

Circumscribed Choroidal Hemangioma

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Abstract

Circumscribed choroidal hemangiomas are benign vascular hamartomas without systemic associations. Generally, they are orange-red elevated masses, which are found posterior to the equator. Lesions are usually solitary and unilateral. Overlying subretinal fluid, serous retinal detachment and cystoid macular edema are common findings. Intravenous fluorescein angiography, indocyanine green angiography, ultrasonography, optical coherence tomography and enhanced depth imaging are helpful ancillary tests for diagnosis of circumscribed choroidal hemangiomas. Asymptomatic circumscribed choroidal hemangiomas do not require treatment. For symptomatic lesions with exudative retinal detachment or cystoid macular edema, photodynamic therapy has emerged as the treatment of choice with high rates of tumor regression, subretinal fluid resorption and minimal complications. Lens-sparing external beam radiotherapy, plaque brachytherapy, proton beam therapy, stereotactic radiosurgery, transpupillary thermotherapy, laser photocoagulation and anti-VEGF injections are other treatment modalities.

Keywords: Circumscribed Choroidal Hemangioma; Photodynamic Therapy; Subretinal Fluid

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INTRODUCTION

Choroidal hemangiomas are benign vascular hamartomas of the choroid that present as two subtypes: Circumscribed and diffuse. The circumscribed type manifests as an isolated unilateral tumor without systemic associations and is considered to be congenital in origin,^[1,2] while the diffuse form occurs frequently in association with Sturge–Weber syndrome. There are rare reports of circumscribed choroidal hemangioma in

patients with Sturge–Weber syndrome.^[3,4] Circumscribed choroidal hemangioma is commonly asymptomatic and usually diagnosed in adulthood during routine eye examinations or when it causes symptoms including decreased vision, visual field defects, or metamorphopsia.^[1] In the present review, we discuss the pathology and clinical features, diagnostic techniques, differential diagnoses, and treatment of circumscribed choroidal hemangioma.

INCIDENCE

Choroidal hemangiomas are probably congenital, however the incidence of the disease is difficult to estimate since most circumscribed choroidal hemangiomas only come to medical attention if the patients become symptomatic or if they are incidentally

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discovered during routine examination. Circumscribed choroidal hemangioma is considered rare. Jarrett et al diagnosed one circumscribed choroidal hemangioma for every 15 cases of choroidal melanoma.^[5] In most clinical series on choroidal hemangiomas, approximately 50% of tumors were circumscribed while 50% were diffuse tumors associated with Sturge–Weber syndrome.^[6] Average patient age for development of symptoms appears to be in the late twenties to fifties, with a range of 6 to 75 years, depending on the series reported.^[1,7] More than 90% of reported cases have been in Caucasian patients but there is no sex predilection.^[1,7]

PATHOLOGY

Hemangiomas of the choroid are probably congenital vascular hamartomas and are classified histopathologically according to the type of vessels within the tumor including cavernous, capillary or mixed.^[7] The cavernous type is composed of large vessels separated by limited connective tissue whereas the capillary type is composed of small vessels separated by loose connective tissue. The mixed type shows both capillary and cavernous features. In a case series on 45 eyes with circumscribed choroidal hemangioma, cavernous, mixed and capillary types were found in 20, 22 and 3 tumors, respectively; meanwhile, all of the 17 cases with diffuse choroidal hemangiomas associated with Sturge–Weber syndrome were of the mixed type.^[7]

Histologically, these tumors are nonproliferative lesions with no evidence of cellular proliferation in their vessel wall.^[7] Enlargement of the hemangioma itself is most likely the result of venous congestion rather than cell proliferation.^[7]

Pigmentary changes, disorganization and proliferation of the overlying retinal pigment epithelium (RPE) along with formation of fibrous plaques on the choroid, and rarely formation of a choroidal neovascular membrane have been reported.^[7,8-10] In long-standing tumors, degenerative changes such as ossification overlying the tumor may occur.^[7] The retina overlying the tumor may show alterations including mild edema or cystic degeneration, loss of photoreceptors, gliosis and occasionally, invasion from the RPE.^[7,10]

Macrophages containing lipofuscin found in both the RPE and the outer plexiform layer may cause orange or orange-yellow spots over the surface of these tumors.^[11] Serous retinal detachment is a common finding in these eyes. The nerve fiber layer and ganglion cells are never affected despite severe retinal changes.^[7]

CLINICAL FEATURES

Circumscribed choroidal hemangioma typically appears as a round or oval, orange-red elevated mass posterior to

the equator.^[12] Lesions are usually solitary and unilateral, although bilateral choroidal hemangiomas have been reported.^[13] The color of this tumor has been described as “salmon-colored”, “yellow-white”,^[14] and “grayish-pink”.^[7] Since the color of choroidal hemangioma is usually similar to the color of the surrounding choroid, it may be difficult to discern on color photographs, and choroidal elevation may be more apparent on clinical examination.

