pISSN 1598-298X / eISSN 2384-0749
J Vet Clin 37(5) : 282-285 (2020)
https://doi.org/10.17555/jvc.2020.10.37.5.282

Journal of Veterinary Clinics
www.ksvc.or.kr

Malignant Anterior Uveal Melanoma Masquerading as Limbal Melanoma in a Shih-Tzu Dog with Recurrences of Hyphema

Lina Susanti, Kangmoon Seo and Seonmi Kang[1]

Department of Veterinary Clinical Sciences, College of Veterinary Medicine and Research Institute for Veterinary Science, Seoul National University, Seoul 08826, Korea

(Received: July 15, 2020 / Accepted: October 14, 2020)

Abstract : A 14-year-old neutered-male Shih-Tzu was referred for glaucoma and hyphema accompanied by systemic hypertension. After topical corticosteroid and antiglaucoma medications, the left eye (OS) progressed phthisically, but ocular hypertension redevelop one-year-and-seven-months later. Suspected limbal melanoma developed in peripheral cornea/limbal sclera with heavily pigmented cornea OS. Ultrasound biomicroscopy and ocular ultrasonography differentiated ciliary body origin-heterogeneous mass from limbal mass. Persistent hyphema and pigmented cornea might obscure intraocular lesion and advanced diagnostic methods played a crucial role. Unlike the generally benign limbal melanoma, aggressive treatment was recommended for uveal tumor. Histopathology of enucleated OS confirmed malignant uveal melanoma with chronic hypertensive vasculopathy.

Key words **:** anterior uveal melanoma, hypertensive vasculopathy, hyphema, limbal melanoma, ocular ultrasound.

Introduction

Limbal melanomas are relatively common in dogs. Originating from the melanocytes in the tissue near the limbus, they often invade cornea and rarely, sclera. Generally benign, they commonly grow outward and protrude into the globe surface, but could sometimes penetrate the sclera and invade iris or ciliary body, in which case, they are often difficult to be differentiated from melanomas originating from the anterior uvea (uveal melanoma) [7].

Unlike limbal melanomas, intraocular tumors are relatively uncommon in dogs. Among the primary intraocular neoplasms in dogs, melanocytic neoplasias, or melanomas, are the most common and often arise into the anterior uvea, originating from iris or ciliary body. Uveal melanomas are typically classified into benign (benign melanocytoma) and malignant (malignant melanoma) [2,4,9]. This paper describes a case of canine malignant anterior uveal melanoma masked by recurrent hyphema resulting from systemic hypertension, which has not been diagnosed until the tumor extended to the limbus.

Case Report

A 14-year-old Shih-Tzu was referred for hyphema and glaucoma of the left eye (OS). The dog had been treated for glaucoma for two months at the referring hospital where ultrasound biomicroscopy (UBM) performed then showed an open ciliary cleft in the right eye (OD) and partially closed in OS. The OS was buphthalmic and not visual. B-mode ocular ultrasonography revealed partial retinal detachment OS. The fundus imaging revealed retinal hemorrhage OU which is likely due to hypertensive retinopathy because the systolic blood pressure was 160 mmHg.

By the time the dog was referred to our animal hospital (Fig 1), the glaucoma was medically controlled with timolol maleate 0.5% TID (Timoptic®, Santen, Korea), dorzolamide 2% TID (Trusopt®, Santen, Korea), and latanoprost 0.005% BID (Xalatan®, Pfizer, Belgium). For the systemic hypertension, amlodipine besylate 0.1 mg/kg q24h PO (Norvasc®, Pfizer, China) was prescribed, and prednisolone acetate 1% SID (Pred Forte®, Allergan, Korea) was also topically medicated to address uveitis OS. Blood pressure measured while the dog was comfortably held by the owner was 155 mmHg. The OD was normotensive (13 mmHg as measured by Ton-

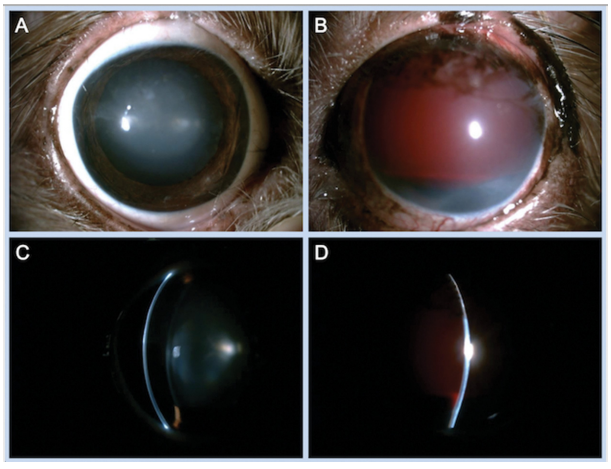

Fig 1. Initial presentation. (A and C) The right eye. (B and D) The left eye. Slit lamp biomicroscopy showed a buphthalmic eye accompanied by hyphema, moderate hyperemia, and corneal pigmentation in the left eye.

