PEER REVIEWED

Amelanotic Choroidal Melanoma

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Abstract

Choroidal melanoma is a common intraocular malignancy among Caucasian adults. This serious and potentially life-threatening lesion is associated with high rates of metastasis. This teaching case report describes an otherwise healthy young patient presenting with amelanotic choroidal melanoma. Differential diagnoses, symptoms, clinical findings, ancillary tests, treatment options and prognosis for amelanotic choroidal melanoma are discussed. Recognition of the clinical manifestations of choroidal melanoma leads to an early diagnosis and timely initiation of treatment.

Key Words: *amelanotic choroidal melanoma, uveal melanoma, intraocular tumor, choroidal nevus, retinal detachment*

Background

Uveal melanoma is the most common intraocular malignancy and involves the choroid in approximately 90% of cases.[1,2] Melanomas are potentially life-threatening lesions that arise from melanocytes at various locations throughout the body, including ocular structures, such as the uvea, conjunctiva, eyelid and orbit.[1,3] Prognosis of uveal melanoma depends on several factors, including tumor size, location and configuration, as well as extraocular extension.[4] The American Joint Committee on Cancer Classification Staging Manual provides a detailed classification for anterior and posterior uveal melanoma prognostication.[4,5] In addition to a dilated fundus exam, ancillary tests provide information and aid in diagnosis confirmation and timely treatment and management.[6] This is a case report of an amelanotic choroidal melanoma in an otherwise healthy 32-year-old white male. Clinical presentation, differential diagnosis, pertinent ancillary tests, treatment options and prognosis for amelanotic choroidal melanoma are discussed. The intended audience is third- and fourth-year optometry students, optometry residents and primary care optometrists.

Case Description

A 32-year-old white male presented with decreased vision in the left eye for three weeks. He complained of seeing a white pulsating obstruction in his left eye. The patient denied symptoms of flashes, floaters or recent history of ocular trauma. Ocular history and medical history were unremarkable, and the patient did not use any medications. His last medical exam was five years prior. The patient reported that he was a heavy smoker with a 15-year one pack per day history.

Best-corrected visual acuity was 20/20 in the right eye and 20/200 in the left eye. Pupils were round and reactive to light with a grade 1 afferent pupillary defect in the left eye. Confrontation visual field testing was full to finger counting in the right eye, and there was inferior-nasal constriction present in the left eye. During red cap desaturation testing, the patient subjectively reported 50% red cap desaturation in the left eye. Intraocular pressure was 16 mmHg in both eyes. Slit lamp exam of the anterior segment was unremarkable in both eyes.

Goldmann visual field testing performed on the same day was reliable in both eyes. Visual field in the right eye was full, while visual field in the left eye revealed nasal hemifield loss, which corresponded to confrontation visual field test results **(Figure 1)**. Optical coherence tomography (OCT) imaging of the left eye was unattainable because views of the optic nerve and macula were obstructed.



Figure 1. Goldmann visual field test in the left eye (left) and right eye (right). Click to enlarge



Figure 2. B-scan ultrasonography of the left eye.
Click to enlarge

Dilated retinal exam was unremarkable in the right eye. Significant posterior segment findings in the left eye included a large bullous, undulating rhegmatogenous retinal detachment superior-temporal with a detached macula. A retinal specialist, who further evaluated the retinal detachment, was consulted on the same day.

Ancillary tests performed at the retinal consultation included B-scan ultrasonography and ultra-widefield retinal photography. B-scan ultrasonography of the left eye revealed a 10-mm dome-shaped lesion with a surrounding retinal detachment **(Figure 2)**. Ultra-widefield (Optos) retinal imaging of the right eye was unremarkable **(Figure 3)**. Retinal imaging of the left eye revealed a large and pale dome-shaped lesion with intrinsic vasculature in the superior-temporal retina with a surrounding retinal detachment **(Figure 3)**. The patient was referred to an ocular oncologist.



