

CE Credit - Case Report(s) & Topic Review

Amela-what?: The Case of the Non-pigmented Choroidal Lesion

Megan D. Tomsik, OD¹

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ABSTRACT

There are numerous tumors that can occur within the choroid, including pigmented and non-pigmented lesions. Generally, clinicians are prone to seeing pigmented lesions, such as a choroidal nevus. Due to the limited exposure that clinicians have with amelanotic lesions, this case report will discuss the differential diagnoses of non-pigmented lesions as well as examine the clinical characteristics, diagnostic tactics, management, and treatment of choroidal osteomas.

INTRODUCTION

Bone formation in the eye is a rare occurrence that is still widely misunderstood. The calcification of bone occurs in areas of the body that have a rich blood supply. This movement of blood carries osteoblasts to the area, forming the complex architecture of bone. Bone ossification intraocularly has been noted through histological studies since the early 1800s and was first introduced as a case study in 1975 by Henry Van Dyk and associates.

Due to the amelanotic features of choroidal osteoma on clinical presentation, diagnosis depends on a thorough workup. There is still much that is unknown about amelanotic lesions of the choroid. Due to this, additional studies with larger pools of patients will be needed to better understand their different distinct properties and to make a diagnosis more easily.

CASE REPORT

A 73-year-old white male presented to the clinic for a full exam. The patient had an ocular history of glaucoma suspect, pseudophakia, and a choroidal nevus in the right eye that was noted on a 2013 examination. The patient had a significant history of prostate cancer and was reported to be currently in remission but was very frail.

The patient's entering corrected acuities were 20/50+2 OD, 20/40 OS. The acuities were reduced secondary to dryness and refractive error. Post-refraction best corrected visual acuities improved to 20/25- OD, 20/30-2 OS. Preliminary testing revealed full and unrestricted EOMs, normal pupils, and full confrontational fields.

Anterior segment displayed clear lids, lashes, conjunctiva, and sclera. Moderate superficial punctate keratitis was seen on the cornea, and the anterior chamber was deep and quiet in both eyes. Goldmann tonometry could not be performed due to patient mobility. Tonopen revealed borderline increased pressures, 21 OD, 23 OS mmHg. The angles were open.

Posterior segment revealed pseudophakia with lenses that were clear and centered. Mildly asymmetric C/D ratios were noted with some crowding. The optic nerve heads revealed 0.30/0.30 (H/V) OD, and 0.25/0.25 (H/V) OS with an intact neuroretinal rim OU. No evidence of hemes, pallor, edema, or NVD in either eye was displayed. A previous drance heme was seen inferiorly in the right eye, but no evidence of pallor was noted on this examination. Both macular areas were flat with even pigment and vessels displayed a normal AV ratio. Vitreous revealed PVDs in both eyes but no holes, breaks, or tears were noted in the periphery. Posterior pole revealed a 1 DD choroidal nevus in the inferior temporal arcades of the right eye. There was no evidence of elevation, drusen, or lipofuscin. This was previously noted on a 2013 examination of the patient. According to the chart review, this finding appeared stable. A 5-7 DD amelanotic lesion was seen in the inferior temporal arcades OS with slight elevation present. This was a new finding for the patient (Figures 1 and 2).

¹Biloxi VA Medical Center, Biloxi, Mississippi, USA

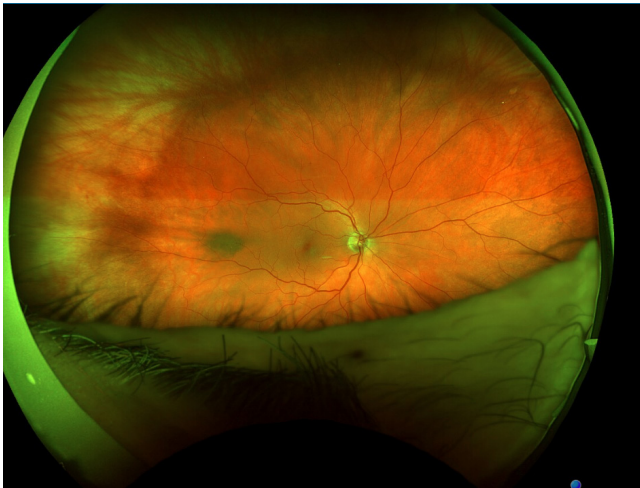


FIGURE 1: Optos of right eye showing choroidal nevus inferior temporal



FIGURE 2: Optos of left eye showing lesion inferior temporal.