[1]Corresponding author.
E-mail : yorong4@snu.ac.kr

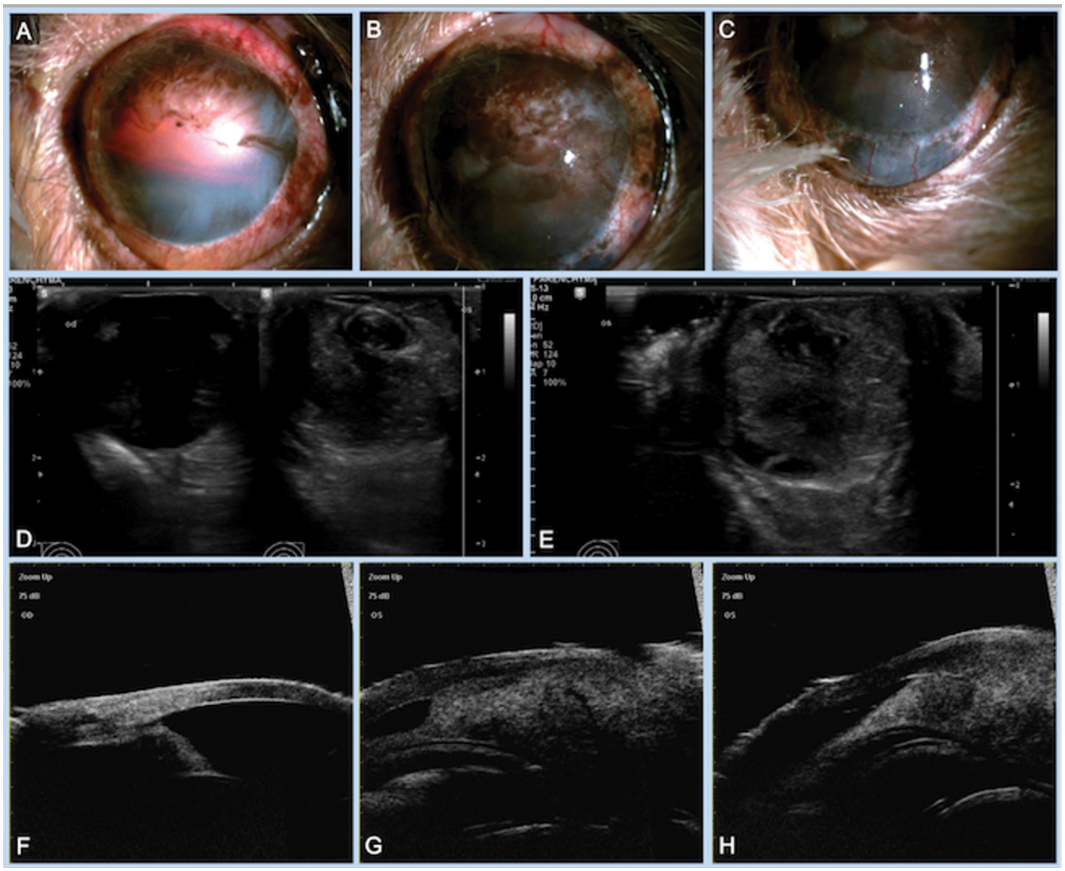

Fig 2. Ocular appearances and the images of ocular ultrasonography and ultrasound biomicroscopy (UBM). (A) The left eye (OS) two months later. Hyphema increased and ocular hypertension redeveloped. (B and C) The OS one year and seven months after the initial presentation. A pigmented lesion in the ventral peripheral cornea and limbal sclera caused an outward bulging. (D and E) Ocular ultrasonography revealed hyperechoic, heterogeneous mass originated from the ciliary body in the OS. (F) A normal UBM image of the right eye. (G and H) The UBM images of the OS showed the iridal mass extended to the sclera.

