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OPHTHALMOLOGY

Clinical Approaches to Common Ocular Tumors

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In companion animals, intraocular tumors are relatively uncommon, but those that do occur can be primary, metastatic, or locally invasive. Tumors can appear as discrete masses, diffuse changes, or even after uveitis. Learning to recognize the presence of a mass and differentiate it from an infectious or benign disease process can help you determine when to recommend medical treatment, surgery, or referral to an ophthalmologist. Here we review the types of intraocular neoplasia most frequently seen in our canine and feline patients, the differentiating features helpful for diagnosis, prognosis, and treatment guidelines. We discuss each species separately.

DOGS

Primary Intraocular Tumors

In dogs, the most common location for primary intraocular masses is the anterior uvea (iris and ciliary body). The most common type of uveal neoplasia is melanocytic tumors, which include melanomas and melanocytomas.[1] These tumors must be distinguished from the following:

- Iris nevi (freckles, flat areas of pigmentation that may become larger but do not progress to inflammation or nodular growth)
- Iris cysts (may be freely moveable within the anterior chamber and generally have a distinctive spherical shape. Iris cysts may be darkly pigmented to fainter brown or even nonpigmented and can generally be distinguished from masses by transillumination (**FIGURE 1A AND 1B**)
- Intraocular extension of limbal melanocytic tumors
- Ocular melanosis (an inherited, bilateral, progressive deposition of pigmented cells that leads to glaucoma, occurring most commonly in Cairn terriers[2])
- Other tumor types

LOW METASTATIC POTENTIAL
The overall prognosis for life in most primary intraocular neoplasias is good.

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Melanocytic tumors can invade the choroid, sclera, filtration angle, cornea, and orbit. Distinguishing outward invasion of an iris melanoma from invasion of the iris by a limbal melanoma can be challenging.[3]

The second most common location for primary intraocular tumors in dogs is the ciliary body. Tumors in this location are generally adenomas or adenocarcinomas. Rarely, they can be medulloepitheliomas (a type of neoplasia from undifferentiated epithelial cell types that can occur in younger dogs). Ciliary body adenomas and adenocarcinomas are usually found in older dogs and can sometimes be seen as a tan/pink mass extending through the pupil (**FIGURE 2**). Labrador and golden retrievers may be predisposed to epithelial ciliary body tumors.[4] These tumors may also invade the iris, cause anterior displacement of the iris, or result in secondary uveitis and glaucoma. Often these masses are not diagnosed until they have caused secondary complications.

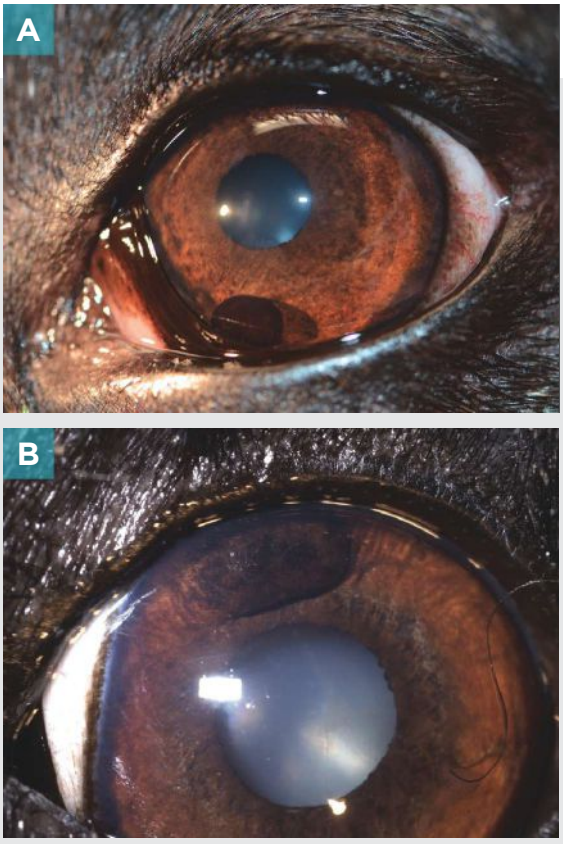

FIGURE 1. (A) Uveal cyst. **(B)** Uveal melanocytic tumor in the dorsal iris of a dog. Note that both are darkly pigmented, but the cyst was freely movable during examination and easily transilluminated.

