Approach to Treatment for Breast Cancer Metastasis To the Orbit: A Case Report

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Abstract

Breast cancer is the most common cancer worldwide and, despite its well-known ability to spread to multiple anatomic sites, orbital metastases are considered an exceptional event.

We present the case of a 53-year-old woman who was diagnosed with luminal B cT4cN1M1 breast cancer with lung metastases (M1PUL) and bone metastases (M1OSS) and was treated with palliative chemotherapy, zoledronic acid, and hormonotherapy with no significant benefit (progressive disease).

Two years after the diagnosis, the patient complained of right eye proptosis, local pain and decrease in visual acuity. Computed tomography (CT) and magnetic resonance imaging (MRI) revealed a soft tissue mass in the right orbit, extending along the right optic nerve, but not invading it. A multidisciplinary team determined that the best next therapeutic step is orbital palliative radiotherapy. Stereotactic body radiation therapy (SBRT) was used because of the location of the metastasis and the high risk of vision loss. Proptosis and local pain were resolved two months after palliative SBRT and an imaging partial response was obtained.

Keywords: breast cancer, orbital metastasis, radiotherapy, SBRT

1. Introduction

Intraorbital metastases are rare, representing 1-13% of the orbital tumors (1,2). Breast cancer is the main primary tumor that metastasizes intraorbitally. In 12 to 31% of the affected patients, intraorbital metastasis was the initial clinical presentation (3,4). An analysis of the histopathologic characteristics of the intraorbital metastasis reported a higher incidence of the luminal subtype of ductal carcinoma, probably explained by the high number of estrogen receptors of the periorbital soft tissues (5). An increased propensity was observed for the lobular type, as compared with the invasive ductal carcinomas (6).

Radiotherapy is the established palliative treatment for orbital metastases, with modern techniques such as SBRT, allowing for the administration of maximal doses of targeted radiation while avoiding the organs at risks and thus, minimizing potential serious adverse events (cataract, radiation retinopathy, neuritis) (7).
2. Case report

2.1. History

A 53 year old patient, without significant personal or family medical history, presented to the emergency department in September 2020 with an ulcerated mass at the junction between the superior inner and outer quadrants of the right breast, associated with hard and freely mobile axillary lymphadenopathy on the soft tissue planes. The mammography described a 77/57 mm spiculated, polilobated nodule with associated micro-calculifications, infiltrating the skin and pectoral fascia. In the axilla multiple lymph nodes with a maximum size of 10/16 mm were observed. The ultrasound-guided biopsy of the breast mass and right axillary adenopathy confirmed the diagnosis of invasive moderately differentiated G2 ductal carcinoma, luminal B subtype, with lymph node metastases. The native and contrast-enhanced cerebral and thoracic-abdominal-pelvic (TAP) CT showed multiple lung nodules suggestive of secondary dissemination, osteolytic lesions in the left coccyx and the thoracic-lumbar vertebrae, which were confirmed by scintigraphy as metastatic disease. The patient was staged as stage IV, cT4cN1M1 (M1OSS, M1PUL) and started on hormone therapy (Letrozole), targeted therapy with cyclin-dependent kinase (CDK) 4/CDK6 inhibitors (Palbociclib) and osteoclasts inhibitors (Zoledronic acid). In January 2022, the follow-up CT scan showed peritoneal nodules and the treatment was changed to Ribociclib and Fulvestrant.

In April 2022 the patient presented with mild exoftalmia, ocular pain and impaired visual acuity in the right eye. The CT scan showed a de novo mass involving the right orbit, and a contrast-enhanced MRI scan was performed. It described a 15/15 mm intra-orbital lesion in contact with the right optic nerve and the right inferior rectus muscle, probably invading the latter. The lesion had malignant characteristics, such as inhomogeneous contrast enhancement (Fig. 4A). The treatment regimen was changed to weekly Paclitaxel and Fulvestrant, which remains the patient’s current treatment.

