Photodynamic Therapy for Choroidal Hemangioma Associated With Serous Retinal Detachment

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Objective: To describe the clinical findings in 3 eyes with circumscribed choroidal hemangioma before and after treatment with photodynamic therapy.

Patients and Methods: In the setting of a tertiary referral center, 2 patients with circumscribed, posteriorly located, choroidal hemangiomas (thicknesses 2.4 and 2.9 mm) contiguous with the superior boundary of the optic nerve and accompanied by serous detachments of the sensory retina extending into the macula were treated with photodynamic therapy using a Zeiss diode laser (692 nm) and a sensitizing dye, verteporfin. A third patient with a circumscribed subfoveal hemangioma (3.9 mm in thickness) and a prominent serous retinal detachment was similarly treated. The tumors were studied with ultrasonography and fluorescein angiography. Visual fields were tested with Goldmann perimetry at follow-up.

Results: Following photodynamic therapy, the serous retinal detachments resolved, and the choroidal hemangioma in each of the 3 eyes regressed to a nonmeasurable thickness within 2 to 5 months. The visual acuity improved from 20/50 to 20/20, 20/150 to 20/20, and 3/200 to 20/200 in the respective cases. Two eyes were treated twice. The tumors have not recurred at follow-up visits from 11 to 16 months. Nerve fiber bundle field defects were not demonstrated with Goldmann field testing.

Conclusions: Photodynamic therapy seems to be effective in the management of circumscribed choroidal hemangioma. Following photodynamic therapy, the choroidal hemangiomas in 3 eyes were no longer measurable by ultrasonography, and the accompanying serous detachments resolved with improvement in the central visual acuities. Nerve fiber bundle defects were not identified.

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INTRAOCULAR CHOROIDAL hemangiomas are benign tumors that, because of location, growth, and the accompaniment of subretinal fluid, may cause symptoms. Ordinarily choroidal hemangiomas have not been treated unless there is either a threatened effect on central vision or an actual effect on central vision from a secondary exudative retinal detachment. Any treatment for choroidal hemangioma ideally should cause a resorption of the subretinal fluid and a regression of the tumor with little collateral damage. This report describes the clinical findings in 3 eyes with circumscribed choroidal hemangioma before and after treatment with photodynamic therapy (PDT).

REPORT OF CASES

CASE 1

A 62-year-old man had a 2-week history of decreased visual acuity in the right eye. He was referred to the Eye Department of the Mayo Clinic, Rochester, Minn, for a second opinion because he had been seen elsewhere and had been advised that his right eye harbored what appeared to be a malignant melanoma.

The ophthalmic examination showed a best-corrected visual acuity of 20/50 OD and 20/20 OS. The fundus of the left eye was normal. The fundus of the right eye showed a 7.5 × 4.0-mm, red-orange choroidal lesion that was contiguous with the optic nerve from approximately the 10-o'clock position clockwise to the 2-o'clock position (Figure 1A). The tumor was not intrinsically pigmented, but some lipofuscin was present on its surface; there was a serous detachment of the sensory retina that extended from the tumor into the macular area and the nasal fundus. There was no evidence of a cutaneous hemangioma.

A clinical diagnosis of circumscribed choroidal hemangioma with an exudative detachment was made. A fluorescein angiogram showed a prearterial...
flush and patchy hyperfluorescence at the time the retinal arterial flow was well defined (Figure 1B). There was late patchy staining of the tumor with some dye leakage into the subretinal space (Figure 1C).

B-scan ultrasonography showed a solid dome-shaped lesion involving the choroid (Figure 1D). Standardized A-scan ultrasonography demonstrated moderate elevation (2.4 mm) and high internal reflectivity, findings consistent with the clinical impression of choroidal hemangioma.