Hemangioma can compress the surrounding choroid imparting a slight brown ring around its margin.^[14] Pigmentary changes and accumulation of lipofuscin pigment (orange pigment) over the lesion have been reported.^[11]

In the largest published series of 200 patients by Shields et al the most common reported symptom was blurred vision in up to 81% of patients, while some patients noted visual field defects, metamorphopsia and floaters. At initial presentation, visual acuity ranged from 20/20 to 20/40 in 24% of subjects, was 20/200 or worse in 54% and 20/400 or worse in 34% of eyes.^[1] In the second-largest series of 45 patients with circumscribed choroidal hemangioma reported by Witschel et al 60% of the eyes were “blind” at presentation.^[7] In the Shields series, 67% of tumors were in the macula, 34% were between the macula and the equator, and no tumor was anterior to the equator. Mean tumor diameter was 6.7 mm, and mean tumor thickness was 3.1 mm. Serous retinal detachment and cystoid macular edema were reported in 81% and 17% of patients, respectively. Epiretinal membrane, subretinal hemorrhage and exudates, total retinal detachment and neovascularization of iris and angle have also been reported.^[1] All circumscribed choroidal hemangiomas reported by Witschel and Font, were located posterior to the equator, and subretinal fluid was noted in 47% of their patients.^[7] Choroidal and retinal neovascularization were found in four and three patients, respectively.^[15,16]

NATURAL COURSE

These lesions usually remain stationary in size, although there are reports of gradually progressive enlargement.^[16,17] Slight enlargement with mean increase of 1.6 × 1.5 mm in basal diameter and 0.9 mm in thickness during an average period of 52 months was reported in five cases.^[17] Vascular congestion of tumor vessels may lead to significant enlargement in tumor size.^[18]

DIAGNOSIS

Ophthalmoscopy

The most characteristic ophthalmoscopic feature of circumscribed choroidal hemangioma is its color,

which has been variously described as pink or flesh-colored, gray or yellow, orange-red, and mottled orange or gray.^[14,7] Clinically, these hemangiomas are elevated and usually round or slightly oval.^[12] Flecks of pigment, splotchy yellow material, or orange pigment may be present over the surface of the tumor which probably develop over time.^[19,20] Orange pigment, however, is more typically observed in patients with choroidal melanomas. Occasionally, there is a whitish or gray pattern over the top of the tumor with a more typical orange or orange-red base.^[21] Tumors which have been photocoagulated almost always show pigmentary changes over their surface as characteristic of photocoagulation scars. Dilated choroidal vessels may occasionally be seen nearby.^[22] "Blackening" of a circumscribed choroidal hemangioma from red-orange to dark gray may occur after surgical manipulation due to extravascular hemorrhage.^[23,24]

Macular changes can include serous retinal detachment, degeneration of the overlying retina, hard exudates, retinal pigment epithelial changes, macular pucker or epiretinal membrane formation and chronic cystic changes.^[19,25]

Visual Fields

A relative scotoma which may be about the size of the lesion, or smaller or sometimes even be? larger than the tumor may be found on visual field examination.^[26,27] The field defects corresponding to the area of the tumor are due to secondary retinal changes over the tumor itself.

Intravenous Fluorescein Angiography

The most common fluorescein angiography (FA) pattern of circumscribed choroidal hemangiomas is mild early lacy hyperfluorescence of the tumor in the pre-arterial and arterial phases, followed by moderate hyperfluorescence during the arteriovenous phase, and increasing hyperfluorescence and progressive staining of the extravascular tissue of the tumor, with variable leakage in the late phase.^[28,29] In the later stages of FA, multiloculated accumulation of dye in the outer retina develops. Occasionally, a zone of hypofluorescence is apparent at the margin of the tumor during the early and middle phases of the angiogram, which probably corresponds to blockage of choroidal fluorescence by melanocytes which are pushed to the margin of the tumor.^[7]

The angiographic appearance is not pathognomonic for choroidal hemangioma. The FA pattern of choroidal hemangioma can be to some extent comparable to other amelanotic choroidal tumors.^[30] FA may also be beneficial for visualization of the extent of serous retinal detachment and cystoid macular edema associated with the tumor.

Indocyanine Green Angiography

Indocyanine green (ICG) angiography using a high-resolution digital photography system is probably the best technique for studying circumscribed choroidal hemangiomas since it provides more ideal visualization of the choroidal vasculature.

Circumscribed choroidal hemangiomas have a characteristic pattern of rapid uniform onset of well-defined hyperfluorescence around 30 seconds which occurs much earlier as compared to other choroidal tumors.^[31] The fluorescence happens in a lacy diffuse hyperintense pattern which fills first peripherally then centrally.^[32] Intrinsic vessels are seen in approximately three-fourths of the patients.^[30] Late in the ICG angiogram, the tumor demonstrates loss of dye which is known as the characteristic "wash out" phenomenon. Schalenbourg et al believe that obscuring of the normal choroidal vasculature beneath the tumor is pathognomonic for hemangiomas. In addition, a late hyperfluorescent rim around the tumor is usually present.

Ultrasonography

The ultrasonographic pattern of choroidal hemangiomas is characteristic. On B-scan ultrasonography, the hemangioma appears as an elevated dome-shaped, acoustically solid mass, which may rarely appear mushroom-shaped or plateau-shaped.^[1,29] Choroidal excavation is not characteristically seen except with unusually large, dome-shaped tumors.^[2]

On A-scan, the choroidal hemangioma demonstrates a high initial spike which corresponds to the anterior tumor surface and high internal reflectivity between 50% and 100% due to multiple vascular channels throughout these tumors.^[33]

Both of these features are useful to distinguish choroidal hemangioma from choroidal melanoma which is usually acoustically hollow with medium to low internal reflectivity.^[1]

Neuroimaging

If a tumor is large enough it will show up on both computed tomography (CT) and magnetic resonance imaging (MRI) scans. The tumor shows moderate enhancement with contrast material on CT scan.^[2]