![Image of the patient’s history](image-url)
2.2. Treatment approach

Palliative stereotactic radiation was chosen for its ability to achieve a quick response to treatment, as well as due to the location of the target volume. Slices of 1.25 mm thickness were acquired using a CT simulation in the supine position with a thermoplastic mask as a contention device and the images were combined with those from the prior cerebral MRI. The planning target volume (PTV) was created by using the gross-tumor-volume (GTV) as the target volume and adding a 1 mm safety margin. Intensity-Modulated-Radiation-Therapy (IMRT) was delivered using a True-Beam-Agility multileaf collimator (MLC). The prescribed dose was 18 Gy in 3 daily fractions, calculated at 80% isodose on the PTV. Image-guided radiotherapy (IGRT) using daily cone-beam CT (CBCT) increased the reproducibility and accuracy of the administration. Five arches treatment planning allowed the dose reduction to the organs at risk, especially for the right optic nerve, situated in the proximity of the target volume. Dose constraints for all the organs at risk (optic nerves, optic chiasm, lens, ocular globes and brain) were respected, including for the right optic nerve (15.2 Gy in 0.2 cm³) (8).

![Figure 2: The spatial distribution of the five dose administration arches. A hot spot of 21.7 Gy within the irradiation volume.](image-url)

2.3. Follow-up

No adverse events were reported during the stereotactic body radiation therapy (G0 according to CTCAE 5.0-Common Terminology Criteria for Adverse Events). Contrast-enhanced cerebral MRI was performed 2 months after last SBRT, and showed regression of the right intraorbital nodule as compared to the pre-stereotactic MRI exam (12/7 mm vs. 15/15 mm, partial response, according to RECIST 1.1 criteria) (Fig. 4B). The ocular pain and exophthalmia also improved. Follow-up MRI is now scheduled every 3 months in the first year, every 6 months in the next 2 years and annually in the following 3 years. An annual ophthalmological examination to assess visual acuity was also recommended as part of the short and long-term follow-up.
Figure 3. Treatment Dose-Volume Histogram (DVH).

Figure 4. Contrast-enhanced MRI (T1, Axial Section): intra-orbital, extra-cone mass in the right orbit before SBRT (A) and after SBRT (B).

3. Discussion

The particularity of this case resides in the intraorbital localization of the metastasis, rapid need for management and lack of any other palliative treatment that would allow preservation of vision. This patient was not a surgical
candidate due to the tumor’s direct contact with the right optic nerve and the lack of a separation plan from the right inferior rectus muscle by imaging. Thus, the stereotactic radiotherapy was considered appropriate as a palliation treatment.

Because the orbit is an unusual metastatic site, the number of studies on stereotactic irradiation of orbital metastases is relatively low, with a reduced number of patients included in each study. In a retrospective study conducted by Klingenstein A et al. on 14 patients treated with a radio-stereotactic method similar to the SBRT, CyberKnife, the irradiated tumor volume ranged from 0.2 to 35 cm³, with dosages of 16.5-21 Gy (median of 18 Gy, average of 18.2 Gy) and the stabilization or regression of orbital metastasis was obtained in 87% of cases (9).

In a retrospective study conducted between 2012-2016 by Riva G et al., 21 patients with 24 intra-orbital metastases treated with SBRT were included. The median dose was 18 Gy (15-24 Gy), administered in 2-3 fractions with a median dose/fraction of 6 Gy. The average follow-up was 6.2 months (1.1-30 months) and 16 out of 24 orbital lesions had no local recurrence. Post-treatment symptoms were improved in all patients. Grade 1 acute toxicities were reported in 33% cases of irradiated tumors, and the most frequently reported ones include: conjunctival erythema (75%), epiphora (37%), and superior palpebral edema (25%). No grade 2 toxicities were reported and only 1 patient developed a long-term adverse event, ipsilateral cataract (10).

In 2008, Hirschbein et al. performed a retrospective analysis of CyberKnife-SRT (stereotactic radiotherapy) in 16 intraorbital lesions (9 of which were malignant). SRT was delivered in 2-5 fractions up to a mean dose of 20 Gy. A decrease or stabilization in the lesion’s size was registered in all patients who underwent radiological post-SRT evaluation after a mean follow-up of 7 months (11). In another retrospective report published by Mehta et al., 13 lesions near the anterior visual pathways were treated with CyberKnife-SRT in 2-5 fractions with a total mean dose of 21.7 Gy; all patients had post-SRT local control without deterioration of the visual pathway (12).