A HVF 24-2 was performed for the patient's glaucoma, revealing a sup nasal step in the right eye and superior nasal and inferior nasal steps in the left eye. Latanoprost was prescribed at this visit to use at bedtime in both eyes due to the visual field findings. Fundus photos and Optos were performed as well to reveal the amelanotic lesion in the OS.

Multiple OCT scans were performed, displaying the lesion in the following images (Figure 3). No subretinal fluid or overlying RPE changes were noted, but a distinct lattice pattern was seen with the use of the EDI-OCT. The lesion is elevated, but measures less than 2 mm thick. Fundus autofluorescence revealed no alteration to the AF signal (Figure 4).

OCT-Angiography was attempted, but due to patient mobility, dryness of the corneas, and the location of the lesion, no distinct or reliable image resulted.

Metastatic signs such as irregular borders, satellite lesions, exudative retinal detachment, and RPE thickening on OCT were not seen upon examination. A diagnosis of an amelanotic lesion was made and a consult to retina was ordered.

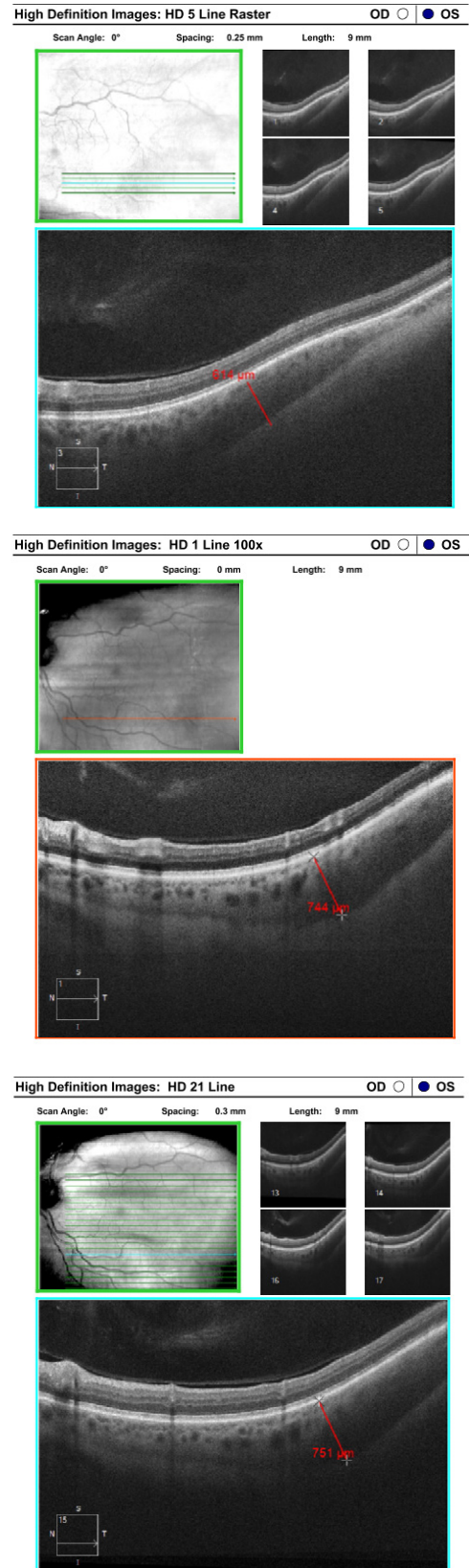


FIGURE 3: (A) OCT of Amelanotic lesion, thickness < 2mm with mild latticework. (B) HD 1 Line with EDI provides a much more detailed view of the elevated choroidal lesion and associated latticework. (C) A slice from HD 21 Line with EDI showing similar findings to (B).

