OCULAR MELANOMAS IN DOGS AND CATS: DIAGNOSIS AND TREATMENT

Author : James Oliver

Categories : Vets

Date : July 2, 2012

James Oliver discusses tumour behaviour in dogs and cats as well as diagnostic tests available and looks at treatment methods, including surgical techniques

MELANOMAS have been documented to affect the eyelids, conjunctiva, corneoscleral limbus, anterior uvea and choroid in dogs and cats.

Tumour behaviour differs between dogs and cats and also varies depending on the location of the melanoma within the eye. Eyelid melanomas are more common in dogs than cats and tend to behave more benignly than their oral counterparts. Conjunctival melanomas have a slightly higher metastatic risk in cats than dogs (14 per cent versus 10 per cent) and a much higher mortality rate (61 per cent versus five per cent). Limbal melanomas tend to be benign in nature, but can be rapidly progressive in young dogs and can occasionally be malignant in cats. Uveal melanomas are the most common intraocular neoplasms in dogs and cats. Anterior uveal melanomas usually behave benignly in dogs with a low metastatic rate (about five per cent), whereas in cats the metastatic rate of diffuse iridal melanomas may be as high as 63 per cent. Choroidal melanomas tend to be aggressive in cats, but are of more variable behaviour in dogs.

Owing to these variations in ocular melanoma behaviour, the most appropriate treatment options also depend on the species affected and tumour location. A non-exhaustive list of factors taken into consideration when choosing an appropriate treatment protocol is provided in **Panel 1**.

Anciliary diagnostic tests

• **Cytology/histopathology**

Fine needle aspiration of ocular melanomas can be performed, although the results are unlikely to provide conclusive results with respect to tumour behaviour. Malignancy may, however, be supported by evidence of pleomorphism and/or anaplasia in a cytological sample. All tissue samples obtained from surgical treatment of ocular melanomas, whether incisional or excisional, should be submitted for histopathological examination. In addition to allowing assessment of surgical margins, histopathological examination allows determination of mitotic index (which is a useful predictor of malignancy) and assessment of malignant transformation in otherwise benign tumours (for example, anaplasia, increased mitotic rates). Histopathology of whole feline eyes with diffuse iridal melanoma is a useful predictor of malignancy and survival. In feline diffuse iris melanoma, neoplastic extension into the sclera has an unfavourable prognosis (Figure 1).

• **Diagnostic imaging**

Ocular ultrasound can be useful in demonstrating the level of extension of ocular tumours when direct ophthalmoscopic examination is precluded. Ultrasound may reveal evidence of ciliary body and scleral extension of anterior uveal melanomas and involvement of structures posterior to melanoma of the choroid. In addition, ultrasonographic evaluation may aid surgical planning for excision of limbal melanomas, although a combination of ophthalmoscopic examination and gonioscopy usually provides sufficient information. Thoraco-abdominal imaging is indicated when there is a suspicion of malignancy, for example in cats with diffuse iris melanoma.

Monitoring

Careful monitoring may be appropriate in certain situations – for example, if there is a low index of suspicion of malignancy and treatment may involve, or risk, the loss of a comfortable and visual eye. This may be the situation for certain nonprogressive limbal melanomas in dogs and cats and anterior uveal melanomas in dogs (Figures 2 and 3). A common dilemma is the case of the cat with a comfortable and visual eye, but which demonstrates increased iridal pigmentation. Careful ophthalmic examination, however, may reveal clinical signs that allude to neoplastic progression to diffuse iridal melanoma. Signs to look out for include:

• change in pupil shape and mobility (this is suggestive of deeper iridal invasion of the tumour; Figure 4);

• formation of distinct masses or nodules (best assessed by slit-lamp biomicroscopy; Figure 5);

• involvement of the iridocorneal angle (best assessed by gonioscopy; Figure 6); and

• glaucoma.

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 for progression of the ocular lesion and for any evidence of metastasis.

Enucleation and exenteration

If a suspected diagnosis of feline diffuse iridal melanoma is provided, then enucleation is usually advised owing to the reported high metastatic rate and increased mortality rates associated with progression of neoplasia (Figures 4, 5 and 6). Enucleation is usually performed after careful systemic evaluation for metastasis (complete physical examination and thoraco-abdominal imaging). The enucleated eye should be submitted for examination by an experienced ocular histopathologist as there is a strong correlation between histopathological findings and malignant behaviour of diffuse iridal melanomas. Based on the results of histopathology and other investigations, further treatment may or may not be necessary. This may include, at the very least, regular systemic re-evaluations for signs of metastasis. Rapidly progressive canine anterior uveal melanomas may increase the clinician's concern about malignancy and may lead to glaucoma and/or blindness (Figure 7).

