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Case Report
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Unusual Extraocular Muscles Involvement from Ductal Breast Carcinoma: A Case Report with Literature Review

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Abstract

The metastatic involvement of the orbit in malignant tumors is a very rare diagnosed condition. Primary breast cancer is incriminated in the majority of these cases. We describe a case of a right orbital metastasis in a 41 year old lady, previously diagnosed stage IV breast cancer with extensive lung and bone metastases, presenting with six nerve palsy. A CT scan and Magnetic Resonance Imaging (MRI) of brain and orbits revealed a right orbital metastatic lesion involving the medial rectus and inferior oblique muscles. At the time of presentation of her eye symptoms, she was on chemotherapy with docetaxel, trastuzumab and pertuzumab. Eye symptoms regressed almost completely during the following months. A follow up orbital CT scan was performed, showing significant regression of the tumor. A review of the literature and the current case, reveal that the appearance of eye symptoms in patients with a history of breast cancer should always be investigated with a consideration of ocular metastatic disease.

Keywords: Orbital metastases; Breast cancer; Ductal carcinoma; Orbit

Introduction

Breast cancer is the most frequent cancer site among women in Saudi Arabia, with its incidence continuing to increase rapidly during recent decades, and it can occur in women at an early age [1]. It represents 28% of all newly diagnosed cancer sites among Saudi women [1]. Such malignancy can metastasize to many sites, but the orbit is an exceptional location and a comparatively sparse site of distribution among the ocular structures [2,3]. Orbital metastases could be the first presentation of an unknown primary tumor [2,3] mostly the Invasive Lobular variant of the breast Carcinoma (ILC), as the orbit represents an area rich in fat niche which may entice disseminated ILC cells [3]. However, the dispersion of the Invasive Ductal variant of breast Cancer (IDC) into the orbit is limit due to the expression of E-cadherin [3]. In this review, we report a case of medial rectus and inferior oblique muscles metastases observed in a 41 year old lady, with metastatic breast cancer. Additionally, we analyzed almost all the previous reported cases of these infrequent however non rare metastases, through the French and English literature.

Case Presentation

We represent a case of 41 year old Saudi lady, with a primary history of ductal adenocarcinoma of the right breast with six nerve palsy. Initial diagnosis was made two months previously and it was initially metastatic to the lung and the bones. Clinical examination revealed large palpable mass in the right breast, measuring about 5 cm. Breast biopsy done and the breast carcinoma was confirmed histopathologically. Workup Staging included CTs of thorax and abdomen, as well as a bone scan showed multiple lung nodules and bony lesions consistent with metastases. The patient developed a back pain and weakness of her lower limbs, due to extensive spinal metastatic disease with T3 pathological fracture causing cord compression. Palliative radiotherapy to spine was performed. The patient was also started on chemotherapy with docetaxel, trastuzumab and pertuzumab.

Two months after, the patient presented six nerve palsy, with diplopia and headache. A CT scan and MRI of the orbits and head were performed, showing infiltrative tumor seen involving the right medial rectus muscle, worrisome of metastasis (Figure 1). Another focal enhancement is seen at the insertion of the right inferior oblique muscle with the globe, representing another lesion. At this time, the patient was already on chemotherapy. Eye symptoms regressed almost completely during the following months. A follow-up orbital CT was performed 3 months after diagnosis of orbital involvement, showing significant regression of the tumor (Figure 2). Currently, the patient remains on palliative systemic therapy, tolerating treatment reasonably well, part from significant

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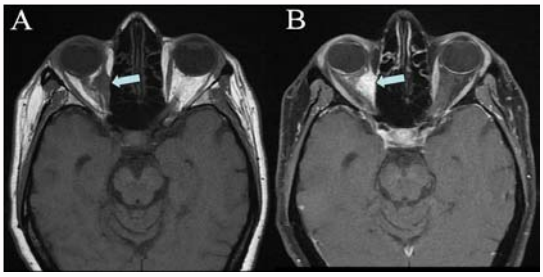

Figure 1: A) T1- MR image depicting the lesion at the time of first diagnosis, as an infiltrative solid nodule (arrow) located on the right orbit involving the medial rectus muscle. B) Post-contrast fat-suppressed T1 image shows enhancement of the lesion (arrow).

