Bilateral Orbital Metastases in Breast Cancer: Literature Review Regarding a Rare Clinical Case

Metástases Orbitárias Bilaterais em Cancro da Mama: Revisão da Literatura Sobre um Caso Clínico Raro

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ABSTRACT

Bilateral orbital metastases from breast cancer are a rare condition, occasionally posing as the initial presentation of an undetected primary tumor. Hormone receptor-positive (HR+)/HER2-negative (HER2-) breast cancer, particularly the lobular subtype, is a common primary source. Despite advancements in breast cancer treatment, managing orbital metastases remains challenging due to limited data and their association with advanced multi-system end-stage disease.

This study reports the first clinical case of bilateral orbital metastases as the initial presentation of bilateral breast cancer, successfully treated with a combination of a CDK4/6 inhibitor and an aromatase inhibitor. Additionally, it comprehensively reviews and analyzes clinical features, histological subtypes, treatment strategies, and outcomes associated with bilateral orbital metastases from breast cancer.

The case involves a 53-year-old woman with elevated intraocular pressure and right optic disc edema in optical coherence tomography (OCT), leading to the discovery of synchronous bilateral orbital metastases and multicentric breast nodules. These were diagnosed as metastatic HR+/HER2- breast lobular cancer, and the patient showed a remarkable response to abemaciclib and letrozole. A review of 48 patients revealed a predominantly female population (96%) with a mean age of 59 years at diagnosis. A substantial proportion (37%) had no prior cancer history at presentation, and 65% had concomitant metastases in other anatomical sites, with 15% involving intracranial metastases. Common clinical findings included limited ocular motility (58%) and vision loss (33%). Imaging often showed infiltrating orbital soft tissues (71%), with 44% involving extraocular muscles. Histologically, most cases exhibited lobular characteristics (71%). Treatment modalities ranged from radiotherapy, chemotherapy, hormone therapy, and surgery, to immunotherapy. The overall mean survival in this cohort was 12 months (ranging from 0.5 to 41 months).

In conclusion, bilateral orbital metastases from breast cancer are a clinically challenging condition. This study highlights their clinical features and treatment outcomes, underscoring the need for innovative therapeutic approaches to enhance their generally poor prognosis. The presented case, where bilateral orbital metastases from bilateral breast cancer responded well to a CDK4/6 inhibitor and an aromatase inhibitor, introduces a promising treatment avenue. Further research is warranted to optimize management and improve overall outcomes for these patients.

KEYWORDS: Breast Neoplasms; Orbital Neoplasms/secondary.

RESUMO

As metástases bilaterais da órbita no cancro da mama são uma condição rara, podendo se apresentar como a manifestação inicial de um tumor primário não detectado. O cancro da mama hormono-positivo (HR +) / HER2-negativo (HER2-), particularmente o subtipo lobular, é a origem primária mais comum. Apesar do progresso no tratamento do cancro da mama, estratégias eficazes na abordagem das metástases da órbita continuam a ser um desafio pela sua associação com doença avançada.

Relatamos o primeiro caso clínico de metástases bilaterais da órbita como manifestação inicial de cancro da mama bilateral, eficazmente tratado com uma combinação de um inibidor de CDK4/6 e um inibidor de aromatase. Revimos e analisamos características clínicas, subtipos histológicos, estratégias de tratamento e resultados associados a metástases bilaterais da órbita de cancro da mama.

O caso envolve uma mulher de 53 anos com aumento da pressão intraocular e edema do disco ótico direito no tomografia de coerência ótica (OCT). A marcha diagnóstica culminou em carcinoma lobular metastizado da mama HR+/HER2-, tendo apresentado uma resposta marcada ao abemaciclib e ao letrozol.

Uma revisão de 48 doentes revelou uma população predominantemente feminina (96%) com idade média de 59 anos. Do total dos casos, 37% não apresentavam história prévia de cancro e 65% apresentavam metástases distantes concomitantes. Limitação da motilidade ocular (58%) e perda de visão (33%) são os sinais mais comuns. Imagiologicamente, frequentemente ocorre infiltração das partes moles (71%), com 44% envolvendo músculos extraoculares. Histologicamente, a maioria dos casos apresenta características lobulares (71%). A sobrevida média global nesta coorte foi de 12 meses (variando de 0,5 a 41 meses).

