



Case report

Orbital metastasis or idiopathic orbital pseudotumor? A case report from a patient previously diagnosed with primary breast cancer

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ABSTRACT

Introduction: Cancer metastatic to the orbit may be difficult to distinguish from idiopathic orbital pseudotumor at clinical and radiological examination. This case report describes clinical, radiological features, differential diagnosis, and treatment options for orbital neoplasms of unknown origin.

Presentation of case: A 63-year-old woman presented to our Unit because of orbital swelling, ocular pain, globe displacement, conjunctival chemosis, and progressive vision loss. The patient had been seen by an ophthalmologist at another hospital. The initial diagnosis was idiopathic orbital pseudotumor. Steroid therapy did not resolve clinical symptoms. Her medical history held decisive clues: ten years before this presentation she had been diagnosed with double primary breast cancer, invasive lobular breast carcinoma, and invasive ductal breast carcinoma. Orbital biopsy was performed for differential diagnosis.

Discussion: Considering the rapid onset and severity of symptoms, the radiological features of the orbit, and the patient's medical history of breast cancer, orbital metastasis should have been the most likely diagnosis. Orbital biopsy was performed because of the history of multiple primary cancers and because metastatic origin had to be determined to define the best treatment strategy.

Conclusion: Biopsy is necessary under specific circumstances in the diagnosis of orbital metastasis, especially when presentation is ambiguous and when differential diagnosis is challenging. A patient's medical history may hold vital clues to correct diagnosis.

1. Introduction

Orbital metastases (OM) account for 4 to 8 % of orbital neoplasms. In almost 40 % of cases, orbital metastases derive from breast carcinoma [1,2], making breast cancer the most common malignancy to spread to the orbit [2]. It has been vastly observed that breast cancer is a rather heterogenous disease: cancers can differ in biology, responsiveness to therapy, survival rate, and metastatic behavior. The two breast cancer subtypes most often diagnosed are invasive lobular carcinoma (ILC) and invasive ductal carcinoma (IDC). ILC accounts for 10 to 15 % of all breast cancers, while IDC accounts for 50 to 70 %. ILC is known to be less responsive to neoadjuvant therapy than IDC [3]. The risk of death at 10 years is 50 % higher for ILC patients than for those affected by IDC [4]. Finally, the two types of breast cancer metastasize differently to the orbit: a meta-analysis of 72 case reports by Raap et al. found that 15 % of orbital metastases were due to ILC whereas only 3 % were related to IDC

[5]. In addition, ILC has a five times greater propensity to metastasize to the orbit than IDC [2,5]. Regarding unusual metastatic sites, the orbit accounts for 25 %, followed by the stomach (23 %), and the rectum (8 %), demonstrating the peculiar organotropism that ILC has for orbital tissues [5]. While clinical history and imaging findings are sufficient for making a correct diagnosis of orbital metastases in most cases, retrobulbar fat and muscular tissue can cause diffuse enhancement in the absence of a well-defined, clearly recognizable lesion [6]. Idiopathic orbital pseudotumor might be an alternative diagnosis, thus posing a dilemma for diagnosis. Here we present a clinical case of orbital metastasis that spread from a primary double breast cancer. Orbital biopsy was performed to identify the histological origin of metastasis and rule out other alternative diagnoses.

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2. Presentation of case

This case report was written in accordance with SCARE criteria [7]. A 63-year-old Caucasian woman presented at the outpatient section of the Maxillofacial Surgery Unit at our Institution because of swelling of the left orbit with ocular pain and globe displacement that had developed over the past three months. Examination of the left eye was notable for conjunctival chemosis, limitation of ocular movement, and progressive vision loss. The patient had been evaluated by an ophthalmologist at another hospital where a magnetic resonance imaging (MRI) study was ordered to better investigate the case. Based on clinical and MRI findings, the consultant diagnosed an orbital pseudotumor. Analgesics and methylprednisolone were prescribed to treat pain and swelling; after initial relief of symptoms, however, headache, swelling, and pain recurred.

The patient was referred to our attention. Clinical examination of the left orbit disclosed proptosis and globe displacement, limited ocular motility, lid edema, conjunctival injection, and loss of vision (Fig. 1). MR with contrast medium demonstrated proptosis with thickening of extraocular muscles and the ipsilateral lacrimal gland, likely of inflammatory origin (Figs. 2 and 3). Though the most plausible hypothesis was idiopathic orbital pseudotumor, the findings for this etiology were inconclusive. Stronger clues were to be found in the patient's clinical history.