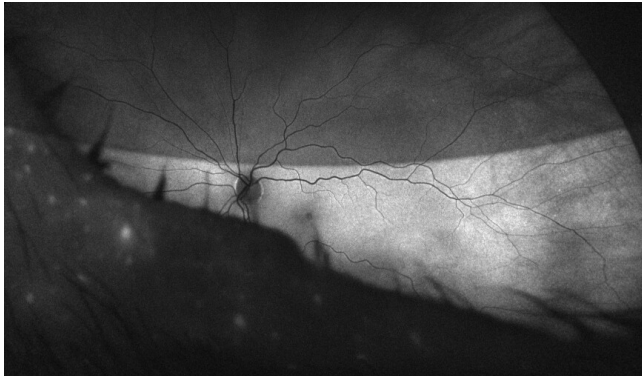


FIGURE 4: Fundus autofluorescence showing no alteration of the AF signal due to a fully calcified lesion. If the lesion was decalcified, AF would show a reduced signal.

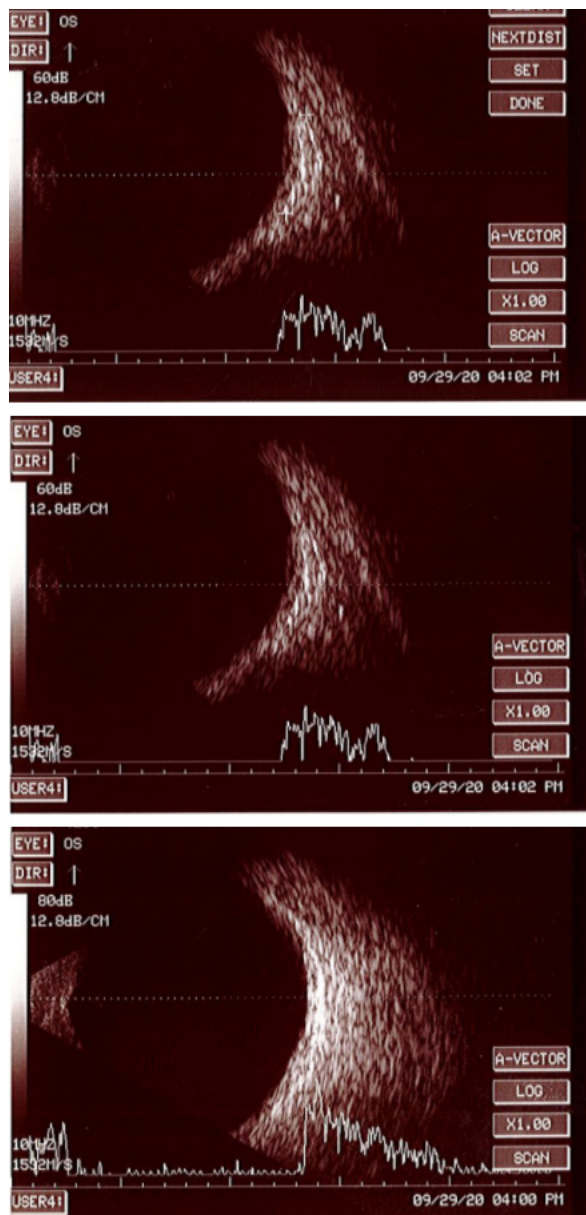


FIGURE 5: B-Scans displaying mild choroidal thickening and anterior hyperreflectivity with low gain.

RETINA VISIT

Retina also noted a past medical history of prostate cancer, but no history of melanoma. The retinal specialist determined a 2 disc diameter flat hyperpigmented choroidal nevus in the right eye with mild drusen along the inferior temporal arcade (no heme/subretinal fluid/orange pigment). A ~5-7 disc diameter amelanotic lesion with slight elevation along the inferior temporal arcade (no heme/SR Fluid/Orange pigment) was also seen in the left eye. Retina diagnosed the patient with a benign choroidal nevus in the right eye that needed periodic clinical monitoring. The retinal specialist considered differentials of amelanotic lesion versus an osteoma or malignant melanoma.

A B-Scan was performed, and it revealed minimal elevation and mild choroidal thickening with increased reflectivity at low gain (Figures 5 and 6). The final diagnosis of this amelanotic lesion is a choroidal osteoma based on the B-Scan findings. Retina proposed that the patient should be clinically monitored by their care every 6 months for a dilated exam, B-scan, and OCT. If any changes occurred within that six months, other differentials would be considered.

