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Case Report

Orbital Metastasis from Triple-Negative Breast Cancer: Case Report and Literature Review

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Orbital metastasis · Breast cancer · Triple-negative breast cancer · Chemotherapy · Radiotherapy

Abstract
Orbital metastases are rare. Breast cancer represents the first etiology to be evoked in carcinomas. We report a rare case of a young 43-year-old patient who developed significant orbital metastasis 2 months after the end of adjuvant treatment for triple-negative breast cancer. Good partial response was shown with an improvement of symptoms under chemotherapy (docetaxel combined with carboplatin), zoledronic acid and palliative radiotherapy. The patient quickly progressed in the pulmonary, hepatic and lymph nodes with mucocutaneous jaundice related to hepatic dysfunction after which she died within 20 days. Different etiologies are responsible for the orbital tumor syndrome. This orbital metastasis may constitute an inaugural mode of expression of the tumor affection. The frequency of metastases of breast cancer overexpressing estrogen receptor can be explained biologically by the presence of estrogen receptors in hormone acting as target choroid tissue steroids for lacrimal secretion. On the other hand, in triple-negative breast cancer, since the hormone receptors are negative, the pathophysiology of these orbital metastases remains unknown. At this stage, the treatment remains palliative, including radiotherapy, chemotherapy, and bisphosphonates, and the prognosis is grim.

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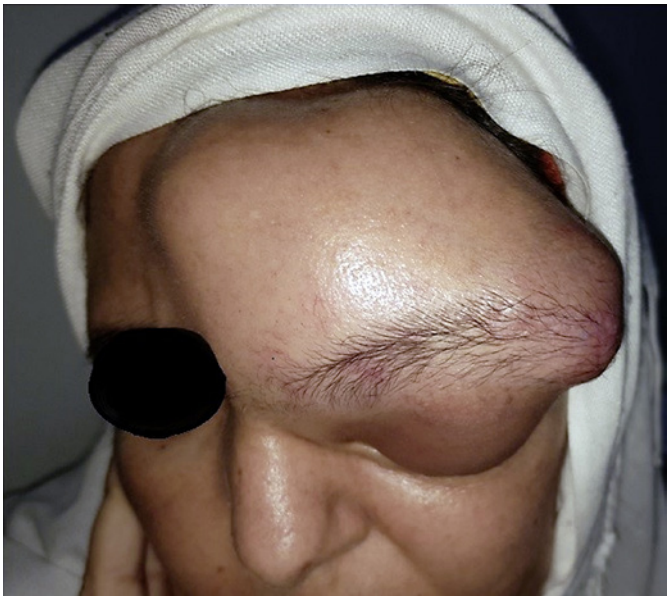

Fig. 1. Significant left orbital metastasis before treatment.

Introduction

The orbit has long been described as a site of tumor proliferation. However, metastases to its level have rarely been reported and may less frequently reveal the primary tumor. They constitute only 3% of orbital lesions and 10% of orbital tumors [1]. Breast cancer is the most common origin of these metastases, followed in sequence by the lung, prostate, kidney, melanoma, and tumors of the digestive tract [2].

The diagnosis is sometimes difficult and only an anatomopathological study with immunohistochemistry allows this diagnosis to be made clear.

We report the case of a 43-year-old patient who developed, during her treatment for triple-negative breast cancer, significant orbital bone metastasis secondary to recurrent breast carcinoma.

Clinical Case

Ms. A.F., 43 years old, mother of 3 children, not menopausal and without a past medical history, was followed for a left breast lesion discovered on self-examination, whose echo mammogram revealed an ACR 5 (Classification of the Americain College of Radiology), lesion of the lower outer quadrant highly suspicious of malignancy. A biopsy with anatomopathological examination objectified an invasive ductal carcinoma, triple-negative to immunohistochemistry: hormonal receptors were negative (ER 0%, PR 0%) and the human epidermal growth factor receptor 2 negative (Her2n) revealed score 1. The extension and tolerance balance were without particulars.

Our patient underwent a lower outer quadrantectomy of the left breast and the anatomopathological study revealed an invasive ductal carcinoma of 4 cm in size, grade SBR III; the lymph node dissection has brought back 20 nodes all negative. The limits were healthy.

