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TUMORS OF THE CANINE GLOBE

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Introduction: This report is a concise summary of primary ocular tumors and their relative frequency in dogs, which is derived from the archives of the Comparative Ocular Pathology Laboratory (COPLOW) a large ocular pathology database.

It is important to have a regional understanding of ocular neoplasia because similar tumors may have a different clinical course depending on location, particularly regarding melanocytic tumors. Melanocytoma (defined as a benign melanocytic tumor) and malignant melanoma of the canine globe have the potential to be locally aggressive, yet enucleation is usually curative for both.¹ Malignant melanoma is common in the conjunctiva and often recurs locally. In contrast, a pigmented tumor in the eyelid is more likely melanocytoma than a malignant melanoma.¹ Hemangiosarcoma in the globe is likely to be a metastatic tumor but primary hemangiomia and hemangiosarcoma of the conjunctiva occur commonly. Although they may recur if inadequately excised, they have very low metastatic potential.

In the COPLOW database, the population of dogs with primary ocular neoplasia was comparable to the total database population, which included all ocular pathology submissions (inflammatory diseases, congenital diseases, trauma, primary and metastatic neoplasia, etc.). There were 6067 cases of primary ocular neoplasia in dogs with a definitive histopathologic diagnosis. Tumors of the globe accounted for 2851 (47.0%) cases and the majority of these were either melanocytic (1842, 64.6%) or iridociliary epithelial tumors (836, 29.3%). Conjunctival and eyelid tumors accounted for 1535 (25.3%) cases and 1399 (23.1%) cases, respectively. Finally, there were 282 (4.6%) orbital tumors.

No gender-specific patterns emerged for any individual tumor type in dogs. Most tumors had a typical age distribution with middle-aged and old dogs most frequently affected. Mean and median ages were 9.2 and 9.5 years, respectively.

A positive correlation based on breed, as determined by odds ratio, was significant for several tumors. The most notable breed predispositions arose in spindle cell tumor of blue eyed dogs (Siberian husky and Australian
shepherd), corneal squamous cell carcinoma (pug), conjunctival hemangiosarcoma (border collie, Australian shepherd, English setter, Basset hound, beagle and boxer), and eyelid melanoma (vizsla and Doberman pinscher). The Siberian husky is significantly less likely to have uveal melanocytic tumors.

The malignancy of melanocytic tumors varied with anatomic location in the eye. Melanocytic tumors in the uveal tract, limbus, and eyelid were more often benign than malignant. There were 1458 of 1842 (79.2%) melanocytic tumors of the uveal tract that were diagnosed as melanocytoma, and the remaining 384 (20.8%) were malignant melanoma. Limbal melanocytoma accounted for 341 of the 343 limbal melanocytic tumors (99.4%). Of the 149 eyelid melanocytic tumors, 126 (84.6%) were melanocytoma and 23 (15.4%) were malignant melanoma. The conjunctiva was the only location where malignant melanoma (180, 88.2%) was more common than benign melanocytoma (24, 11.8%).

Primary Tumors of the Globe

Melanocytic Tumors of the Globe

Uveal melanocytoma was approximately four times more common than malignant melanoma of the uvea. With respect to location within the uveal tract, anterior uveal (iris and/or ciliary body) melanocytic tumors are at least ten times more common than those in the choroid. Melanocytoma frequently invades the sclera and may extend into the episclera in advanced cases. Malignant uveal melanoma exhibits pleomorphism and may be locally invasive, although metastasis is uncommon. Malignant melanoma is more frequently amelanotic than melanocytoma. Enucleation with complete excision is generally curative for both melanocytoma and malignant melanoma of the uvea.4