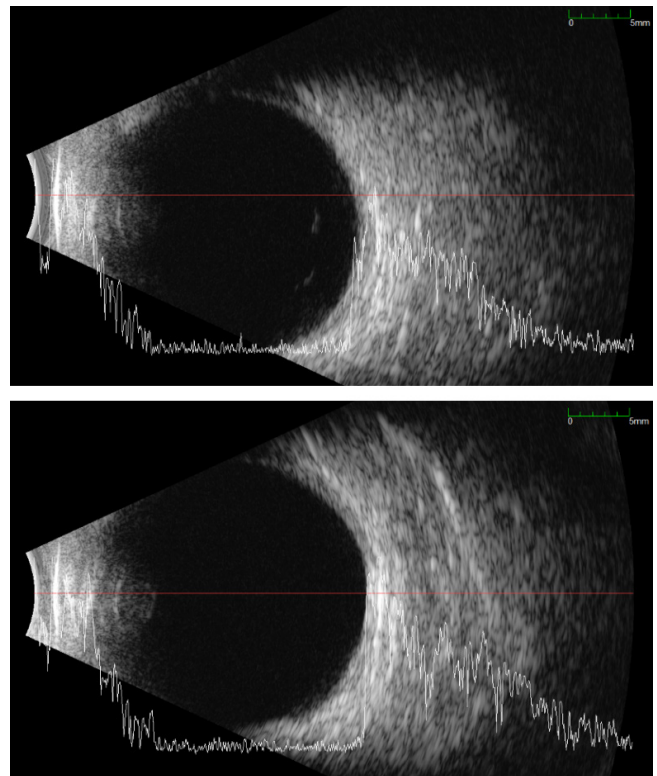


FIGURE 6: EYECUBE: Multiple images displaying mild choroidal thickening and anterior hyperreflectivity with low gain. All testing was very difficult due to patient mobility and frailty.

DISCUSSION

Pigmented lesions of the choroid are very common presenters in ocular examinations. Non-pigmented lesions are much less common, hence making them less known clinically. It is important to know your differentials, perform a thorough exam, and know a good referral source when diagnosing and managing amelanotic lesions of the choroid. Due to the difficulty in making a diagnosis with non-pigmented lesions fundoscopically, it is important to rely on systemic cues and additional testing.

Any diagnosis of choroidal lesions should be observed quickly after discovery. The first observation after diagnosis should be at a minimum of 3-4 months after diagnosis to confirm if the lesion is stable. Afterward, the lesion should be evaluated 1-2 times annually. Low-risk lesions can be followed yearly, whereas high-risk lesions should be followed every 3-6 months. "The published data suggest a low rate (1/8845) of malignant transformation of a choroidal nevus in the white population."

A detailed drawing or photo with the lesion size and location is important, but relying on clinical presentation alone makes it difficult to make an accurate diagnosis. The clinical course of the lesion, associated signs and symptoms visually and systemically, and additional ancillary testing are critical in making the right diagnosis.

Differential diagnoses for an amelanotic choroidal lesion include amelanotic choroidal nevus, choroidal hemangioma, metastatic carcinoma, solitary choroidal granuloma (e.g., sarcoidosis, tuberculosis), posterior scleritis, sclerochoroidal calcification, and a choroidal osteoma. The following paragraphs will discuss briefly each differential and a more in-depth discussion of a choroidal osteoma.

The most common choroidal lesions are the choroidal nevus. These are typically pigmented but can present without pigment. Choroidal nevi are most commonly found in the Caucasian race, presenting in roughly 5-10% of the race and approximately 30% of eyes. It is rare to see choroidal nevi in darker-skinned races. Most nevi appear early in a person's life. Growth during puberty is common and it is rare for a new nevi formation in adulthood. Clinically, this is helpful because if a lesion appears de novo, this should alert suspicion for malignancy. They are thought to even be present at birth. ,

There is no absolute definition of a choroidal nevus, but the Collaborative Ocular Melanoma Study states that a melanocytic choroidal lesion that is ≤ 5 mm in the largest basal dimension and is ≤ 1 mm in height is classified as a choroidal nevus. Choroidal melanomas rarely contain calcium and lack distinct margins.

The majority of choroidal nevi are asymptomatic and can be detected on clinical examinations. If there is ever a question on examination that a pigmented nevus is present,

the red free filter can be used. Retina remains with red free. Therefore, a choroidal nevus should "disappear" with the red free filter. They usually display a grey-green appearance and are oval or circular. Depigmented halos and overlying drusen are common. Amelanotic choroidal nevi represent 6-10% of the choroidal nevi population. No solitary hyporeflective lesion was seen on B Scan in this case eliminating this as a diagnosis.