Invasive lobular carcinoma (ILC) of the right breast and invasive ductal carcinoma (IDC) of the left breast had been diagnosed 10 years earlier. The patient had undergone neoadjuvant therapy, then bilateral mastectomy and adjuvant chemotherapy and radiotherapy to the right breast. She had been prescribed Tamoxifen for five years and had been regularly followed up. The current presentation was strongly suggestive of metastasis to the orbit. Surgical biopsy was performed: upper blepharoplasty to dissect the orbit; a skin-muscle flap was created medially and laterally, passing through the orbicularis oculi muscle, and a specimen from the intra-orbital peri-bulbar tissue was taken. The patient received therapy with steroids and antibiotics for 6 days to reduce swelling and risk of infection, respectively.

Histological and immunohistochemical analysis confirmed the diagnostic suspicion of breast cancer metastasis: the pattern of cellular infiltration and the cellular markers (ER 90 %, PgR 50 %, Ki-67 15 %, and HER-2 0) were compatible with infiltrating lobular carcinoma (ILC). Orbital metastasis was identified, and a PET-CT study was performed as required by protocol for the management of orbital metastasis [8]. The PET-CT images showed metastases involving the axial skeleton and the kidney. Owing to the systemic spread of cancer, chemotherapy and metastasis-localized radiotherapy were the treatments of choice. After 9 months of combined systemic and radiation therapy, follow-up MRI scans revealed treatment response at the bone and disease stability in the orbital-periorbital tissues. Ophthalmologic and maxillofacial examinations showed no substantial changes in clinical findings. The patient referred symptom improvement.

3. Discussion

Orbital metastasis exhibits a variety of etiological, clinical,



Fig. 1. Frontal view. Note ptosis and swelling of the left orbit and eyelids.

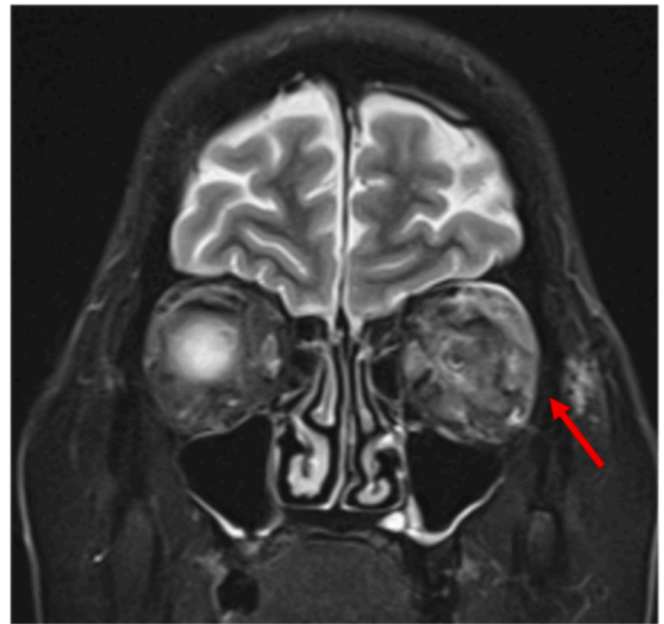


Fig. 2. MR, coronal view.

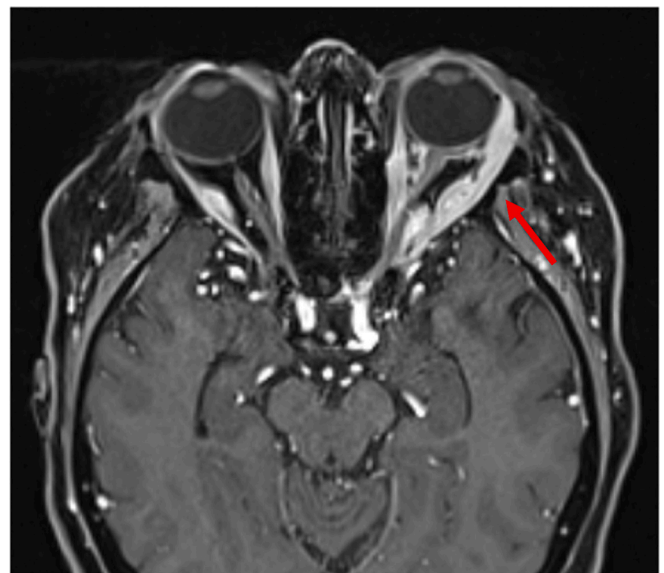


Fig. 3. MR, axial view.

radiological, and histological variations [9], which is why management and treatment of orbital neoplasms often require multimodal strategies and approaches involving diverse medical specialties [10]. The most evident shortcoming in the management of this case is the lack of interdisciplinary discussion at the time of initial examination. While multidisciplinary discussion rarely leads to changes in clinical diagnosis [10], we believe that, given the suspected etiology, clinical discussion by specialists might have saved time and improved diagnostic-therapeutic management of this case.