Iridociliary epithelial tumors

Iridociliary epithelial tumors (IET) are the second most common intra-ocular tumor of dogs. Canine iridociliary epithelial tumors vary considerably with respect to pigmentation, invasiveness and morphology (solid vs. papillary). The definition of adenoma versus adenocarcinoma is based on histologic evidence of scleral invasion in the latter. We did not differentiate between adenoma and the scleroinvasive adenocarcinoma in this review, although previous studies suggest that IET adenoma is approximately 6-8 times more frequent than adenocarcinoma.5,6 Deposition of a thick, often arborizing, periodic acid Schiff (PAS)-positive basement membrane is often helpful in diagnosing poorly-differentiated or extensively necrotic IETs in dogs. Like native iridociliary epithelium, canine iridociliary epithelial tumors are generally positive for vimentin and negative for cytokeratin immunohistochemical stains. However, there is some tendency for the more invasive iridociliary adenocarcinomas to coexpress cytokeratin and vimentin.6,7

Iridociliary epithelial tumors, including the invasive adenocarcinoma, are clinically benign and generally well-differentiated. However, a previous study identified 16 cases of “pleomorphic” iridociliary adenocarcinomas.5 The term pleomorphic iridociliary adenocarcinoma applies to a similar malignant primary uveal tumor in humans, and is the only ocular tumor in humans associated with prior trauma.8 In dogs, the diagnosis applies to iridociliary tumors with pronounced cellular and nuclear features of malignancy and infiltrative behavior. They often arise in globes with long-standing intraocular disease, including previous intracameral gentamicin injection.5 Pulmonary metastasis was previously reported in one of the cases of pleomorphic iridociliary adenocarcinoma reported here.9
Spindle cell tumor of blue-eyed dogs

Spindle cell tumor of blue-eyed dogs (SCTBED) is the third most common intra-ocular tumor in dogs. In dogs that have at least a partially blue iris, these tumors arise diffusely in the iris, may extend to the ciliary body, and rarely involve the choroid. SCTBED are frequently not recognized clinically as neoplastic disease and may cause secondary glaucoma without an obvious mass lesion. Immunohistochemistry staining characteristics (GFAP positive and Melan A negative) is consistent with Schwann cells of non-myelinating nerves, furthermore, the tumors are morphologically consistent with a schwannoma. SCTBED must be distinguished from other intra-ocular spindle cell tumors of dogs, namely, melanocytic tumors and metastatic sarcomas. There are definite breed predispositions for SCTBED, generally any breed in which blue eye color occurs regularly. Siberian husky dogs and Australian shepherds are over-represented with respect to SCTBED in the COPLow collection.

Corneal Squamous Cell Carcinoma

The cornea may be the primary site of squamous cell carcinoma (SCC), particularly in dogs with long-standing keratitis. Corneal SCC may occur in situ or as an extension of conjunctival SCC. There is some evidence that dogs treated with topical medications for keratoconjunctivitis sicca at increased risk. Brachycephalic breeds are reported to be predisposed to corneal squamous cell carcinoma, and we found a statistically significant association in pugs.

Primitive Neuroectodermal Tumor

Intra-ocular primitive neuroectodermal tumors (PNET) are poorly differentiated embryonal tumors of neural tissue origin and include medulloepithelioma and retinoblastoma. Of the 27 cases of ocular canine PNET reported here, most (11) have a pattern characteristic of medulloepithelioma. Medulloepithelioma is rare in domestic animals, reported most frequently in dogs and horses. Medulloepithelioma may be fairly well-differentiated, resembling an iridociliary epithelial tumor. Like ciliary body epithelium, cells are negative for cytokeratin.

True retinoblastoma is almost exclusively a human disease, and is often associated with mutation of the retinoblastoma (rb) tumor suppressor gene. Of the 27 PNET tumors included here, two were diagnosed as retinoblastoma. They must be distinguished from medulloepithelioma based on strict morphologic criteria.

Glioma

Gliomas associated with the eye are rare in both the dog and cat. Ocular gliomas may be associated with either the retina or the optic nerve and may extend up the optic nerve tract toward the optic chiasm. They are generally astrocytomas with positive immunolabeling with glial fibrillary acidic protein (GFAP), and rarely oligodendroglioma.
References:
5. Bell CM, Dubielzig RR. Canine Iridociliary Epithelial Tumors: A Morphologic Case Series of 702 Cases, in proceedings. 60th Annual Conference of the American College of Veterinary Pathologists 2009; abstract #172.