Canine uveal melanoma: examination, differential diagnoses and treatment

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JAMES OLIVER provides an overview of benign and malignant intraocular tumours in dogs, discussing presenting signs and treatment options

UVEAL melanoma is the most common intraocular neoplasm in the dog, frequently seen by both general practitioners and specialists.

In dogs, the term melanoma is usually used to describe uveal melanocytic neoplasms of both benign and malignant behaviour.

Strictly speaking however, the term melanoma should be reserved for malignant melanocytic neoplasms and melanocytoma used in preference for benign tumours. The distinction between the two is made by histopathological examination.

This is not always clear-cut, as melanocytoma can undergo gradual malignant transformation. Furthermore, the histopathological characteristics of canine uveal melanoma tend to be poorly predictive of tumour behaviour. Histologically, classified malignant uveal melanoma does not metastasise frequently and there are reports of recurrence of benign uveal melanocytoma in the orbit as malignant melanoma following enucleation.

Uveal melanocytoma

Uveal melanocytoma is generally a disease of older dogs and those affected have a mean age of
9.7 years. Interestingly, however, there is a spike in incidence of disease in dogs under two years of age. German shepherd dogs and retrievers are the most commonly affected breeds, but it is yet to be confirmed by population statistics whether this represents a true breed predisposition.

In dogs, 94 per cent of reported cases of uveal melanocytoma affect the iris and ciliary body and six per cent affect the choroid (Figures 1, 2, 3, 4 and 5). It is likely, however, that choroidal involvement is more common, as melanocytomas in this region are more likely to go unnoticed. Definitive diagnosis requires histopathological examination (see later), but biopsies are rarely performed in visual eyes owing to the risk of inadvertent damage to intraocular structures that could result in blinding complications. Fine-needle aspiration of uveal melanocytic neoplasma can be performed, although the results are unlikely to be conclusive and also risks causing damage.

For these reasons, slowly growing and well-defined pigmented masses within the canine uvea usually receive a presumptive diagnosis of melanocytoma. Treatment of presumed uveal melanocytoma is increasingly being carried out by veterinary ophthalmologists. This is because growth of the tumours can cause secondary glaucoma and blindness and also because it is known that melanocytomas can undergo malignant transformation. The current treatment of choice for presumed iris melanocytoma is laser photoagulation. In one study, a semiconductor diode laser was used to treat presumed iris melanomas in 23 dogs (Cook and Wilkie, 1999). Laser energy was delivered either via an operating microscope adaptor or a laser indirect ophthalmoscope with a 20D lens. All masses reduced in size following treatment, although five cases required more than one treatment. Follow-up varied from six months to 4.5 years and no increase in size of the pigmented masses was noted in any case. Some minor complications occurred, including iris hyperpigmentation, dyscoria and corneal oedema. The authors concluded that non-invasive diode laser photoagulation was a safe and effective method of treatment for isolated, pigmented iris masses in dogs.

Although this treatment is relatively non-invasive, it remains controversial and careful monitoring is still required. If monitoring is elected without any treatment, then careful client counselling is paramount. It is never possible to provide a guarantee of non-malignancy and regular re-examinations need to be performed to evaluate both progression of the lesion and any evidence of metastasis. Careful ophthalmic examination may reveal clinical signs, which demonstrate progression although not necessarily malignant transformation. Signs to look for include the following:

- change in pupil shape and mobility (this is suggestive of deeper invasion of the tumour, Figure 1);
- involvement of the iridocorneal angle (Figure 2);
- scleral extension (Figure 3); and
- glaucoma (Figure 8).
**Malignant uveal melanoma**

Malignant uveal melanoma is much less common in dogs than its benign counterpart. As with melanocytoma, the anterior uvea is affected with much greater frequency than the choroid. The average age of dogs with malignant uveal melanoma is 10.3 years and there is no spike in incidence in dogs under two years of age. Malignant uveal melanoma frequently occurs in eyes with melanocytoma and occasionally in eyes with melanosis. Melanocytomas are usually made up of heavily pigmented, large round and spindle cells in varying proportions.

As malignant transformation occurs, the proportion of spindle cells and the mitotic index increase and cells tend to become less pigmented. Some malignant melanomas can even be amelanotic (Figure 6). A mitotic index of greater than four per 10 high power fields is indicative of malignancy, as is the presence of nuclear atypia (Figure 7b).

Clinical signs suggestive of malignancy include rapid growth, which can lead to secondary glaucoma (Figure 8), depigmentation and extraocular extension. Ocular ultrasound is useful in demonstrating the extension of ocular tumours when direct ophthalmoscopic examination is precluded and can help in surgical planning (Figure 9a). Ultrasound examination may reveal evidence of ciliary body and scleral extension of anterior uveal melanomas and involvement of structures posterior to melanoma of the choroid. In blind and painful eyes, enucleation or exenteration is warranted and this treatment is usually curative if performed before the melanoma has spread beyond the globe.