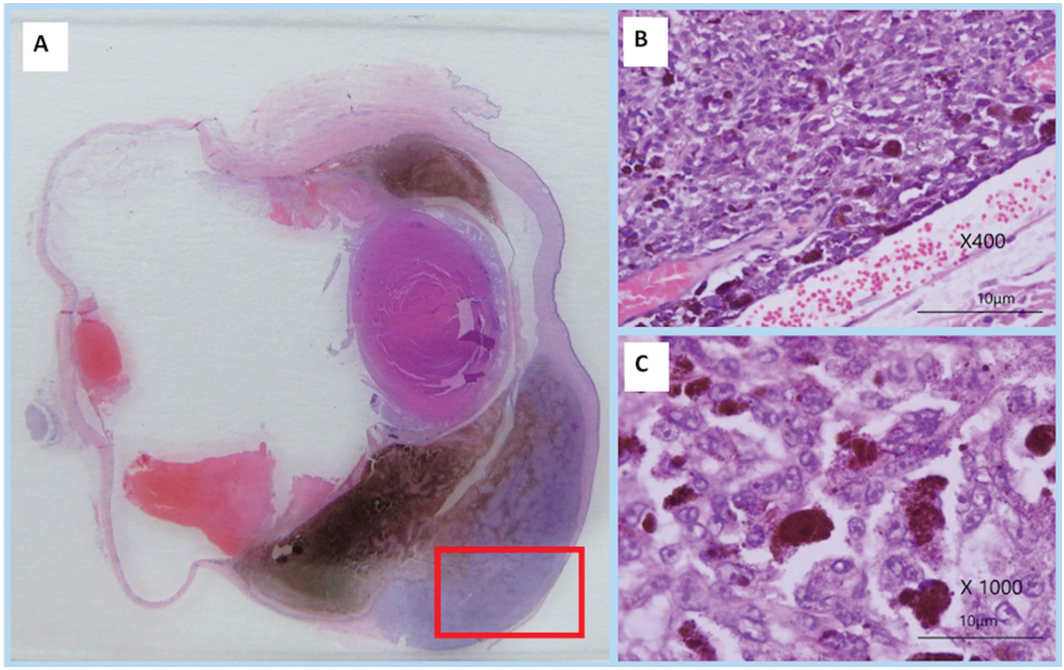

Fig 3. Histopathologic images from the enucleated left eye. (A) Subgross image from the enucleated left eye. An uncapsulated, poorly demarcated and variably densely cellular mass infiltrates, expands, and effaces the iris circumferentially and extends into the ventral peripheral cornea and limbal sclera, causing an outward bulge. (B) 400x magnification; (C) 1000x magnification. The cells exhibit mild to moderate anisocytosis and anisokaryosis and are polygonal to spindle in shape.

ovet; Icare®, Finland), had uveitis and focal retinal hemorrhage. The OS was buphthalmic with the intraocular pressure (IOP) of 20 mmHg. The intraocular structure OS could not be assessed due to severe hyphema (Fig 1B and D). Schirmer tear test (Merck, NJ, USA) were 19 OD and 22 mm/min OS.

The uveitis OU persisted two months later, and so did the retinal hemorrhage OD. Hyphema OS was largely resolved but the lens and posterior chamber still could not be observed. The IOP were 10 OD and 3 mmHg OS. The OS was no longer buphthalmic but instead slightly phthisical (Fig 2A). Glaucoma medication was stopped at this point. Three months later, ocular hypertension reoccurred OS (IOP 25 mmHg) and the eye was buphthalmic again. Trusopt® was prescribed TID. The anterior chamber was again obscured by hyphema.

One year and seven months after the initial presentation, the dog was presented with limbal outward bulging mass with heavily pigmented cornea OS (Fig 2B and C). Ocular ultrasonography revealed intraocular mass (Fig 2D and E) and UBM showed the limbal mass extended to iris through sclera (Fig 2G and H). UBM OD was normal (Fig 2F) and both eyes had normal IOP (14 OD/20 mmHg OS). There was no evidence of metastases on thoracic and abdominal radiography and ultrasonography. Enucleation and histopathology were performed and an informed consent was made that the results could be reported.

Histopathologically, the melanoma lesion showed an unencapsulated, poorly demarcated and variably densely cellular mass (Fig 3A). The cells were polygonal to spindle-shaped with variably distinct cell borders. The cells exhibited mild to moderate anisocytosis, and anisokaryosis and mitotic figures were present with 4 mitotic figures in ten 400x fields within the less pigmented areas (Fig 3B and C). Histological lesions associated with systemic hypertension were including intraocular hemorrhage and fibrinoproliferative lesion, retinal detachment and necrosis, and hypertensive chorioretinal vasculopathy. A fibrovascular membrane lines the anterior iris surface, crosses the iridocorneal angle and continues across the anterior lens capsule as pupillary membrane and posteriorly where it blends with a cyclitic membrane.