She then received adjuvant chemotherapy, sequential type 3AC60 (doxorubicin with cyclophosphamide and –docetaxel) followed by adjuvant radiotherapy. Three months later, we report the onset of a gradually increasing left orbital lesion (Fig. 1) associated with a slight decrease in visual acuity. The scans of the extension showed a bone metastasis of the roof of the left orbit with extra-axial and endo-orbital endocranial extension without invasion of the eyeball or other parenchymal brain damage or other damage of the bone (Fig. 2).

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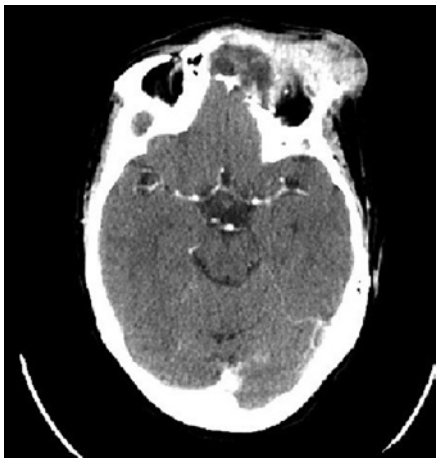

Fig. 2. Radiological image of an orbital metastasis before treatment.

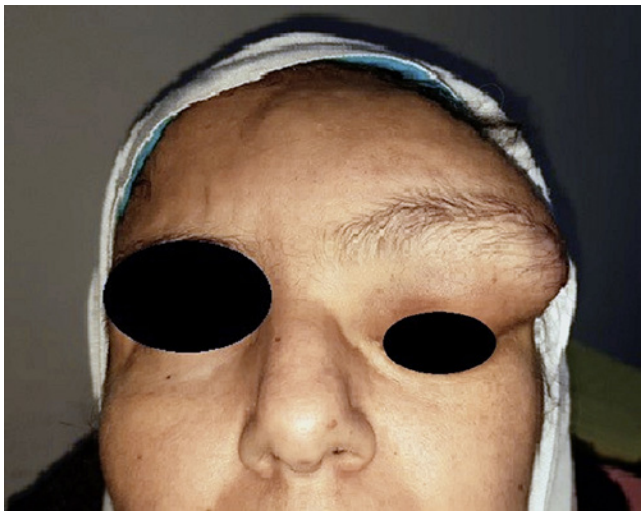

Fig. 3. Good clinical response after treatment.

The biopsy with an anatomopathological examination of this mass concluded that it was a bone metastasis of a poorly differentiated carcinoma, CK7 positive, CK20 negative, RH negative and Her2n negative pointing to a breast origin.

The decision of the multidisciplinary concertation meeting was as follows: as the tumor was inoperable, palliative radiotherapy after neoadjuvant chemotherapy was indicated. Excellent clinical response to the docetaxel/carboplatin cycle every 21 days was reported and zoledronic acid was administered with better tolerance followed by radiotherapy on the orbital mass (60 Gy; 2 Gy per session, 5 sessions/week; Fig. 3).

We continued chemotherapy for 12 months then as maintenance Endoxan 50 mg per day per os and zoledronic acid were administered; 2 months after the end of chemotherapy, diffuse pulmonary lymph nodes and hepatic secondary lesions with jaundice were observed and balanced hepatic disturbance.Under palliative care, the patient died within 20 days.

Discussion

Different etiologies are responsible for the orbital tumor syndrome. In adults, lesion lymphomas are the most common followed by inflammatory lesions. The metastases of carcinomas remain rare, accounting for only 1–13% of all orbital tumors, but they should be mentioned [1, 3, 4]. Breast cancer is the most common cause explaining between 10 and 61% of cases [5]. The most common symptoms are orbital pain, decreased visual acuity and binocular diplopia [2, 5], while exophthalmos is more frequent in cases of orbital fat infiltration. The differentiation of idiopathic inflammation, lymphoma, and metastasis is not always possible in imaging and the histopathological study of tissue biopsy is sometimes the only way to make a definitive diagnosis [6].

