

CASE REPORT

Primary central corneal hemangiosarcoma in a dog

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Abstract

Purpose To report a case of primary central corneal hemangiosarcoma in the dog.

Methods An 11-year-old, neutered, female, German shepherd mixed breed dog was referred to the Hospital Veterinario Sierra de Madrid (Spain) for evaluation of an enlarging corneal mass of the left eye (OS). The dog was predominantly housed outdoors and was diagnosed with a history of chronic superficial keratitis of both eyes (OU) by the referring veterinarian. The corneal mass was resected by routine superficial keratectomy and submitted for histopathology and Factor VIII immunohistochemical staining.

Results The mass was diagnosed as a corneal hemangiosarcoma with complete excision. Postoperatively, the keratectomy site healed without complication and there was no evidence of recurrence three and a half months postoperatively. Complete systemic evaluation, including abdominal ultrasound and CT scan of the head and thorax, indicated no other detectable neoplasia in the dog.

Discussion Outdoor housing and ultraviolet exposure, breed, and chronic superficial keratitis were all suspected as contributing factors to the development of a primary corneal hemangiosarcoma. Surgical removal and postoperative treatment for chronic superficial keratitis provided effective therapy.

Key Words: canine, hemangiosarcoma, cornea, ultraviolet light, superficial keratectomy

INTRODUCTION

Primary corneal neoplasia has been described in the dog,¹ cat,² horse,³ cow⁴ and human.⁵ Primary canine corneal neoplasms are rare. Primary corneal tumors that have been described in the dog include papilloma, limbal melanoma, squamous cell carcinoma, hemangioma, limbal hemangiosarcoma, adenocarcinoma, and lymphoma.¹ Canine corneal tumors of vascular origin have been described to involve the cornea by extension from the conjunctiva and limbus.⁶ To the authors' knowledge, central, primary, corneal hemangiosarcoma (HSA) has not been reported in the dog or any other species.

Hemangiosarcoma is a malignant neoplasm of vascular endothelial origin.⁷ HSA occurs more frequently in the dog than other species, may originate anywhere in the body with a blood supply and represents 5% of all nonskin primary canine malignant neoplasms.^{8,9} German Shepherds are overrepresented in the literature for visceral HSA,¹⁰

however they are not known to be overrepresented for ocular tumors. In addition, German Shepherds are overrepresented for the development of chronic superficial keratitis, of which ultraviolet light is thought to be a causative agent, thus encouraging corneal vascularization.¹¹

CASE REPORT

History and initial ophthalmic examination

An 11-year-old, female-spayed, mixed German Shepherd breed dog was referred to the Hospital Veterinario Sierra de Madrid in Spain for evaluation of a red, central corneal mass of the left eye (OS) and corneal melanosis of the right eye (OD). The owners reported that the mass had rapidly enlarged since observed 1 month prior to presentation. The OS was being treated with gentamicin, dexamethasone, and atropine 1% of unknown frequency by the referring veterinarian for a corneal mass and keratitis, however, no clinical response was seen after these initial treatments. Several years



Figure 1. Appearance of the OS of an 11-year old dog. This is a large, vascularized, tubular-like mass extending from the central cornea with small superficial corneal vessels extending to the mass from the limbus.

prior, the OD was believed by the owners to be blind for unknown reasons. The dog was predominantly housed outdoors and there was no previous history of trauma to either eye. No other systemic problems were reported.

Initial ophthalmic examination revealed a large, red, irregular mass located in the axial cornea OS (Fig. 1). Blepharospasm and serosanguineous ocular discharge were present OS. Menace and dazzle responses and palpebral and oculocephalic reflexes were all normal OS. Menace response OD was negative. Pupillary light reflexes could not be evaluated due to atropine induced mydriasis OS and severe corneal pigment OD. Schirmer tear test values were 20 mm/min OU. Intraocular pressure, as measured by applanation tonometry (TonoPen Vet[®], Medtronic, Florida, USA), was 19 mmHg OD and 9 mmHg OS. The intraocular pressure of the OS was taken in the peripheral cornea rather than the standard axial location due to the large mass. Fluorescein stain uptake was negative OU. Biomicroscopy OS revealed a large, vascularized, tubular-like mass extending from the central cornea with small superficial corneal vessels extending to the mass from the limbus. The remainder of the anterior segment appeared normal. Corneal melanosis with inactive corneal vessels and without any signs of active keratitis was present OD and prevented intraocular examination. The OD at this time was determined to be blind as there was no menace response. Indirect ophthalmoscopy revealed no abnormalities OS and the fundus was not visible OD. Physical examination, routine hematology, and biochemistry were all within normal limits.