In these cases, enucleation is warranted and usually curative if performed before the melanoma has spread beyond the globe. Enucleation or exenteration may also be advised in cases of progressive choroidal melanomas where there is a suspicion of malignancy. Evisceration with placement of an intrascleral prosthesis is contraindicated if intraocular neoplasia is present.

Surgical excision and grafting techniques

Surgical excision with or without adjunctive therapy (cryotherapy, laser treatment, strontium plesiotherapy) is usually advised for eyelid, conjunctival (Figure 9) and limbal melanomas (Figure 10a). Melanomas involving the eyelid skin can usually be excised with low recurrence rates. Those arising from the lid margins tend to be more locally aggressive and removal requires reformation of the eyelid margin with blepharoplastic techniques. In dogs, small, non-invasive conjunctival melanomas can usually be excised by simple excision without the need for suturing.

The majority of conjunctival melanomas in dogs are benign, but they can be malignant and progress to invade the orbit, therefore early treatment is advised. Wide surgical margins have been advised in cats with conjunctival melanomas, in which case they are associated with an increased risk of metastasis and mortality. However, unless the tumour is located on the third eyelid, this is not usually possible without sacrificing the eye. Excision of limbal melanomas is a specialist procedure. Careful preoperative evaluation is required to establish the extent of the melanoma and includes gonioscopy and, occasionally, ocular ultrasound.

The superior resolution afforded by high frequency ultrasound is particularly useful for evaluation of intraocular invasion, but is rarely available. Haemostasis (such as electrocautery) is essential during scleral dissection and access to viscoelastic materials should be immediately available to maintain the anterior chamber in the event of globe perforation. Excision of limbal melanomas

usually needs to be combined with a grafting technique to re-establish structural support. Materials that have been used for grafting include autologous conjunctiva and third eyelid cartilage, homologous cornea and sclera, and porcine small intestine submucosa (Lewin, 1999; Kanai et al, 2006; Featherstone et al, 2009). When porcine small intestine submucosa is used to repair corneoscleral defects, it is usually combined with an overlying conjunctival graft to provide vascular and further mechanical support to the region.

Cryotherapy

Cryotherapy has been advised following surgical removal/ debulking of melanomas of the conjunctiva, cornea and sclera (Figures 10a, 10b and 10c). In one retrospective study, 14 dogs that underwent partial lamellar resection to treat limbal melanomas were also treated with cryotherapy as an adjunctive treatment (Featherstone et al, 2009). Following tumour resection and before adjunctive graft procedures, cryotherapy (1,1,1,2-tetrafluoroethane) was applied to the surgical site in either a double or a triple freeze-thaw cycle.

Recurrence did not occur in any of the eyes. Early complications included anterior uveitis (n = 7) and corneal ulceration (n = 5) and the main late complication was corneal lipidosis (n = 3). In another case of canine limbal melanoma, nitrous oxide was applied to the surgical site in a double freeze-thaw cycle, but, in this case, the cryotherapy was used after placement of a donor corneal graft (Norman et al, 2008). Again, no recurrence was reported.

Laser photocoagulation

Semiconductor diode lasers and neodymium:yttrium-aluminium- garnet (Nd:YAG) have both been used in the treatment of ocular melanomas in certain situations. In 23 dogs, a semiconductor diode laser was used to treat presumed iris melanomas (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 four and a half 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 noninvasive diode laser photocoagulation was a safe and effective method of treatment for isolated, pigmented iris masses in dogs. Nd:YAG laser photocoagulation has been used as both a sole treatment and as an adjunctive therapy to treat limbal melanomas in cats and dogs (Sullivan et al, 1996; Plummer et al, 2008). When used as adjunctive therapy following lamellar resection of the tumour, laser energy is applied to the surgical site with the aim of destroying any residual tumour cells. In 15 cases (13 dogs and two cats) in which Nd:YAG laser photocoagulation was used as the only treatment for limbal melanomas, all tumours responded, but there was recurrence in three cases. Another potential use of laser therapy for ocular melanomas is for presumed choroidal melanomas. In this situation, laser

photocoagulation is used as a sole treatment in a transpupillary fashion.