Enucleation/exenteration should be performed after careful systemic evaluation for metastasis (complete physical examination and thoracoabdominal imaging) and all enucleated globes should be submitted to an experienced ocular pathologist for examination. Although histologically malignant uveal melanomas do not metastasise frequently, metastasis to the lung, heart and vertebrae has been reported, as has local extension into the brain (Friedman et al, 1989; Minami and Patnaik, 1992; Rovesti et al, 2001; Yi et al, 2006; Galán et al, 2009).

Another potential treatment for malignant canine uveal melanoma is vaccination. A xenogeneic murine tyrosinase DNA vaccine has been developed for canine malignant melanoma and the United States Department of Agriculture has issued a conditional licence for its use (Oncept). The vaccine appears to be safe and effective when used in conjunction with local and regional disease control (Manley et al, 2011). Use of the vaccine in the UK is off-licence, but it can be imported and used following successful application of a Special Treatment Certificate from the VMD. There are no publications reporting its use in dogs with uveal melanoma specifically, but the author sees no real reason why the vaccine may not be used in cases of malignant uveal melanoma.

**Differential diagnoses of canine uveal melanoma**

Melanoma is not the only pigmented disease of the canine uveal tract and some important
differential diagnoses should be considered.

**Iris freckles and nevi**

The canine iris is frequently affected by non-neoplastic areas of hyperpigmentation. These areas are referred to as freckles or nevi and, to some extent, the terms are interchangeable. An iris freckle is a cluster of pigmented cells that represent either a region of benign hyperplasia or increased pigmentation of normal melanocytes. These are located in the superficial iridial stroma, can be slightly raised, but do not cause pupil distortion. Iris nevi tend to occur in young dogs and represent proliferations of melanocytes that form well-circumscribed and slightly elevated masses on the iris surface ([Figure 9b](#)). Mitotic figures are not observed and the cell population is relatively homogeneous. It is known, however, that benign nevi can undergo malignant transformation.

**Uveal cysts**

Uveal cysts are a common finding in dogs and the Labrador retriever appears to be predisposed. The cysts, which are usually dark brown and spherical, may arise from the pupillary margin, the posterior pigmented iris epithelium or the pars plicata of the ciliary body. They may remain attached to their site of origin or “bud off” and move anteriorly through the pupil into the anterior chamber where they may be freefloating or become permanently lodged in the ventral anterior chamber ([Figure 10](#)). Occasionally, the cysts rupture, leaving their pigmented shell adherent to the corneal endothelium or anterior lens capsule. The diagnosis of uveal cysts is made on clinical appearance. Cysts are easily transilluminated, whereas neoplastic pigmented lesions do not transilluminate. Uveal cysts are usually benign, but have been associated with glaucoma in the golden retriever and great Dane (see below).

Treatment of uveal cysts is rarely required, but may be necessary if so many are present they obstruct vision. Treatment strategies include laser photocoagulation and aspiration.

**Pigmentary uveitis**

Pigmentary uveitis occurs almost exclusively in the golden retriever and is a common cause of secondary glaucoma in this breed in the US (Sapienza et al, 2000). The most common early sign is pigmentation on the anterior lens capsule, which may or not be associated with uveal cysts that can be blood-filled ([Figure 11](#)). Later, there are obvious clinical signs of anterior uveitis with fibrin within the anterior chamber and posterior synechiae. The majority of eyes with pigmentary uveitis develop secondary glaucoma and need to be enucleated. Fortunately, this disease is rarely seen in European golden retrievers, although a similar disease has been reported in great Danes on the continent (Speiss et al, 1998).
• Ocular melanosis

Ocular melanosis or “pigmentary glaucoma” occurs most frequently in the Cairn terrier, and thus has been most extensively investigated in this breed (Petersen-Jones et al, 2007). The iris becomes progressively pigmented and develops a prominent, circumferential ridge at its root (Figure 12). As disease progresses, pigmentation of the sclera and episclera becomes evident and, in some cases, pigmentation of the posterior segment occurs. Melanosis differs from melanocytoma, as the pigmentation is diffuse, which is caused by both an increase in size and an increase in number of pigmented cells. The predominant cell type is melanocytes with a smaller subpopulation of melanophages. No specific treatment exists for ocular melanosis, although enucleation is usually carried out when eyes develop secondary glaucoma. Histopathological examination of enucleated eyes should be performed to rule out neoplasia.

Summary

In summary, the canine uvea can be affected by a number of melanocytic disorders. Careful ophthalmic examination, occasionally assisted by ancillary diagnostic tests, usually helps in their differentiation. Definitive differentiation between benign melanocytoma and malignant melanoma requires histopathological examination. Fortunately, in the dog even malignant uveal melanomas do not metastasise commonly.

References