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CLINICAL PRESENTATION, DIAGNOSTIC AND THERAPEUTIC APPROACH OF OCULAR MELANOSIS IN A GOLDEN RETRIEVER- CASE STUDY

Andra ENACHE[1], Iuliana IONAŞCU[1], Pip BOYDELL[2], Tim SCASE[3]

[1]University of Agronomical Sciences and Veterinary Medicine, Faculty of Veterinary Medicine, Bucharest, Romania, andraenache@yahoo.com
[2]Animal Medical Centre Referral Services, Manchester, United Kingdom, www.amcreferrals.com
[3]Bridge Pathology, www.bridgepathology.com

Corresponding author email: andraenache@yahoo.com

Abstract

Ocular melanosis represents an abnormal pigment proliferation that involves the iris, ciliary body, choroid and filtration angle leading to secondary glaucoma. This report presents a Golden Retriever with excessive pigment deposition and corneal infiltration diagnosed with uveal melanoma. A 6 year-old male Golden Retriever presented with a four-week history of corneal degeneration and excessive pigmentation of the right eye. Full ophthalmic examinations and investigations including gonioscopy, ocular ultrasound and magnetic-resonance imaging were performed. Initial ophthalmic examination showed a central area of corneal degeneration, excessive melanin deposition on the right corneal endothelium and slightly irregular pupil with iris degeneration. There were also two melanin clumps on the left corneal endothelium. Initial ultrasound showed a mass posterior to the right iris into the vitreous with blood flow on the anterior margin and bilateral vitreous degeneration. Nonsteroidal and steroidal eye drops and topical interferon-alpha were initiated. MRI scan revealed an intraocular mass ventro-laterally situated posterior to the iris likely to be consistent with uveal melanoma. Fine needle aspirates were nondiagnostic. Enucleation was initially declined and progression was monitored. Six months later, ocular ultrasound showed extensive subretinal invasion. The eye was enucleated and histopathology described uveal melanoma originated within the iris with local infiltration. A low dose oral interpheron-alpha was administered for a long term management. Clinical progress was monitored and one year follow up revealed no signs of metastasis.

Key words: *enucleation, infiltration, ocular melanosis, uveal melanoma.*

INTRODUCTION

Ocular melanosis represents an abnormal pigment proliferation that may involve the anterior uvea, ciliary body, choroid with infiltration of the sclera, episclera and optic nerve. This has been primarily described as likely inherited in the Cairn terrier but was also reported in the Boxer, Labrador retriever, Boston terrier and Dachshund breeds.

The condition starts with increased pigmentation of the iris then it progresses to scleral involvement and intraocular invasion.

There are three reports of ocular melanosis in the Cairn terrier breed that were subsequently diagnosed with neoplastic uveal melanocytomas (Petersen-Jones, 2007) and other report describe concurrent limbal melanocytoma (Dees, 2013).

Many cases of anterior uveal melanocytoma were proven to arise from ocular melanosis or heavily pigmented globes and many cases of anterior uveal malignant melanoma arised from melanocytoma or melanosis. (Dubielzig, 2011)

This report presents a Golden Retriever with excessive pigment deposition with corneal infiltration subsequently diagnosed with uveal melanoma.

Primary canine intraocular melanomas commonly originate from the anterior uvea (Diters et al., 1983; Dubielzig, 1985; Wilcock, 1986) with primary choroidal melanomas being less frequently reported. (Bospene, 2008; Morgan, 1993; Weisse, 1985; Ryan, 1984)

The most clinically useful classification scheme classifies these tumors simply as melanocytoma benign and potentially

malignant melanoma based on the nuclear features of the tumor cells and the mitotic rate. (Wilcock, 1986) Benign tumors have fewer than 2 mitotic figures/10 high power fields and malignant tumors demonstrate nuclear pleomorphism and a mitotic index of at least 4 and often more than 30. (Withrow, 2013)

Other studies showed no correlation between histopathological description and the biological behavior and further studies of flowcytometry have been suggested. (Bolon, 1990)

The prognosis for histologically benign melanomas appears to be excellent and enucleation is curative. (Withrow, 2013) In one study, approximately 25% of histologically malignant melanomas demonstrated metastasis, typically within 3 months of enucleation. (Wilcock, 1986)

Choroidal melanomas are rare intraocular melanocytic tumors, representing only 4 to 7% of canine uveal melanomas, with no breed or sex predisposition. (Withrow, 2013; Giuliano et al., 1999) common in Middle-aged (6-7 years old), medium to large dog breeds. (Nasisse, 1993) Generally, these tumors are well-defined, raised subretinal pigmented masses with bulging centers and a tendency to invade the peripapillary region and the optic nerve. (Collinson PN, 1993; Dubielzig et al., 1985; Hyman, 2002)

MATERIALS AND METHODS

A 6 year-old male Golden Retriever was referred at the Ophthalmology Service with a four-week history of unilateral keratopaty and progressive pigmentation of the right eye.

