

Case Report

# Orbital Metastases as a Manifestation of Breast Cancer: Case Series and Diagnostic Approach

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## Abstract

**Background:** Orbital metastases from breast cancer are uncommon and may present with nonspecific ophthalmologic symptoms, complicating early diagnosis and management. This report highlights the variable clinical presentations and histopathological features observed in three such cases.

**Cases Description:** Three female patients, with a median age of 70.6 years, presented with progressive orbital symptoms. The first case involved ptosis, orbital pain and ophthalmoplegia in a patient without prior cancer history. The second case manifested as ptosis, diplopia and periorbital pain in a patient with a remote history of breast cancer treated 29 years earlier. The third patient, 16 years post-breast cancer surgery, presented with orbital pain exacerbated by horizontal eye movements, diplopia and enophthalmos. Imaging confirmed orbital masses in two cases, and an enlarged extra ocular muscle in the third case. Histopathology revealed lobular breast carcinoma metastases.

**Conclusion:** Presentation may differ in each case and histology of the primary tumour may differ from that of the metastasis. Ophthalmological evaluation should be performed on all patients with known breast cancer and mild ocular symptoms, as early local treatment may help to prevent severe complications.

**Keywords:** Orbital Surgery; Eyelid Mechanical Ptosis; Orbital Tumors; Breast Carcinoma Orbital Metastases; Breast Carcinoma Lobular Histotype

## Introduction

Orbital metastases from breast carcinoma, while relatively uncommon, represent the most frequent source of secondary orbital malignancies in adults. These lesions present a considerable diagnostic challenge owing to their often insidious and nonspecific clinical manifestations that can mimic benign orbital conditions, potentially leading to delays in diagnosis and appropriate treatment.

Breast cancer-related orbital metastases are clinically significant due to both their prevalence and their prognostic implications. They account for approximately 30-60% of all orbital metastases, reflecting a substantial proportion of secondary orbital tumors in clinical practice. Notably, up to 10% of patients may develop orbital involvement within 3 to 8 years following an initial breast cancer diagnosis, frequently coinciding with widespread systemic metastases and suggesting a progression to an advanced

disease stage [1]. In this report, we present three cases of orbital metastases from breast carcinoma, each exhibiting distinct clinical features. These cases were diagnosed and managed within an 11-month period at the Orbital Service of Tiberia Hospital, highlighting the heterogeneity in presentation and the importance of maintaining a high index of suspicion in patients with a history of breast cancer and new-onset orbital symptoms.

### Cases Series

Written informed consent including permission for the use of clinical photographs was obtained from all the study participants. Patients' data have been anonymized and this has not distorted the scholarly meaning. The study was performed in accordance with the tenets of the Declaration of Helsinki.