Other primary ocular tumors have been reported in dogs but are extremely rare, and few have shown evidence of metastatic disease. One of these is schwannomas of blue-eyed dogs, a form of peripheral nerve sheath tumor. These tumors typically arise in the iris and ciliary body but are not common.[5]

Metastatic Neoplasia

Secondary, metastatic neoplasia in the eye can result from hematogenous spread and is most commonly seen with lymphoma or local invasion from adjacent structures. One study reported that 14.8% of all intraocular tumors in dogs were metastatic disease and that 6.3% of metastases were from lymphoma.[6] Reportedly, a wide variety of tumors metastasize to the eye: histiocytic sarcoma, mammary adenocarcinoma, hemangiosarcoma, malignant melanoma, and osteosarcoma.[5] Because the metastatic potential of most primary intraocular neoplasms is low, the presence of disseminated disease generally indicates that the intraocular tumor is metastatic. Ocular manifestations may be the first signs noticed but further workup can reveal a primary tumor elsewhere. Primary intraocular neoplasms are generally unilateral, whereas bilateral disease suggests metastatic disease. Bilateral ocular neoplasia should prompt a complete workup to evaluate for primary neoplasia elsewhere in the body, which can often be life-threatening. For any patient with unexplained hyphema, the differential diagnosis should include neoplasia, and ocular ultrasonography may help identify the presence

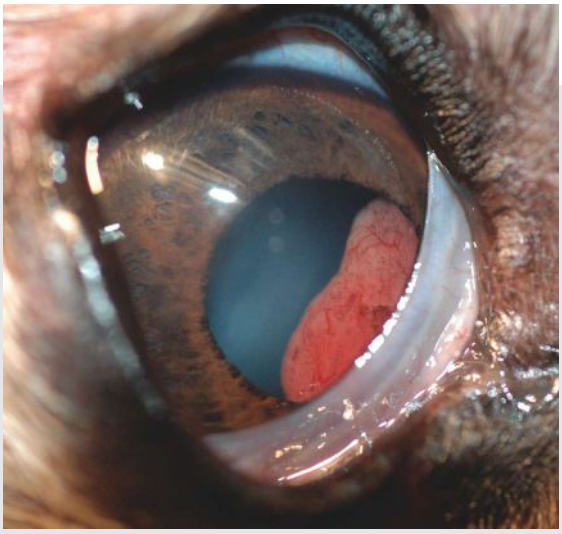

FIGURE 2. Red, vascularized mass originating posterior to the iris in the pupil of a dog. Histopathologic diagnosis was adenoma of the ciliary body.

Courtesy of Dr. Ellen Belknap (3)

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of a mass. Sometimes diagnosis can be based on histopathologic appearance of enucleated globes.

Ciliary body tumors often go undiagnosed until they have caused significant uveitis and secondary glaucoma.

Diagnosis and Prognosis

Canine uveal melanomas tend to grow in a distinctive nodular fashion, but diagnosis may still be challenging. Clients may note a color change in the eye as the first sign of a problem, or the mass may go unnoticed until it causes uveitis and/or secondary glaucoma. Melanocytic tumors are diagnosed clinically, based on location in the iris, nodular appearance, and typical dark pigmentation, although some can be nonpigmented. Large masses can cause dyscoria, anterior displacement of the iris, or lens subluxation. For patients with dramatic uveitis or hyphema that prevents direct examination, use of ocular ultrasonography may help you determine the diagnosis and anatomic location. Melanocytic tumors have a low metastatic potential (4% to 6%), and the prognosis for the patient's overall health is good, but secondary complications may necessitate enucleation.[1,5,7-9]