Discussion

Eyes are known as major target organ damaged from systemic hypertension [5]. Ocular findings associated with hypertensive injury include hemorrhage within the retina, vitreous, or anterior chamber; retinal detachment and atrophy; retinal edema; perivasculitis; retinal vessel tortuosity; and glaucoma [1]. In this case, persistent hyphema, which manifested from systemic hypertension, obscured the intraocular lesion OS and therefore the intraocular melanoma was only diagnosed after it had extended into the limbus, which at first, diagnosed as a limbal melanoma. UBM performed then showed the melanoma also extended intraocularly. Although melanomas of limbal origin might invade the intraocular structure [6], melanomas originating from the anterior uvea that penetrated perilimbal sclera are more common and comprises the majority of canine ocular melanomas [4].

The histopathologic report of hypertensive chorioretinal vasculopathy [5], including retinal detachment/necrosis and intraocular hemorrhage with a fibrinoproliferative lesion were all shown in this case. Systemic hypertension in dogs is frequently diagnosed in association with primary diseases, including renal failure, hyperadrenocorticism, diabetes mellitus, etc [5]. In this case, the systemic hypertension was associated with chronic renal disease. Amlodipine was prescribed to address the systemic hypertension which act mainly as an arteriolar vasodilator [12]. Through the course of the treatment, the blood pressure was ranging from 155 to 160 mmHg. The response of ocular lesions to antihypertensive therapy are expected to be varied and are influenced by duration and aetiopathogenesis of hypertension itself [8]. A study on 65 cases of ocular lesion associated with hypertension in dogs showed 10/15 dogs receiving antihypertensive drugs still had > 1 type of ocular lesion which wasn't necessarily represent the failure of medication in controlling the ocular target organ damage as other factors such as capillary fragility and increased vascular permeability could also play a role [5].

Pre-iridal fibrovascular membrane is a neovascularization membrane resulted from chronic uveitis [13] which in this case existed pre- and post iridally. A possible stimulus for this neovascularization could be an angiogenic stimulating factors released by the hypoxic retina, by tumor cells, or by some component of host response (macrophages) to an injured retina or neoplasm [11]. Pre-iridal fibrovascular membrane were frequently found in globes diagnosed with chronic endophthalmitis, chronic glaucoma, ocular melanoma, ciliary epithelial tumors, and other neoplasms [11].

Secondary glaucoma often occurs on eyes with melanoma [4], however, in this case, glaucoma already occurred at the first presentation to the referring veterinarian, where OS was presented with buphthalmos and blindness resulting from glaucoma. UBM and B-mode ultrasound performed at that time didn't show intraocular nor limbal neoplasia but the OS showed a semi-closed ciliary cleft while OD had an open angle with a normal range IOP. It was also revealed that OS had a retinal detachment but only partial, therefore suggesting that the blindness was due to chronic glaucoma which is supported further by the buphthalmic condition of the eye.

By the time this dog was presented to our animal hospital, glaucoma OS had been medically managed for 2 months and the OS was slightly becoming phthisical during following 7 months, until when the ocular hypertension (IOP 25 mmHg) reoccurred. At this point, it was possible the uveal melanoma had developed and caused the secondary ocular hypertension but was obscured by persistent hyphema. Ocular hypertension was resolved by the prescription of Trusopt® and IOP was maintained throughout the following 10 months until the limbal melanoma was diagnosed. Distinguishing between limbal melanoma and malignant intraocular melanoma that penetrates the sclera are known to be challenging and require careful clinical examinations to accomplish [7,10]. Complete intraocular examination, gonioscopy, and high-resolution ultrasonography or UBM along with ocular ultrasonography are generally required to differentiate between the two ocular melanomas [6].

Based on histopathologic examination, the melanomas are diagnosed as malignant anterior uveal melanoma in this case. Metastatic rate for uveal melanomas in dogs was reported to

be around 4-10% with mitotic index considered to be the superior criterion for predicting malignancy [4]. Generally, canine anterior melanomas do not tend to metastasize and cause death even though they are defined as malignant, but if metastasis does occur it typically involves thoracic and abdominal viscera [4]. For this reason, thoracic and abdominal radiography and ultrasonography were performed but no evidence of metastasis was found. In this study, aside from malignancy, mitotic index could also be suggested as a prognosis indicator, although it is considered to be unreliable in predicting the survival of the dog [3,9,10,14]. In this case, the tumor penetrated the sclera. In general, the prognosis for survival has been known to be good if the eye is enucleated before the tumor penetrates the sclera in dogs [4].