#### Case 1

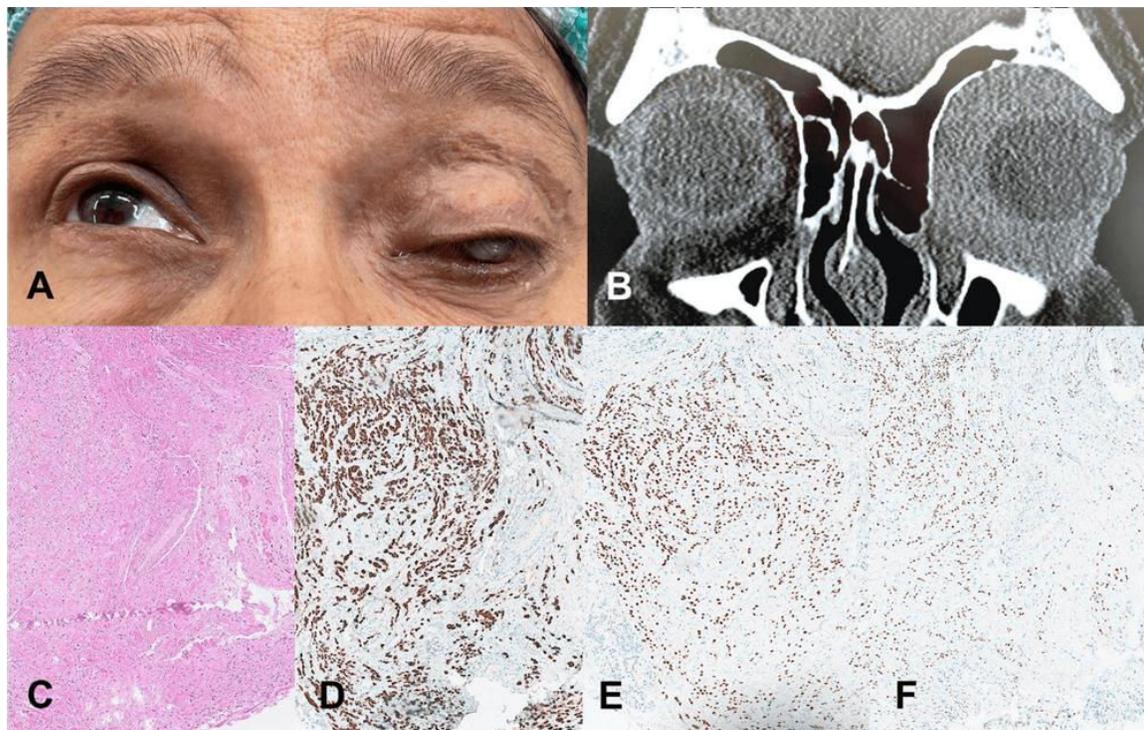
A 62-year-old woman presented with a chief complaint of left upper eyelid ptosis with a fix upper eyelid with incomplete closure. She had an epithelial ulcer in the lower corneal quadrants, no light perception, severe impairment of eye movements and diffuse orbital pain (Fig. 1). CT scan showed a diffuse left orbital involvement (Fig. 1). She had previously been submitted elsewhere to an unsuccessful left ptosis correction, then to a left orbital biopsy with diagnosis of left orbital inflammatory disease and no signs of malignancy. There was no known history of breast cancer. She was then submitted to a repeated left orbital biopsy. Histology showed tissue infiltration by moderately atypical epithelioid neoplastic elements (ER+, PR+, CK7+, GATA3+) organized in small nests, cords and elongated duct-like structures, compatible with metastatic localization of breast carcinoma (Fig. 1). Estrogen-receptor was expressed in 90% of neoplastic cells, progesterone-receptor was expressed in 75% of neoplastic cells, Ki67-receptor was expressed in 10% of neoplastic cells and Her2-Pathway Ventana (Clone 4b5) showed mild positivity. She underwent a systemic work-up and a small, previously undetected breast nodule was excised, with diagnosis of invasive ductal breast carcinoma with a tubular-type differentiating aspect. The patient is under oral therapy with hormonal and cyclin inhibitors drugs. After 10 months of follow-up there are no other metastases and the orbital mass has greatly reduced in size.

#### Case 2

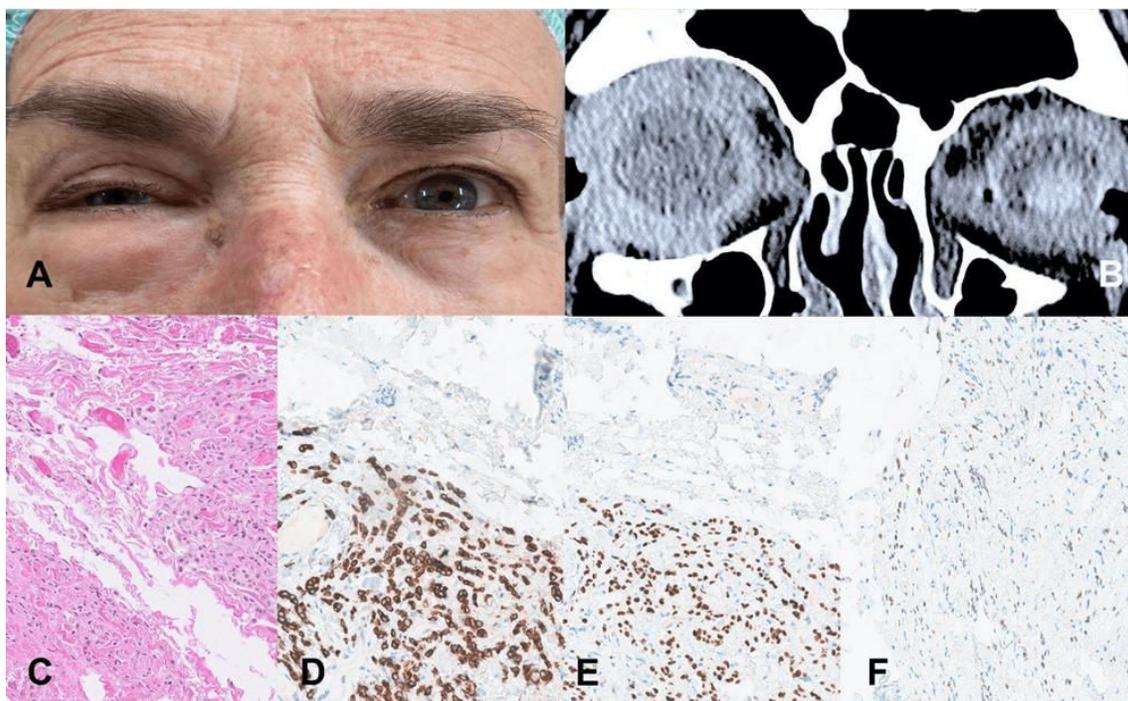
An 85-year-old woman presented with right ptosis, diplopia and recent onset right periorbital pain (Fig. 2). There was a palpable mass in the right superior and inferior orbital quadrants. She had left breast cancer removal in 1994, adjuvant chemotherapy and subsequently maintenance therapy with Tamoxifen for 5 years, with regular follow-up. CT scan showed a diffuse right orbital mass (Fig. 2). She was submitted to right orbital biopsy that revealed fibroadipose and skeletal muscle tissue site with infiltration by poorly cohesive epithelioid cells (CKAE1/3+, ER+, CK7+, GATA3+), arranged in single elements and cord-like structures (Fig. 2). This finding was compatible with the localization of carcinoma of breast origin with morphological aspects referable to a lobular isotype. The patient has interrupted the oral therapy for the advanced stage of the disease and is under palliative treatment.