The initial diagnosis was idiopathic orbital pseudotumor (IOP), which is a benign, non-infectious inflammation of the orbit without identifiable local or systemic causes [11]. IOP usually involves one orbit and presentation may vary in degree of inflammation, fibrosis, and mass effect. Patients usually have a dramatic response to corticosteroid therapy [12]. Mombaerts et al. [13] reported that corticosteroid responsiveness cannot be considered diagnostic for lesions occupying

the orbital space. In the present case, steroid therapy achieved only temporary relief from symptoms, arousing the suspicion of malignancy.

The differential diagnosis will include lymphomas and thyroid ophthalmopathy, the latter of which is often bilateral and spares tendinous insertions. Also, granulomatous disease such as sarcoidosis may resemble orbital metastasis and involve the extraocular muscles, the optic nerve, the optic chiasm, and the lacrimal gland. Differentiating non-neoplastic infiltration from orbital metastasis may be particularly difficult. Orbital metastases behave differently and tend to disseminate to adipose tissue, bone or muscle tissue, depending on where the primary cancer arose: breast, prostate or skin, respectively. In their study involving a sample of Egyptian patients with orbital metastases, Eldesouki et al. found that imaging studies (MR or CT) showed infiltrative patterns in 62.2 % of cases, a mass lesion in 21.6 %, isolated muscle thickening in 10.8 %, and bone metastasis in 5.4% [14]. The radiological findings were ambiguous in the present case: the orbital metastases were similar in appearance to IOP on the scans.

Considering the rapid onset and severity of symptoms, which would have been unusual in orbital benign tumor or lymphoma [15], the radiological features of the left orbit and, above all, the medical history of breast cancer, orbital metastasis should have been the leading diagnostic option since the first consultation. In general, a diagnosis of orbital metastasis is based on these three fundamental elements. In addition, when primary lobular breast cancer is documented in the medical history, the suspicion of orbital metastases is particularly strong, notwithstanding a primary diagnosis made more than 10 years earlier [5].

Fine-needle aspiration biopsy (FNAB) or open biopsy are necessary for final diagnosis [15], especially under certain circumstances. According to the Anderson Cancer Center, FNAB or open surgical biopsy may be performed to confirm clinical suspicion of orbital metastasis: when the lesion suspected to be orbital metastases is the only metastatic lesion found, raising the concern that the lesion differs from orbital metastases; when the patient has undiagnosed primary cancer; when there is a multiplicity of primary cancer and biopsy is performed to identify the metastatic origins; when the immunohistochemical profile of the tumor provides vital information for target therapy. In the present case, open biopsy was performed to obtain a reliable histopathological sample from a patient with a history of double primary breast cancer and negative for cancer during the 10-year follow-up period. The biopsy would have sorted out whether the neoplasm was a metastasis or not and from which tumor (ILC or IDC) the metastasis had spread.

Invasive radical surgery was not considered. Orbital exenteration is rarely necessary in patients with periorbital, conjunctival or primary orbital carcinomas, whereas it may be necessary in patients with multiple recurrences, when multiple eye-sparing treatments fail, and in patients with high T stages [9], when the craniofacial neoplasm is aggressive to such an extent that surgical radicalization is unquestionably beneficial for limiting the risk of recurrence and the need for future re-intervention [1]. Since prognosis in cancer patients is influenced more by systemic control of the disease than by local treatment of metastasis, orbit exenteration may be unnecessary in the treatment of orbital metastases in patients with a history of systemic cancer.

4. Conclusion

Recognizing the clinical presentation and the radiological features of orbital metastases is fundamental for timely diagnosis and correct treatment of patients with an orbital neoplasm of unknown origin. The medical history must never be underestimated. The diagnosis of orbital metastasis may require biopsy under specific circumstances, especially when presentation is ambiguous or when differential diagnosis is particularly challenging.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

Giorgio Barbera: conceptualization, methodology, writing - review & editing; Vittorio Favero: conceptualization, methodology, resources, writing - review & editing; Guido Lobbia: writing - original draft, investigation, writing - review & editing; Riccardo Nocini: conceptualization, methodology, supervision, writing - review & editing. The published version of the manuscript was read and accepted by all authors.

Guarantor

Guido Lobbia.

Research registration number

This case report was not a first in man study.

1. Name of the registry: NO REGISTRY WAS EMPLOYED.
2. Unique identifying number or registration ID: NONE.
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): NONE.

Conflict of interest statement

The authors declare no conflict of interest.

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