Choroidal hemangioma is typically a circumscribed or diffuse red-orange lesion and can be elevated. They can appear like an early choroidal osteoma before depigmentation occurs. Diffuse lesions occur almost exclusively with Sturge Weber patients. Isolated hemangiomas most often occur in the posterior pole near the macula or optic nerve. They are often well-circumscribed and are typically dome shaped. OCTs can display atrophy, retinoschisis, or sub and intraretinal fluid. A serous retinal detachment is a common finding. The chart below indicates the patterns and findings of different kinds of testing. In this case, the hemangioma was ruled out due to B scan patterns. The choroidal hemangioma typically shows a solid lesion with a well-defined anterior surface. The anterior surface does not display high reflectivity compared to a choroidal osteoma.

Metastatic carcinoma is similar to choroidal osteomas in color. It presents as a cream or light brown lesion and can be slightly elevated with extensive sub-retinal fluid. These lesions can be bilateral in 25% of cases or multifocal. Patients can also have a history of cancer, especially breast or lung cancer. Patients typically display minimal symptoms, such as mild blur. The lesion is oftentimes quick to grow and differs from the choroidal osteoma because the margins are usually indistinct. Typically, most melanomas are pigmented and metastasis is often associated with an exudative retinal detachment. The OCT of a metastatic lesion shows RPE thickening versus a choroidal osteoma with RPE thinning. FA is also distinctly different, showing early hypofluorescence and hyperfluorescence with the metastatic carcinoma and choroidal osteoma, respectively.

Solitary choroidal granuloma (e.g., sarcoidosis, tuberculosis) can also cause lesions in the choroid. If either of these diagnoses is suspected, a systemic work-up is in order. Sarcoid choroidal lesions can appear as a solitary granuloma or in multiples, displaying a punched-out appearance. Most inflammatory choroidal lesions are bilateral due to the systemic nature of the diseases but can be unilateral too. Choroidal neovascularization and scarring are common findings with this diagnosis.

Tuberculosis manifests as tubercles or tuberculomas in the choroid. The tubercles can be unilateral or bilateral and are typically white to yellow in color with indistinct borders. FA shows late hyperfluorescence. The tuberculomas appear as a white, solitary subretinal mass that is accompanied by an exudative retinal detachment. Echography shows solid, elevated lesions with moderate to low internal reflectivity.

Both forms of these granulomas are typically associated with indistinct margins and vitreous cells. These lesions also do not demonstrate a specific pattern on FA. This patient did not display an inflammatory response nor a solid lesion on B-Scan, ruling out this differential.

Posterior scleritis can appear as an amelanotic mass fundoscopically due to an inflamed sclera causing edema into the adjoining choroid. The lesion is almost always unilateral and usually has an orange-brown appearance with indistinct margins. Typically, these patients can be distinguished from a nevi through the presence of ocular pain, choroidal folds, anterior uveitis, or proptosis. B scan ultrasonography will show marked thickening of the sclera and choroid. A “T” sign is formed in the potential space located between Tenon’s capsule and the sclera when fluid is present. The cross bar of the T represents the enlargement of the potential space caused by fluid in Tenon’s space and the optic nerve forms the stem. IVFA will show increased areas of hypofluorescence. MRI and CT imaging display scleral thickening and proptosis.

Sclerochoroidal calcification is an uncommon clinical finding that usually presents in a multifocal pattern of yellow placoid lesions and is more likely to be bilateral. It can be dystrophic or metastatic but is usually idiopathic in nature. It is commonly confused with choroidal osteomas due to the similar appearance in the retina.

Dystrophic calcification displays calcium deposition with normal serum calcium-phosphorus levels. It is associated with chronic intraocular inflammation and ocular trauma. Very commonly, it is seen with phthisis bulbi. This form of sclerochoroidal calcification is easily differentiated from choroidal osteomas because of the strong correlation with trauma, congenitally deformed eye, or inflammation.

Metastatic calcification includes calcium in normal tissues with abnormal calcium-phosphorus metabolism. This typically occurs with hyperparathyroidism, pseudohypoparathyroidism, vitamin D intoxication, sarcoidosis, and chronic renal failure. Patients are typically asymptomatic. The most common location for sclerochoroidal calcification was superotemporal and post equatorial. They are usually not found juxtapapillary. These lesions greatly resemble the choroidal osteoma, but typically, the lesions occur in relation to one of the systemic diseases listed. The patient in this case had none of the associated systemic diagnoses.