#### Case 3

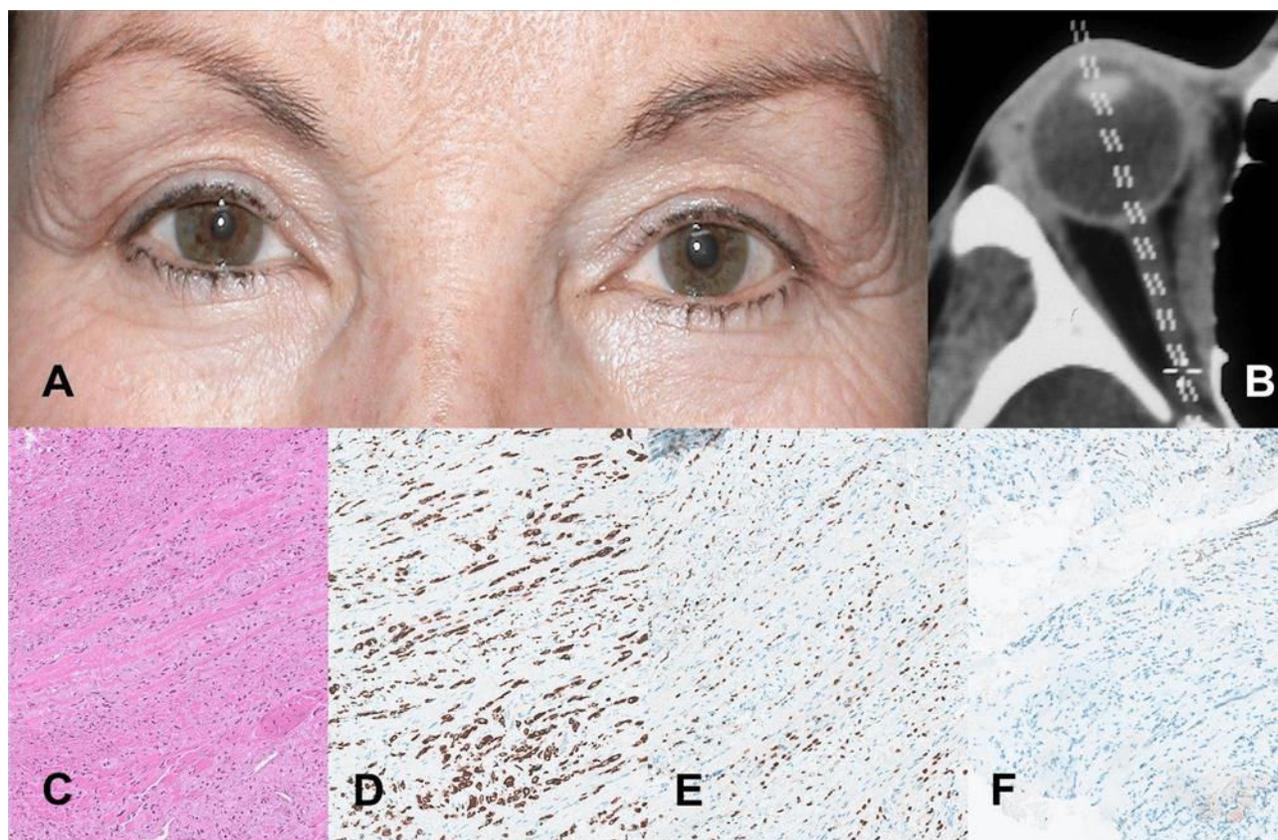
A 65-year-old woman with history of breast cancer operated 16 years before presented with mild pain in her right orbit increasing with horizontal movements, horizontal diplopia in right and left gaze and mild right enophthalmos (Fig. 3). She had been submitted to treatment with Tamoxifen for 5 years, with no chemo or radiotherapy and no other general disease or other known metastases. CT scan showed a right medial rectus muscle increased in size, with mild and diffuse enlargement of the entire muscle (Fig. 3). She underwent biopsy of the right medial rectus muscle, which revealed infiltration of poorly cohesive epithelioid neoplastic cellular elements (ER+; CK7+; GATA3+) disposed in single cells and single cell files, compatible with lobular breast carcinoma (Fig. 3). The patient succumbed after 8 months.