Magnetic resonance imaging (MRI) of choroidal hemangiomas typically shows hyperintensity as compared to the vitreous on T1-weighted images, and hyperintensity or isointensity on T2-weighted images.^[1] Choroidal hemangiomas enhance with gadolinium contrast.^[1] The MRI findings are helpful for differentiation from choroidal melanoma and metastases which show bright signals on T1-weighted images and low signals on T2-weighted images.^[1] Enhancement is earlier and much stronger for hemangioma as compared

to uveal melanoma.^[34] However, these characteristics are not pathognomonic for discrete choroidal hemangiomas and have been found with a few choroidal melanomas.^[35]

Autofluorescence

Fundus autofluorescence (AF) increases in eyes with dysfunctional RPE and decreases in with photoreceptor and RPE loss.^[36] The intrinsic AF of untreated circumscribed choroidal hemangiomas is iso-autofluorescent (58%) or hypo-autofluorescent (42%); however, treated circumscribed choroidal hemangiomas are thoroughly hypo-autofluorescent (100%).^[37]

Optical Coherence Tomography and Enhanced Depth Imaging

In choroidal tumors, traditional time-domain and spectral-domain optical coherence tomography (SD-OCT) are most useful for visualizing secondary changes in the retina and retinal pigment epithelium (RPE).^[38] In choroidal hemangiomas, OCT can be used to demonstrate macular edema, epiretinal membranes and subretinal fluid.^[39] In a report of three circumscribed choroidal hemangiomas, enhanced depth imaging (EDI) showed low to medium homogeneous reflective signals from the lesions. Moreover, small and large (possibly vascular) spaces were identified within the tumors.^[40]

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of circumscribed choroidal hemangioma is of high importance due to the probability of confusion with other lesions including choroidal nevus, amelanotic choroidal melanoma, choroidal metastasis, choroidal osteoma, central serous chorioretinopathy and posterior scleritis. It was previously reported that 5-10% of eyes enucleated for choroidal melanoma actually contained a choroidal hemangioma.^[41,42]

On clinical examination, choroidal hemangiomas have a characteristic orange-red color, unlike choroidal metastases which usually appear in creamy-yellow color and amelanotic melanomas which often tend to be yellow-tan.^[1] Ancillary modalities such as ultrasonography, indocyanine green angiography, CT scan and MRI imaging are also of benefit in distinguishing these conditions as formerly discussed.

CHOROIDAL HEMANGIOMA AND PREGNANCY

Little is known regarding the behavior of choroidal hemangioma in pregnancy. There is one report of leakage from a circumscribed choroidal hemangioma in pregnancy, and the fluid resolved following full-term normal delivery.^[43] In another report of three

patients with choroidal hemangioma, exudative retinal detachments developed during the third trimester of pregnancy.^[44] None of these patients had symptoms or signs of pre-eclampsia. Victoria et al reported that following delivery, the subretinal fluid tends to reabsorb and the hemangioma ceases to leak. The retina was flat at 5 months after delivery following one episode of thermotherapy in one case. In another case, the retina was flat at month 9 postpartum with no treatment. However, resolution of an exudative detachment after delivery does not occur as a rule. The third patient suffered from total retinal detachment and secondary glaucoma, and finally required enucleation.^[44]

Isolated hemangiomas are known to remain stable or grow very slowly.^[17] Shields et al demonstrated that enlargement was the result of venous congestion and not due to cell multiplication.^[18] The altered hemodynamic state in pregnancy may result in engorgement of vascular networks within the hemangioma, leading to increased transudation of fluid into the subretinal space. This can explain the observed leakage from a choroidal hemangioma in the late stages of pregnancy. The effect of hormonal changes on the growth of vascular malformations is unknown.

TREATMENT

Observation alone may be indicated in cases of asymptomatic hemangiomas demonstrating no subretinal fluid and also in subfoveal tumors which have resulted in hyperopic amblyopia.^[1] Hemangiomas with advanced visual deficits and minimal anticipated visual potential may also be observed but one should consider that progressive subretinal fluid may lead to neovascular glaucoma and ultimately the need for enucleation.

There are different treatments for symptomatic serous retinal detachment associated with choroidal hemangiomas including photodynamic therapy (PDT), plaque brachytherapy, external beam and proton beam radiation, stereotactic radiosurgery, transpupillary thermotherapy, laser photocoagulation, oral propranolol and anti-VEGF injections.

Photodynamic Therapy (PDT)

Photodynamic therapy (PDT) currently appears to entail the best results in treating symptomatic circumscribed choroidal hemangioma with exudative retinal detachment.^[45]

PDT is typically performed with administration of intravenous verteporfin at a dose of 6 mg/m² followed by treatment with laser wavelengths of 689, 690, or 692 nm at an intensity of 600 mW/cm² with durations ranging from 83 to 166 seconds (50–100 J/cm²).^[46-50] PDT has been shown to eliminate subretinal fluid caused by subfoveal neovascularization. Although the non-growing vascular

channels in choroidal hemangiomas are different as compared to those of neovascular tissue, PDT might be able to cause atrophy of the hemangioma vessels and thus decrease leakage and the associated vision loss. The reason for the relative specificity of PDT for hemangioma vessels with respect to normal choroidal and retinal vessels can only be postulated. Perhaps the relatively large caliber of the cavernous hemangioma vessels, and thereby the greater blood volume relative to the thinness of their vascular walls, leads to more effective treatment using activated verteporfin.^[51] Cellular injury by PDT is mediated by singlet oxygen. The main advantage of PDT is selectivity of the treatment and minimal disruption of normal tissues. In various studies, visual acuity improvement or stabilization after PDT for choroidal hemangioma ranged from 73% to 100%.^[52] Blasi et al reported the five-year outcomes of 25 patients treated with PDT for circumscribed hemangioma and found that visual acuity improved by two lines in 76% of patients with complete resolution of macular exudation in all cases and no complications were observed.^[46] There have been numerous case series describing patients with circumscribed choroidal hemangioma in which the majority of subjects received one PDT treatment.^[46-54]