Initial ophthalmic examination showed a central area of corneal degeneration, excessive melanin deposition on the right corneal endothelium and slightly papillary irregularity with iris degeneration (Figure 1, Figure 3).

There were two small melanin clumps on the left corneal endothelium as well (Figure 2).

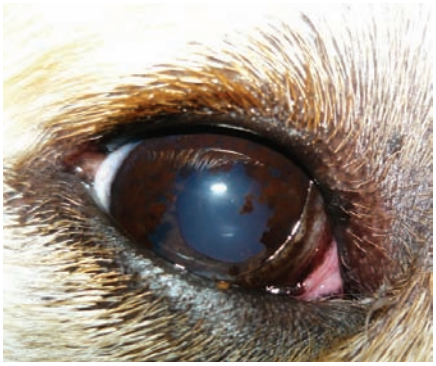

Figure 1. Right eye extensive melanin infiltration in the corneal endothelium (Golden Retriever, 6 years old)

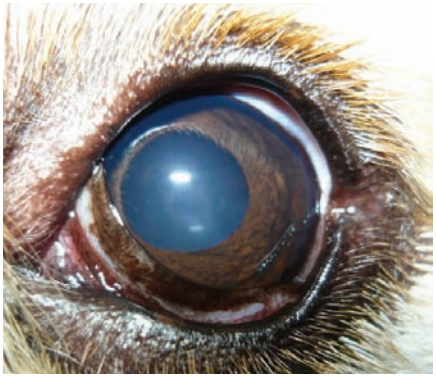

Figure 2. Two iridal hyperpigmented areas were noted at 4 and 5 o'clock with no architectural changes (Golden Retriever, 6 years old)

Both eyes were visual and comfortable. The fluorescein test was negative for both eyes and the direct ophthalmoscopic examination (PanOptic, Welch Allyn) was unremarkable.

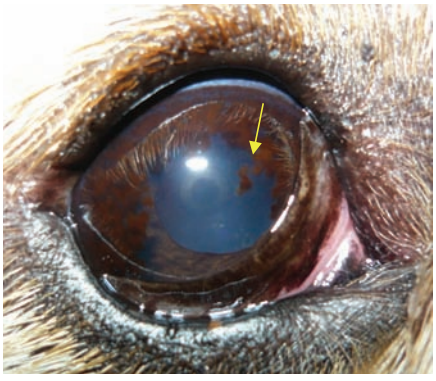

Figure 3. Right eye melanin deposition in the corneal endothelium and the presence of free melanin in the anterior chamber (yellow arrow)

Blood sample was sent out for cell blood count, biochemistry, protein electrophoresis, thyroid hormone testing and serologic investigations for Neospora and Toxoplasma.
Ocular ultrasound, chest and abdomen radiographic studies and gonioscopy were performed.
Investigations continued with magnetic resonance imaging and fine needle aspirates performed under general anaesthesia.

RESULTS AND DISCUSSIONS

Biochemistry results were unremarkable and hematology showed a borderline anaemia and hyperglobulinaemia that could reflect the presence of chronic disease and potentially inflammation.
Protein electrophoresis suggested antigenic stimulation in the absence of skin or hepatic disease. Thyroid hormones levels, T4 and TSH, free T4 were consistent with normal thyroid function and there was no serological evidence of exposure to Toxoplasma or Neospora.
Initial ultrasound showed a round-shaped mass posterior to the right iris into the vitreous with blood flow on the anterior margin and bilateral vitreous degeneration (Figure 4).

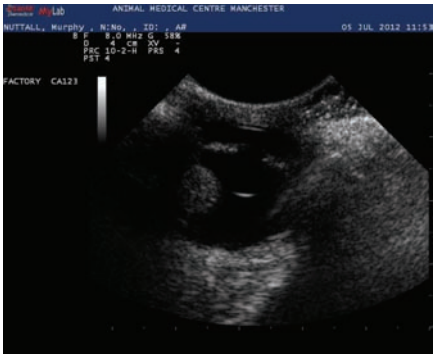

Figure 4. Ultrasound examination of the right eye showing a round-shaped mass posterior to the iris and the lens (Golden Retriever, 6 years old)

Gonioscopy was performed under general anaesthesia and the irido-corneal angle could not be visualized due to the infiltration of the pigment in this area.
Magnetic Resonance Image investigations revealed a hypointense signal ventrolaterally, posterior to the iris consistent with an intraocular mass. Intraocular melanoma was considered (Figure 6). Although the mass looked very well demarcated, different images taken suggest anterior extension of the mass (Figure 7).

