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Case Report

# Orbital Metastases from Breast Cancer with BRCA2 Mutation: A Case Report and Literature Review

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## Keywords

Orbital metastases · Breast cancer with BRCA2 mutation

## Abstract

Breast cancer is the second leading cause of cancer-related deaths in women in the United States. Of these women, 5–10% have an inherited form of breast cancer with a mutation in a major gene, such as the breast cancer susceptibility genes 1 or 2 (*BRCA1* or *BRCA2*). Triple negative (the most common subtype of *BRCA1*-associated breast cancers) and Her2-positive breast cancer patients have more frequently been observed to develop central nervous system (CNS) metastases compared to other molecular subtypes of breast cancers. However, it remains an open question if *BRCA2*-associated breast cancers also have a higher propensity to develop CNS metastases. Here we report a rare case of recurrent *BRCA2*-associated breast cancer which manifested as orbital metastases. At the time of this publication, this is one of the first cases of *BRCA2*-associated breast cancer to present with orbital metastases. In this article, we discuss the diagnostic challenges and review the literature regarding this rare presentation.

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## Introduction

Breast cancer is the second leading cause of cancer-related deaths in women in the United States. Of these women, 5–10% have an inherited form of breast cancer with a mutation in a major gene, such as the breast cancer susceptibility genes 1 or 2 (*BRCA1* or *BRCA2*) [1]. *BRCA1*-associated breast cancers often do not express the estrogen receptor (ER), progesterone receptor (PR), or Her2 gene and have been commonly described as “triple negative” [1]. In contrast, the gene expression pattern of *BRCA2*-associated breast cancers has usually been found to be ER- and PR-positive, and sometimes also Her2-positive [1]. Triple negative (the most common subtype of *BRCA1*-associated breast cancers) and Her2-positive breast cancer patients have more frequently been observed to develop central nervous system (CNS) metastases compared to other molecular subtypes of breast cancers [2, 3]. In comparison, it is not clear if *BRCA2*-associated breast cancers also have a higher propensity to develop CNS metastases and this is still an open question. Here we report a rare case of *BRCA2*-associated breast cancer who complained of diplopia and was found to have recurrent disease that manifested as orbital metastases. In this case report, we discuss the diagnostic challenges and review the literature on this rare clinical presentation.

## Case Presentation

A 38-year-old female was diagnosed with stage I (T1cN0M0) moderately differentiated invasive ductal carcinoma of the breast, which was ER- (97%) and PR-positive (28%). Due to her young age of presentation, she underwent genetic testing and was also found to have a *BRCA2* mutation (E49X: 373G>T). She received neoadjuvant chemotherapy with carboplatin, paclitaxel, and bevacizumab, which was then followed by a bilateral mastectomy. Analysis of the surgically resected sample found that the patient had a pathological stage of T1N0M0 with molecular analysis showing ER/PR-positive (IHC ER100% and PR1%) and Her2-positive expression (IHC Her2 0, Her2 FISH ratio at 2.3). As a result, the patient underwent adjuvant chemotherapy and received trastuzumab with pertuzumab for a total of 6 cycles. She was then started on adjuvant endocrine therapy with toremifene (due to adverse effects from tamoxifen). The patient did well for 2 years without any signs of recurrence until she noticed she had an enlarged left axillary lymph node. This lymph node was biopsied and found to be a recurrent metastatic carcinoma that was positive for ER/PR consistent with recurrence of her breast cancer.

Three weeks after undergoing axillary lymph node biopsy, the patient presented to the emergency department with progressively worsening diplopia and weight loss. Additionally, the patient complained of frequent urination and stated that she had been drinking approximately 2 L of water daily for the past year. Brain MRI showed multiple metastases centered in the lacrimal gland/lateral rectus muscle of the left orbit, superior, inferior, and medial rectus muscles of the right orbit, pituitary stalk/gland, skull base, cervical spine, and right mandibular condyle as well as cervical lymphadenopathy with mass effect on the left globe and optic chiasm (Fig. 1a). The patient was initially started on steroids. Additional liver ultrasound showed multiple metastases to the liver with the largest being 5 mm. As the lesion could not be surgically removed, the patient began radiation therapy to the orbits with possible radiation therapy to the pituitary. She was restarted on trastuzumab/pertuzumab and also received treatment with fulvestrant/goserelin and zoledronic acid. During the next 3 months,

the patient continued to show good treatment response with significant improvement in her diplopia and is still undergoing care for her metastatic disease (Fig. 1b).