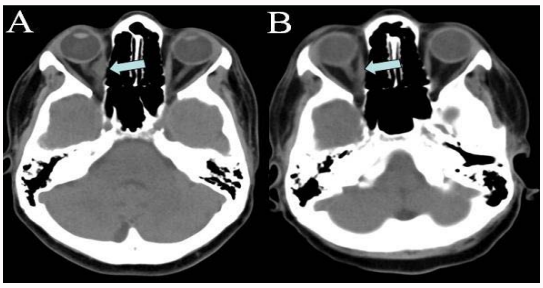

Figure 2: A) Initial axial CT scan images demonstrate an infiltrative solid nodule (arrow) located on the right orbit involving the medial rectus muscle. B) Axial CT scan images show further shrinkage of the lesion (arrow) after the chemotherapy.

bone marrow suppression.

Discussion

Orbital metastases represent an infrequent but increasing percentage of all orbital tumors, reported in the literature to have an incidence of 1% to 13%. The breast cancer (mainly the ILC) accounts by far the most frequent primary cause, with 28% to 58% of cases of orbital metastases, followed by lung, prostate, gastrointestinal, kidney and melanoma [4]. Extraocular muscles involvement could represent the first manifestation of other underlying unknown malignancies, such as renal cell carcinoma [2,4]. In this review, we analyzed all the previous cases of extraocular muscle metastases from breast cancer reported in the English and the French literature, from 1899 until 2019. The total of the cases was 78 patients with extraocular muscle metastases from breast cancer. Literature review produced 77 patients [2,5-58], in addition to our case. Unluckily, a lot of reviewed studies did not provide age, histological type of breast cancer, treatment modality, and overall survival data.

The mean age of our provided cases was 50.7 years (range 31 to 83). Twenty patients had extraocular muscle metastases from ILC whereas in 14 patients (including our case) IDC was the primary source. Five patients had an undifferentiated BC a one patient had poorly differentiated BC. Unfortunately, there was no histology detail in the rest of patients.

The orbital involvement was unilateral in 48 patients, including the present case, and bilateral in 13, whereas in 16 women laterality was not identified. The mono-treatment modality was founded on surgery in 4 patients, radiotherapy in 6 patients, chemotherapy in 4 patients and hormonal therapy in 2 patients. In the other hand, combined treatments were used in 20 patients, as follows: Chemo-radiotherapy in 12, chemo-radiotherapy plus hormonal therapy with Selective Estrogen Receptor Modulators (SERMs) or Aromatase Inhibitors (AI) in 2, radiotherapy and hormonal therapy in 5 and radiotherapy and surgery in one case. For the present case, we selected chemotherapy with docetaxel, trastuzumab and pertuzumab.

Unfortunately, again the lack of data according to the clinical outcome was a limitation of our study. The most outcomes were the partial response with partial improvement of the eye symptoms and partial regression of the tumor. In Table 1, we try to provide the collected data with the clinical and histological types, treatments, outcomes of almost all the published cases included in the literature review. Unilateral disease is the most common presentation, with predominantly involvement within the lateral and superior quadrants [4]. Orbital metastatic lesions usually occur in patients with previously established diagnosis of advanced metastatic cancer, after a long medial time interval of 4.5 to 6.5 years from the initial diagnosis for breast carcinoma [4,20]. The longest intervals from the baseline status and the presentation of orbital metastasis are 25 and 28 years respectively [4,20]. However, orbital metastases could be the initial presentation of unknown primitive, in up to 25% of cases [4,30,34].

The common eye symptoms include diplopia, which is the prevalent symptom, followed by proptosis, pain, eyelid swelling or visible mass, ptosis, bulb divergence and blurred vision, caused by infiltration or compression [2,4]. The final proof of an orbital lesion requires histological proven by an orbital biopsy (either FNA or open biopsy). However, in patients with well-established metastatic cancer, as in our case, the latter may be avoided. It should only be reserved for patients with unknown history of cancer and in patients in whom the orbit is the only site of suspected metastasis.

Suspected metastatic lesions to the orbit usually present as irregularly soft tissue masses on non-contrast CT, isodense to the muscle, with slight enhancement after contrast injection [4]. On MRI, metastatic lesions present usually as hypointense to fat on T1-Weighted Images (T1WI) and hyperintense to fat on T2WI [4]. This hypersignal in T2 may help to differentiate metastatic lesion from an orbital pseudotumor, which is usually isointense to fat on T2WI [35]. In all cases, treatment for orbital metastases is necessary palliative, given that hematogenous spread of cancer to the orbit is worrisome of systemic disease and involvement of other sites [2,24]. Surgical intervention is generally not advised, unless it is performed for diagnostic purpose (biopsy) in patients for need of histological proof of orbit metastases or as palliation (tumor resection or enucleation) in cases of uncontrolled local symptoms [4,24].