In two case series, the vast majority of patients required more than one PDT treatment because the treatment goal was complete resolution of the tumor, not just resolution of subretinal and intraretinal fluid.^[50,51] Considering several case series on PDT for choroidal hemangioma, the baseline tumor thickness ranged from 2.6 to 3.8 mm. Subretinal and/or intraretinal exudation resolved in 93-100% of patients. All patients displayed tumor regression to some extent, and 7-100% had complete tumor resolution.^[46-54]

More sessions of PDT may increase the risk of choroidal atrophy and neurosensory retinal degeneration.^[51] Visual acuity improvement has been shown to be inversely associated with the number of PDT sessions. Whether this is a side effect of PDT *per se* or because larger tumors need more PDT sessions is unknown.^[50-52] In a study including 50 patients, 95% of the subjects required only one session of PDT with complete resolution of the tumor and fluid. A second session was needed in 5% to resolve persistent or recurrent subretinal fluid.^[55] Long-term recurrence of subretinal fluid is uncommon.^[55,56]

Laser Photocoagulation

Laser photocoagulation (Xenon or Argon) has been an effective treatment modality for hemangiomas for many years prior to development of PDT. Anand et al using argon or xenon laser, showed a 79.2% improvement in visual acuity and subretinal fluid, with a 40% rate of recurrent subretinal fluid after initial treatment.^[57] Shields et al reported 62% resolution of subretinal fluid and 71% stability of vision with argon laser photocoagulation.^[1]

However, laser photocoagulation does not reduce tumor size and cannot be used to treat subfoveal lesions.^[45] The main complication of laser photocoagulation is extension of RPE atrophy and coexistent scotomas. Other reported complications include epiretinal membrane, choroidal neovascularization, vascular occlusion and retinal bleeding, and higher rates of recurrent subretinal fluid.^[1,45] Diode laser photocoagulation has been shown to be equally effective with probably lower absorption by RPE.^[8] Currently, laser photocoagulation is rarely used to treat hemangiomas as it has been largely replaced by photodynamic therapy.

Transpupillary Thermotherapy

Transpupillary thermotherapy (TTT) utilizes 810 nm diode laser with a large spot size and long exposure time leading to increased temperature and irreversible cytotoxic effect, sclerosis of vascular channels and partial or complete tumor regression in many patients.^[58] The use of TTT is limited to extrafoveal post-equatorial circumscribed choroidal hemangiomas with shallow subretinal fluid with basal tumor diameter <10 mm and tumor thickness <4 mm.^[58,59] If the tumor margin touches the optic disc, TTT is not a proper treatment as it may induce thermal papillitis.^[60] TTT leads to tumor regression in many patients (42%, complete and 53%, partial regression), however it carries a risk of cystoid macular edema, preretinal fibrosis, focal iris atrophy and retinal vascular occlusion.^[58] Gunduz found that all tumors ceased leaking following TTT along with resolution of subretinal fluid. Visual acuity improved by two or more Snellen lines in 77% of eyes and remained unchanged in 23%.^[58] Indocyanine green dye can be injected before TTT to enhance heat uptake.^[61] Few authors believe that tumors larger than 10 mm in diameter and thicker than 4 mm may respond to TTT.^[62]

Radiation

Radiation therapy has been recommended for choroidal hemangiomas with extensive subretinal exudation and retinal detachment which are difficult to treat with PDT. Radiation therapy often results in retinal reattachment and tumor regression, though it carries the risk of radiation-induced side effects such as cataract, subretinal fibrosis, radiation retinopathy, and optic neuropathy.^[63]

External Beam Radiotherapy

Lens sparing external beam radiotherapy (EBRT) has predominantly been used for diffuse choroidal hemangioma with a dose range of 20 to 25 gray (Gy) in some cases and 35 to 40 Gy in others.^[64] More precise radiation in a single session has been performed for circumscribed hemangioma with gamma knife radiosurgery. Kong et al reported three patients

treated with a maximal dose of 10 Gy with acceptable anatomical and functional outcomes, and no side effects with follow-up period of 18 to 36 months.^[65] EBRT treats the entire choroid with a homogeneous dose of radiation.^[63]

In the largest series of choroidal hemangiomas treated with EBRT, subretinal fluid resolved in 63.8% and visual acuity was stable or improved in 78% of patients.^[66] Ritland et al reported tumor regression in all nine treated eyes with EBRT.^[64] Some studies also reported successful treatment of circumscribed choroidal hemangioma with lens sparing-EBRT.^[1,67]