Possible differential diagnoses for the corneal mass included granulation tissue, hemangioma, hemangiosarcoma, squamous cell carcinoma, lymphoma and adenocarcinoma.¹ The location and appearance of the tumor supported squamous cell carcinoma based on history of chronic pigmentary keratitis.¹² After discussion with the owner, a diagnostic and therapeutic superficial keratectomy

was performed to obtain histopathology for a definitive diagnosis.

Surgical Procedure

The dog was premedicated with meloxicam 0.2 mg/kg subcutaneously (Boehringer, Ingelheim, Germany), metadone 0.2 mg/kg intramuscularly (Novest Esteve, Barcelona, Spain), and dexmedetomidine 2 µg/kg intravenously (Orion Pharma, Espoo, Finland). Anesthesia was induced with propofol 2 mg/kg intravenously (Fresenius EFG, Friedberg, Germany), and maintained with isoflurane (NPIL Pharmaceuticals, Huddersfield, UK) and topical 2% mepivacaine (Braun, Barcelona, Spain). The OS was routinely clipped and prepared for surgery using dilute povidone iodine. The lesion was delineated using a #64 beaver blade (Swann-Morton, Sheffield, England) and a 30% depth lamellar keratectomy was performed excising the mass including a 2 mm margin of normal corneal tissue circumferentially. The excised mass was placed in 10% neutral buffered formalin and submitted for histological evaluation. Recovery was uneventful. Postoperative medications included Neomycin, Polymixin B, and Gramicidin triple antibiotic ointment (Oftalmowell, UCB Pharma, Madrid, Spain) OS every 6 h for 3 weeks, diclofenac 1% (Novartis Farmaceutica, Barcelona, Spain) solution OS every 6 h for 3 weeks, and atropine ophthalmic solution (Alcon CUSI, Barcelona, Spain) OS every 12 h for 3 weeks. No medications were prescribed for the OD.

Histopathologic examination

The corneal stroma was infiltrated, distorted and replaced by a non-encapsulated, moderately cellular mass in addition to large aggregates of erythrocytes and a coagulum of eosinophilic amorphous material (fibrin). The mass consisted of haphazardly arranged trabeculae of collagen and reactive fibroblasts which formed interconnected spaces containing free erythrocytes. Neoplastic spindle cells formed irregularly shaped and sized vascular spaces supported by cells containing scant amounts of eosinophilic homogenous cytoplasm and exhibited minimal to mild anisocytosis (Fig. 2). The nuclei were oval to spindle shaped, contained clumped chromatin and rarely contained a single prominent nucleolus. Minimal to mild anisokaryosis was present. Mitoses were not observed in ten 400× fields. Multifocal areas of fibrin thrombosis were observed in areas of the mass. The overlying corneal epithelium was multifocally ulcerated. The adjacent corneal stroma exhibited mild to moderate edema. Immunohistochemical staining for factor VIII was performed via the streptavidin-biotin method with counterstain and the neoplastic cells exhibited moderate positive cytoplasmic staining (Fig. 3). The histologic diagnosis was a corneal hemangiosarcoma.

Follow-up ophthalmic examination

The patient was examined three and a half months postoperatively. Based on the diagnosis of a corneal HSA, cardiac and

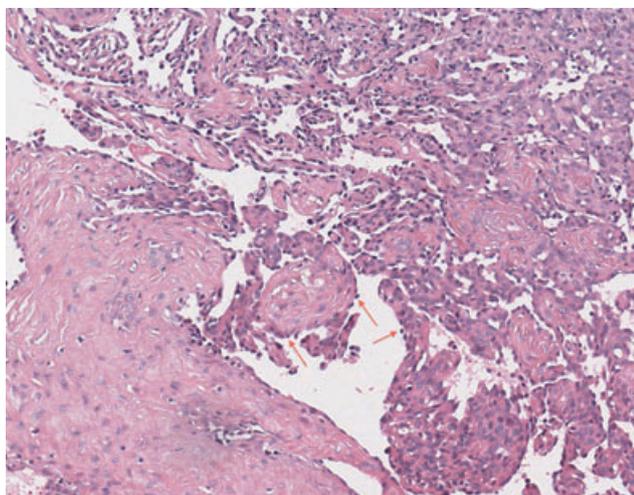


Figure 2. Hematoxylin and eosin (H&E) photomicrograph. Haphazardly arranged trabeculae of collagen and reactive fibroblasts. Trabeculae are lined by spindle cells bulging slightly into the lumens of these spaces (arrows). 40 \times .