Choroidal osteomas are characterized as a rare and benign ossifying tumor that includes only 4% of all choroidal masses. Under most circumstances, choroidal osteomas affect young adults in the second and third decades of life, with a common predilection towards females of approximately 90%.¹⁰ Lesions are bilateral in about 25% of cases.¹¹

The etiology, pathophysiology, and treatment are unknown. There are many theories associated with each subject. It is thought that inflammatory or hormonal conditions are associated with the etiology, as well as congenital causes. Despite the theories mentioned, there has been no ocular or systemic condition linked to choroidal osteoma. In addition, there is no association with blood lab panels relating to an inflammatory or endocrine disorder.

These lesions consist of cancellous mature bone in the choroid. Initially, the lesions appear orange in color and gradually change to a yellow-white appearance with time as the RPE atrophies. The lesions primarily affect the juxtapapillary and macular areas.¹² Small vascular networks can be seen on the lesion’s anterior surface and just under Bruch’s membrane. These pathognomonic vessels, called spider vessels, consist of thin walls and are dilated. The lesions can be elevated, but are typically well-defined. Growth can occur with time, but it is often slow. The 10-year probability for tumor growth noted to date is 41-64%.¹³ Although a rare occurrence, spontaneous decalcification can sometimes take place. Decalcification is usually associated with increased visual loss. There have been no cases documented with the tumor possessing malignant capabilities.

Patients who are diagnosed with choroidal osteoma are often initially asymptomatic. Visual symptoms can include mild to severe blur, metamorphopsia, and even scotomas. Visual loss can occur secondary to atrophy of the RPE, spontaneous decalcification, serous retinal detachments, and most commonly from choroidal neovascular membranes. The 10-year probability for poor visual acuity is 56-58%.¹² CNV has been reported in 31-47% of cases and is thought to be associated with the decalcification of the tumor and disruption to the RPE and Bruch’s membrane according to two long-term studies by Shields et al and Aylward et al, respectively.¹⁰ Serous retinal detachments are thought to be a result of many pinpoint RPE disruptions that cause leaking and are seen most clearly with fluorescein angiography.

Making a diagnosis for choroidal osteoma is incredibly difficult without the use of different technologies. These include, but are not limited to, optical coherence tomography (OCT), fluorescein angiography (FA), fundus autofluorescence (FAF), indocyanine green angiography (ICGA), magnetic resonance imaging (MRI), computed tomography (CT or CAT), and ultrasonography. As with the other pigmented and non-pigmented lesions, ancillary testing is incredibly useful in making a diagnosis and with overall clinical monitoring.

It is difficult to obtain distinct images of a choroidal osteoma using the time domain OCT due to the poor visibility to the choroid. OCT is more useful once decalcification begins due to changing features in the choroid. It is used to document any subretinal fluid, drusen, lipofuscin, CNV, or any other overlying retinal features. Enhanced-depth imaging optical

coherence tomography (EDI-OCT) is a more effective and promising tool when looking at the lesion. EDI-OCT uses a strong light source to pass through the lesion to the sclera. With this image, a lattice pattern, or shadowing beneath the choriocapillaris, is noticed in the calcified tumor. This lattice pattern looks similar to cancellous bone.

Because of the small vascular networks on the anterior surface of the lesion, a recent trend in research has been the use of OCT-Angiography (OCT-A) on the lesion. OCT-A uses the motion of blood to reveal vascular structure and form angiographic images. This is an excellent, cost-effective, and non-invasive test that can aid in the determination of different lesions. Varying case studies have shown that OCT-A may aid in detection of CNV in patients with choroidal osteoma. OCT-A has shown a hyporeflective, granular plexus with distinct borders when the lesion is calcified.¹⁴

Fundus autofluorescence is also used to aid in diagnosing different lesions. It is especially helpful when determining if any lipofuscin or RPE disruption is present. Unfortunately, unless there is an abnormality with the RPE or outer retina, AF is not very helpful. Therefore, a fully calcific lesion will show no AF signal, but a decalcified lesion that possesses RPE atrophy will show a decreased AF signal.