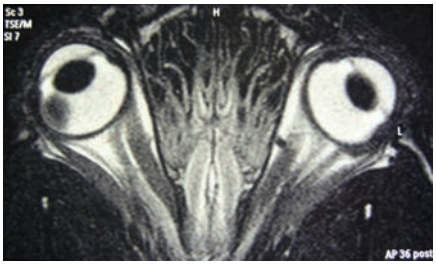

Figure 6. MRI scan of the brain, sagital section, showing the mass situated posterior to the iris with possible choroid infiltration

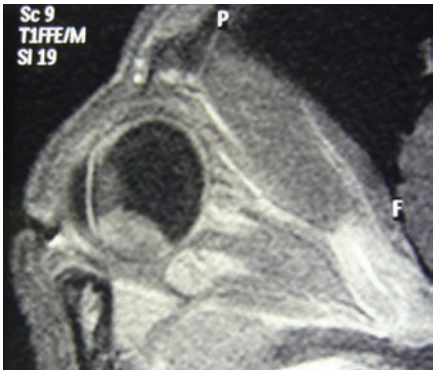

Figure 7. MRI scans showing posterior uveal tract involvement with anterior extension.

Fine needle aspirates performed under general anaesthesia revealed a high numbers of small dark melanin granules with occasional erythrocytes and rare neutrophils. Therefore, the cytological findings were nondiagostic in this case.
Enucleation was initially declined having considered the low rate of metastasis of uveal melanoma in dogs. Treatment consisted in prevention and management of secondary uveitis with topical nonsteroidal (Acular, ketorol tromethamine) and steroidal eye drops, Maxitrol (neomycin, polymyxin and dexamethasone), in the affected eye four times a day.
Oral low dose of interferon-alpha (Roferon A), 30 IU/ml was also advised topically four times a day.

Progression was monitored and one month later the eye was still visual and the mass could be visualized ophthalmoscopically.
Six months later the dog presented with no visual function of the right eye and ocular ultrasound showed marked changes in the posterior segment and extensive subretinal invasion (Figure 8, 9).

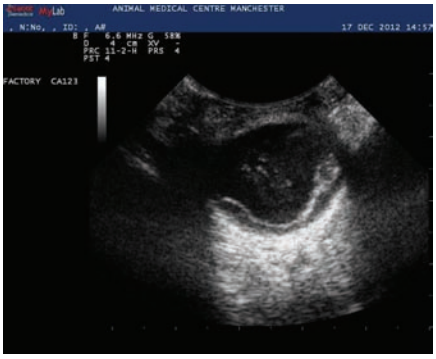

Figure 8. Right eye, loss of details of the lens with obvious lining of the retina suggesting retinal detachment
(Golden Retriever, 6 years old)

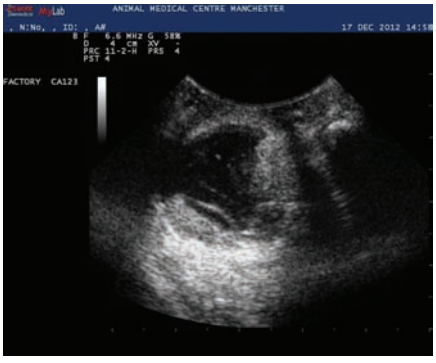

Figure 9. Right eye, anterior uveal invasion and subretinal extension of the mass with choroid thickening. (Golden Retriever, 6 years old)

Radiographic studies of the chest at the time were unremarkable.
The eye was enucleated and histopathological examination described uveal melanoma.
Neoplastic cells were seen expanding the iris, forming a dense, nodular mass, extending throughout the iris, ciliary body and choroid, around the optic nerve (Figure 10, 11, 12, 13). Focally, the neoplastic cells were extending into the choroid and cornea at the limbus, with clusters of neoplastic cells extending into the central portions of the cornea.
The neoplastic cells were moderately large, polygonal and contained abundant cytoplasm within which there were very large amount of dense intracytoplasmic brown granular pigment (Figure 10).
Nuclei were oval and obscured by the melanin pigment. Mitoses were 1 per 10 high power fields that describeed a low mitotic activity and therefore a low risk of metastasis.