Plaque Brachytherapy

Plaque radiotherapy (brachytherapy) has been applied for treatment of multiple ocular disorders, most commonly choroidal melanomas. Plaque brachytherapy allows more targeted treatment of the hemangioma, minimizing radiation-induced side effects but the dose is not homogeneous with higher doses at the tumor base than the apex.^[63,67] Plaque radiotherapy is usually used for choroidal hemangioma with extensive subretinal fluid in which PDT would not be advised. Low-dose treatment is sufficient using 20 Gy apex dose.^[64] Aizman et al reported five patients treated with palladium-103 plaque for circumscribed hemangiomas. All patients showed complete resolution of subretinal fluid with tumor height decreasing by a mean of 50%.^[68] Brachytherapy with palladium-103, cobalt-60, ruthenium-106, and iodine-125 have all been used for treatment of circumscribed choroidal hemangioma.^[1,68-72] Tumor regression and resolution of subretinal fluid was noted in all patients treated with iodine-125 plaque, and signs of radiation retinopathy were noted in 38% of subjects.^[70] Zografos et al reported the largest series of 39 patients with circumscribed choroidal hemangioma treated with cobalt-60 plaque brachytherapy who showed 100% retinal reattachment. Complications included pigment migration into the treated area, subretinal fibrosis and an areolar atrophic scar.^[71] Subretinal fluid was resolved in all patients treated by Shields et al and visual acuity improved or became stable in 53 % of cases.^[1] The disadvantage of plaque brachytherapy is the necessity for two surgeries for plaque placement and removal.

Proton Beam Radiation

Proton beam radiation involves delivery of a precise dose of radiation to a target tissue. Surgical intervention is necessary prior to radiation to place tantalum clips for tumor localization. Protons unlike other rays deposit high energy when they slow down reducing the scattering effect on surrounding tissues. In a retrospective review of 71 patients with choroidal hemangioma treated with

20 Cobalt Gray Equivalent of proton beam radiation, improvement in visual acuity, resolution of subretinal fluid and tumor regression were observed in 52%, 100% and 91.5% of subjects, respectively. Meanwhile, cataract and radiation maculopathy developed in 28% and 8% of patients, accordingly.^[72]

In 2004, at 2-year follow-up, 94% of patients treated by Frau et al with proton beam radiation had visual acuity improvement of two or more lines, and 65% of subjects showed complete tumor resolution.^[63] Zografos et al^[73] reported a series of 48 eyes with circumscribed choroidal hemangioma treated with a radiation dose ranging from 16.4 to 27.3 Gy and all of the patients had resolution of exudative retinal detachment but three patients treated with 27.3 Gy developed optic neuropathy.

Disadvantages of proton beam radiation include the necessity to travel to an equipped center, need for one surgery and greater cost as compared with other treatments.

Gamma Knife Radiosurgery

Gamma knife radiosurgery allows accurate focusing of radiation along with a single session treatment and less effect on surrounding structures such as the lens and optic nerve.^[74] It can also be used for large choroidal hemangiomas where transpupillary thermotherapy, PDT and photocoagulation may not be feasible.^[74] Kim et al treated three patients with circumscribed choroidal hemangioma with a marginal dose of 10 Gy; exudative retinal detachment resolved completely within 3 months and visual acuity improved in all three cases.^[74] Song et al treated two patients with marginal dose of 26.7 Gy and reported that retinal detachment resolved in both cases, but vision worsened in one patient and was stable in the other case.^[73]

Stereotactic radiotherapy (gamma knife) does not require any surgical intervention, though the case series are quite small and clinical experience with this procedure is limited.

Anti-vascular Endothelial Growth Factor Agents

Anti-vascular endothelial growth factor (anti-VEGF) agents are known to reduce vascular permeability and are effective for resolution of subretinal and intraretinal fluid in multiple ophthalmic pathologies. The role of anti-VEGF agents in treatment of choroidal hemangioma is still uncertain and more studies are required. Sagong et al^[76] reported beneficial effect from bevacizumab for three patients with circumscribed hemangiomas. One patient was treated with bevacizumab alone for recurrence following laser photocoagulation and two patients were treated with bevacizumab and PDT as primary treatment. All patients showed improvement in visual acuity with resolution of subretinal fluid and

edema. At mean follow-up of 8 months, none of the patients showed any evidence of recurrence or adverse effects.

The authors hypothesized that the use of bevacizumab prior to PDT reduces tumor thickness through resorption of subretinal fluid, and this may maximize the effect of PDT.

Oral Propranolol

Propranolol is a nonselective beta-blocker commonly used in cardiology. Capillary endothelial cells express beta adrenergic receptors.^[77] Sanz-Marco et al^[78] treated one circumscribed choroidal hemangioma with 120 mg/day oral propranolol. Visual acuity improved to 20/20 and the macular detachment resolved without systemic or local adverse effects. The authors explained that propranolol may induce vasoconstriction, decrease expression of bFGF, HIF-1 and VEGF, and inhibit endothelial proliferation. Indeed, propranolol induces apoptosis of cultured capillary endothelial cells.^[79] Good visual results after treatment with oral propranolol may open a new treatment research line for choroidal hemangioma.

SUMMARY

Circumscribed choroidal hemangiomas are benign vascular hamartomas and have a typical clinical appearance. The diagnosis can be confirmed by ancillary tests such as ultrasonography, FA and ICG angiography. No systemic work up is needed because there is no systemic association. Although circumscribed choroidal hemangioma is a benign tumor, it may be a cause of visual impairment through subretinal fluid, refractive errors, intra-retinal edema and amblyopia. Photodynamic therapy is the treatment of choice for symptomatic hemangiomas with high rates of tumor regression, subretinal fluid resorption and minimal complications. Different types of radiation therapy are reserved for larger hemangiomas with extensive retinal detachment which are not amenable to treat with PDT. Recently, new therapies such as oral propranolol and intravitreal injection of anti-VEGF agents have been introduced.