**Figure 1:** Case 1. A: Pre-op picture shows left ptosis, left corneal ulcer and fix left upper eyelid; B: CT shows left diffuse orbital mass. C-D-E-F; photomicrograph of orbital metastasis, HER-2 pathway +, E-caderine negative, PR + (stain at 400x). Histology showed diffuse infiltration by poorly cohesive neoplastic epithelioid elements (C) with strong and diffuse expression of Citokeratin 7 (D) and GATA3 (E) and a variable degree of nuclear expression of estrogen receptors (F). These findings are consistent with metastatic localization of breast carcinoma.



**Figure 2:** Case 2. A: Pre-op picture shows right ptosis and inferior orbital mass; B: CT shows right diffuse orbital mass; C-D-E-F: photomicrograph of orbital metastasis, HER-2 pathway +, E-caderine negative, PR + (stain at 400x). Histology showed diffuse infiltration by poorly cohesive neoplastic epithelioid elements (C) with strong and diffuse expression of Citokeratin 7 (D) and GATA3 (E) and a variable degree of nuclear expression of estrogen receptors (F). These findings are consistent with metastatic localization of breast carcinoma.



**Figure 3:** Case 3. A: Pre-op picture shows mild right enophthalmos; B: CT shows right medial rectus increased in size; C-D-E-F: photomicrograph of orbital metastasis, HER-2 pathway +, E-cadherine negative, PR + (stain at 400x). Histology showed diffuse infiltration by poorly cohesive neoplastic epithelioid elements (C) with strong and diffuse expression of Cytokeratin 7 (D) and GATA3 (E) and a variable degree of nuclear expression of estrogen receptors (F). These findings are consistent with metastatic localization of breast carcinoma.

### Discussion

Orbital metastases due to breast cancer can be the result of a cellular tropism caused by estrogens produced by periorbital fat, which correlates with most cases secondary to hormone-sensitive tumours. The orbit represents a rich in fat niche which may attract disseminated invasive lobular breast cancer cells [2]. The majority of orbital metastases from breast cancer are linked to invasive lobular carcinoma, a subtype known for its proclivity to disseminate widely due to its lack of E-cadherin expression. This characteristic allows for greater cell dispersion and infiltration into fatty tissues like the orbit. In contrast, invasive ductal carcinoma, which expresses E-cadherin, is less likely to metastasize to the orbit due to its more cohesive cell structure [2]. It has been shown that a significant majority of patients with orbital metastases from breast cancer have a luminal profile, with estrogen and progesterone receptor positivity being common. This aligns with the notion that ER-positive breast cancer, which benefits from long-term hormone therapy, has a greater likelihood of leading to orbital metastases due to prolonged patient survival [1]. Pierson, et al., also reported that most cases of orbital metastases in their series were ER-positive and HER2-negative, further supporting the correlation between hormone receptor positivity and the development of orbital metastases [2]. Interestingly, some cases have shown discrepancies in histological subtypes between primary tumors and orbital metastases, suggesting the possibility of selective pressures within the orbital microenvironment influencing the histological characteristics of metastases [3]. The average age at diagnosis for orbital metastasis from breast cancer is approximately 61 years, with a significant lag time from the initial diagnosis of the primary tumor to the appearance of orbital metastases ranging from 2 to 8.5 years [1,4]. Cases with longer intervals have been described and of our patients had presented an orbital metastasis 29 years after the diagnosis of primary tumor, this being the longest reported interval as far as we are aware [5]. Presentation may differ in each case and histology of the primary tumour may differ from that of the metastasis. Orbital metastasis may sometimes be the first symptom of an undiagnosed primary breast tumor, as in one of our cases, although mainly in case of invasive lobular carcinoma [2]. This necessitates a high index of suspicion and a thorough systemic evaluation in patients presenting with orbital masses, particularly in women over the age of 60 [6]. The involvement of a single extraocular muscle by breast metastatic tumors as in one of our

cases is rare and this is probably due to the continuous movement of the muscles, that creates an unfavorable environment for tumor cell implantation [7]. However, breast carcinoma metastases to the orbit do tend to infiltrate extraocular muscles and orbital fat [5]. The pattern of orbital metastasis from breast carcinoma typically spares bilateral involvement, this occurring in less than 10% of cases [8].

### Conclusion

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) play a pivotal role in detecting and characterizing orbital metastases. Biopsy remains essential for definitive diagnosis, as it can confirm the histopathological subtype and receptor status of the metastatic lesion [9]. The management of orbital metastases from breast cancer typically involves a combination of surgery, radiotherapy and systemic treatments such as chemotherapy and hormone therapy. Despite these interventions, the prognosis for patients with orbital metastases remains poor, with median survival times reported to be between 17.5 and 26.4 months from the onset of orbital involvement [2]. As treatments for primary breast cancer have improved, leading to increased survival rates, the incidence of orbital metastasis is expected to rise [10]. This underscores the importance of long-term surveillance and the need to remain vigilant for symptoms indicative of orbital involvement in breast cancer survivors [11].

### Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article. The authors alone are responsible for the content and writing of the paper.

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### References

1. Grajales-Alvarez R, Gutierrez-Mata A. Orbital metastases from breast cancer: A retrospective analysis of 28 cases. *Cancer Treat Res Commun.* 2020;24:10018.
2. Pierson T, Tebit E, Sayed AE, Smolkin M, Dillon P. Orbital metastases from breast cancer: Retrospective analysis at an academic cancer center. *Breast J.* 2016;1-4.
3. Aurilio G, Goldhirsch A, Nolè F. A meta-analysis of oestrogen receptor, progesterone receptor and human epidermal growth factor receptor 2 discordance between primary breast cancer and metastases. *Eur J Cancer.* 2014;50(2):277-89.
4. Shields JA, Shields CL, Scartozzi R. Survey of 1264 patients with orbital tumors and simulating lesions: The 2002 Montgomery Lecture, part 1. *Ophthalmol.* 2004;111(5):997-1008.
5. Milman T, Pliner L, Langer PD. Breast carcinoma metastatic to the orbit: An unusually late presentation. *Ophthal Plast Reconstr Surg.* 2008;24:480-2.
6. Ahmad SM, Esmali B. Metastatic tumors of the orbit and ocular adnexa. *Curr Opin Ophthalmol.* 2007;18:405-13.
7. Ashton N, Morgan G. Discrete carcinomatous metastases in the extraocular muscles. *Br J Ophthalmol.* 1974;58:112-7.
8. Rossi L, Zanca S, Civitelli L, Ranieri E. An unusual orbital metastasis of breast cancer. *Breast Dis.* 2014;34:173-6.
9. Blohmer M, Zhu L, Atkinson JM, Jankowitz RC. Patient treatment and outcome after breast cancer orbital and periorbital metastases: a comprehensive case series including analysis of lobular versus ductal tumor histology. *Breast Cancer Res.* 2020;22(1):70.
10. Saad ESP, Bakri HM, Rayan A, Barakat D, Khalel MM. Eye metastasis in breast cancer: case report and review of literature. *E Cancer Medical Science.* 2022;16:1353.
11. Strianese D, Iuliano A, Quaranta Leoni FM. Secondary orbital tumours and orbital metastases. In *oculoplastic, lacrimal and orbital surgery: The ESOPRS Textbook.* Cham: Springer Nature Switzerland. 2024;2:351-69.

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