Management options that were discussed with the patient included observation, brachytherapy, transpupillary thermotherapy (TTT), and photodynamic therapy (PDT). Photodynamic therapy was chosen and administered on November 7, 2000, using a modified PDT protocol. A pretreatment sketch outlining the hemangioma and the retinal vessels was prepared to help define landmarks during the laser treatment (Figure 2A). Ten minutes after infusing 6 mg/m² of verteporfin, 3 overlapping laser applications (laser spot sizes of 4000 µm) were directed to the tumor. Each application was delivered by the Zeiss laser (692 nm), using a power calculated to be 50 joules/cm² at an intensity of 600 mW/cm² over an interval of 83 seconds. The 4000-µm spot size appeared adequate to encompass the vertical dimension of the tumor. The first application was directed toward the more temporal part of the tumor; immediately following this application, a second application to the more central part of the tumor was delivered, and a third application was finally directed to the more nasal portion of the tumor; the central application overlapped the nasal and temporal applications by approximately 1000 to 1500 µm (Figure 2B). There was no change in the clinical appearance of the retina, the retinal vasculature, or the tumor immediately after administering the laser treatment.

At a follow-up visit 6 weeks after PDT, visual acuity had improved to 20/30+ OD. B-scan ultrasonography at this time showed a reduction in the thickness of the tumor to approximately half its original thickness. Although there was no subretinal fluid recognized in the fovea, additional PDT was given. Four exposures (4000 µm in diameter) were used, with the first 3 exposures identical to those given previously, and a fourth exposure overlapping the superior boundaries of the first, second, and third exposures.

The patient returned 3 months later with a visual acuity of 20/20 OD. There was no subretinal fluid, and the tumor was no longer detectable clinically or by ultrasonography. There was subtle evidence of subretinal fibrosis, but the primary ophthalmoscopic appearance was rarefaction of the pigment epithelium at the site occupied by the original tumor (Figure 3). There was no re-
The occurrence of the tumor at a follow-up visit 14 months later. Perimetric fields using a Goldmann perimeter showed no peripheral field defects.

CASE 2

A 46-year-old man was seen in the Eye Department of the Mayo Clinic with a 1-week history of photopsias (flickering lights) and decreased visual acuity in the left eye. His general health was satisfactory; he was receiving no medication.

The best-corrected visual acuity was 20/20 OD and 20/150 OS. The pupils were equal; there was no afferent defect. The right fundus was normal. The left fundus showed an elevated orange-red choroidal tumor with some lipofuscin on its surface. There was no recognizable intrinsic pigmentation. The tumor measured 7 × 7.5 mm in base dimension and was contiguous with the superior 120° of the optic disc (Figure 4A). There was a serous detachment of the sensory retina that extended from the tumor into the macula. The clinical diagnosis was a circumscribed choroidal hemangioma. There was no evidence of a skin hemangioma. A fluorescein angiogram showed a prearterial patchy filling of the tumor with late patchy staining and dye leakage into the subretinal space, consistent with the clinical impression of choroidal hemangioma (Figure 4B). B-scan ultrasonography showed a solid dome-shaped tumor and a secondary retinal detachment (Figure 4C); standardized A-scan echography demonstrated a tumor thickness of 2.9 mm and high internal reflectivity consistent with the clinical impression of choroidal hemangioma.

Options in management were discussed with the patient. The patient chose to proceed with PDT. Ten minutes after infusing 6 mg/m² of verteporfin, 6 overlapping 83-second laser applications (laser spot sizes of 5400 µm) were directed to the tumor using the same power and intensity as described for patient 1. The first application overlapped the nasal perimeter of the tumor adjacent to the nasal edge of the disc. The second application overlapped the nasal perimeter of the tumor adjacent to the nasal edge of the disc. The second application was slightly temporal overlapping the first, and the third was located further slightly temporally overlapping the second. The fourth, fifth, and sixth applications were administered more superiorly, overlapping each other and overlapping the first 3 by approximately 2000 µm (Figure 5). There was no change in the clinical appearance of the retina, the retinal vasculature, or the tumor immediately after the laser treatment. No adverse
symptoms occurred at the time of the treatment or the following day as determined by a telephone call. When the patient returned 1 month later, the tumor measured 1.8 mm in maximum thickness, there was decreased fluid under the retina, and the visual acuity had improved to 20/60 OS. No additional treatment was given.

