports of orbital metastases from breast cancer in English literature from 2000 to 2009.

Ref	Histology	Age	Extra-orbital metastases	Intra-/para-orbital localisation	Treatment	Evolution
6	ductal	83	bone, muscles, lymph nodes, pancreas	L inferior oblique, L inferior rectus, R lateral, superior, medial rectus muscles	L transconjunctival orbitotomy (diagnostic), letrozole	partial improvement in ocular motility, decrease in systemic metastatic burden
7	lobular	73	laterocervical and axillary lymph nodes (subsequent)	extrinsic muscles and the surrounding tissues	tamoxifen	modest improvement of the clinical picture
25	NA	66	hepatic, bone	R diffuse infiltrative soft-tissue mass surrounding the orbit, the frontal sinus, and the dura of the brain	CT (trastuzumab, docetaxel, tegafur, cyclophosphamide)	the eyelid edema disappeared post-cycle 1, the previous infiltrating soft tissue in the orbit and tumor disappeared, shrinkage in the frontal sinus
22	lobular	54	multiple locations	bilateral extraocular muscles	high dose RT, HT, CT	persistence of diplopia
26	ductal	70	ethmoid sinuses, cavernous sinus	mass in the posterior orbit	anticancer treatment not otherwise specified	death 2 months post-1st symptoms from diffuse brain infiltration
27	NA	60	none	choroidal mass	RT (44Gy), anastrozole	total disappearance of lesion, normal vision 24 months post-therapy
28	ductal	30	none	lateral rectus muscle, 2.7 × 1.6 × 0.9 cm mass	R lateral orbitotomy (diagnostic), RT, tamoxifen	no evidence of local recurrence
29	NA	36	central nervous system	both optic nerves, mass lateral to the lateral rectus of the L orbit	corticosteroids, RT (4000 cGy to the orbits, 3500 cGy to the whole brain), VP-16, L optic nerve sheath fenestration	modest improvement in vision and resolution of disc edema
30	lobular	58	none	lower eyelids and deeper tissues limited by the bony orbital rim	NA	NA
15	ductal	81	none	extraconal mass adjacent to the L superior orbital rim extending to the soft tissues	RT	NA
8	lobular	53	none	intraorbital, intraconal infiltrative process of the medial wall of the L orbit	NA	NA
18	ductal (case 1), ductal (case 2)	82, 67	none (case 1), bone (case 2)	mass at the level of the internal wall on the R orbit following the line of the internal rectum muscle, adhered to the eye globe (case 1), mass almost covering the whole L orbit and compressing the eye globe	HT (case 1), none (case 2)	stable 5 years post-diagnosis (case 1), death 6 months post-diagnosis from other reasons (unrelated to her disease) (case 2)



31	NA	52	NA	extraocular muscles	NA	NA	NA
10	ductal	50	bone marrow	superior medial fat space of the R orbit, upper eyelid	RT (30Gy) to the R orbit, high-dose CT with FAC (5-fluorouracil, doxorubicin, cyclophosphamide) followed by autologous bone marrow rescue	pain and diplopia completely resolved, 10-year survival	
12	NA	75	none	retrobulbar fat, medial rectus muscle	CT with cyclophosphamide, doxorubicin, HT (letrozole), split-beam RT (30Gy)	full range of ocular motion	
17	lobular	35	mediastinum, bones	R lateral rectus, levator muscle of R upper lid, frontal sinuses	CT	death 10 days post-diagnosis	
21	NA	59	NA	17 × 13-mm tumor in the R orbit, posterior and medial to the bulb	stereotactic radiation (45Gy), vinorelbine	marked improvement of local symptoms for 10 months	
9	lobular	63	none	bilateral diffuse infiltration of extraocular muscles, extra-intraconal compartments	NA	NA	
23	ductal	57	axillary, mediastinal, retroperitoneal lymphadenopathy	choroidal mass	trastuzumab, vinorelbine	resolution of visual disturbance 1 month post-diagnosis	
24	NA	NA	none	medial upper quadrant of the L orbit, (1st) lateral region of the L lower eyelid (2nd), progression of the tumour in the eyelid (3rd)	RT 5Gy (1st), surgery, RT 30Gy (2nd), local hyperthermia (3rd)	complete tumour regression maintained for 21 months, dry left eye	
11	lobular	61	none	retrobulbar mass	RT (3000rad) to the L orbit, tamoxifen	no recurrence 8 years post-diagnosis	
13	lobular	52	none	no metastatic lesion has been found in her orbit	no change of treatment, patient already on tamoxifen, continuous review	stable for 2 1/2 years	
32	NA	40	none	R choroid	RT, CT, acetazolamide	clinical and radiological remission	

Abbreviations: NA, not-available; R, right; L, left; CR, complete response; PR, partial response; CT, chemotherapy; RT, radiation therapy; HT, hormone therapy.



