Photodynamic Therapy for Choroidal Metastasis

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• PURPOSE: **To evaluate the effectiveness of photodynamic therapy (PDT) in the management of choroidal metastasis.**
• DESIGN: **Retrospective, interventional case series.**
• METHODS: **Patients with choroidal metastasis treated with PDT at a single institution were reviewed. PDT was applied with verteporfin at a dose of 6 mg/m^2 body surface area and a 689 nm diode laser for 83 seconds. Visual acuity, tumor basal diameter, tumor thickness by ultrasonography, and enhanced depth imaging optical coherence tomography (EDI-OCT), as well as associated features including subretinal fluid, were recorded before PDT and during follow-up examinations.**
• RESULTS: **Twenty-one tumors in 13 eyes of 10 patients were included. Eight tumors were treated with a single session of PDT, 11 tumors received 2 sessions, 1 tumor received 3 sessions, and 1 tumor received 5 sessions. At the end of a mean follow-up of 12 months (range, 3–42 months), 9 eyes (69%) had stable or improved visual acuity, while 4 eyes (31%) had decreased visual acuity. Mean logMAR change in visual acuity was −0.09 (range, −1.3 to 0.8). Seventeen of 21 tumors (81%) were flat at last follow-up. The mean decrease in ultrasound-measured thickness was 0.83 mm (range, 2.6 mm decrease to 1.4 mm increase), while the decrease in EDI-OCT-measured thickness was 400 μm (range, 1280 μm decrease to 280 μm increase). Eighteen tumors (86%) had complete resolution of subretinal fluid. There were no PDT-related complications.**
• CONCLUSIONS: **Photodynamic therapy may be an effective therapeutic option for the management of choroidal metastasis in selected cases. (Am J Ophthalmol 2016;161:104–109. © 2016 by Elsevier Inc. All rights reserved.)**

CHOROIDAL METASTASIS IS THE MOST COMMON intraocular malignancy.[1] The mean survival of patients with choroidal metastasis is short: 18 months in patients with tumors originating from primary breast cancer and 8 months in patients with tumors originating from primary lung cancer.[1,2] Since most cases of choroidal metastasis have poor systemic prognosis, treatment of ocular manifestations should fit in the holistic care of the patient. Current treatment modalities include external beam radiotherapy, systemic chemotherapy, hormonal therapy, brachytherapy, and enucleation. External beam radiotherapy takes several weeks and multiple sessions of treatment to deliver the total required radiation dose. It can also cause anterior segment and retinal complications in some cases. Chemotherapy and hormonal therapy are usually associated with a variety of systemic side effects.

Photodynamic therapy (PDT) is a safe, noninvasive, outpatient procedure with the ability to target choroidal lesions with precision. It has been used with limited side effects in the treatment of multiple retinal and choroidal disorders including age-related macular degeneration, chronic central serous chorioretinopathy, and choroidal hemangiomas. It is also approved by the Food and Drug Administration (FDA) for the treatment of cancer including esophageal cancer, non–small cell lung cancer, and skin cancers. In 2004, Harbour first reported the use of PDT for choroidal metastasis in a patient with primary pulmonary carcinoid tumor who had failed treatment with both chemotherapy and external mean radiotherapy.[3] Since then, there have been a few additional case reports and a small case series for choroidal metastasis from breast cancer,[4–6] lung adenocarcinoma,[6,7] carcinoid tumor,[8] and leiomyosarcoma.[6] In this study, we report our experience with 21 tumors in 13 eyes of 10 patients with choroidal metastasis treated with PDT.

METHODS

THIS STUDY WAS A RETROSPECTIVE, INTERVENTIONAL CASE series of all symptomatic patients with choroidal metastasis less than 2.6 mm in thickness on ultrasonography that were managed with PDT between January 1, 2011 and June 1, 2015 at the Kellogg Eye Center, University of Michigan. No patients were excluded.

The review of existing patient records and imaging was approved retrospectively by the Institutional Review Board at the University of Michigan and adhered to the tenets of the Declaration of Helsinki. Twenty-one tumors in 13 eyes of 10 patients were included in the study. All patients underwent examination with indirect ophthalmoscopy, ultrasound measurement of tumor thickness, and enhanced depth imaging optical coherence tomography (EDI-OCT) before PDT and during follow-up visits. The data extracted from the medical record included age, sex, types of previous treatment, location of primary tumor, treatment of primary

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tumor, other systemic metastases, tumor laterality, number of tumors per eye, anteroposterior location of tumor epicenter, best-corrected visual acuity, presence of subretinal fluid, largest tumor basal diameter by indirect ophthalmoscopy, tumor thickness by ultrasound, and tumor thickness by EDI-OCT. Any available outpatient oncology records were also reviewed for information about the primary tumor, including metastasis locations, previous systemic treatment, and histopathology.

