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CASE REPORT

Response of bilateral choroidal metastases of breast cancer to therapy with trastuzumab

E. Munzone*, F. Nolè, G. Sanna, A. Goldhirsch

Department of Medicine, Division of Medical Oncology, Day Hospital Unit, European Institute of Oncology, Via Ripamonti 435, 20141 Milan, Italy

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Summary Intraocular metastases, especially those of the choroidal plexus, are not common in metastatic breast cancer patients and are typically associated with a poor prognosis and impaired quality of life. A 45-year-old woman with breast cancer overexpressing HER2 and metastasizing to choroidal plexus, lymph nodes and skin received a combination of trastuzumab and paclitaxel as first-line treatment. Subsequently, at progression, trastuzumab was reintroduced together with vinorelbine. Administration of trastuzumab with either paclitaxel or vinorelbine led to a rapid improvement of the ocular symptoms, associated with a rapid objective response of all metastatic lesions and a prompt improvement in the quality of life. Choroidal metastases from breast cancer overexpressing HER2 are responsive to trastuzumab and chemotherapy (paclitaxel or vinorelbine). The susceptibility of ocular metastases to this approach seems different to that of other sanctuary disease sites.

Introduction

Breast cancer can affect the eye and the orbit by way of metastatic neoplastic infiltration. The choroid is the most common site of presentation, with 40% of metastatic lesions located within the temporal retinal vascular arcades.[1] The incidence of ocular metastases in patients with breast cancer has been reported to be about 3% when they are the initial manifestation and about 16% when the eye is the first systemic metastatic site of a previously diagnosed breast cancer. In one study, ocular metastases were reported to be bilateral in 38% of patients and unilateral in 62%.[2] Wiegel et al.[3] conclude that the incidence of asymptomatic choroidal metastases is about 5%, increasing to 11% when more than one organ is involved in metastatic spread; the risk is even higher in patients with lung or brain metastases. These lesions are located

Abbreviations: ER, estrogen receptor; PgR, progesterone receptor; NMR, nuclear magnetic resonance; CNS, central nervous system

*Corresponding author. Tel.: +39 257489460; fax: +39 257489457.
E-mail address: elisabetta.munzone@ieo.it (E. Munzone).

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predominantly in the posterior uveal tract, which includes the choroid and the ciliary body. The predilection of metastases for the choroid is unexplained, but it may be related to the vascular architecture. Tumor cells may pass through the internal carotid artery to the ophthalmic artery and so reach the intraocular and orbital structures. The most common presenting signs and symptoms are diminished visual acuity, metamorphosia, pain, proptosis, and conjunctival hyperemia; retinal detachment and ophthalmoplegia have also been reported, especially in patients with disease infiltrating the orbital soft tissues.[4] There is no well-established standard management of choroidal metastases, but the treatment usually includes radiotherapy, with a reported response rate of approximately 75%, the immediate goals being pain control and visual improvement.[5,6] Radiotherapy using a direct anterior field provided effective palliation for this disease site in about 72% of Doig et al.'s 32 advanced breast cancer patients with symptomatic choroidal metastases. Objective improvement was seen in about 53% of these patients, and stabilization in 19%.[7] Chemotherapy and/or hormonal therapy can also result in stabilization or regression of disease comparable to the results in other metastatic lesions.[8]

Case report

In September 1999, a 45-year-old woman was diagnosed with carcinoma in the right breast. The pathological stage and biological characteristics at diagnosis were pT1a pNo(i-)(Sn)MoG2, estrogen receptor (ER) 40%, progesterone receptor (PgR) 0%; c-erbB-2 was not determined in the primary tumor. After conservative surgery, the patient received locoregional radiotherapy without adjuvant systemic treatment.

After 2 years, the patient experienced significant visual loss with blurred vision. On examination, bilateral choroidal metastases were found. Visual acuity was reduced to 5/10 in the right eye and 9/10 in the left. The patient underwent complete restaging and was found to have multiple metastases to the skin and to the supraclavicular and mediastinal lymph nodes. Nuclear magnetic resonance (NMR) examination of the brain found smooth enhancement areas that aroused the suspicion of metastases, but no clear evidence of metastatic lesions.

A supraclavicular lymph node was biopsied, and the pathological diagnosis confirmed its metastatic origin from breast carcinoma with the following biological characteristics: ER 30%, PgR 30% and c-erbB2 overexpressed (HercepTest™: 3+, Dako, Carpinteria, Calif).

In November 2001, the patient started a treatment with trastuzumab (Herceptin™, Hoffman La-Roche, Basel, Switzerland), 2 mg/kg per week i.v., after an initial loading dose of 4 mg/kg plus paclitaxel (Taxol®, Bristol-Myers Squibb Company, Princeton, N.J.), 90 mg/m^2 per week i.v., for 3 consecutive weeks, repeated every 4 weeks. After 1 month of therapy the patient reported significant visual improvement; skin nodules and palpable lymph nodes were found to be in partial remission. After 2 months of treatment, all the palpable lesions were in complete remission and the patient had regained full visual acuity with 10/10 bilaterally. The choroidal lesions were no longer visible on ophthalmoscopy, and ultrasound showed them to be in partial remission.

After 3 months of chemotherapy the patient was still asymptomatic: a repeat CT scan of the thorax showed that the metastatic disease in the mediastinal lymph nodes was also in complete remission. Clinical examination also confirmed complete remission of the skin metastases.

Ophthalmoscopy revealed a scar on each eye, and the lesions measured on ultrasound were also reduced in size. Interestingly, angiography with Indochina Green suggested that the lesions were vascularized, and the vascular pattern of the subjacent choroid was not modified. There was no obvious exudation in the late sequences except for retention of the dye in the injured parts of the pigmentary epithelium (Figs. 1 and 2).

The patient underwent repeated brain NMR every 45–60 days during the treatment, and these exams showed evident and progressive advancement of the cerebral lesions, albeit without concomitant symptoms.

This finding led the patient to discontinue trastuzumab plus paclitaxel after 4 months of therapy and to start a new chemotherapy regimen (cyclophosphamide, methotrexate, 5-fluorouracil, vincristine, prednisone) with concomitant radiotherapy to the whole brain. After 3 months of chemotherapy, a further brain NMR was performed, which showed a reduction in the dimensions and the number of cerebral metastases (partial remission). A neck and thorax CT scan showed stability of the metastatic disease in the lymph nodes. A hormonal 'maintenance' treatment with letrozole was then started.

In November 2002, the patient again started to complain of bilateral loss of vision and blurred vision. She underwent a repeat ophthalmologic examination, which showed progression of the