## Discussion

As discussed above, it has been observed that triple negative (the most common subtype of BRCA1-associated breast cancers) and Her2-positive breast cancer patients have more frequently been observed to develop CNS metastases compared to other molecular subtypes of breast cancers [2, 3]. It remains an open question if BRCA2-associated breast cancers also have a higher propensity to develop CNS metastases. Distant metastases occur frequently in breast cancer, with the majority of metastases occurring to the bone, lungs, liver, brain, and regional lymph nodes [4]. Spread to the head and neck region is uncommon and can present a diagnostic challenge for physicians with orbital metastases occurring in 2–3% of all cancer patients [5, 6]. Clinical signs and symptoms of orbital metastases include proptosis, diplopia, pain, exophthalmos, blurry vision and a visible or palpable mass in the orbital or periorbital region. Unfortunately, patients with orbital metastases generally have a poor prognosis [7, 8].

Although metastases to the head and neck region are uncommon, breast cancer accounts for the majority of head and neck metastases with estimates ranging from 15 to ~20% [9, 10]. For patients with metastatic breast cancer, metastases to the head and neck region can be the presenting finding and can occur many years after the original diagnosis. Although our patient presented within 4 years of diagnosis, the majority of head and neck metastases present 5 or more years after diagnosis [11]. This reflects the already established long intervals to metastases in breast cancer seen with other organs such as the brain, lung, and bone [4]. Most orbital metastases arise from lobular breast carcinoma; however, our case demonstrates a unique example of orbital metastases arising from invasive ductal carcinoma [11, 12]. Studies speculate that lobular carcinoma's predilection for the orbit may be due to the more invasive nature of lobular carcinoma; however, the exact cause is unknown [11].

Treatment of metastatic breast cancer is generally palliative and focused on improving the quality and length of life. Median survival for metastatic breast cancer has been reported to be between 18 and ~24 months with a mean survival for patients with orbital metastases being 31 months [13]. Treatment of metastatic breast cancer generally involves hormone therapy, chemotherapy or radiation therapy for symptomatic metastases. Due to our patient's diplopia, she elected to proceed with radiation therapy prior to any chemotherapy. Radiation therapy for orbital metastases is both safe and effective with response rates reaching up to 79% and resolution of symptoms being seen in approximately 80% of patients [14]. Orbital surgery is generally not recommended as it can result in extensive morbidity and is additionally not curative [15]. Treatment for orbital metastases should include a multidisciplinary approach including oncology, neurology, and ophthalmology.

In conclusion, head and neck metastases, particularly orbital metastases, are rare but represent an important and challenging finding in breast cancer. Though treatment is not curative, significant symptomatic improvement can be achieved through radiation and chemotherapy. Presenting symptoms can include proptosis, diplopia, pain, or blurry vision all of which warrant further investigation by clinicians particularly in patients with a history of breast carcinoma.

### Statement of Ethics

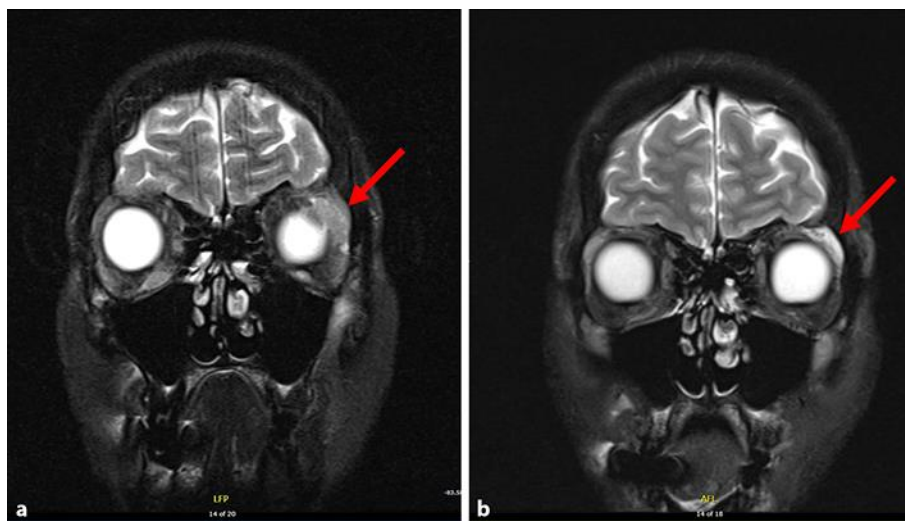
The authors have no ethical conflicts to disclose.

### Disclosure Statement

The authors have no conflicts of interest to declare.

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**Fig. 1.** MRI image of orbital metastases. T2 MRI image of the orbits shows a metastatic lesion to the left lateral rectus muscle (arrow) which responded to treatment. **a** MRI orbits before treatment. **b** MRI orbits after receiving 3 months of treatment.