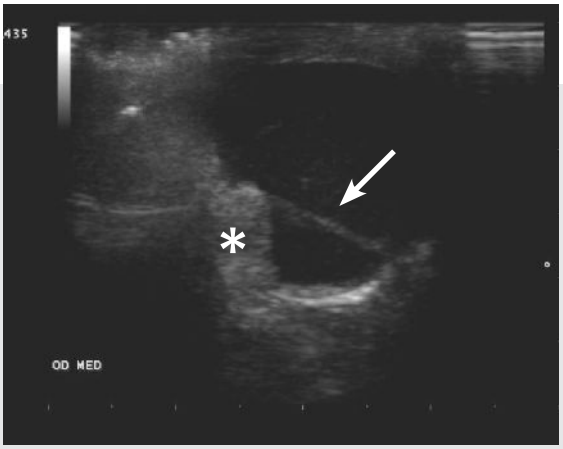

FIGURE 3. Ultrasonography image of a globe from a patient with hyphema, partial anterior lens luxation, and secondary glaucoma; image obtained by use of B-mode ultrasonography. Ultrasonography revealed retinal detachment (arrow) and possible ciliary body mass (asterisk). Because of secondary complications, this eye was enucleated. Histopathologic examination revealed retinal detachment and a blood clot in the posterior chamber.

Courtesy of Dr. Ellen Belknap (3)

Ciliary body tumors often go undiagnosed until they have caused significant uveitis and secondary glaucoma. Because of their location posterior to the iris, they often remain unseen until they have grown quite large. Occasionally, they can be seen as a tan or pink mass behind the lens or extending through the pupil. In most cases, however, they are detected by ocular ultrasonography or even histopathology after globe enucleation because of intractable glaucoma. Fortunately, although about 15% of these tumors are malignant, their metastatic potential is low and the prognosis for overall health is good.[5]

Ocular ultrasonography is a valuable, noninvasive imaging tool and can generally be performed by an ophthalmologist or radiologist to help make a diagnosis and further recommendations. It is particularly useful for patients with opacities in the clear ocular media that prevent direct examination, and it can generally be performed without sedation. Even for patients in which the mass can be directly observed, ultrasonography can help you determine the origin of the mass as well as enable its measurement. Most practitioners use B-mode ultrasonography for image capture, although A-mode can be useful for taking measurements and is used in human ophthalmology for evaluating the internal structure of some masses.[10] The accuracy of ultrasonography for identification of intraocular masses is good, but occasionally intraocular blood clots can mimic masses[10] (**FIGURE 3**). For avoiding misdiagnosis of blood clots as tumors, standardized imaging protocols performed by an experienced operator can be helpful; for some animals, serial ultrasonography can also be beneficial. For obtaining images of the best possible quality, appropriately sized probes for ocular imaging are needed.

For some patients, computed tomography or magnetic resonance imaging is helpful. These modalities can be used to detect bony involvement, extra-ocular soft tissue extension, or local invasion from an intraocular tumor. They can also provide information for surgical planning and help determine whether further treatment with chemotherapy or radiation might be needed.

Treatment

Treatment of any intraocular neoplasia in the dog is

based on multiple factors, including the suspected tumor type, evidence of metastatic disease, secondary complications, and overall patient health.

Enucleation is indicated when the patient has intractable secondary uveitis, glaucoma, or ocular discomfort unresponsive to medications or when the goal is to obtain a diagnosis. Patients with severe uveitis obscuring a definitive diagnosis may warrant aggressive medical treatment with topical and systemic anti-inflammatories before definitive therapy. Treatment can help clear anterior chamber hemorrhage and inflammation to enable direct examination of the eye, which may reveal an obvious mass and prompt enucleation. Even in the absence of an obvious mass, discomfort and secondary glaucoma may prompt enucleation and submission of the globe for histopathology. For tumors that have extended outside the globe, exenteration (removal of the globe and surrounding orbital tissues) may be recommended. Any enucleated eyes or locally excised tumors should be submitted for histopathology to determine the type of neoplasm and whether any further treatment (e.g., chemotherapy or radiation) is recommended.