Figure 3. Ultra-widefield retinal images (Optos) of the right eye (left) and left eye (right). Click to enlarge

Two weeks later, the patient was diagnosed with amelanotic choroidal melanoma by the ocular oncologist and underwent plaque brachytherapy. Three days after treatment, the patient presented to the emergency department actively vomiting with 10/10 left-side head pain and an intraocular pressure of 53 mmHg in the left eye. Maximum medical therapy, including administration of intravenous Diamox, resulted in minimal intraocular pressure-lowering effect. Due to poor response to this treatment and possible adverse reactions from previous therapies, enucleation of the left eye was performed the following day. The patient was scheduled for magnetic resonance imaging (MRI) of the abdomen, computed tomography (CT) scan of the chest, and liver function tests to evaluate for metastasis. The patient was instructed to return for follow-up in one, three and six months, and every six months thereafter.

Education Guidelines

Completion of courses in ocular disease and optometric theory and procedures are recommended for third- and fourth- year optometry students to actively participate and benefit from this case discussion.

Key concepts

1. Recognition of the clinical manifestations of uveal melanoma
2. Treatment options and management of uveal melanoma
3. Differential diagnoses when encountering uveal melanoma

Learning objectives

At the conclusion of this case report, readers should be able to:

1. Understand clinical findings associated with amelanotic choroidal melanoma
2. Differentiate amelanotic choroidal melanomas from pseudo-melanomas
3. Know how to use ancillary tests to aid in diagnosis and management

Discussion points

1. What differential diagnoses should be considered in cases of suspected choroidal melanoma?
2. What symptoms are associated with choroidal melanoma?
3. What clinical findings are associated with choroidal melanoma?
4. What ancillary tests can aid in the diagnosis of choroidal melanoma?
5. What are current evidence-based treatment and management strategies for choroidal melanoma?
6. What is the prognosis for choroidal melanoma?

Literature review

Amelanotic choroidal tumors can have various presentations, including melanoma, nevus, metastasis, hemangioma, peripheral exudative hemorrhagic chorioretinopathy, scleral calcification, osteoma, lymphoma, solitary idiopathic choroiditis and choroidal effusion, among others.[7,8] In a report of 5,586 amelanotic choroidal tumors in 4,441 patients, the demographics of patients with amelanotic choroidal melanomas were Caucasians (97%) who presented with a unilateral lesion (100%) at a mean age of 57 years.[7] Additionally, prevalence was equal among males and females.[7,9] A meta-analysis found that predisposing factors for uveal melanoma included light eye color, fair skin color and inability to tan.[10] Identifying pre-existing and predisposing factors for amelanotic choroidal melanoma aids in diagnosis.

Discussion

Teaching methodology: To facilitate active learning, participants should read each discussion question and formulate answers. This should be carried out before reading the discussion section. Participants are encouraged to read reference articles and research independently to aid in making evidence-based answers. Participants should partake in group discussion and share their evidence-based answers with one another. Learning objectives are to be assessed by comparing participants' responses with the information provided.

What differential diagnoses should be considered in cases of suspected choroidal melanoma?

The leading differential diagnoses for choroidal melanoma are choroidal nevus, peripheral exudative hemorrhagic chorioretinopathy, congenital hypertrophy of the retinal pigment epithelium (RPE), hemorrhagic RPE detachment, choroidal hemangioma, age-related macular degeneration, RPE hyperplasia and several others.[11] Choroidal nevus is the most common differential diagnosis and can be the most difficult to differentiate from a choroidal melanoma.[11] The rate of malignant transformation of a choroidal nevus is 1 in 8,845, based on the premise that all melanomas arise from pre-existing nevi.[12] Risk factors for nevus transformation into melanoma include thickness greater than 2 mm, subretinal fluid, symptoms, orange pigment, tumor proximity within 3 mm of the optic disc, ultrasound hollowness, halo absent, and drusen absent, which can be remembered by the mnemonic "To Find Small Ocular Melanoma Using Helpful Hints Daily."[13] The first letter of each word in the mnemonic corresponds to a risk factor:

To	**T**hickness greater than 2 mm
Find	**F**luid present in subretinal space
Small	**S**ymptoms

Ocular	**O**range pigment overlying the lesion
Melanoma	**M**argin within 3 mm of the optic disc
Using **H**elpful	**U**ltrasound **H**ollowness
Hints	**H**alo absence
Daily	**D**rusen absence

A study comparing 5,586 amelanotic choroidal tumors found that amelanotic choroidal melanoma demonstrated significantly larger basal diameter, greater thickness, more frequent association with subretinal fluid and ultrasound hollowness compared with other amelanotic choroidal lesions.[7] Early detection of choroidal melanoma leads to improved patient prognosis; therefore, ancillary tests and referral to an ocular oncologist may be necessary to ensure proper diagnosis.

What symptoms are associated with choroidal melanoma?

Patients with choroidal melanoma may present with symptoms of flashes, floaters, decreased vision and visual field defects.[4,14,15] Often, patients are asymptomatic.[4,15] This highlights the importance of routine dilated eye exams as choroidal melanoma can be detected on routine eye exam in asymptomatic patients. When patients experience reduced vision, it is usually caused by tumor involvement of the macula or by exudative retinal detachments.[14]

What clinical findings are associated with choroidal melanoma?

The majority of choroidal melanomas are pigmented, but they can also present as non-pigmented or a combination of pigmented and non-pigmented.[9] Choroidal melanomas are typically elevated masses that appear dome-shaped or mushroom-shaped.[4,16] Most choroidal melanomas are large (thickness >2 mm), but smaller melanomas should not be mistaken for choroidal nevi.[2,13] The presence of subretinal fluid is very common in choroidal melanoma.[4,7] The melanoma disrupts the architecture of the retina and its vascular supply, which leads to subretinal fluid accumulation. There is a strong association of exudative retinal detachment with choroidal melanoma.[17] In contrast, the presentation of rhegmatogenous retinal detachment with choroidal melanoma is rare, accounting for less than 1% of choroidal melanoma cases.[18] Retinal detachment is a major source of vision loss, regardless of the type.[17] The presence of orange pigment (representing lipofuscin deposits at the level of the RPE) is another clinical finding characteristic of choroidal melanoma.[14] Using the mnemonic “To Find Small Ocular Melanoma Using Helpful Hints Daily” can help the clinician to identify clinical features consistent with choroidal melanoma.[13]

What ancillary tests can aid in the diagnosis of choroidal melanoma?

Diagnosis of choroidal melanoma can be made without the use of ancillary tests by assessing clinical features on dilated fundus exam. Ancillary tests help to confirm diagnosis. These tests may include OCT, optical coherence tomography angiography (OCTA), fluorescein angiography (FA), indocyanine green angiography (ICGA), retinal imaging and B-scan ultrasonography.

Spectral domain OCT uses enhanced depth imaging for visualization of the posterior segment of the eye.[16] OCT imaging can aid in the precise localization of intraocular tumors. OCT findings characteristic of choroidal melanoma include deep optical shadowing, overlying choriocapillaris compression, subretinal lipofuscin deposition, RPE atrophy and the presence of subretinal fluid with overlying “shaggy” photoreceptors.[19] Subretinal fluid is an important characteristic in choroidal melanoma.[4,7] OCT can detect the presence of subretinal fluid before it becomes clinically visible.[20] In a study of 20 patients with

untreated choroidal melanoma, OCT detected subretinal fluid in all cases.[20]

OCTA is a non-invasive imaging technique that allows visualization of the retinal and choroidal vasculature.[6] Pellegrini et al.[6] analyzed swept source OCT-A images in 22 eyes with choroidal melanoma and found that tumor intrinsic microvasculature was detected in all cases. OCTA is a relatively novel imaging technique and therefore not widely utilized. OCTA may have a prominent role in the near future given its ability to detect tumor intrinsic vasculature.