Em conclusão, as metástases bilaterais da órbita em cancro da mama são uma condição desafiadora. Este estudo destaca as características clínicas e resultados de tratamento, ressaltando a necessidade de abordagens terapêuticas inovadoras para melhorar o prognóstico geralmente reservado.

PALAVRAS-CHAVE: Neoplasias da Mama; Neoplasias da Órbita/secundária.

INTRODUCTION

Orbital metastases pose a complex and clinically significant challenge, accounting for 1%–13% of all orbital neoplasms and affecting 2%–5% of individuals with systemic malignancies.[1] Among these cases, breast cancer, a global health concern and a leading cause of cancer-related mortality in women stands out as a primary source of orbital metastases.[2–4] Bilateral orbital metastases occur in 4%–10% of cases with orbital involvement and can occasionally be the initial presentation of an undetected primary tumor, posing significant diagnostic and therapeutic challenges.[5]

Despite notable progress in breast cancer therapeutics, devising effective strategies for managing orbital metastases remains a formidable task, primarily due to limited available data and their association with advanced multi-system end-stage disease.[6] Palliative care remains the cornerstone of treatment, underscoring the advanced stage at which orbital metastases typically become clinically evident.[6]

In this report we present a unique case involving a patient with bilateral orbital metastases as the presenting feature of bilateral breast cancer, demonstrating a substantial response to a first-line treatment regimen combining abemaciclib, a CDK4/6 inhibitor, and letrozole, an aromatase inhibitor.

Additionally, we conducted a critical and comprehensive review of cases involving bilateral orbital metastases originating from breast cancer. This review was conducted using PubMed/Medline, and Google Scholar databases

and employed appropriate controlled [MeSH] keywords, including "breast cancer," "bilateral," "metastases," and "orbit" and acknowledging references list. The selected articles included case reports and case series that provided detailed clinical, histological, and treatment descriptions.

CASE REPORT

A 53-year-old female, asymptomatic, was observed in a routine ophthalmology appointment. Her medical history included essential hypertension, dyslipidemia, adenomyosis, a benign thyroid nodule, major depression, and a smoking history of 30 pack years. She was currently taking candesartan, rosuvastatin, mirtazapine, and bupropion. Additionally, she reported a family history of prostate cancer in two brothers. There was no relevant ophthalmic history. The best-corrected visual acuity (BCVA) was 20/20 OD *vs* 20/20 OE. Examination only revealed a mildly elevated intraocular pressure (IOP) of 22 mmHg in the right eye (OD) and 20 mmHg in the left eye (OS). Biomicroscopy and ocular fundoscopy were unremarkable.

DIAGNOSTIC ASSESSMENT

Five months later, following the initial ophthalmology appointment and to evaluate the raised IOP, an optical coherence tomography (OCT) surprisingly revealed a raised neuro-retinal rim and increased RNFL thickness, consistent with subclinical optic disc edema OD (Fig. 1), prompting further investigation with a computed tomography (CT) scan, which revealed infiltration of soft tissues within the right orbit. A magnetic resonance imaging (MRI) was requested to provide a more comprehensive characterization. The MRI revealed extensive intra- and extraconal orbital infiltration involving the optic nerve, extraocular muscles, and lacrimal gland in the right orbit. Additionally, similar discrete signal alterations were identified within the left orbit, primarily located between the optic nerve and the medial and inferior rectus muscles (Fig. 1). The patient was subsequently referred to an orbital specialist for further evaluation.

During the follow-up appointment, the patient reported painful periorbital edema and limitation of extraocular movements on the right side. At this time, physical examination revealed inferior dystopia of the right eye and restricted horizontal motility, although diplopia was not reported (Fig. 1). BCVA was 20/30 OD and 20/20 OS. A relative afferent pupillary defect (RAPD) was detected in the right eye. Ocular fundoscopy revealed a grade 1 optic disc edema OD. Hertel exophthalmometry showed mild asymmetry, with 15 mm OD and 16 mm OS measurements. Visual field testing revealed an inferonasal paracentral scotoma in the right eye, while the left was normal. OCT still showed optic disc edema in the right eye, with no changes observed in the left. Biomicroscopy remained unchanged.