The two diagnostic hypotheses in our patient were malignant lymphoma or recurrent breast carcinoma. The pathology and immunohistochemical examination confirmed the diagnosis by showing positivity for CK7 and negativity for CK20.

Generally, metastases from solid tumors involve the orbit less frequently than the eye. Choroid metastasis is the most common eye tumor linked to breast cancer [7]. Orbital bone and fat are the most common extra-orbital locations and metastatic localization in the ocular extrinsic muscles is extremely rare [8, 9].

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The prevalence of breast cancer as a metastatic origin in the orbit is lacking with a clear pathophysiological explanation and from the histological point of view, the lobular subtypes of breast cancer are the most frequently reported [10, 11].

This orbital metastasis can constitute an inaugural mode of expression of the tumor affection [12]. In the series of Shields et al. [13] concerning 100 cases of orbital metastasis, metastasis was the original complaint in 19 cases (19%), including 10 cases with no found primary tumor and bilateral involvement observed in only 4 cases. In another series by Goldberg et al. [1], a little more than 25% of metastatic orbit breast cancer cases had an orbital tumor as the first sign of cancer.

Triple-negative breast cancer is defined in immunohistochemistry by the negativity of receptors to estrogen and progesterone as well as a lack of expression of human epidermal growth factor receptor 2 (Her2). This molecular subtype represents 10–15% of all breast cancers and is very heterogenous; these cases are characterized by the paradox of being very chemosensitive but remaining very aggressive with early recurrences and poor survival. 14–20% of triple-negative breast cancers present with BRCA1/2 mutations that are targets of new treatments with anti-PARP at the metastatic stage and by neoadjuvant therapy. Immunotherapy with anti-PDL1 is also shown to be effective when PDLs are expressed above 1%. Frequent metastatic sites for triple-negative breast cancer are the pulmonary, hepatic, cerebral level and bony sites [14]; on the other hand, orbital metastases are exceptional.

Pierson et al. [15] reported in a retrospective study 20 cases of orbital metastases of breast cancer; the majority (80%) were ER-positive and Her2-negative and had a more favorable survival under treatment with hormone therapy. The frequency of metastases of breast cancer overexpressing ER can be explained biologically by the presence of estrogen receptors in hormone acting as target choroid tissue steroids for lacrimal secretion [16]. On the other hand, the literature on orbital metastases in triple-negative breast cancer patients is very poor. The treatment of orbital metastases is mainly palliative since these metastases secondary to breast carcinoma usually occur in the context of a disseminated disease [8, 10]. The pillars of treatment in this indication are radiotherapy, chemotherapy combined with bisphosphonates and hormone therapy when the hormonal receptors are positive [17].

Radiotherapy gives objective response rates of more than 70% according to various studies [15]. It may be used in doses of 30–50 Gy as a single treatment or in combination with chemotherapy and hormone therapy [8]. Kouvaris et al. [4] used a high dose of radiotherapy (47.5 Gy) with greater survival (13 months). Systemic treatment with chemotherapy and bisphosphonates also increases the rate of objective response with significant improvement in symptoms.

Surgery was used as a treatment, but without any improvement in symptoms [10]. Surgical excision of an orbital metastasis may only be indicated in certain well-selected patients because it is always associated with significant morbidity and no benefit demonstrated on global survival [17].

Orbital metastases of breast cancer are characterized by their rapid progression over 2 months on average and the prognosis is generally poor with an average survival of 31 months (1–116 months) [9, 12]. The median overall survival of our patients is 26 months.

Conclusion

Orbital metastases, admittedly rare, deserve to be mentioned even outside of any history of neoplastic disease. Orbital metastasis of triple-negative breast cancer is exceptional and of unknown pathophysiology. The diagnostic approach is sometimes difficult, treatment remains palliative and the prognosis remains grim.

Statement of Ethics

The patient has given her written informed consent to publish her case (including publication of images).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Authors Contributions

Kamal El Bakraoui (principal author): data gathering, drafting of the manuscript and literature review. Bader El Morabit: (coauthor): manuscript review.

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