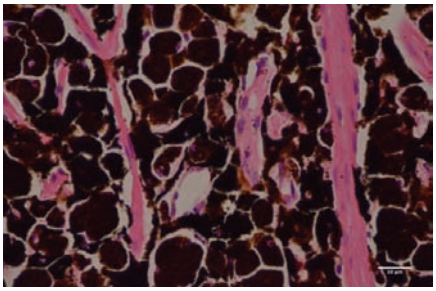

Figure 10. Uveal melanoma. Large, polygonal neoplastic cells with abundant cytoplasm with very large amount of dense intracytoplasmic brown granular pigment (100x)
(Courtesy of Tim Scase)

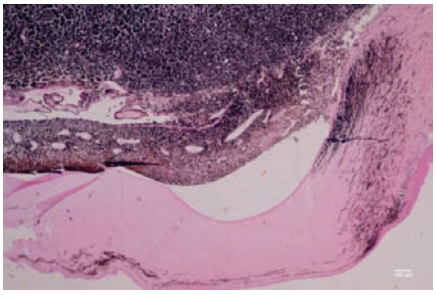

Figure 11. Iris and mass posterior to iris, low power field (Courtesy of Tim Scase)

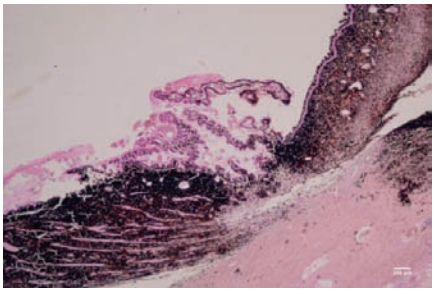

Figure 12. Iris and the ciliary body, low power field (Courtesy of Tim Scase)

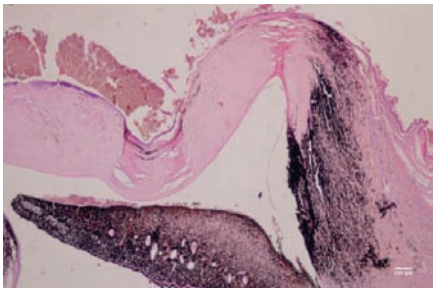

Figure 13. Iris and irido-corneal angle
(Courtesy of Tim Scase)

At the Comparative Ocular Pathology Laboratory of Wisconsin (COPLOW), uveal melanocytic tumors represent up to 27% of all ocular tumors and most of the uveal tumors of melanocytic origin are benign melanocytomas, the malignant melanomas representing only 20%. (Bospene, 2008; Esson, 2009)

Benign tumors also tend to be more darkly pigmented than malignant tumors. (Withrow, 2013)

There is no age predisposition but most affected dogs are older than 7 years of age. (Withrow, 2013) Although no breed predisposition was demonstrated, German Shepherds and Retrievers are highly represented in the literature. (Cook, 1999; Giuliano, 1999)

In dogs, uveal melanomas are locally invasive leading to secondary glaucoma, retinal detachment, and intraocular hemorrhage resulting in blindness. (Willis, 2001)

Magnetic resonance images of melanoma masses usually reveal high signal intensity on T1- weighted images and low signal intensity on T2-weighted images. In this case, the mass could be observed as low signal intensity, probably due to the presence of large amount of melanin. (Kato, 2005; Miwa, 2005)

The overall rate of metastasis of intraocular melanomas is approximately 4% and this usually occurs via the hematogenous route. (Bussanich, 1987) Local invasion is possible along ocular vessels and nerves or via direct penetration of the sclera or cornea. (Withrow, 2013)

The reported low risk of metastasis and unproved efficacy of enucleation at preventing metastasis make it difficult to advise enucleation of normotensive, noninflamed, visual eyes. (Wilcock, 1986; Withrow, 2013) Enucleation is therefore advised if there is a concern about metastasis or if complications such as uveitis or secondary glaucoma occur. (Nasisse, 1993; Withrow, 2013) In the reported case, enucleation was advised six months after the initial presentation as the eye was no longer visual and ultrasound examination showed extensive invasion.

Isolated primary iris or ciliary body masses may be amenable to local resection by sector iridectomy. (Diters et al., 1983; Gelatt, 1979) transscleral and transcorneal Nd:YAG or diode laser theray had induced remission in some small sized primary intraocular tumors. (Nasisse, 1993; Cook, 1999)

The process of pigment proliferation and deposition may be similar to that described in the Cairn terrier and long term management usually requires monitoring of the changes that the pigment may occlude the visual axis and accumulate and block the drainage angle. (Withrow, 2013)

It results in thickening and pigmentation of the iris, release of pigment in the aqueous, pigment deposition in the sclera, and to a lesser extent posterior segment pigment deposition. Secondary glaucoma is common and uveal melanocytic neoplasia occurs in a small percentage of dogs. (Petersen-Jones et al., 2007)

CONCLUSIONS

In this case the debate is whether the tumor has arised from the ocular melanosis and was subsequently diagnosed or the excessive endothelial melanosis is secondary to the local tumoral invasion.

Corneal and irido-corneal angle infiltration was reported in the literature with anterior uveal melanoma. (Friedman, 1989)

Choroidal melanomas are likely to invade the peripapillary region and the optic nerve, with no reported corneal invasion to the authors' knowledge. As the mass was well-delineated and originated within the posterior iris, it is likely to have caused local infiltration and anterior invasion of the neoplastic cells, also suggested by the presence of free pigment in the anterior chamber.

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