An incisional biopsy of the right orbit was conducted through an anterior orbitotomy. The procedure included the collection of multiple tissue samples from the superior and superior-temporal areas (Fig. 2). Histopathologic examination unveiled the presence of moderately differentiated lobular carcinoma cells (Fig. 2). Immunohistochemical analysis further revealed positivity for GATA3 and CK7 markers and 100% of tumor nuclei expressed estrogen receptors (ER+) (Fig. 2). The c-ERB-B2 (HER2/neu) score was

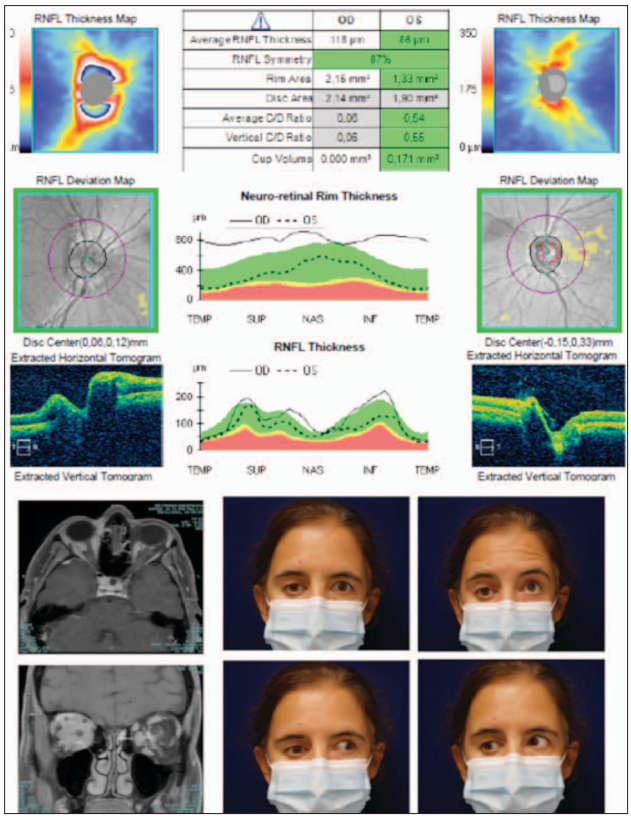

Figure 1. Clinical presentation, OCT and orbital findings before treatment. (A) The OCT reveals a optic disc edema of the right eye. (B) Orbit axial and coronal T1 MRI showing post-gadolinium enhancing lesions (intra and extra-conal), with mass effect and inflammatory changes of orbital fat. (C) Right inferior dystopia with restriction in extraocular elevation and adduction of the right eye.

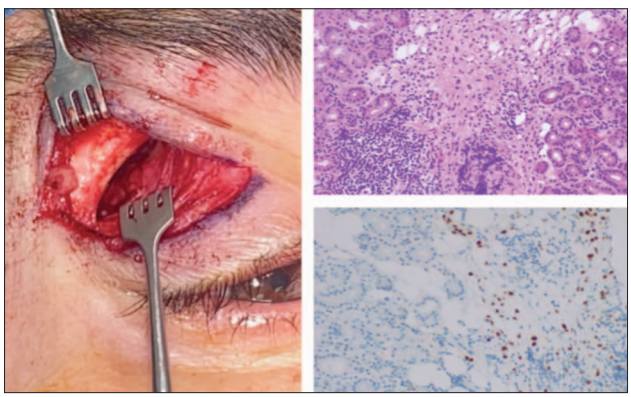

Figure 2. Orbital biopsy. (A) Incisional biopsy of the right orbit through a lid crease incision. (B) Lacrimal gland showing discohesive cells with nuclear atypia, many resembling signet-ring cells and containing intracellular mucin. Thickened fibrous tissue where isolated cells and cell rows of similar histologic characteristics are identified. (C) Infiltrating cells exhibiting immunoreactivity for estrogen receptors, suggesting breast origin.

