Case Report

Photodynamic Therapy with Verteporfin for Choroidal Metastasis Refractory to Radiotherapy

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Keywords

Choroidal metastasis · Ocular oncology · Photodynamic therapy · Radiotherapy

Abstract

A 54-year old female with longstanding metastatic breast cancer was referred for management of choroidal metastases. She was first treated with external beam radiotherapy and experienced some response before later suffering progression of her eye disease. We then treated her using full fluence Photodynamic therapy (PDT) with Verteporfin, which resulted in regression of her lesions until she passed away due to other illnesses. This is the first documented successful application of PDT for choroidal metastasis from a primary breast cancer refractory to external beam radiotherapy.

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Introduction

Breast cancer is the most common cancer to metastasize to the choroid (47% total in men and women combined) [1, 2]. Choroidal metastases are usually located between the macula and equator (80%), and mean tumor thickness is 3 mm. Our patient's tumors were representative of typical choroidal metastases. Affected patients most often present with blurred vision (70%), flashes and floaters (12%), and eye pain (7%) [2].

Radiation (delivered by plaque and/or external beam) or chemotherapy are the traditional therapies employed to manage choroidal metastases [2, 3]. However, full fluence photodynamic therapy has proven effective when chemotherapy or radiotherapy is not possible or convenient for the patient [4–8]. In this report, we describe a case of multiple choroidal metastases from breast cancer that were responsive to photodynamic therapy after radiotherapy and chemotherapy failed.

Case Report/Case Presentation

A 54-year-old female with a history of metastatic breast carcinoma presented with left-sided photopsias and decreased vision. Her breast cancer had previously been treated with lumpectomy without adjuvant radiotherapy to the breast, and she was taking Anastrozole for maintenance at the time of presentation.

Visual acuity was 20/20 in both eyes. Intraocular pressure by Tonometry was 25 mm Hg in the left eye and 24 mm Hg in the right eye. Slit-lamp examination of the external eye and anterior segment were normal in both eyes. Fundoscopic visualization and photography of the peripheral left eye showed 3 poorly defined amelanotic subretinal lesions (see Fig. 1A). Fluorescein angiography of the left eye showed mild hyperfluorescence, and optical coherence tomography (OCT) demonstrated multiple subretinal masses. Examination of the right eye was unremarkable. Choroidal metastasis of the left eye was diagnosed and the patient received whole-eye external beam radiotherapy delivered in multiple fractions to a total dose of 35 Gy. One month after the last fraction, repeat examination demonstrated stability of the lesions without obvious growth. Two months following treatment however, all left eye choroidal metastases demonstrated growth (see Fig. 1B). The patient was treated with full fluence Photodynamic therapy using a Verteporfin photosensitizer to all lesions in a single setting. One month following PDT (4.5 months after presentation), all metastases had regressed with stability of visual acuity and symptom improvement (see Fig. 1C). The patient expired three months following her last follow up due to progressive thoracic and intracranial metastases.

Discussion/Conclusion

Radiation therapy mediates cell death by direct and indirect mechanisms [9]. Direct mechanisms involve the formation of double-stranded DNA breaks, ultimately leading to death of rapidly proliferating cell populations. Indirect mechanisms involve the production of reactive oxygen species, by interaction with biomolecules to form organic free radicals, or by ionization of H₂O molecules to form hydroxy radicals [10]. Reactive oxygen species further contribute to cell death through DNA oxidation, protein oxidation, lipid peroxidation, and inactivation of enzymes [11].

In comparison, PDT acts via three mechanisms [7, 12]. PDT produces a highly reactive oxygen species, singlet Oxygen, which also directly damages tumor cells. In addition, PDT activates the immune response against tumor cells, and damages tumor-associated vasculature. In particular, Verteporfin photosensitizers selectively target vascular endothelial cells to cause photothrombosis. Thus, PDT with the use of Verteporfin is particularly effective against hypervascular tumors, such as choroidal metastases.

Photodynamic therapy (PDT) was popularized in the late 1990s for the treatment of wet age-related macular degeneration and choroidal neovascularization secondary to pathologic

myopia. Since then, the use of PDT has been explored in the treatment of various orbital tumors [9].

For choroidal metastases from breast, lung, and carcinoid primaries, whole-eye external beam radiotherapy is the therapy of reference and treatment is usually palliative [2, 3, 13]. The average life expectancy of patients diagnosed with choroidal metastases is less than one year; our patient expired 7.5 months after her initial presentation. In these cases, the type and duration of therapy should be selected with great care.

PDT can be administered in the outpatient setting during a single day, unlike chemotherapy and radiotherapy. By avoiding hospitalization and interventional surgery, PDT is likely to have decreased costs on the quality of life for patients with limited survival. Furthermore, as previously mentioned, PDT is able to target tumor-associated vasculature for hypervascular tumors, unlike radiation therapy.

Although radiotherapy is generally effective in controlling progression of choroidal metastases, a significant proportion of patients do not respond. Previous studies used PDT to treat choroidal metastases (from breast, lung, carcinoid, etc.) that were refractory to external beam radiotherapy, with generally successful results [4, 7, 8]. To our knowledge, this is the first documented successful application of PDT for choroidal metastasis (from a primary breast cancer) refractory to external beam radiotherapy. In agreement with the trends reported [7, 8], our patient experienced improved visual acuity associated with resolution of subretinal fluid, without PDT-related complications. Our case expands on existing literature to underscore the value of PDT in comparison to other options for management of choroidal metastasis.

In conclusion, PDT utilizing Verteporfin has unique benefits in the treatment of patients with choroidal metastases. PDT should be strongly considered in cases refractory to external beam radiotherapy and explored for potential role as first-line therapy.

Statement of Ethics

The study complied with guidelines for human studies. The subject gave informed consent for use of clinical images, and the case report was deemed exempt by the institute's committee on human research.

Disclosure Statement

The authors have no conflict of interest to disclose.

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Author Contributions

Raymond Zhou reviewed health records related to the case and researched relevant literature. He drafted and completed the Abstract, Introduction, Case Presentation, Discussion,

and References. He also edited the Figure legend. He compiled the different components of the Case Report into its finalized version, and served as corresponding author for submission.

David Reichstein served as the treating clinician in the case and shared his clinical experience. He collected retinal fundus photographs, produced the Figure, and Figure legend. He reviewed and edited the Abstract, Introduction, Case Presentation, Discussion, and References. He advised Raymond on submitting the case report for publication.

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Fig. 1. **A.** Optos widefield photograph of the left fundus taken at the time of presentation demonstrates three creamy yellowish choroidal or subretinal lesions superonasal, superior, and superotemporal to the optic nerve. The lesions are consistent with choroidal metastases secondary to systemic breast cancer. **B.** Optos widefield photograph taken six weeks following the completion of external beam radiotherapy to the whole left eye. Lesions have shown no regression and slight growth of the superotemporal lesion despite whole eye radiotherapy. **C.** Fundus montage photograph taken with Topcon color camera of the left fundus one month following full fluence photodynamic therapy to each lesion demonstrates RPE change and lesion flattening of all three metastases. The choroidal lesions' regression occurred despite systemic progression in the brain and lungs. **D.** Fundus montage photograph of the left fundus taken 4 months following photodynamic therapy demonstrates continued choroidal lesion regression despite systemic worsening in the head and thorax.