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Orbital infiltration mimicking pseudotumor as first manifestation of cancer of unknown primary

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Abstract

Orbital metastases are rarely the first and sole presenting feature of distant carcinoma and extremely rare as the presenting sign of Cancer of Unknown Primary (CUP).

We report the case of a previously healthy woman who presented with diplopia and left orbital pain and underwent contrast enhanced orbit MRI: Imaging findings were interpreted as left orbital pseudotumor, so she began a treatment with steroids.

Despite the treatment, the patient's symptomatology did not improve. After 2 months, she noticed a left axillary lymphadenopathy; therefore she started a series of investigations which turned to be within normal limits. A Positron Emission Tomography (PET) and a total body computed tomography with contrast medium injection were executed, showing a left axillary lymphadenopathy with pathologic FDG uptake and the left orbital infiltration without pathologic FDG uptake. The axillary lymphadenopathy was biopsied and turned out to be a nodal metastasis of adenocarcinoma. Four months after the onset, the ocular symptoms still persisted, therefore the hypothesis of orbital metastasis was considered and a left orbital biopsy was executed, revealing microfoci of carcinoma compatible with metastasis from breast primary tumor.

After a while a follow-up contrast enhanced orbit MRI was executed showing a mild increase in retrobulbar fat tissue infiltration.

The appearance of an orbital metastasis as first and sole manifestation of a breast cancer is extremely rare. Breast carcinoma is the most common primary source of orbital metastases, followed by prostate, lung, and melanoma.

From a radiological point of view orbit CT and MRI can show the presence of a mass or a retrobulbar infiltration, which can involve one or more extra ocular muscles; certain diagnosis is not possible on imaging. Therefore, in a female patient with suspected orbital pseudotumor with no response to steroids, orbital biopsy or fine needle aspiration of any mass should be considered recommended.

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Introduction

Orbital metastases are rarely the first and sole presenting feature of distant carcinoma and extremely rare as the presenting sign of Cancer of Unknown Primary (CUP). When orbital metastases present in patients without history of tumors, they can be a diagnostic problem and be misunderstood as pseudotumor.

We report the case of a previously healthy woman who presented with diplopia and left orbital pain and underwent contrast enhanced orbit MRI. Her symptoms and imaging findings were initially diagnosed as orbital pseudotumor and treated with steroids. However, 2 months later, she developed a left axillary lymphadenopathy, and began a series of investigations, including the biopsy of the intraorbital fat tissue.

Case description

A 56 year old female patient presented with a sudden onset of left orbital pain and diplopia. The pain was subacute, worsened by ocular movements. Ocular examination, including visual acuity, pupillary light reflex and ocular motility, was within normal range.

Patient's medical history was unremarkable and no other symptoms were present. Neurological examination did not show any focal neurological deficit. Laboratory tests, including C reactive protein, white blood cells, and thyroid hormones were within normal range. The patient executed contrast enhanced orbital MRI: Imaging findings were interpreted as left orbital pseudotumor (Figure 1,2) and a treatment with prednisone was prescribed (1 mg/kg/day per os for 1 week, then every other day for 5 weeks, followed by a progressive dose reduction).