0. E-cadherin and PD-L1 (combined positive score) expressions were found to be negative.

Following these findings, an extensive work-up was initiated to identify the primary tumor. This evaluation encompassed breast ultrasonography, mammography, breast MRI, esophagogastroduodenoscopy, gynecological transvaginal ultrasound, lumbar puncture, and positron emission tomography (PET)/CT scan employing 18-fluorodeoxyglucose (18F-FDG). The PET/CT 18-FDG scan revealed moderate heterogeneous radiopharmaceutical uptake in both orbits, the right axillary lymph node, and moderate metabolic activity in the stomach. Esophagogastroduodenoscopy uncovered hyperemic gastropathy without evidence of neoplastic or dysplastic tissue. A lumbar puncture detected suspected neoplastic cells, prompting a neuroaxis MRI that did not indicate invasive disease. Breast imaging unveiled bilateral multicentric nodular formations along with enhancing right axillary lymph nodes. Ultrasound-guided core biopsies were performed on breast nodules and the right axillary node. Histological analysis revealed a moderately differentiated (G2) invasive carcinoma with a lobular pattern. ER was positive in 90% of cells, while progesterone receptor (PR) in 100%. HER2 was negative, as was E-cadherin. The dominant lesion in the right breast exhibited a proliferation index (Ki67) of 10%, and in the left breast, it was 7%.

As a result, the patient was diagnosed with metastatic lobular breast cancer, classified as stage IV disease according to the AJCC 8th edition TNM staging.[7] The case was discussed in a multidisciplinary breast cancer tumor board, and, considering the metastatic and unresectable nature of the disease, along with its unsuitability for local intervention, it was decided to initiate systemic treatment with a CDK4/6i plus an aromatase inhibitor.

THERAPEUTIC INTERVENTION

In December of 2021, based on the MONARCH 3 clinical trial results,[8] the patient initiated treatment with abemaciclib 150 mg twice daily, combined with letrozole 2.5 mg once a day.

FOLLOW-UP AND OUTCOME

In January 2022, just one month after starting systemic therapy, the patient developed analytical toxic hepatitis, marked by elevated transaminases levels at grade 3, along with serum creatine grade 2 elevation, as classified by the Common Terminology Criteria for Adverse Events (CTCAE),[9] which contributed to the temporary withdrawal of treatment. After a two-week interval, during which laboratory parameters were reassessed and showed progressive improvement, the patient resumed letrozole, while the dose of abemaciclib was adjusted to 100 mg twice a day. Rigorous monitoring of laboratory values was maintained. Over the following four months, hepatic parameters and serum creatinine gradually normalized.

Concomitantly, the patient reported grade 1 diarrhea that was effectively managed through conservative measures.

During follow-up, the patient exhibited a marked clinical response to treatment, with significant recovery of visual acuity and extraocular motility, which occurred as early as the first cycle of abemaciclib and continued despite the reduced dosage of 100 mg twice daily. The patient underwent repeated orbital MRI, breast MRI, and PET/CT with 18F-FDG imaging, all of which confirmed a favorable response, on both orbits and breast areas.

In September 2023, after twenty months of systemic therapy, the patient achieved a complete response in both breasts and a significant improvement on orbital imaging, with only a minor residual metabolic fixation detected in the left orbit (Fig. 3). Visual acuity remained stable at 20/20 OI, with visual field recovery, and extraocular motility improved, persisting only a mild limitation of right eye adduction and elevation (Fig. 3). Diplopia continued not to be reported. OCT revealed an improvement in both the retinal ganglion cell layer and the retinal nerve fiber layer thickness. Hertel exophthalmometry was 14 mm OD and 15 mm OS, and the rest of the physical examination yielded unremarkable findings.

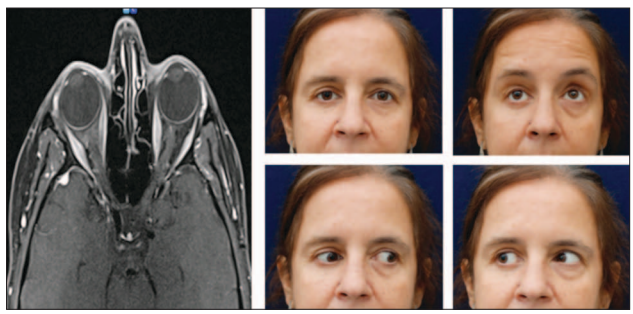

Figure 3. Orbital findings after twenty months of systemic treatment and clinical presentation. (A) Orbit axial and coronal T1 MRI showing imaging improvement in both orbits, marked by repermeabilization of intraorbital fat. (B) Significant clinical improvement in ocular movement restrictions, with only partial limitation remaining on right adduction and elevation.