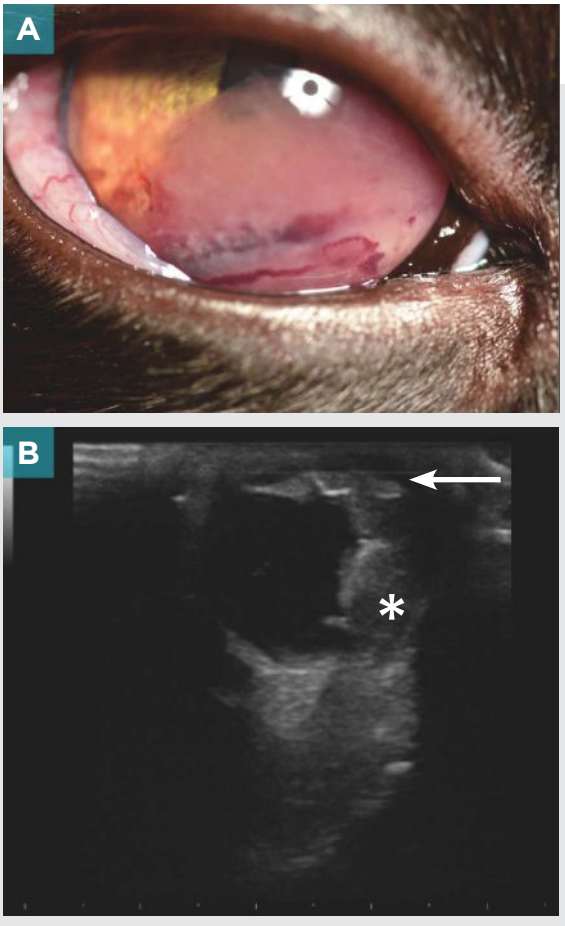

FIGURE 4. (A) Gross image of a large, pink, vascular mass and associated fibrin in the anterior chamber of a cat. **(B)** B-mode ultrasonography image from the same patient, demonstrating an extensive mass in the anterior chamber (arrow) as well as invading the posterior chamber (asterisk). Histopathologic diagnosis after enucleation was undifferentiated sarcoma.

Treatment by enucleation is controversial for the many dogs that have melanocytic uveal tumors in an eye that is still functional (i.e., can see) and that have no evidence of inflammation and glaucoma. Some practitioners elect to monitor apparent uveal melanomas because of their slow progression and low risk for metastasis. Some melanocytic tumors are amenable to laser photocoagulation.[5] Laser photocoagulation can be performed with endolaser, transscleral, or transcorneal diode or Nd:YAG laser and is best suited to focal tumors with no extension into the iridocorneal angle. To preserve vision in dogs with no secondary complications, local excision of a mass with iridectomy or iridocyclectomy procedures has been described.[11] Clients interested in vision-sparing surgical or laser treatment options for their pet should be referred to an ophthalmologist for further evaluation.

CATS

As for dogs, the most common primary intraocular tumor of cats is iris melanoma. Generally, cats with melanocytic lesions are brought to the veterinary clinic for iris color change or for iris melanosis, which is benign. Uveal cysts, although less common in cats than in dogs, can also mimic melanoma, and methods for differentiation are similar.[12]

The second most common tumor in cats is posttraumatic sarcoma (**FIGURE 4A AND 4B**), which is incited by ocular trauma and inflammation (e.g., trauma to the lens, chronic uveitis, and gentamicin injections into the posterior segment for ciliary body ablations).[1,13–16] This tumor is specific to cats. Specific tumor types reported include fibrosarcoma, osteosarcoma, and undifferentiated sarcoma.[17] These tumors are postulated to arise from malignant transformation of lens epithelium, a process that has not been reported for other species, and they share similarities with feline vaccine-induced sarcomas because both apparently result from an initial insult and subsequent chronic inflammation.[18] Although iridociliary epithelial adenomas and adenocarcinomas are rare in cats, they have been reported.[4]

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Because of the high rate of malignancy of posttraumatic ocular sarcomas in cats, any blind eye that resulted from trauma should be considered for early enucleation.

Other primary intraocular neoplasms are uncommon in cats, but as in dogs, intraocular disease can be metastatic.

Diagnosis and Prognosis

Feline diffuse iris melanosis begins as benign, flat, hyperpigmented nevi on the iris. Over months to years, diffuse melanosis may progress to malignancy and should be monitored closely for changes. Photographs of the affected eye can help you evaluate these eyes over time. Melanoma lesions are distinguished by the spread of pigment, thickening of the iris, or irregular iris surface (**FIGURE 5**). Eventually, these changes can invade the ciliary body, iridocorneal angle, and sclera, and may result in secondary glaucoma.[4,19–21] Rates of metastasis range from 55% to 66% after the lesions have become malignant, and the overall prognosis is poorer if the tumor has invaded the ciliary body or sclera at the time of enucleation.[1,3,7,12] The prognosis is also worse for cats that have secondary glaucoma.