This appearance may help to differentiate it from an orbital pseudotumor, which is usually isointense to fat on T2WI. When hyperintense lesions are seen on T1WI, a very vascular metastasis (e.g. thyroid, renal) or melanoma metastasis should be suspected.¹⁶ The combined involvement of the orbit and adjacent structures, such as the paranasal sinuses, is a rare condition revealed by imaging studies.¹⁷

In addition to metastasis, differential diagnosis of an orbital process should include inflammatory lesions, benign tumors (such as hemangiomas) and lymphoproliferative disorders. Idiopathic orbital inflammatory syndrome (IOIS or orbital pseudotumor), sarcoidosis and Wegener granulomatosis are inflammatory conditions that may present in similar manners. Given that inflammatory signs are common in orbital metastases from breast cancer, they could be misdiagnosed as thyroid orbitopathy, cellulitis, myositis, scleritis or endophthalmitis. The distinguishing feature of orbital metastases is a rapid onset and progressive course with combined motor and sensory deficits, non-responding to antibiotics or steroids.^{18,19}

Treatment for orbital metastases is inevitably palliative, given that hematogenous spread of cancer to the orbit is a sign of systemic disease and involvement of other sites. Surgical intervention is generally not recommended, unless it is performed for diagnostic purpose (biopsy) in patients with no previous history of cancer^{20–28} or as palliation (tumor resection or enucleation) in cases of unmanageable local symptoms.¹

The main treatment option is radiotherapy, with high rates (60%–80%) of clinical improvement of local symptoms and vision. External-beam irradiation is the most common and accessible modality, with a total dose of 20–40 Gy delivered in fractions over 1–2 weeks.^{1,5}

Stereotactic radiation therapy (SRT) has recently evolved as an alternative modality, in an effort to apply high doses of radiation to a well-defined volume with steep dose gradients outside the target volume.²⁰ A complex mixture of image-guided radiation using CT, MRI and stereotactic localization defines stereotactic radiosurgery (SRS). Although not available in all treatment settings, SRT and SRS require a shorter treatment course compared with external-beam irradiation, thus contributing to a better quality of life.²⁰ To our knowledge, only two other

cases of orbital metastases from breast cancer treated with the stereotactic method have been reported.²¹

Due to the fact that most patients have concomitant progressive systemic disease, chemotherapy followed by hormone therapy in cases of hormone-sensitive tumors is indicated in patients with good performance status. A contribution to the palliative result obtained by radiotherapy can be expected with systemic treatment.²² In contrast, responses with systemic chemotherapy alone have been reported in choroidal metastases. In one recent case of choroidal metastasis of breast cancer a dramatic response was observed with trastuzumab and vinorelbine.²³

The combination of radiotherapy, delivered in eight fractions of 4Gy, and hyperthermia was recently proposed as a treatment for patients with recurrent breast cancer in the orbital region. Local hyperthermia treatment feasibility in the orbit is restricted by the depth of the tumor from the skin and the need to avoid microwave-induced high temperatures reached in the lens.²⁴

Prognosis of patients with metastatic orbital tumors is rather poor, with a median survival ranging from 22 to 31 months for breast cancer.^{1,5} Nevertheless, rare cases of long-term survival after the diagnosis of breast cancer presenting as an orbital mass have been reported.^{10,11,18}

Table 1 summarises recent cases of orbital metastases from breast cancer reported in English literature. Oncologists and ophthalmologists should be vigilant for the observation and interpretation of symptoms and signs compatible with ocular disease in patients with an established diagnosis of breast cancer. A combination of local and systemic treatments may help preserve vision and patients' quality of life.

Disclosures

The authors declare no conflicts of interest related to this article.

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