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Conflicts of Interest

There are no conflicts of interest.

REFERENCES

- Shields CL, Honavar SG, Shields JA, Cater J, Demirci H. Circumscribed choroidal hemangioma: Clinical manifestations and factors predictive of visual outcome in 200 consecutive cases. *Ophthalmology* 2001;108:2237-2248.
- Shields JA, Shields CL. Circumscribed choroidal hemangioma. In: Shields JA, Shields CL, editors. *Intraocular Tumors: An Atlas and Textbook*. 2nd ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2008. p. 230-245.
- Scott IU, Alexandrakis G, Cordahi GJ, Murray TG. Diffuse and circumscribed choroidal hemangiomas in a patient with Sturge-Weber syndrome. *Arch Ophthalmol* 1999;117:406-407.
- Cheung D, Grey R, Rennie I. Circumscribed choroidal haemangioma in a patient with Sturge Weber syndrome. *Eye (Lond)* 2000;14(Pt 2):238-240.
- Jarrett WH 2nd, Hagler WS, Larose JH, Shields JA. Clinical experience with presumed hemangioma of the choroid: Radioactive phosphorus uptake studies as an aid in differential diagnosis. *Trans Sect Ophthalmol Am Acad Ophthalmol Otolaryngol* 1976;81:862-870.
- Reese AB. *Tumors of the Eye*. 3rd ed. Hagerstown, MD: Harper and Row; 1976.
- Witschel H, Font RL. Hemangioma of the choroid. A clinicopathologic study of 71 cases and a review of the literature. *Surv Ophthalmol* 1976;20:415-431.
- Lanzetta P, Virgili G, Ferrari E, Menchini U. Diode laser photocoagulation of choroidal hemangioma. *Int Ophthalmol* 1995-1996;19:239-247.
- Leys AM, Bonnet S. Case report: Associated retinal neovascularization and choroidal hemangioma. *Retina* 1993;13:22-25.
- Jones IS, Cleasby GW. Hemangioma of the choroid: A clinicopathologic analysis. *Am J Ophthalmol* 1959;48:612-628.
- Shields JA, Rodrigues MM, Sarin LK, Tasman WS, Annesley WH Jr. Lipofuscin pigment over benign and malignant choroidal tumors. *Trans Sect Ophthalmol Am Acad Ophthalmol Otolaryngol* 1976;81:871-881.
- Boixadera A, García-Arumí J, Martínez-Castillo V, Encinas JL, Elizalde J, Blanco-Mateos G, et al. Prospective clinical trial evaluating the efficacy of photodynamic therapy for symptomatic circumscribed choroidal hemangioma. *Ophthalmology* 2009;116:100-105.e1.
- Schepens CL, Schwartz A. Intraocular tumors. I. Bilateral hemangioma of the choroid. *AMA Arch Ophthalmol* 1958;60:72-83.
- Hogan MJ. Choroidal hemangioma. *Arch Ophthalmol* 1964;71:69-70.
- Ruby AJ, Jampol LM, Goldberg MF, Schroeder R, Anderson-Nelson S. Choroidal neovascularization associated with choroidal hemangiomas. *Arch Ophthalmol* 1992;110:658-661.
- Leys AM, Silva R, Inhoffen W, Tatar O. Neovascular growth following photodynamic therapy for choroidal hemangioma and neovascular regression after intravitreal injection of triamcinolone. *Retina* 2006;26:693-697.
- Medlock RD, Augsburger JJ, Wilkinson CP, Cox MS Jr, Gamel JW, Nicholl J. Enlargement of circumscribed choroidal hemangiomas. *Retina* 1991;11:385-388.
- Shields JA, Stephens RF, Eagle RC Jr, Shields CL, De Potter P. Progressive enlargement of a circumscribed choroidal hemangioma. A clinicopathologic correlation. *Arch Ophthalmol* 1992;110:1276-1278.
- Gass JD. *Differential Diagnosis of Intraocular Tumors*. St. Louis: Mosby; 1974.
- Shields JA, Rodrigues MM, Sarin LK, Tasman WS, Annesley WH Jr. Lipofuscin pigment over benign and malignant choroidal tumors. *Trans Sect Ophthalmol Am Acad Ophthalmol Otolaryngol* 1976;81:871-881.
- Rosen E. Hemangioma of the choroid. *Ophthalmologica* 1950;120:127-149.
- Duke-Elder S, Perkins ES. *Diseases of the uveal tract. System of*