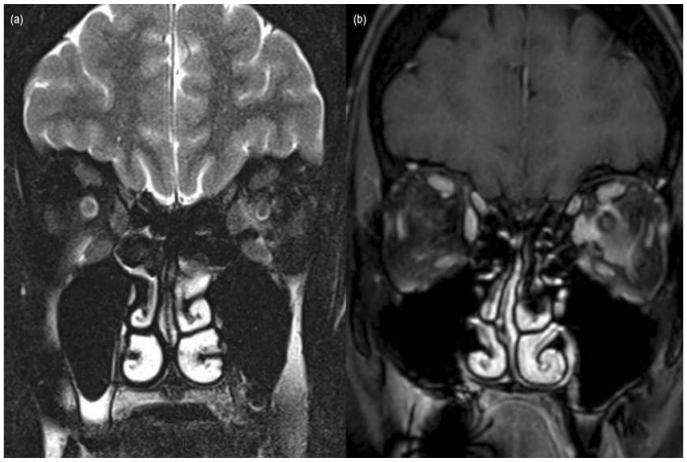

Figure 1: Orbital MRI
(a) coronal T2 weighted sequence with fat saturation showing infiltration of the retro-orbital fat tissue surrounding the left optic nerve.
(b) coronal T1 weighted sequence with fat saturation post contrast medium injection showing postseptal infiltration with enhancement of the retro-orbital fat tissue surrounding the left optic nerve and mild thickening and contrast enhancement of the medial rectus muscle.

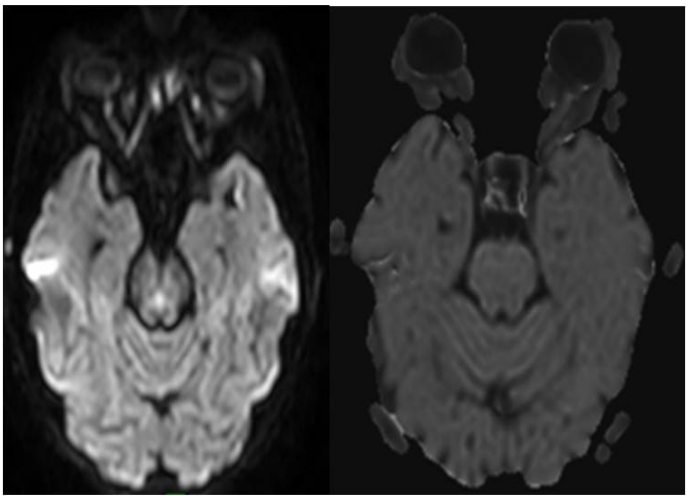

Figure 2: Orbital MRI:
(a) diffusion weighted imaging (DWI; b=1000 s/mm²): no significant signal hyperintensity corresponding to diffusion restriction is visible.
(b) ADC map: no areas of restricted diffusion are visible in the left orbit.

Despite the treatment, the patient's symptomatology did not improve. After 2 months, she noticed a left axillary lymphadenopathy, therefore she started a series of investigations: Breast clinical examination, mammography, breast ultrasound and contrast enhanced breast MRI: All these investigations were within normal limits. A Positron Emission Tomography (PET) and a total body computed tomography with contrast medium injection were executed, showing a left axillary lymphadenopathy with pathologic FDG uptake and the left orbital infiltration (Figure 3) without pathologic FDG uptake.

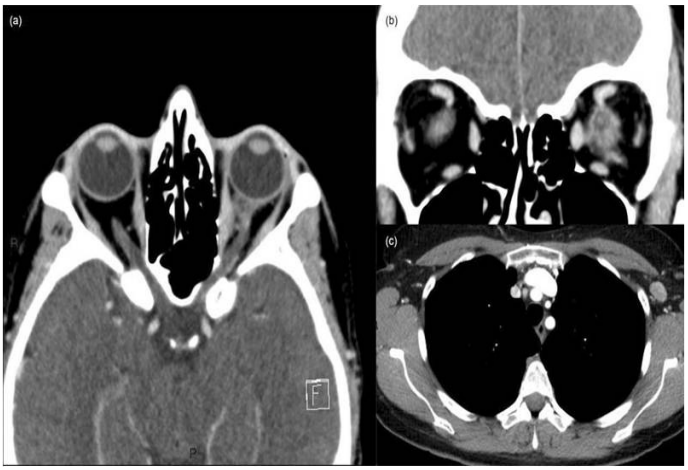

Figure 3: Total body CT with contrast medium
(a) axial orbit CT post contrast medium injection and (b) coronal MPR reconstruction: mild thickening and contrast enhancement of the medial rectus muscle; infiltration of the retro-bulbar fat tissue not dissociable from the optic nerve.
(c) chest CT with contrast medium injection. Presence of a pathologic lymphnode in the left axilla.