CLINICAL CASE AND LITERATURE ANALYSIS

GENERAL DATA AND DEMOGRAPHICS

In our comprehensive review, which encompassed English and non-English papers published from 1960 to 2023, we systematically examined 38 articles focused on synchronous bilateral orbital metastases secondary to breast cancer.[6,10–43] This extensive analysis identified a total of 48 patients, predominantly females (96%), with only two cases involving males. The mean age at diagnosis was 58.7 years, ranging from 35 to 83 years. Remarkably, 63% of these patients had a documented history of breast cancer. The onset of orbital metastases, on average, occurred approximately 10 years after the initial breast cancer diagnosis, with the most extended interval being 30 years. Table 1 summarizes these findings.

Table 1. Clinical data of 48 clinical cases of bilateral orbital metastases from breast cancer.

Demographics Characteristics	
N	48
Female (n,%)	46 (96)
Age (mean, SD)	58.7 (12)
Previous known diagnosis (%)	63
Time since diagnosis (mean, SD)	10 (8.85)
Histology subtypes (%)	
Lobular	71
Ductal	18
Poorly differentiated	7
Mixed (lobular-ductal)	6
Metastatic sites (%)	
Bone	45
Lymph nodes	18
Brain	15
None	35
Treatment (%)	
RT	68
Systemic treatment (CHT, HT)	81
Surgery	5

CHT chemotherapy, HT hormonotherapy, RT radiotherapy, SD standard deviation.

CLINICAL PRESENTATION

Patients who are affected by bilateral orbital metastases arising from breast cancer commonly present with various clinical manifestations, as summarized in Table 2. Limited ocular motility was the most prevalent sign, affecting 58% of the cases. Vision loss was noted in 33% of patients, while periorbital edema was observed in 25%. Diplopia was described in 23% of cases, pain in 17%, proptosis in 15%, upper lid ptosis in 13%, a palpable mass in 8%, and globe dystopia, upper eyelid retraction, and enophthalmos in 6% each.

Table 2. Clinical presentation in 48 clinical cases of bilateral orbital metastases from breast cancer.

Symptoms and signs*	No	%
Limited ocular motility	28	58.33333
Vision loss	16	33.33333
Periorbital edema	12	25
Diplopia	11	22.91667
Pain	8	16.66667
Proptosis	7	14.58333
Ptosis	6	12.5
Palpable mass	4	8.333333
Enophthalmos	3	6.25
Dystopia	3	6.25
Upper lid retraction	3	6.25

Data extracted from 48 patients explicitly checked by the authors and in whom details of history and examination were available.

* Several patients had more than one complaint, explaining why numbers and percentages add to more than the number of patients.

HISTOLOGICAL SUBTYPES

Histologically, most orbital metastases exhibited lobular characteristics, accounting for 71% of cases (Table 1). Ductal histology was identified in 18% of cases, while poorly differentiated and mixed histological subtypes were observed in 9% and 6% of cases, respectively.

ORBITAL IMAGING AT PRESENTATION AND METASTATIC SITES

Imaging studies revealed that the majority of metastases displayed a diffuse pattern within the orbit, with a predilection for infiltrating orbital soft tissues in 71% of cases. In 44% of these cases, metastases extended to involve the extraocular muscles.

In 65% of cases, orbital metastases were found to be concurrent with metastases in other anatomical sites. In a subset of cases (15%), tumors exhibited intracranial extension (Table 1).

TREATMENT AND OUTCOME

Due to the heterogeneity of treatment approaches in the reviewed cases, conducting a comprehensive comparative analysis of treatment methods was not feasible. However, we observed a diverse range of treatments employed, including radiation therapy, systemic chemotherapy and immunotherapy, and surgery. Our findings indicated that the most common outcome was death secondary to the cancer, occurring in 56% of cases. The prognosis for patients diagnosed with orbital metastases from breast cancer yielded a mean survival of 12 months, with a range spanning from 0.5 to 41 months.