Four months later (5 months after the single session of PDT), the visual acuity measured 20/20 OS. There was no visible tumor by ophthalmoscopy (Figure 6A), biomicroscopy, or ultrasonography (Figure 6B). There was pigment rarefaction and some granularity of the retinal pigment epithelium in the area occupied by the original tumor along with some delicate subretinal fibrosis. A fluorescein angiogram showed a choroidal vascular pattern superior to the disc where the pigment in the pigment epithelium was rarefied; more temporally there was some late hyperfluorescence from dye accumulating in the region of the subretinal fibrosis.

There was no recurrence of the tumor at a 13-month follow-up visit. A formal Goldmann visual field showed no evidence of a peripheral field defect to suggest nerve fiber bundle damage.

CASE 3

A 67-year-old man was initially seen in the Eye Department of the Mayo Clinic in 1996 at the age of 62 years because of a posteriorly located submacular choroidal lesion that had caused a reduction in the visual acuity in his left eye. Ophthalmic examination documented a visual acuity of 20/20 OD and 20/100 OS. Intraocular tensions were 18 mm by applanation tonometry. There was no evidence of a skin hemangioma. The anterior segments showed early nuclear sclerosis in each lens. There were some drusen in the right macula. In the left eye there was a red-orange lesion in the subfoveal area, overlying lipofuscin deposits; there was some subtle pigmentation involving the superficial parts of the tumor. There was no subretinal fluid. The clinical diagnosis was choroidal hemangioma. B-scan ultrasonography showed a solid dome-shaped lesion; standardized A-scan echography demonstrated high internal reflectivity and a tumor thickness of 2.9 mm.

Figure 4. Case 2. A, Choroidal hemangioma located superior to the optic disc measuring $7 \times 7.5$ mm in base dimension and 2.9 mm in thickness. B, Fluorescein angiogram showing the patchy hyperfluorescence within the tumor at the early arterial phase of angiography. C, B-scan ultrasonography showing a dome-shaped tumor with a secondary retinal detachment. A-scan echography demonstrated high internal reflectivity and a tumor thickness of 2.9 mm.

Figure 5. Case 2. Sketch showing the outline of the choroidal hemangioma, the extension of the exudative detachment through the macula, and the relative locations of the overlapping laser application following the infusion of verteporfin.
had a thickness of 3.9 mm (Figure 7B). A-scan echography demonstrated high internal reflectivity. The choroidal hemangioma was contiguous with the superior and temporal boundary of the optic nerve for approximately 4 clock hours and had a base dimension estimated to be 9 × 8 mm. Photodynamic therapy was recommended and given in 2001 after infusing 6 mg/m² of verteporfin. Four overlapping laser applications (spot size, 5500 µm) were directed to the tumor to cover its entire surface (Figure 8). The power was calculated to be 50 joules/cm² at an intensity of 600 mW/cm² over an 83-second interval. The patient returned 2 months later and noted improvement in his visual acuity (20/200 OS) and a reduction in the size of the central scotoma. The serous detachment of the sensory retina had resolved, and the tumor was barely discernible (Figure 9A). Additional treatment was given for residual tumor using 3 overlapping laser applications with spot sizes of 5400 µm. At follow-up 6 weeks later, the tumor was not recognizable either clinically or by ultrasonography (Figure 9B). The tumor has not recurred during follow-up of 11 months.

**COMMENT**

The management of circumscribed choroidal hemangiomas with secondary retinal detachments has included photocoagulation, cryotherapy, radiation from proton beam, episcleral plaque brachytherapy, and, more recently, TTT. Laser photocoagulation may be successful in causing a regression of the exudative detachment, but recurrence of the detachment often is evident within a year, and the body of the tumor usually is not significantly affected.
Brachytherapy using radiolabeled iodine 125 or rhenium 106 has been reported as being effective by Madreperla et al. Brachytherapy using radiolabeled cobalt 60 or 106Ru has also been reported as being effective by Zografos et al in 1996 but, more recently, Zografos et al advocated proton beam therapy. Successful treatment with proton beam was also reported by Hannouche et al. While radiotherapy may destroy the hemangiomas, late complications of radiotherapy, including radiation maculopathy and optic neuropathy, may limit the therapeutic benefit.