Beta irradiation

Adjunctive strontium-90 beta ($_{90}$Sr-?) plesiotherapy has been used in the management of canine limbal melanoma (Figure 11). In one retrospective study, 30 cases underwent lamellar resection to remove the tumours followed by $_{90}$Sr-? plesiotherapy (Donaldson et al, 2006). One case suffered recurrence and side effects occurred in 16 cases. Shortterm side effects included corneal scarring, neovascularisation and granulation tissue formation. Long-term side effects were less frequent, but more severe, and included deep scleral thinning, focal scleromalacia and globe perforation.

Vaccination

A xenogeneic murine tyrosinase DNA vaccine has been developed for canine malignant melanoma and the US Department of Agriculture has issued a conditional licence for its use (Oncept, Figure 12). 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 the vaccine 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 ocular melanomas specifically, but there is no reason why the vaccine may not be used in cases of malignant ocular melanoma. The vaccine holds no licence in cats, although it has been used anecdotally in cases of diffuse iridal melanoma. There are, however, no published reports of the benefit or safety of the vaccine in cats and so this treatment cannot be recommended.

Summary

Ocular melanomas in dogs and cats come in many shapes and forms, thus current advocated therapies vary greatly. As our understanding of the behaviour of canine and feline ocular melanomas is in continuous development, our recommendations for treatment will also need continuous reassessment. Of particular interest for the veterinary ophthalmologist is the development of a melanoma vaccine. This may, in the future, prove useful for feline diffuse iridal melanoma – a potentially highly malignant tumour that, when extensive, usually carries a very poor prognosis.

References

- Cook C S and Wilkie D A (1999). Treatment of presumed iris melanoma in dogs by diode laser photocoagulation: 23 cases, *Veterinary Ophthalmology* **2**(1): 217-225.
- Donaldson D, Sansom J and Adams V (2006). Canine limbal melanoma: 30 cases

(1992-2004). Part 2. Treatment with lamellar resection and adjunctive strontium-90? plesiotherapy – efficacy and morbidity, *Veterinary Ophthalmology* **9**(3): 179-185.
- Featherstone H J, Renwick P, Heinrich C L and Manning S (2009). Efficacy of lamellar resection, cryotherapy, and adjunctive grafting for the treatment of canine limbal melanoma, *Veterinary Ophthalmology* **12**(supplement): 65-72.
- Kanai K, Kanemaki N, Matsuo S, Ichiwaka Y, Okujima H and Wada Y (2006). Excision of a feline limbal melanoma and use of nictitans cartilage to repair the resulting corneoscleral defect, *Veterinary Ophthalmology* **9**(4): 255-258.
- Lewin G A (1999). Repair of a full thickness corneoscleral defect in a German shepherd dog using porcine small intestinal submucosa, *Journal of Small Animal Practice* **40**(7): 340-342.
- Manley C A, Leibman N F, Wolchock J D, Riviere I C, Bartido S, Craft D M and Bergman P J (2011). Xenogeneic murine tyrosinase DNA vaccine for malignant melanoma of the digit of dogs, *Journal of Veterinary Internal Medicine* **25**: 94-99.
- Norman J C, Urbanz J L and Calvarese S T (2008). Penetrating keratoplasty and bimodal grafting for treatment of limbal melanocytoma in a dog, *Veterinary Ophthalmology* **11**(5): 340-345.
- Plummer C E, Kallberg, Ollivier F J, Gelatt K N and Brooks D E (2008). Use of a biosynthetic material to repair the surgical defect following excision of an epibulbar melanoma in a cat, *Veterinary Ophthalmology* **11**(4): 250-254.
- Sullivan T C, Nasisse M P, Davidson M G and Glover T L (1996). Photocoagulation of limbal melanoma in dogs and cats: 15 cases (1989- 1993), *Journal of the American Veterinary Medical Association* **208**(6): 891-894.

PANEL 1

• Species (dog versus cat)

• Location

• Rate of progression of tumour

• Results of ancillary diagnostic tests (cytology/ histopathology, diagnostic imaging)

• Index of suspicion of malignancy (dependent on above)

• Availability of treatment

• Level of technical expertise required

- Side effects of treatment
- Likely prognosis with/without treatment
- Owner’s attitude to treatment
- Costs