A scan and B-scan ultrasonography aids in measuring the tumor's thickness and other properties. Echography is highly effective and cost-efficient in practice. It is very sensitive to detect calcification such as in the choroidal osteomas. Ultrasonography in choroidal osteomas typically shows an increased reflectivity on the anterior surface. When the gain is reduced, the lesion can be seen more clearly in relation to the choroidal tissue due to the extreme reflectivity. It can also show orbital shadowing of the sclera and tissue posterior to the lesion. This orbital shadowing gives the appearance of a pseudo-optic nerve.

Angiographic imaging aids in detecting CNV formation, RPE atrophy, and spider vessels. FA shows an early and irregular hyperfluorescence with late intense and diffuse staining. The calcified areas show early hyperfluorescence of the vasculature on the anterior surface of the tumor. ICG angiography can show early hypofluorescence and late staining. The lesion appears well-demarcated and the procedure can make the lesion appear larger after the procedure than during posterior segment evaluation. Hypercyanescent dots may correspond to spider vessels.

A CT scan or MRI could be helpful for patients with opaque media. A CT scan for choroidal osteomas appears as a dense plate of plaque-like tissue in the posterior choroid. MRI shows hyperintense signal with gadolinium-DPTA on T1-weighted images and hypointensity on T2-weighted images.⁸

Numerous treatment modalities have been attempted for choroidal osteomas with secondary CNV, including surgical removal of the CNV, laser photocoagulation, transpupillary thermotherapy (TTT), and photodynamic therapy (PDT). The management depends on the location of the lesion. Surgical removal of the CNV does not prove to be beneficial for maintaining or improving visual acuity. For lesions outside the fovea, argon and krypton lasers have been attempted with a success rate of around 45%, although it ultimately leads to poor visual acuity.⁹ This method is less effective than its use in age-related macular degeneration. Conventional photocoagulation lasers are not recommended because of their dependency on pigment. This tumor's lack of melanin makes it difficult for the laser to be effective.

Photodynamic therapy (PDT) has shown promising results with both subfoveal and extrafoveal CNVs. It is thought that this is because PDT is independent of pigment.¹⁵ Other conventional lasers depend on pigment to work properly and because a choroidal osteoma is amelanotic, a laser that does not need pigment is more beneficial. PDT has been shown to instigate decalcification of the lesion and can also stunt the lesion's growth occasionally.⁹ This is helpful in areas outside the fovea to prevent the lesion from growing into more visually critical areas. This therapy was noted to need multiple attempts and overall may lead to a decrease in best corrected visual acuity if in conjunction with the fovea.¹⁶

For lesions involving the fovea, transpupillary thermotherapy has been attempted in various case reports, resulting in a positive light. In some case reports, the CNVs have been shown to resolve and even maintain vision after multiple treatment sessions.¹⁷

Overall, the most effective treatment to date is associated with the anti-vascular endothelial growth factor intravitreal injections (anti-VEGF). These injections block VEGF activity in the eyes with CNV. There have been several case reports documenting the use of bevacizumab and ranibizumab with CNVs related to choroidal osteoma. With the use of either drug, CNVs were noted to regress, prevent acuity loss, and also improve visual acuity. The intravitreal injections are thought to improve the subfoveal and extrafoveal CNVs by decreasing the permeability of the choroidal vessels and also by penetrating the atrophied RPE of the lesion more easily.¹⁸ Favorable outcomes from the effects of bevacizumab were sustained anywhere from one to four years, with an average of 1.8 anti-VEGF injections for most patients. Some patients required the use of combination therapy with PDT or TTT.^{19,20}

The plan for the choroidal osteoma in this case is thankfully straightforward at this time. Periodic observation is in order to decrease visual acuity loss from potential CNV. Although our knowledge is limited due to small sample sizes, we know to follow this patient closely for the likelihood of CNV in 10 years. Larger sample sizes are needed to study the long-term management of this lesion.

CONCLUSION

Non-pigmented choroidal lesions have a wide-ranging list of differential diagnoses and are difficult to diagnose due to the various clinical features that may or may not be present. Without appropriate expertise and knowledge of a variety of ocular and systemic tests, it is difficult to make a diagnosis of these lesions. As optometrists, it is important to make the diagnosis, document it with appropriate testing, and, when necessary, refer to a specialist who can aid in proper management. These decisions may not only help preserve vision but could also lead to life-saving diagnoses.

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