The axillary lymphadenopathy was biopsied and turned out to be a nodal metastasis of adenocarcinoma with diffuse growing pattern, with small mucinous type cellular component, according with breast, endometrial or ovarian primary. Endovaginal ultrasound and hysteroscopy executed in order to exclude a uterine/ovarian primary were unremarkable.

Four months after the onset, the ocular symptoms still persisted, therefore the hypothesis of orbital metastasis was considered and a left orbital biopsy was executed, revealing microfoci of carcinoma compatible with metastasis from breast primary tumor positive for estrogen (ER:75%) and progesterone (PgR:60%) receptors. The patient started chemotherapy (5-fluoruracil, epirubicin, cyclophosphamide, docetaxel).

45 days after the execution of the orbital biopsy, a follow-up contrast enhanced orbit MRI was executed, showing a mild increase in retrobulbar fat tissue infiltration (Figure 4).

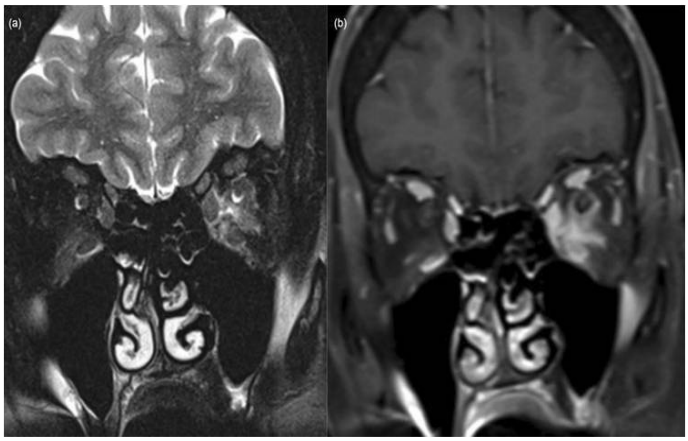

Figure 4: Orbit follow up MRI
(a) coronal T2 weighted sequence with fat saturation and
(b) coronal T1 weighted sequence with fat saturation post contrast medium injection showing slight increase of retro-orbital fat tissue infiltration.

During a follow up of 1 year, no palpable mass become identifiable in the breast and the mammography and breast US executed after 12 months from the onset of the symptomatology were still unremarkable.

Discussion

To the best of our knowledge no data regarding the incidence of orbital metastases in breast CUP syndrome has been reported. Orbital metastases can occur in patients with breast cancer in 0.2% of cases, but about the 80% of these present in patients with a known history of breast carcinoma, usually after 40-70 months from the diagnosis of the primary cancer, but they can also occur as late as 20-25 years after the diagnosis of the primary cancer [1], therefore the appearance of an orbital metastasis as first and sole manifestation of a breast cancer is extremely rare [2]. Our patient had no history of disease and all her breast examinations, including contrast enhanced MRI, were unremarkable.

Breast carcinoma is the most common primary source of orbital metastases, followed by prostate, lung, and melanoma; the choroid is a frequent location of metastases, while the orbit is quite rare [3]; orbital metastases occur most commonly in the 5th decade of life, are mostly unilateral, but they can also be bilateral in 15 % of cases; metastases from breast cancer involve most frequently the right side, while other types of metastases are equally distributed. The primary tumor is typically diagnosed long before the appearance of orbital metastases, but in a small rate of patients, orbital metastases may be the presenting manifestation [4], also in cases of breast cancer [5-10].

Ocular metastases can occur with different symptoms and signs including pain, mass effect, ptosis, enophthalmos, visual problems, and impaired extraocular movements [11]; the different manifestations can be linked to the various histologic types of the lesions. Scirrhous carcinoma with a high collagen component may cause exophthalmos, ocular palsy, blepharoptosis, due to a scar retraction mechanism [12-13]; lobular carcinoma tends to infiltrate extraocular muscles and is more frequently associated with diplopia [14], but it can also occur with pain, ptosis, and ophthalmoplegia [15].