In comparison to OCTA, FA and ICGA are invasive imaging techniques used to visualize intrinsic vasculature of choroidal tumors. ICGA is preferred over FA for angiography of choroidal tumors because of the improved visualization of the choroidal vasculature by indocyanine green.[21]

Retinal imaging techniques such as fundus photography and ultra-widefield retinal imaging are useful ways to document tumor appearance. Clinicians can better monitor tumor response to treatment by comparing tumor size to previous retinal images. Ultra-widefield retinal imaging may aid in identifying large tumors that are otherwise difficult to appreciate with clinical exam alone.

B-scan ultrasonography is the most important ancillary test.[14] In cases when visualization of the tumor is obscured by retinal detachment or vitreous hemorrhage, ultrasonography can make the tumor visible.[4] B-scan ultrasonography can aid in characterizing the tumor by obtaining tumor dimensions.[14] Typical findings in large choroidal melanomas include acoustic hollowness, choroidal excavation and orbital shadowing.[7,14] Choroidal melanomas typically have a mushroom-shaped configuration and display low to medium reflectivity on B-scan ultrasonography.[22]

What are current evidence-based treatment and management strategies for choroidal melanoma?

Selection of treatment and management strategies must take into account tumor size, tumor location, associated features, status of the opposite eye, patient's systemic health condition, patient's age and, most importantly, patient's desire.[4,15] Management choices for choroidal melanoma include enucleation, surgical resection, radiotherapy and laser therapy.[23] The majority of choroidal melanomas are treated with plaque brachytherapy.[15,23] Brachytherapy involves adhering a radioactive plaque to the episclera to deliver a fixed dose of focal radiation to the tumor.[14,23] The plaque is surgically removed after several days of treatment.[14] Potential complications that may arise include radiation-induced retinopathy, cataracts, neovascular glaucoma and macular edema.[23] Transpupillary thermal therapy is a type of laser therapy that focuses energy to destroy tumor vasculature, and is typically used as an adjuvant therapy after brachytherapy.[23] Besides plaque brachytherapy, other types of radiation therapy include photon-based external-beam radiation, and charged particle raditation.[23] Enucleation is the most common surgery performed for uveal melanoma, but other surgical strategies include transretinal endoresection and transscleral resection.[23] There are higher rates of tumor recurrence with transscleral resection when compared to enucleation or brachytherapy, which is an important consideration.[23] The Collaborative Ocular Melanoma Study found no difference in patients' five-year survival rate when comparing enucleation vs. pre-enucleation radiation treatment for large choroidal melanomas.[24]

What is the prognosis for choroidal melanoma?

Choroidal melanoma can spread to numerous organ systems including the lungs, skin, gastrointestinal tract and liver, which is the primary site of metastasis for uveal melanoma.[23,25] Despite excellent rates of local disease control, approximately 50% of patients develop metastatic disease.[23] Systemic monitoring with liver function tests twice yearly and an annual physical exam, MRI of the abdomen and CT scan of the chest are advised.[4] Prognosis with uveal melanoma varies depending on tumor size, location, configuration and extraocular extension.[2,4] In a study involving 8,033 patients with uveal melanoma, each millimeter increase in tumor thickness was found to be associated with an approximately 5% increased

rate of metastasis.[2] The Kaplan-Meier estimates for metastasis at 5, 10 and 20 years was 35%, 49% and 67%, respectively, for large melanoma (>8 mm).[2]

Conclusion

Choroidal melanoma is a common intraocular tumor in Caucasian adults. Several conditions mimic amelanotic choroidal melanoma leading to a diagnostic dilemma. Understanding the clinical presentation of choroidal melanoma aids in differentiation. Because these malignant tumors are capable of metastasis, early diagnosis and initiation of treatment are essential.

Disclosure

The authors declare that there are no financial nor intellectual conflicts of interest.

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