- Ophthalmology. Vol. 9. St. Louis: Mosby; 1966.
23. Schalenbourg A, Zografos L. Blackening of choroidal hemangioma after tantalum clip surgery. *Arch Ophthalmol* 2007;125:1136.
 24. Bosch MM, Helbig H. Blackening of a choroidal hemangioma after photodynamic therapy. *Klin Monbl Augenheilkd* 2005;222:258-260.
 25. Bonnet M. Cavernous hemangioma of the choroid. Clinical review of 10 cases. *Ophthalmologica* 1981;182:113-118.
 26. Flindall RJ, Drance SM. Visual field studies of benign choroidal melanomata. *Arch Ophthalmol* 1969;81:41-44.
 27. Maclean AL, Maumenee AE. Hemangioma of the choroid. *Am J Ophthalmol* 1960;50:3-11.
 28. Norton EW, Gutman F. Fluorescein angiography and hemangiomas of the choroid. *Arch Ophthalmol* 1967;78:121-125.
 29. Singh AD, Kaiser PK, Sears JE. Choroidal hemangioma. *Ophthalmol Clin North Am* 2005;18:151-161, ix.
 30. Arevalo JF, Shields CL, Shields JA, Hykin PG, De Potter P. Circumscribed choroidal hemangioma: Characteristic features with indocyanine green videoangiography. *Ophthalmology* 2000;107:344-350.
 31. Shields CL, Shields JA, De Potter P. Patterns of indocyanine green videoangiography of choroidal tumours. *Br J Ophthalmol* 1995;79:237-245.
 32. Schalenbourg A, Piguet B, Zografos L. Indocyanine green angiographic findings in choroidal hemangiomas: A study of 75 cases. *Ophthalmologica* 2000;214:246-252.
 33. Long RS. Problems of diagnosis and treating choroidal hemangiomas. *Ophthalmol Times* 1981;6:144.
 34. Stroszczynski C, Hosten N, Bornfeld N, Wiegel T, Schueler A, Foerster P, et al. Choroidal hemangioma: MR findings and differentiation from uveal melanoma. *AJNR Am J Neuroradiol* 1998;19:1441-1447.
 35. Peyster RG, Augsburger JJ, Shields JA, Hershey BL, Eagle R Jr, Haskin ME. Intraocular tumors: Evaluation with MR imaging. *Radiology* 1988;168:773-779.
 36. Schmitz-Valckenberg S, Holz FG, Bird AC, Spaide RF. Fundus autofluorescence imaging: Review and perspectives. *Retina* 2008;28:385-409.
 37. Ramasubramanian A, Shields CL, Harmon SA, Shields JA. Autofluorescence of choroidal hemangioma in 34 consecutive eyes. *Retina* 2010;30:16-22.
 38. Shields CL, Materin MA, Shields JA. Review of optical coherence tomography for intraocular tumors. *Curr Opin Ophthalmol* 2005;16:141-154.
 39. Spaide RF, Koizumi H, Pozzoni MC. Enhanced depth imaging spectral-domain optical coherence tomography. *Am J Ophthalmol* 2008;146:496-500.
 40. Torres VL, Brugnoli N, Kaiser PK, Singh AD. Optical coherence tomography enhanced depth imaging of choroidal tumors. *Am J Ophthalmol* 2011;151:586-593.e2.
 41. Ferry AP. Lesions mistaken for malignant melanoma of the posterior uvea. A clinicopathologic analysis of 100 cases with ophthalmoscopically visible lesions. *Arch Ophthalmol* 1964;72:463-469.
 42. Shields JA, Zimmerman LE. Lesions simulating malignant melanoma of posterior uvea. *Arch Ophthalmol* 1973;89:466-471.
 43. Pitta C, Bergen R, Littwin S. Spontaneous regression of a choroidal hemangioma following pregnancy. *Ann Ophthalmol* 1979;11:772-774.
 44. Cohen VM, Rundle PA, Rennie IG. Choroidal hemangiomas with exudative retinal detachments during pregnancy. *Arch Ophthalmol* 2002;120:862-864.
 45. Tsipursky MS, Golchet PR, Jampol LM. Photodynamic therapy of choroidal hemangioma in Sturge-Weber syndrome, with a review of treatments for diffuse and circumscribed choroidal hemangiomas. *Surv Ophthalmol* 2011;56:68-85.
 46. Blasi MA, Tiberti AC, Scupola A, Balestrazzi A, Colangelo E, Valente P, et al. Photodynamic therapy with verteporfin for symptomatic circumscribed choroidal hemangioma: Five-year outcomes. *Ophthalmology* 2010;117:1630-1637.
 47. Zhang Y, Liu W, Fang Y, Qian J, Xu G, Wang W, et al. Photodynamic therapy for symptomatic circumscribed macular choroidal hemangioma in Chinese patients. *Am J Ophthalmol* 2010;150:710-715.e1.
 48. Barbazetto I, Schmidt-Erfurth U. Photodynamic therapy of choroidal hemangioma: Two case reports. *Graefes Arch Clin Exp Ophthalmol* 2000;238:214-221.
 49. Singh AD, Kaiser PK, Sears JE, Gupta M, Rundle PA, Rennie IG. Photodynamic therapy of circumscribed choroidal haemangioma. *Br J Ophthalmol* 2004;88:1414-1418.
 50. Porrini G, Giovannini A, Amato G, Ioni A, Pantanetti M. Photodynamic therapy of circumscribed choroidal hemangioma. *Ophthalmology* 2003;110:674-680.
 51. Schmidt-Erfurth U, Hasan T, Gragoudas E, Michaud N, Flotte TJ, Birngruber R. Vascular targeting in photodynamic occlusion of subretinal vessels. *Ophthalmology* 1994;101:1953-1961.
 52. Jurkles B, Bornfeld N. The role of photodynamic therapy in the treatment of symptomatic choroidal hemangioma. *Graefes Arch Clin Exp Ophthalmol* 2005;243:393-396.
 53. Jurkles B, Anastassiou G, Ortman S, Schüler A, Schilling H, Schmidt-Erfurth U, et al. Photodynamic therapy using verteporfin in circumscribed choroidal haemangioma. *Br J Ophthalmol* 2003;87:84-89.
 54. Verbraak FD, Schlingemann RO, Keunen JE, de Smet MD. Longstanding symptomatic choroidal hemangioma managed with limited PDT as initial or salvage therapy. *Graefes Arch Clin Exp Ophthalmol* 2003;241:891-898.
 55. Shields CL, Materin MA, Marr BP, Mashayekhi A, Shields JA. Resolution of advanced cystoid macular edema following photodynamic therapy for choroidal hemangioma. *Ophthalmic Surg Lasers Imaging* 2005;36:237-239.
 56. Tuncer S, Demirci H, Shields CL, Shields JA. Polypoidal choroidal vasculopathy following photodynamic therapy for choroidal hemangioma. *Eur J Ophthalmol* 2009;19:159-162.
 57. Anand R, Augsburger JJ, Shields JA. Circumscribed choroidal hemangiomas. *Arch Ophthalmol* 1989;107:1338-1342.
 58. Gündüz K. Transpupillary thermotherapy in the management of circumscribed choroidal hemangioma. *Surv Ophthalmol* 2004;49:316-327.
 59. García-Arumí J, Ramsay LS, Guraya BC. Transpupillary thermotherapy for circumscribed choroidal hemangiomas. *Ophthalmology* 2000;107:351-356.
 60. Shields CL, Shields JA, Perez N, Singh AD, Cater J. Primary transpupillary thermotherapy for small choroidal melanoma in 256 consecutive cases: Outcomes and limitations. *Ophthalmology* 2002;109:225-234.
 61. Kamal A, Watts AR, Rennie IG. Indocyanine green enhanced transpupillary thermotherapy of circumscribed choroidal haemangioma. *Eye (Lond)* 2000;14(Pt 5):701-705.
 62. Rishi P, Sharma T. Transpupillary thermotherapy for large-sized subfoveal circumscribed choroidal hemangioma. *Retina* 2006;26:974-976.
 63. Frau E, Rumen F, Noel G, Delacroix S, Habrand JL, Offret H. Low-dose proton beam therapy for circumscribed choroidal hemangiomas. *Arch Ophthalmol* 2004;122:1471-1475.
 64. Ritland JS, Eide N, Tausjø J. External beam irradiation therapy for choroidal haemangiomas. Visual and anatomical results after a dose of 20 to 25 Gy. *Acta Ophthalmol Scand* 2001;79:184-186.
 65. Kong DS, Lee JI, Kang SW. Gamma knife radiosurgery for choroidal hemangioma. *Am J Ophthalmol* 2007;144:319-322.
 66. Schilling H, Sauerwein W, Lommatzsch A, Friedrichs W, Brylak S, Bornfeld N, et al. Long-term results after low dose