Conclusions

Limbal melanoma was a presenting sign of uveal melanoma. Persistent hyphema developed as an ocular manifestation of systemic hypertension, masking intraocular lesions. In order to differentiate between the uveal melanoma from the benign limbal melanoma, especially when intraocular lesion is unable to be visualized, UBM and ocular ultrasonography plays a crucial role in confirming the diagnoses.

Acknowledgments

This study was supported by BK21 FOUR Future Veterinary Medicine Leading Education and Research Center and the Research Institute for Veterinary Science (RIVS), College of Veterinary Medicine, Seoul National University, Seoul 08826, Republic of Korea.

Conflict of Interest

The authors declare no conflicts of interest and there was no financial support of manufacturer associated with the products used in this case report.

References

1. Brown SA, Henik RA. Systemic hypertension. In: Smith FWK, Tilley LP, Oyama MA, Sleeper MM, editors. Manual of Canine and Feline Cardiology. 5th ed. Missouri: Elsevier. 2016: 275-284.
2. Esson DW. Uveal melanoma. In: Clinical Atlas of Canine and Feline Ophthalmic Disease. 1st ed. IOWA: Wiley-Blackwell. 2015: 200-201.
3. Giuliano EA, Chappell R, Fischer B, Dubielzig RR. A match observational study of canine survival with primary intraocular melanocytic neoplasia. Vet Ophthalmol 1999; 2: 185-190. doi: 10.1046/j.1463-5224.1999.00080.x.
4. Hendrix VHD. Diseases and surgery of the canine anterior uvea. In: Gellat KN, Gilger BC, Kern TJ, editors. Veterinary Ophthalmology. 5th ed. IOWA: Willey-Blackwell. 2013: 1146-1198.
5. LeBlanc NL, Stepien RL, Bentley E. Ocular lesions associated with systemic hypertension in dogs: 65 cases (2005-2007). J Am Vet Med Assoc 2011; 238: 915-921. doi: 10.2460/javma.238.7.915.
6. Ledbetter EC, Gilger BC. Diseases and surgery of the canine cornea and sclera. In: Gellat KN, Gilger BC, Kern TJ, editors. Veterinary Ophthalmology. 5th ed. IOWA: Willey-Blackwell. 2013: 976-1049.
7. Maggs DJ. Diseases of the cornea and sclera. In: Maggs D, Miller P, Ofri R, editors. Slatter's Fundamentals of Veterinary Ophthalmology. 6th ed. Missouri: Elsevier. 2018: 213-253.
8. McLelllan GJ, Narfstrom K. The fundus. In: Gould D, McLellan G, editors. BSAVA Manual of Canine and Feline Ophthalmology. 3rd ed. Gloucester: BSAVA. 2017: 322-356.
9. Miller PE. Diseases of the uvea. In: Maggs D, Miller P, Ofri R, editors. Slatter's Fundamentals of Veterinary Ophthalmology. 6th ed. Missouri: Elsevier. 2018: 254-278.
10. Mitchell N. The sclera, episclera and limbus. In: Gould D, McLellan G, editors. BSAVA Manual of Canine and Feline Ophthalmology. 3rd ed. Gloucester: BSAVA. 2017: 232-240.
11. Peiffer RL, Wilcock BP, Yin H. The pathogenesis and significance of pre-iridal fibrovascular membrane in domestic animals. Vet Pathol 1990; 27: 41-45. doi: 10.1177/030098589002700106.
12. Sisson D, Kittleson MD. Management of heart failure: principles of treatment, therapeutic strategies, and pharmacology. In: Sisson D, Moise NS, Fox PR, editors. Textbook of Canine and Feline Cardiology. 2nd ed. Philadelphia: Saunders. 1999: 216-250.
13. Watte C, Pot S. The uveal tract. In: Gould D, McLellan G, editors. BSAVA Manual of Canine and Feline Ophthalmology. 3rd ed. Gloucester: BSAVA. 2017: 241-272.
14. Wilcock BP, Peiffer RL. Morphology and behavior of primary ocular melanomas in 91 dogs. Vet Pathol 1986; 23: 418-424. doi: 10.1177/030098588602300411.