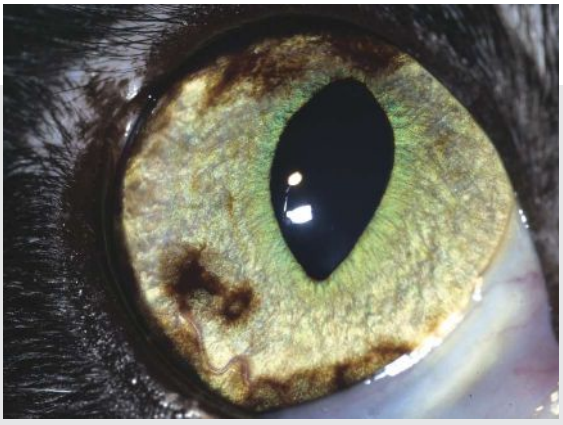

FIGURE 5. Photograph of the iris of a cat, showing flat, pigmented nevi (iris melanosis), which have not progressed to melanoma.

Courtesy of Dr. Ellen Belknap

Posttraumatic ocular sarcomas in cats are highly malignant; these tumors should be suspected in cats with a history of trauma to the globe and evidence of uveitis, glaucoma, intraocular hemorrhage, and visible masses. For cats in which intraocular evaluation is inhibited by anterior segment opacity, ocular ultrasonography can facilitate characterization of the intraocular disease and its extent. The prognosis is poorer if the tumor has invaded beyond the sclera because it can involve the optic nerve and invade the brain; most of these cats die or are euthanized within months because of metastatic disease.[14]

Iridociliary epithelial adenomas and adenocarcinomas in cats are generally solid and nonpigmented, as they are in dogs, and they are often accompanied by secondary complications, including retinal detachment and glaucoma. Although the prognosis for the globe is poor, as with other intraocular neoplasms, the potential for metastasis is low.[4]

With regard to metastatic disease, lymphoma is the most common offender and can appear as anterior uveitis, an intraocular mass, or both. As previously discussed, bilateral ocular disease is suggestive of metastatic neoplasia. Cats with signs of metastatic intraocular neoplasia should also be tested for FeLV and FIV, both of which can predispose the cat to systemic neoplasia and thus intraocular metastasis. Treatment is systemic therapy, such as for lymphoma, as well as topical management of uveitis and secondary glaucoma, if present. Intraocular metastatic neoplasia can be difficult to distinguish from other causes of feline uveitis (e.g., feline infectious peritonitis, toxoplasmosis, or other infectious causes). Signalment and other systemic signs can help you determine the underlying cause, but any cat with profound bilateral uveitis should be evaluated for evidence of neoplasia in addition to infectious diseases.

Treatment

Enucleation is the treatment of choice for feline diffuse iris melanoma; however, for many patients, it is difficult to decide when to enucleate because of the slow disease progression as well as reluctance to remove a comfortable, visual eye. Close monitoring of these patients over time is imperative; look for significant changes of the pigmented areas, which may indicate the need for surgical intervention. Alternative techniques (e.g., diode laser ablation or sector iridectomy) have not been

widely used. They would probably be appropriate only for cats with small, focal lesions and are not guaranteed to prevent progression.

Because of the high rate of malignancy of posttraumatic ocular sarcomas in cats, any blind eye that resulted from trauma should be considered for early enucleation. After a sarcoma has developed, exenteration is the recommended treatment, along with staging to evaluate for involvement of the regional lymph nodes and for distant metastasis.

CONCLUSION

Intraocular neoplasia is uncommon in companion animals but should be considered in the differential diagnosis for patients with uveitis and glaucoma as well as for those with discrete masses. The most common primary intraocular tumor of both dogs and cats is uveal melanoma, although epithelial tumors and feline intraocular sarcomas are possible. Animals with bilateral disease should be evaluated for evidence of primary neoplasia elsewhere with metastatic spread to the eyes. For all species, knowing the most common tumor types and their appearance can help you determine the prognosis. Although the sequelae of tumor growth often necessitate enucleation of the affected eye, most primary intraocular neoplasia has low metastatic potential, so the overall prognosis for life is good. A good first-line tool for identifying intraocular masses is ultrasonography. When neoplasia is suspected, consider referring the patient to a veterinary ophthalmologist. For some patients, vision-sparing surgical procedures are available. TVP

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