LITERATURE REVIEW

Orbital metastases are a challenge within the field of oncology. Notably, breast cancer (36%), melanoma (10%), and prostate cancer (8.5%) emerge as the most common primary sources of orbital metastases.[2-5] This study presents a unique clinical case and a comprehensive review that analyzed 48 clinical cases of bilateral orbital metastases secondary to breast cancer. The preponderance of females in these cases aligns with the well-established gender distribution of breast cancer.[4] Notably, the range of ages at diagnosis emphasizes the diverse age interval at which this presentation can manifest.[1,3] This supports the imperative need for clinicians to consider orbital metastases as a potential indicator of breast cancer across the entirety of a patient's clinical journey.

An important finding in this review is that only 2/3 of reports had a documented history of breast cancer at the time

of their diagnosis with orbital metastases. Nevertheless, it is crucial to always consider the possibility of orbital metastases in a patient with a history of breast cancer who presents with orbital symptoms.[5] Notably, the time interval between the initial breast cancer diagnosis and the development of orbital metastasis ranged widely. This protracted timeframe highlights the necessity for prolonged surveillance, as orbital metastases can surface as a delayed complication.

These metastases often present as space-occupying lesions, with significant clinical symptoms.[5] Limited ocular motility emerged as the most prevalent sign, which can be attributed to the infiltrative nature of orbital metastases, potentially involving the extraocular muscles. Vision loss, observed in 1/3 of patients, reflects the potential severity of this condition, often associated with compression of the optic nerve or other critical orbital structures.[2,3] The occurrence of enophthalmos, noted in 6% of cases,[22,38,41] is a rarely observed manifestation in other types of metastases and should raise suspicion of breast cancer metastization. This phenomenon likely arises from neoplastic cell infiltration into the extraocular muscles and retro-bulbar stromal tissues, leading to desmoplasia, fibrosis, and globe retraction.[45]

The array of tumors and tumor-like lesions that can involve the orbit underscores the importance of thorough imaging as a crucial step in the initial differential diagnosis for patients presenting with new symptoms or lack a prior diagnosis.[46,47] Conditions such as thyroid eye disease, granulomatosis with polyangiitis, amyloidosis, sarcoidosis, lymphoproliferative disease, idiopathic orbital inflammation, IgG4-related disease, as well as solid tumors, infectious agents, and vascular conditions should all be diligently considered when radiologic changes are observed in the orbital area.[48] In cases where clinicoradiologic findings remain inconclusive or when previous histological diagnoses are questioned, a biopsy should be considered.[48,49]

Our findings indicate that the majority of orbital metastases tend to occur at later stages after primary tumors, often showing a diffuse location within the orbit, and rarely invading intracranial structures.[2] In several instances, the tumor's location within the orbit allows for an open incisional biopsy, which can be performed through either a conjunctival or cutaneous approach.[5] If the tumor is well-demarcated and amenable to complete removal, a complete excisional biopsy should be pursued.[5] However, if there is a confirmed primary cancer diagnosis, fine-needle aspiration biopsy (FNAB) can also be justified.[50]

Histologically, the majority of orbital metastases exhibited a lobular subtype. When considering the histological subtypes, lobular breast carcinoma, which accounts for approximately 10%-15% of all breast cancer cases,[51] exhibits an increased expression of estrogen receptors (ER) and progesterone receptors (PR) but a decreased human epidermal growth factor receptor 2 (HER2) positivity compared to the no special type (NST)/ductal carcinoma.[52] The propensity of lobular breast carcinomas for estrogen-rich sites, such as periocular tissues and orbital fat, may explain their tendency for orbital metastases.[53] Conversely, ductal breast carcinoma, characterized by E-cadherin expression that limits cellular dispersion, is less likely to result in orbital metastases.[34]

The prognosis for patients diagnosed with orbital metastases from breast cancer is invariably poor, highlighting the aggressive nature of these metastases and their close association with advanced, often multi-system, end-stage disease.[6] Treatment strategies for bilateral orbital metastases from breast cancer display significant heterogeneity, reflecting the intricate nature of managing such cases. Available modalities encompass radiation therapy, systemic treatments (including chemotherapy and hormonotherapy), and surgical interventions for disease control.