Orbital metastases can have variable imaging appearances [16]. From a radiological point of view, the case described by Gupta et al [5] was similar to ours and showed a thickening of the left medial and inferior extraocular muscle and infiltration with enhancement surrounding the optic nerve. After the onset of ocular symptoms, an irregular breast mass was found.

Lell et al [6] presented a case of a 63-year-old woman with bilateral swelling of eyelids and impaired eye movements; her CT showed diffuse infiltration of both intra and extraconal compartments and infiltration of the extraocular muscles. A palpable breast mass of 5 x 5 cm was identifiable at the onset of ocular symptomatology.

Wolstencroft at al [7] reported a case of orbital metastasis due to interval lobular carcinoma that was first misdiagnosed as orbital lymphoma: CT and MRI showed an intraconal and extraconal mass extending from the apex. In that case, the identification at ultrasound of a small breast lesion and a fine needle aspiration helped a correct diagnosis of metastatic lobular carcinoma. The patient described by Francone [8] et al presented with right swelling of the lower orbit and executed an orbit CT showing thickening of periorbital soft tissues. Imaging findings were first interpreted as a lymphoproliferative process, but, together with orbital symptoms, the patient has a palpable breast mass which was submitted to fine needle aspiration, and turned out a poorly differentiated breast carcinoma.

Kadivar et al [9] reported a case of a 53-year- woman with left orbital pain and proptosis; CT proved an intraorbital intraconal mass in the medial part of the orbit that was diagnosed at biopsy as metastasis from a primitive breast cancer. Also this patient showed a right breast mass.

Reeves et al [10] described a patient with left upper eyelid ptosis, red and painful eye, with a history of previous resection of a poorly differentiated uterine adenocarcinoma; her CT showed a diffuse infiltrating mass in the left orbit, extending forward in the lids. The execution of a mammography revealed a suspicious opacity in the left breast. Biopsies of both breast and orbital masses diagnosed a breast infiltrating adenocarcinoma.

In general, orbit CT and MRI can show the presence of a mass or a retrobulbar infiltration, which can involve one or more extraocular muscles [4-10,16]; differential diagnosis between idiopathic inflammation [17,18], lymphomas, reactive lymphoid hyperplasia and metastases is not possible on imaging, particularly because metastases from breast carcinoma can grow along the extraocular muscles and fascial planes and are more irregular-shaped and diffuse, in comparison to other types of metastases that tend to present with nodular enlarge-

ment of the muscles. The execution of diffusion weighted imaging can help the differential diagnosis with lymphoproliferative disorders due to the marked restricted diffusion [19]. Orbital metastatic involvement can also be bilateral in up to 40 % of cases [15], making the diagnosis more difficult, and many cases of orbital metastases can present with inflammatory signs and be misdiagnosed as orbital pseudotumor, especially in absence of a known primary cancer [20].

Therefore, in a female patient with suspected orbital pseudotumor, a series of investigations to exclude breast carcinoma and other possible cancers, thyroid orbitopathy, infections, autoimmune diseases should be performed.

As in our case, orbital biopsy or fine needle aspiration of any mass should be considered especially in cases refractory to steroids [11]: the biopsy is the preferred option when a previous known primary cancer is absent or when the lesion mimics inflammatory or lymphoproliferative disease, while fine needle biopsy (better if under radiological guidance) is the best approach in patients with a known history of primary cancer, or in patients considered high-risk for biopsy [6]. The contribution of histological diagnostic procedures is essential to make a diagnosis.

The treatment for orbital metastasis consists of systemic chemotherapy or hormonal therapy for the underlying cancer with or without local radiation and/or surgical resection [10].

Conclusions

An orbital metastasis can be the primary and sole presentation of a breast cancer, therefore metastatic breast cancer has to be included in the differential diagnosis of orbital infiltration in a woman. It can occur also in the presence of normal breast examination and negative breast imaging.

It can be misdiagnosed as orbital pseudotumor, therefore, in a patient with unclear infiltrative orbital process, biopsy and histopathological examination of the orbital lesion should be considered, especially in cases refractory to steroids.

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