Transpupillary thermotherapy has gained advocates of this modality as a primary treatment for circumscribed hemangioma. Although successful tumor regression has been reported, the regressions have often been incomplete with conventional TTT, and there is the real potential TTT may produce nerve fiber bundle defects as well as preretinal fibrosis in the macular region. Both of these complications have been observed in cases with small choroidal melanomas that have been successfully treated with TTT. However, published reports of choroidal hemangioma managed with TTT do not mention the complications of visual field defects from nerve fiber bundle damage.

To minimize the potential for retinal damage with TTT, Kamal et al advocated enhancing the absorption of heat energy in the choroid by using an infusion of indocyanine green 20 seconds prior to treatment. The authors were able to deliver the energy with 1-minute applications using powers up to 1250 mW. Half of the patients reported by Kamal et al received 2 treatments; the tumors regressed to a nonmeasurable scar in 5 of 6 eyes. Visual fields were not reported.

The successful treatment of circumscribed choroidal hemangioma with PDT, reported by Barbazetto and Schmidt-Erfurth, prompted the consideration of PDT as an attractive management option for treating the choroidal hemangiomas in the present series. Because the success of PDT depends not on a thermal effect but a photochemical effect, it was predicted that PDT could successfully cause regression of the hemangiomas without causing retinal damage and nerve fiber bundle field defects. This was a particularly important consideration because, in each of the cases in this report, the tumor abutted the optic nerve for approximately 120°, and nerve fiber bundle damage could potentially cause a considerable loss of peripheral field.

The thickness of the choroidal hemangiomas in the present series ranged from 2.4 to 3.9 mm, and exudative retinal detachments involved the macula in each. Following PDT the serous detachment resolved in all eyes. The visual acuity improved to 20/20 in the 2 eyes with extrafoveal hemangiomas, and the tumors regressed to nonmeasurable thicknesses in all. Two patients were treated with 2 sessions of PDT because of incomplete tumor regression observed at a 6-week follow-up. Based on the complete regression of the tumor at 5 months for patient 2, it seems reasonable to wait for up to 5 months before considering the need for a second treatment.

After images induced by staring for 83 seconds at the retina illuminated by the red aiming beam during treatment can confuse identification of the boundaries of the choroidal hemangiomas that subtly blend in with the color of normal choroid. Because of these disturbing after images, a preoperative sketch outlining the tumor and the related retinal vessels has proven valuable in helping define landmarks during treatment.

The successful short-term results with complete resolution of the choroidal hemangioma in these cases and the absence of nerve fiber bundle defects after PDT, as determined by Goldmann field perimetry, suggest that PDT may offer significant advantages over other treatment modalities. Although long-term complications are not expected after either PDT or TTT, the lack of consistent complete tumor regression with TTT and the complete regression in 5 cases of choroidal hemangioma (the 2 cases reported by Barbazetto and Schmidt-Erfurth and the 3 cases reported herein) suggest PDT is a satisfactory primary treatment for circumscribed choroidal hemangioma when treatment is indicated because of the presence of an exudative detachment extending into the macula. Although it is possible that overlapping laser exposures, as used in these cases, may increase the risk for damage to the retina by overexposure, the Goldmann visual fields did not demonstrate a nerve fiber bundle-type field defect as I have commonly observed after treat-
ing choroidal melanomas with TTT. Whereas it may be possible to treat choroidal hemangiomas without overlapping lesions, this treatment was given for the choroidal hemangioma without any treatment precedent except the 2 case reports published by Barbazetto and Schmidt-Erfurth. Subsequent to the submission of this manuscript, 3 additional cases of circumscribed choroidal hemangiomas have been successfully treated with PDT. Details regarding administration of PDT were not given for those cases.

Presently PDT seems to be an attractive and an effective option for treating circumscribed choroidal hemangiomas that are threatening central vision or have caused visual loss from a secondary exudative retinal detachment. Tumor recurrences have not been seen at follow-ups from 11 to 16 months. However, longer follow-up will be important to observe for tumor recurrences.

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REFERENCES