In a retrospective clinical evaluation conducted by Desheng Xu et al. on 202 patients treated with GammaKnife-SRT with dosages of 10 to 40 Gy (202 lesions, 82 of which malignant) the tumor volume irradiated ranged from 0.04 to 35 cm³. The follow-up ranged from 12 to 114 months and the local control was obtained in 93.6% of patients.

Post-treatment symptoms were improved in all patients. Grade 1 acute toxicities were reported in 9.4% cases (mostly transient conjunctival edema) (13).

Table 1. Stereotactic Radiotherapy for the treatment of orbital lesions (orbital metastases included); LC= local control, R- retrospective, pts= patients.

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients (no. of lesions)</th>
<th>Follow-up (months)</th>
<th>Treatment</th>
<th>Total Dose (range)</th>
<th>Outcome</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Klingenstein A. et al. (2012,R)</td>
<td>14 (16, all metastases)</td>
<td>6 (mean)</td>
<td>CyberKnife</td>
<td>16.5-21 Gy in 1 fx</td>
<td>LC 87%</td>
<td>No adverse effects during follow-up.</td>
</tr>
<tr>
<td>Hirschbein M.J. et al. (2008,R)</td>
<td>16 (16, 9 malignant)</td>
<td>7 (mean)</td>
<td>CyberKnife</td>
<td>10-25 Gy in 2-5 fx</td>
<td>LC 100%</td>
<td>1 pt G1 (nausea)</td>
</tr>
<tr>
<td>Mehta V.K. et al. (2002,R)</td>
<td>13 (13, 3 malignant)</td>
<td>18 (median)</td>
<td>CyberKnife</td>
<td>17.8-25 Gy in 3-5 fx</td>
<td>LC 100%</td>
<td>N/A</td>
</tr>
<tr>
<td>Riva G. et al. (2018,R)</td>
<td>21 (24, all metastases)</td>
<td>6.2 (median)</td>
<td>CyberKnife</td>
<td>15-24 Gy in 2-3 fx</td>
<td>LC 100%</td>
<td>8 pts G1 (75% conjunctival erythema, 37% increased tearing, 25% upper eyelid edema) No ≥ G2</td>
</tr>
<tr>
<td>Xu D. et al. (2010,R)</td>
<td>202 (202, 82 malignant)</td>
<td>34.5±14.7 (median)</td>
<td>GammaKnife</td>
<td>10-40 Gy in 1-2 fx</td>
<td>LC 93.6%</td>
<td>19 pts G1 (transient conjunctival edema)</td>
</tr>
</tbody>
</table>
In the case of stereotactic radiation treatment of orbital lesions, the main concern remains radiation induced optical pathway neuropathy. In a retrospective study conducted by Stafford et al. which included 215 patients treated with single stereotactic radiotherapy for benign tumors of the sellar or parasellar regions, the rates of optic nerve neuropathy were 1.7% when the dose was less than 8 Gy, 1.7% when it was between 8 and 10 Gy, and 6.9% when the dose was in excess of 12 Gy (14). For the current case, the mandatory optic pathway constraints for SBRT in 3 fractions established by the latest trials and studies were applied: \( D_{\text{Max}} (0.1\text{cm}^3) < 15\text{Gy} \) and \( D(0.2\text{cm}^3) < 15.3\text{Gy} \) (8,16-20).

SBRT gradually improves its status of optimal palliative treatment for orbital metastases, implying less risks as compared to surgery (15).

### 4. Conclusion

The orbital metastases continue to be a challenge for the short-term management of the oncologic patient due to their close anatomic relationship with radio-sensitive organs, requiring rapidly implemented treatment, without which imminent vision loss is likely to occur. The scientific and technological advances in radiotherapy allowed for the rapid and optimal approach of these metastases and SBRT represents a quick, safe and efficient method for the management of the orbital metastases.

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**Abbreviations:**

- CT – computed tomography
- MRI – magnetic resonance imaging
- SBRT – Stereotactic Body Radiation Therapy
- GTV – gross tumor volume
- LC – local control
- PTV – planning tumor volume
- IMRT – intensity-modulated radiation therapy
- M1OSS – bone metastases
- M1PUL – lung metastases
- MLC – multileaf collimator
- IGRT – image-guided radiation therapy
- CTCAE – Common Terminology Criteria for Adverse Events
- OS – overall survival
- RECIST – Response Evaluation Criteria in Solid Tumor

**Statements:**

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References:


