Although ocular cancer is extremely rare relative to its systemic counterparts, a general awareness of its major signs and symptoms will serve you well as the US population continues to age. Enhancements to existing diagnostic devices and the development of new technologies are making it slightly easier to detect ocular cancer. With earlier diagnosis comes more opportunities not only to save vision, but also to reduce the risk of mortality associated with some forms of this disease. This article reviews three forms of ocular cancer commonly encountered by eye care practitioners and how to recognize them early to ensure prompt and appropriate management.

**CHOROIDAL METASTASIS**

Choroidal metastasis is far and away the most common type of cancer in the posterior pole. As cancer treatment improves, patients with metastatic disease are living longer, and metastasis to the choroid is becoming more prevalent as a result. Systemic medications can diffuse freely through the choroid, so some small areas of metastasis may never be detected because they can improve with systemic therapy alone.1

Primary sources of choroidal metastasis vary based on gender, with men more likely to have lung cancer and women more likely to have breast cancer. Approximately 25% of patients with this type of pathology will not have a cancer diagnosis when they present to your clinic. It is vital for you to bear this in mind when you observe amelanotic choroidal lesions and are making a differential diagnosis.

**AT A GLANCE**

- Choroidal metastasis is the most common type of cancer in the posterior pole, yet an estimated 25% of patients with this type of pathology will not have a cancer diagnosis when they present to your clinic.

- Small choroidal melanomas are challenging to identify (roughly 30% of these masses are < 3 mm thick).

- Intraocular lymphoma may be classified as either primary vitreoretinal lymphoma or uveal lymphoma, and a majority of the latter are found within the choroid.
Clinical Appearance
Choroidal metastasis presents as a solitary yellow amelanotic choroidal mass of minimal thickness accompanied by overlying changes to the retinal pigment epithelium (RPE) and/or lipofuscin (Figure 1A). This form of cancer is often unilateral (breast cancer is the exception), and patients commonly present with a complaint of visual disturbances because the lesion is often located in the posterior pole. As these tumors grow, they generally do not thicken drastically, unlike choroidal melanoma. Instead, it is far more likely that the basal diameter of a choroidal metastasis will expand.

Auxiliary Testing
You can use OCT to document the size and location of these tumors. A choroidal metastasis will often appear as an elevated, lumpy, bumpy mass with overlying subretinal fluid (Figure 1B). Small subretinal deposits, photoreceptor loss, and possible intraretinal edema have also been observed. Historically, spectral-domain OCT has been limited to imaging the anterior surface of the mass, but advances in enhanced depth imaging OCT (EDI-OCT) are enabling thickness measurements in some situations. Interestingly, the gold standard of ultrasonography (B-scan) was found to overestimate the thickness of these tumors compared with high-resolution EDI-OCT (2.3 vs 0.987 μm). Although the use of OCT angiography is still in its infancy for choroidal tumor management, this technology can provide an interesting in vivo analysis of tumor margins and vascular supply. However, its utility is limited by scan size and segmentation artifacts.

Another recent advance in imaging is fundus autofluorescence (FAF). Its value for ocular cancer lies in its ability to identify lipofuscin (typically from degradation of adjacent photoreceptors). Natesh and colleagues have suggested that hyperautofluorescence can be utilized to image tumor margins and to track growth objectively.

Long-Term Prognosis
A continuing increase in systemic treatment options suggests that the long-term prognosis for patients with choroidal metastasis will improve; however, certain metastases still carry significant morbidity, while others do not. Oncologists may come to use these intraocular growths to monitor the progression of other metastases throughout the body and their response to treatment.

CHOROIDAL MELANOMA
Choroidal melanoma is the most common primary ocular malignancy, and there is a significant risk of metastasis depending on tumor size and genetic composition (up to a 50% risk for metastasis). Although the estimated conversion rate from benign nevus to melanoma ranges from 1:8,000 to 1:9,000, it is important to detect choroidal melanoma early and initiate treatment in order to lower the risk of metastasis.

Clinical Appearance
Choroidal melanoma presents as an elevated pigmented mass that has indistinct borders, a thickness of greater than 2 mm, and an increased basal diameter (> 6 mm). The mass will likely be located adjacent to the optic nerve. It is frequently accompanied by subretinal fluid and overlying lipofuscin but not by a halo (Figure 2).

Patients are more likely to experience visual symptoms (photopsia, scotoma, etc.) if they have a melanoma versus a benign mass, but the absence of symptoms is not a guarantee of a benign mass. Routine observation will help you to identify changes in size, which typically indicate malignancy. Small choroidal melanomas are challenging to identify, and an estimated 30% of these masses are less than 3 mm thick. As they grow, they can break through Bruch membrane, causing the overlying retinal tissue to detach.

Auxiliary Testing
Auxiliary testing has been paramount for the early identification of choroidal melanomas. Ultrasonography (B-scan)
continues to be the gold standard for identifying tumor thickness and internal reflectivity, with lower reflectivity suggesting more disorganization and, therefore, a greater chance of malignancy.

OCT has facilitated earlier detection by revealing additional risk factors, specifically the disruption of overlying photoreceptors and the presence of subretinal fluid, both of which indicate a significant risk for metastasis. As mentioned earlier, the initial limitation of this technology was signal penetrance, but, with resolution reaching the posterior face of a tumor, EDI-OCT can be used in certain situations to accurately measure tumor thickness. OCT angiography has successfully identified additional risk factors. One is a hyporeflective plexus or hyperreflective ring within the choriocapillaris layer that increases the risk of malignancy. Investigators are currently studying whether differences in the foveal avascular zone (between eyes) and heterogeneity of the venous plexus affect overall risk.

FAF is a valuable tool for identifying the presence of lipofuscin, but this pigment will fade over time with overlying retinal atrophy.

Long-Term Prognosis

A patient’s long-term prognosis depends on the size of the tumor, his or her age, and genetic mutations associated with metastasis. Ocular oncologists have benefitted from advances in genetic sequencing. Fine needle aspiration biopsy of tumors at the time of treatment have aided in the identification of mutations associated with metastasis and of patients at risk for systemic involvement, thereby lessening the need for enucleation.

INTRAOCULAR LYMPHOMA

This type of non-Hodgkin lymphoma may be subdivided into two subtypes: primary vitreoretinal lymphoma (PVRL) and uveal lymphoma. The latter may be further classified as choroidal, ciliary body, or iris lymphoma. A majority of uveal lymphomas are found within the choroid.

Although uveal lymphoma is frequently associated with ocular adnexal involvement (up to 60%), its systemic involvement is uncommon. PVRL, however, is often found to coexist with central nervous system (CNS) lymphoma, and between 16% and 34% of patients are estimated to have CNS involvement at the time of PVRL diagnosis. New-onset seizures are a strong indicator of CNS involvement.

Clinical Appearance

PVRL can easily be mistaken for posterior uveitis. The former is a low-grade vitritis. It is often accompanied by minimal anterior chamber reaction and minimal pain, and cystoid macular edema is absent, meaning patients have better vision than you might expect. Symptoms are often limited to slightly blurred vision and/or floaters. Symptoms may be bilateral at presentation but are often asymmetric. The vitritis may respond positively to initial treatment with topical steroids, further complicating diagnosis.

As the lymphoma progresses, signs frequently include creamy yellow-white, multilobulated subretinal lesions with overlying leopard spot changes to the RPE and possible involvement of the optic nerve. Choroidal lymphoma has a similar subretinal appearance, but it is often unilateral and grows slowly.

Auxiliary Testing

Auxiliary testing facilitates the diagnosis of orbital lymphoma. Vitreoretinal biopsy is often used to confirm the diagnosis when neuroimaging (MRI) and cerebrospinal fluid cytology are negative.

On EDI-OCT scans, choroidal lymphoma appears as a placid, flat infiltration of the choroid if the lesion is thin, and has a rippled or undulating appearance if the lesion is thick. FAF can serve as a useful adjunct to color fundus photography by revealing adjacent RPE atrophy and overlying lipofuscin accumulation. In certain situations, FAF has been used to help monitor disease progression and therapeutic response by quantifying the overlying hyperautofluorescence.

Figure 2. A large choroidal melanoma with overlying lipofuscin (A). OCT can be used to detect subtle subretinal fluid and shaggy photoreceptors or disruption of the outer photoreceptor layer (B).
Long-Term Prognosis

A patient’s long-term prognosis heavily depends on CNS involvement. Uveal lymphoma is often indolent and responds well to treatment, whereas PVRL with CNS involvement is frequently aggressive and associated with a poor prognosis. Ocular lymphoma is often referred to as a masquerade syndrome, with many overlapping signs and symptoms of subsequent infectious or inflammatory retinal diseases. A careful and multidisciplinary approach is often required to correctly diagnose lymphoma.

A LITTLE KNOWLEDGE COULD GO A LONG WAY

Just knowing a few key signs and symptoms of ocular cancer could enable you to make an early diagnosis in patients and consequently save their vision and possibly even their lives. It’s a relatively small investment with the potential for a huge payoff.


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