In general, in these cases orbital surgery for the removal of tumor masses is not recommended, as it is non-curative and may result in substantial morbidity.[44] When surgical debulking is considered appropriate, it can effectively reduce mass-related symptoms. Nonetheless, it risks severe complications, including permanent visual deficits.[44] Chemotherapy, hormonal therapy, and targeted therapy offer the advantage of simultaneous control over primary and metastatic lesions.

Our case report highlights a unique instance of metastatic breast cancer classified as hormone receptor-positive (HR+) and HER2-negative (HER2-). Luminal HR+/HER2- breast cancer constitutes the most prevalent subtype, making up approximately 65% of cases.[54] This subtype shares the feature of hyperactivity in the CDK4/6 pathway, contributing to resistance against endocrine therapy.[55] Notably, the emergence of CDK4/6 inhibitors, such as abemaciclib, has revolutionized the treatment landscape for advanced and/or metastatic HR+/HER2- breast cancer.[56–61] Abemaciclib, an oral selective small molecule targeting the CDK-RB1-E2F pathway critical for cell cycle progression, has garnered significant attention.[62]

CDK4/6 inhibitors have the capability to impede the hyper-phosphorylation of retinoblastoma protein, inducing G1 arrest and halting proliferation.[62,63] The MONARCH 3 trial, a phase 3, double-blind, randomized study, demonstrated that abemaciclib plus letrozole significantly extended progression-free survival compared to placebo plus aromatase inhibitor (hazard ratio, 0.54; 95% CI, 0.41 to 0.72; $p = 0.000021$; median: not reached in the abemaciclib arm, 14.7 months in the placebo arm).[8] Notably, abemaciclib has exhibited efficacy in managing intraocular metastases arising from breast cancer, as evidenced by previous case reports.[64,65] In one report, a 57-year-old woman presented with iris metastases, which regressed within four months and remained undetectable through an eight-month follow-up after using a combination of abemaciclib and letrozole.[65] In a second case, a woman in her 50s with bilateral choroidal metastases stemming from breast cancer positively responded to abemaciclib and fulvestrant within four months after the beginning of treatment.[64] The significant response observed to abemaciclib in treating intraocular metastases aligns with preclinical and clinical evidence showing its ability to penetrate the central nervous system.[66] This suggests that abemaciclib holds promise as a viable therapeutic option in this specific clinical scenario. No cases of orbital metastases treated with these targeted therapies were found. Our case report underscores

that even with a reduced dose of 100 mg due to analytical toxicity, abemaciclib demonstrated efficacy without compromising the outcome. This observation sparks the intriguing concept of tailoring treatment by personalizing doses for individual patients based on their unique responses and tolerances. It is also noteworthy that adverse events and toxicities observed during treatment may offer predictive factors for treatment success, a concept that warrants further exploration in the realm of breast cancer therapy.

Rigorous investigations are imperative to comprehensively understand the potential of CDK4/6 inhibitors in managing orbital metastases. Robust studies should evaluate the safety and efficacy of different CDK4/6 inhibitors through head-to-head comparisons and explore the impact of varying doses. Such research endeavors will provide invaluable insights into optimizing treatment strategies and potentially enhancing outcomes for HR+/HER2- breast cancer patients presenting with orbital metastases.

Nevertheless, it is imperative to acknowledge that single-case reports have inherent limitations, and their results should be extrapolated to similar presentations with caution, especially when considering their long-term effects. It is crucial to recognize the limitations inherent to literature reviews, including potential publication bias and incomplete data within certain case reports.

In conclusion, this comprehensive review advances our understanding of synchronous bilateral orbital metastases from breast cancer, shedding light on their demographic, clinical, histological, and imaging characteristics, as well as the available treatment options. These findings underscore the necessity for increased awareness and vigilance among clinicians, which can lead to earlier detection and comprehensive multidisciplinary care. As research in this field continues to progress, a deeper understanding of prognostic factors and refined treatment strategies will contribute to the improved management of this complex clinical entity. By addressing these critical aspects, this review enriches the knowledge base and offers valuable insights for clinicians, researchers, and patients. Ultimately, it aims to optimize patient care and outcomes in the challenging landscape of orbital metastases from breast cancer.

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CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

All authors declare that they had a substantial and direct intellectual contribution in the design and elaboration of this article, that they participated in the analysis and interpretation of the data, in the writing of the manuscript, in the revision of versions and critical revision of its content and in the approval of the final version.

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