The principal treatment option is radiotherapy, with very high rates (60% to 80%) of clinical improvement of local symptoms and vision. The most common modality is the external-beam irradiation, with a total dose estimated at 20 Gy to 40 Gy delivered in fractions over one to two weeks [2-5]. In case of the patients has concomitant progressive systemic disease, chemotherapy followed by hormone therapy is indicated, in cases of hormone-sensitive tumors, if there is good performance status [4]. In the other hand, the responses with systemic chemotherapy alone have been noted in case of choroidal metastases [38]. Recent articles proposed the combination of radiotherapy, delivered in eight fractions of 4 Gy, and hyperthermia, as a treatment for recurrent breast cancer in the orbital region; however, local hyperthermia treatment feasibility is limit in the orbit by the depth of the tumor from the skin and the need to avoid microwave-induced high temperatures arrived to lens [39].

Table 1: Clinical and histological data of patients with extraocular muscles metastases from BC. Literature review.

Year of publication	ref	age	histology	Intra-/para-orbital localization	Treatment	Evolution
2019	[2]	44	lobular	Right IR	RT (40 Gy)+Fulvestrant+Palbociclib	Total regression of the orbital lesion at PET/TC without improvement in eyesight.
2019	[5]	60	Ductal	Left IR	RT+ Fulvestrant+Palbociclib	Total regression
2017	[6]	47	lobular	MR	NS	NS
		63	lobular	NS	NS	NS
		67	lobular	MR, LR	NS	NS
		68	Not biopsied	Right LR, IR	NS	NS
		64	lobular	Rectus muscle	NS	NS
2017	[7]	47	ductal	EOM bilaterally	CT	Death of the patient
2016	[8]	NS	NS	NS	NS	NS
		NS	NS	NS	NS	NS
		NS	NS	NS	NS	NS
		NS	NS	NS	NS	NS
		NS	NS	NS	NS	NS
		NS	NS	NS	NS	NS
2016	[9]	66	Ductal	Four recti unilaterally	Anastrozole+RT(35 Gy-40 Gy)	NS
2015	[10]	NS	Ductal	Right LR, left IR, LR	Whole brain RT	Partial response
2015	[11]	43	Ductal	IR, LR	RT	Improvement
2015	[12]	NS	Undifferentiated	IR	NS	NS
2015	[13]	49	NS	Right IR	RT+CHT	Partial response
		45	NS	Four recti bilaterally right SO	RT+CHT	Partial response
2014	[14]	84	Undifferentiated	Right infiltrative soft-tissue mass surrounding the orbit	RT+CHT	Partial response
2012	[15]	73	Lobular	IR	RT+CHT	Improvement
2011	[16]	61	Lobular	Right SR, LR, IR, left SR	RT (54 Gy)+Tamoxifen	Complete resolution at TC/ PET, improvement of the ocular motility and resolution of diplopia but mild bilateral ptosis
2009	[17]	NS	NS	NS	NS	NS
		NS	NS	NS	NS	NS
		NS	NS	NS	NS	NS
		NS	NS	NS	NS	NS
		NS	NS	NS	NS	NS
		NS	NS	NS	NS	NS
2008	[18]	83	Ductal	Right LR, MR, SR	Letrozole	Partial response
2008	[19]	50	Lobular	All EOM bilaterally	RT (47.5 Gy)+Anastrozole+CHT (vinorelbine and mitomycin)+Local Hyperthermia.	Diplopia partial amelioration
2008	[20]	73	Lobular	All EOM bilaterally	tamoxifen	Partial response
2008	[21]	66	NS	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
2008	[22]	70	Ductal	Mass in the posterior orbit	NS	death 2 months post-1st symptoms from diffuse brain infiltration
2008	[23]	60	NS	Choroidal mass	RT (44 Gy), anastrazole	total disappearance of lesion, normal vision 24 months post therapy
2007	[24]	30	Ductal	lateral rectus muscle, 2.7 cm × 1.6 cm × 0.9 cm mass	R lateral orbitotomy (diagnostic), RT, tamoxifen	no evidence of local recurrence
2007	[25]	36	NS	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