All patients gave informed written consent for treatment with PDT. Full-fluence PDT was performed according to standard institutional protocols. Intravenous verteporfin (6 mg/m^2) was infused over 10 minutes. Five minutes after completion of infusion, a 689 nm diode laser was delivered to areas of angiographic leakage for 83 seconds at an intensity of 600 mW/cm^2 (50 J/cm^2). A single spot or multiple overlapping spots were used to cover the largest diameter of the tumor with a 1 mm free margin. Follow-up examination was performed after 6 weeks and subsequently determined by clinical response to treatment. The need for additional PDT was determined by change in tumor appearance, increasing tumor size or thickness, or recurrence of subretinal fluid.

Data recorded at each follow-up visit included best-corrected visual acuity, presence of subretinal fluid, largest tumor basal diameter by indirect ophthalmoscopy, tumor thickness by ultrasound, and tumor thickness by EDI-OCT if the anterior and posterior margins of the tumor were visible. All Snellen acuities were converted to their respective logarithm to the base 10 of the mean angle of resolution (logMAR) score. Counting fingers, hand motion, and light perception were represented by 2.3, 2.6, and 2.9, respectively.[9] Tumor thickness by EDI-OCT was measured by selecting the line scan with the greatest tumor thickness. Software calipers were used to measure tumor thickness from the base of the retinal pigment epithelium to the base of the tumor demarcated by the junction of the hyperreflective inner sclera. Since previous studies have shown unreliable EDI-OCT measurements of choroidal tumor thickness larger than 2–2.5 mm, tumors with initial or final ultrasound-measured thickness greater than 2 mm were excluded from measurement with EDI-OCT.[10,11] Complications during PDT and at each follow-up visit were recorded.

RESULTS

TWENTY-ONE TUMORS OF 13 EYES OF 10 PATIENTS WITH choroidal metastasis were treated with PDT. Five eyes were treated with a single session of PDT, 6 eyes received 2 sessions, 1 eye received 3 sessions, and 1 eye received 5 sessions. Patient demographics and systemic features of the primary tumor are listed in Table 1. The mean patient age at the first session of PDT was 58 years (range, 41–70 years). Nine patients (90%) were female. The most common primary tumor was breast cancer, in 7 women. The mean interval of detection of primary to first treatment with PDT was 83 months (range, 5–264 months).

Preoperative features of each choroidal tumor are listed in Table 2. Six eyes had a solitary tumor, 6 eyes had 2 tumors, and 1 eye had 3 tumors. Nine tumors had the tumor epicenter outside of the macula, 4 were juxtapapillary, and 8 were in the macula. The mean basal diameter by indirect ophthalmoscopy was 8.6 mm (range, 3–16 mm). All tumors treated with PDT were less than or equal to 2.6 mm in ultrasound-measured thickness. The mean preoperative ultrasound-measured tumor thickness was 1.3 mm (range, 0–2.6 mm). Six tumors were excluded for EDI-OCT-measured thickness since initial or final ultrasound-measured thickness was greater than 2 mm. Of the 15 included tumors, the mean preoperative EDI-OCT-measured thickness was 974 μm (range, 340–1600 μm). All 21 tumors were initially associated with subretinal fluid. Prior to their first session of PDT, 2 patients with unilateral involvement had intravitreal Avastin injection without improvement and 2 patients received EBRT to the eye without adequate response (Table 2).

The response to treatment of each tumor is listed in Table 3. Eight tumors were treated with a single session of PDT, 11 tumors received 2 sessions, 1 tumor received 3 sessions, and 1 tumor received 5 sessions. At the end of a mean follow-up of 12 months (range, 3–42 months), 9 eyes (69%) had stable or improved visual acuity, while 4 eyes (31%) had decreased visual acuity. Mean logMAR change in visual acuity was −0.09 (range, −1.3 to 0.8). Seventeen of 21 tumors (81%) were flat at last follow-up. The mean decrease in ultrasound-measured thickness was 0.83 mm (range, 2.6 mm decrease to 1.4 mm increase), while mean decrease in EDT-OCT-measured thickness was 400 μm (range, 1280 μm decrease to 280 μm increase). Three tumors (14%) increased in ultrasound-measured thickness. Eighteen tumors (86%) had complete resolution of subretinal fluid. Two tumors had decreased but persistent subretinal fluid and 1 tumor had unchanged subretinal fluid at last follow-up. The systemic status of the primary tumor at final ophthalmic follow-up after PDT is listed in Table 1. Seven patients (70%) had increasing tumor markers or new systemic metastasis at final follow-up. There were no PDT-related complications.

DISCUSSION

DESPITE IMPROVEMENTS IN SYSTEMIC TREATMENTS OF PRIMARY cancers such as breast and lung adenocarcinoma, patients with uveal metastasis have high mortality. Patients with breast cancer metastatic to the uvea show survival rates of 65% at 1 year, 35% at 3 years, and 24% at 5 years.[12] In uveal metastasis from lung cancer, there is tumor-related