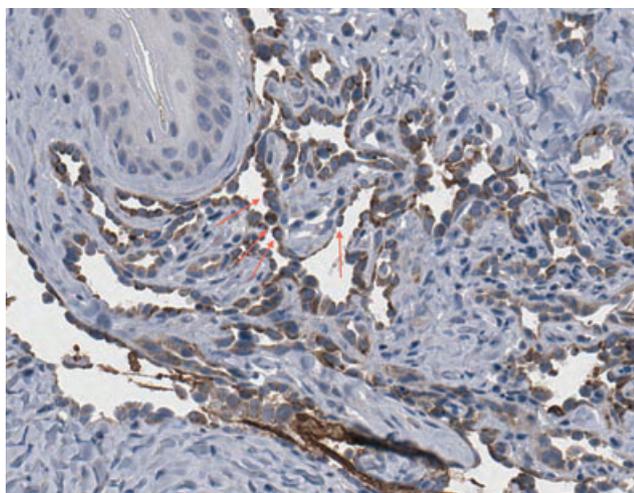


Figure 3. Factor VIII immunohistochemistry via streptavidin-biotin method with counterstain. 40 \times magnification showing neoplastic cells (arrows) exhibiting moderate positive cytoplasmic staining.

abdominal ultrasonography and CT scan of the skull and thorax were performed. These did not reveal a primary tumor elsewhere in the body. At the time of follow-up, there was no evidence of ocular discomfort. Menace response, dazzle response, palpebral reflex, and oculocephalic reflex were normal OS. Direct pupillary light reflex was normal OS, however the pupil could not be visualized OD. Schirmer tear test values were 20 mm/min OU and intraocular pressure as measured by applanation tonometry were 16 mmHg OD and 15 mmHg OS. Fluorescein stain was negative OU. Biomicroscopy revealed a moderate hyperemic conjunctiva, inactive corneal vascularization and corneal edema OS (Fig. 4). There was no evidence of recurrence of the tumor. Treatment with topical 0.1% dexamethasone solution



Figure 4. Three and a half month postoperative photograph showing moderate hyperemic conjunctiva, inactive corneal vascularization and corneal edema OS. This is prior to the initiation of topical therapy.

(Alcon CUSI, Barcelona, Spain) every 8 h was recommended OS and the patient was then lost to follow-up.

DISCUSSION

Hemangiosarcoma is a malignant neoplasm of vascular endothelial origin.⁷ HSA occurs more frequently in the dog than other species, may originate anywhere in the body and represents 5% of all nonskin primary canine malignant neoplasms.^{8,9} Visceral HSA occurs in any breed of dog but the majority are large breed dogs with the German Shepherd overrepresented.¹⁰ Several reports indicate a higher incidence of HSA in males although others do not cite a sex predilection.^{9,13,14} To the authors' knowledge, this is the first case reported of a primary, central corneal HSA reported in any species. Canine corneal tumors include squamous cell carcinoma, limbal hemangioma, limbal HSA, adenocarcinoma, and lymphoma.¹ Cutaneous HSAs are found more frequently in dogs with decreased pigmentation and light hair and may be associated with ultraviolet light exposure.¹⁵ In a report of temporal limbal HSA in a research colony of Beagles, the lesions developed under circumstances which suggested that solar radiation was involved in the pathogenesis.¹⁵ In the dog, primary HSA has been reported in many locations including spleen, right atrium, skin, subcutaneous tissue, liver, lungs, kidneys, oral cavity, muscle, bone, urinary bladder, peritoneum, third eyelid, conjunctiva, limbus, and iris.^{6,8-10,16-18} A retrospective review study performed by Pirie *et al.* showed that out of 108 primary vascular tumors of the conjunctiva, 70 tumors were identified as hemangiomas, and 38 as hemangiosarcomas. In this study, the German Shepherd was not overrepresented.¹⁹

The fact that this dog was predominantly housed outdoors, was a German shepherd mix, had bilateral keratitis

diagnosed by the referring veterinarian and had decreased skin pigmentation may have predisposed this dog to developing primary chronic superficial keratitis OU followed by a central corneal hemangiosarcoma OS. In a study by Chavkin *et al.*, it was determined that altitude was a significant risk factor to developing chronic superficial keratitis and that German Shepherds were overrepresented.¹¹ Other factors implicated in the initiation and potentiation of chronic superficial keratitis include high altitude,^{20,21} low humidity,²¹ UV radiation,^{20–22} breed,^{20,21,23} and gender.²⁴

In this case, there was vascular progression across the cornea secondary to chronic superficial keratitis of unknown duration with subsequent development of a primary corneal hemangiosarcoma. Surgical excision and medical treatment for the chronic superficial keratitis resulted in a favorable outcome at the time of the last examination.

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