2007	[26]	45	NS	NS	NS	NS
2007	[27]	75	Lobular	EOM bilaterally	NS	NS
2006	[28]	58	Lobular	lower eyelids and deeper tissues limited by the bony orbital rim	NS	NS
2006	[29]	81	Ductal	extraconal mass adjacent to the L superior orbital rim extending to the soft issues	RT	NS
2006	[30]	53	Lobular	intraorbital, intraconal infiltrative process of the medial wall of the L orbit	NS	NS
2006	[31]	82	Ductal	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	HT	stable 5 years post-diagnosis
		67	Ductal	mass almost covering the whole L orbit and compressing the eye globe	NS	death 6 months post-diagnosis from other reasons (unrelated to her disease)
2006	[32]	52	NS	EOM	NS	NS
2005	[33]	50	Ductal	superior medial fat space of the R orbit, upper eyelid	RT (30 Gy) to the R orbit, high-dose CT with FAC (5-fluorouracil, doxorubicin, and cyclophosphamide) followed by autologous bone marrow rescue.	pain and diplopia completely resolved, 10-year survival
2005	[34]	75	NS	retrobulbar fat, medial rectus muscle	CT with cyclophosphamide, doxorubicin, HT (letrozole), split-beam RT (30 Gy)	full range of ocular motion
2004	[35]	35	lobular	Right LR	CT	death 10 days post-diagnosis
2004	[36]	59	NS	17 mm × 13 mm tumor in the R orbit, posterior and medial to the bulb	stereotactic radiation (45Gy), vinorelbine	Marked improvement
2004	[37]	63	Lobular	EOM bilaterally	NS	NS
2004	[38]	57	Ductal	Choroidal mass	trastuzumab, vinorelbine	resolution of visual disturbance 1 month post-diagnosis
2004	[39]	NS	NS	medial upper quadrant of the L orbit, (1st) lateral region of the L lower eyelid (2^{nd}), progression of the tumour in the eyelid (3^{rd})	RT 5 Gy (1^{st}), surgery, RT 30 Gy (2^{nd}), local hyperthermia (3rd)	Complete regression
2004	[40]	53	NS	LR	RT	Complete recovry
2002	[41]	61	Lobular	Retrobulbar mass	RT (3000 rad) to the L orbit, tamoxifen	no recurrence 8 years post-diagnosis
2001	[42]	40	NS	R choroid	RT, CT, acetazolamide	clinical and radiological remission
2000	[43]	79	NS	Left MR	Orbital surgery	NS
1999	[44]	NS	Lobular	MR and IR bilaterally	NS	NS
1998	[45]	47	Lobular	ALL EOM Bilaterally	Surgery	NS
1991	[46]	47	Lobular	Right IR and IO	NS	NS
1991	[47]	64	NS	Right MR, left MR, LR	Tamoxifen+RT (35 Gy)+CHT	No response
1990	[48]	71	NS	MR and LR Bilaterally	refused	NS
1987	[49]	65	NS	Right SO	RT	Partial response
1987	[50]	NS	NS	Left MR	NS	NS
		NS	NS	Right LR	NS	NS
		NS	NS	LR Bilaterally	NS	NS
1984	[51]	66	Lobular	Left MR	NS	NS
		57	Lobular	Left SR, LR	NS	NS
1984	[52]	56	NS	Right LR	CHT+RT	NS
		55	NS	Left MR	CHT+RT	NS
		53	Undifferentiated	Left SR	CHT+RT	NS
1981	[53]	62	NS	Left LR	NS	NS
1979	[54]	40	PD	Left LR	RT+CHT	Complete regression
1979	[55]	NS	NS	MR	Surgery	ns
1974	[56]	58	Undifferentiated	NS	NS	NS
			Undifferentiated	NS	SURGERY	NS
1960	[57]	72	NS	All OEM Bilaterally	NS	NS
1899	[58]	58	NS	Right MR, IR	NS	NS

EOM: Extra Ocular Muscle; NS: Not Specified; PD: Poorly Differentiated; MR: Medial Rectus; SR: Superior Rectus; LR: Lateral Rectus; IR: Inferior Rectus; SO: Superior Oblique; IO: Inferior Oblique; NT: No Treatment; RT: Radiotherapy; CHT: Chemotherapy

Conclusion

A review of the literature and the current case, reveal that the appearance of eye symptoms in patients with a history of breast cancer should always be investigated with a consideration of ocular metastatic disease. Eventual combination of adequate local and systemic treatments may help preserve both vision and patients' quality of life.

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