- ocular irradiation for choroidal haemangiomas. *Br J Ophthalmol* 1997;81:267-273.
67. Madreperla SA, Hungerford JL, Plowman PN, Laganowski HC, Gregory PT. Choroidal hemangiomas: Visual and anatomic results of treatment by photocoagulation or radiation therapy. *Ophthalmology* 1997;104:1773-1778.
68. Aizman A, Finger PT, Shabto U, Szechter A, Berson A. Palladium 103 (103Pd) plaque radiation therapy for circumscribed choroidal hemangioma with retinal detachment. *Arch Ophthalmol* 2004;122:1652-1656.
69. Chao AN, Shields CL, Shields JA, Krema H. Plaque radiotherapy for choroidal hemangioma with total retinal detachment and iris neovascularization. *Retina* 2001;21:682-684.
70. López-Caballero C, Saornil MA, De Frutos J, Bianciotto C, Muiños Y, Almaraz A, et al. High-dose iodine-125 episcleral brachytherapy for circumscribed choroidal haemangioma. *Br J Ophthalmol* 2010;94:470-473.
71. Zografos L, Bercher L, Chamot L, Gailloud C, Raimondi S, Egger E. Cobalt-60 treatment of choroidal hemangiomas. *Am J Ophthalmol* 1996;121:190-199.
72. Levy-Gabriel C, Rouic LL, Plancher C, Dendale R, Delacroix S, Asselain B, et al. Long-term results of low-dose proton beam therapy for circumscribed choroidal hemangiomas. *Retina* 2009;29:170-175.
73. Zografos L, Egger E, Bercher L, Chamot L, Munkel G. Proton beam irradiation of choroidal hemangiomas. *Am J Ophthalmol* 1998;126:261-268.
74. Kim YT, Kang SW, Lee JI. Gamma knife radiosurgery for choroidal hemangioma. *Int J Radiat Oncol Biol Phys* 2011;81:1399-1404.
75. Song WK, Byeon SH, Kim SS, Kwon OW, Lee SC. Gamma knife radiosurgery for choroidal haemangiomas with extensive exudative retinal detachment. *Br J Ophthalmol* 2009;93:836-837.
76. Sagong M, Lee J, Chang W. Application of intravitreal bevacizumab for circumscribed choroidal hemangioma. *Korean J Ophthalmol* 2009;23:127-131.
77. Giatromanolaki A, Arvanitidou V, Hatzimichael A, Simopoulos C, Sivridis E. The HIF-2alpha/VEGF pathway activation in cutaneous capillary haemangiomas. *Pathology* 2005;37:149-151.
78. Sanz-Marco E, Gallego R, Diaz-Llopis M. Oral propranolol for circumscribed choroidal hemangioma. *Case Rep Ophthalmol* 2011;2:84-90.
79. Sommers Smith SK, Smith DM. Beta blockade induces apoptosis in cultured capillary endothelial cells. *In Vitro Cell Dev Biol Anim* 2002;38:298-304.