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## OCULAR AND PERIOcular TUMORS IN CATS

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

Ocular neoplasia is a common reason for enucleation in cats. Previous studies have correctly identified diffuse iris melanoma as the most common tumor of the feline globe; however, these surveys exclude several recently characterized feline ocular tumors (e.g. feline restrictive orbital myofibroblastic sarcoma and conjunctival surface adenocarcinoma) and do not differentiate between the various subtypes of feline ocular post-traumatic sarcoma. Because of the greater frequency of malignant ocular neoplasia in cats, relative to dogs, clinicians should take care to avoid evisceration and scleral prosthesis in cases of possible neoplasia in cats.

Tumors of the globe that occur subsequent to ocular trauma are a particularly interesting phenomenon in cat eyes. These tumors are sub-divided into spindle-cell variant, round-cell variant, and osteosarcoma/chondrosarcoma. Because of the relationship between trauma and neoplasia in the feline globe, procedures like intraocular surgery or chemical ablation of the ciliary body are complicated by the risk imposed by the potential of a malignant neoplasm in much the same way that feline vaccine associated sarcoma impacts the way vaccinations are performed in cats.

The population of cats 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 2614 cases of primary ocular neoplasia in cats with a definitive histopathologic diagnosis. Tumors of the globe accounted for 2136 (81.7%) of all cases and the majority was melanocytic (1754, 82.1%). Conjunctival and eyelid tumors accounted for 319 (12.2%) and 111 (4.2%) of the total cases, respectively. Finally, there were 48 (1.8%) orbital tumors.

Intraocular tumors, in general, are most common in middle age to old cats. Mean and median ages were 10.6 and 11 years, respectively. Post-traumatic sarcomas are more common in male cats than females. Squamous cell carcinoma occurs more commonly in slightly older cats, having a mean and median age of 11.8 and 12 years, respectively.

Persian cats were over-represented among cases of hidrocystoma and slightly more likely to have melanocytic tumors of the globe. Persians accounted for 5 of 9 (55.6%) cases of hidrocystoma with an odds ratio of 7.71 and approximated 95% confidence interval of 1.48-40.2 ( $p = 0.01$ ). For feline diffuse iris melanoma, 125 of 1676 (7.5%) cases were in Persians, with an odds ratio of 1.93 and approximated 95% confidence interval 1.19-3.11 ( $p = 0.009$ ).

### **Primary Tumors of the Globe**

Previous reviews of feline ocular neoplasia identify melanoma and iridociliary tumor as the most common tumor of the feline globe.<sup>1-4</sup> Feline diffuse iris melanoma (FDIM) and feline ocular post-traumatic sarcoma (FOPTS) are the most common in our database.

### ***Uveal Melanocytic tumors***

In the cat, melanocytic tumors occur in one of three distinct patterns within the globe, from most frequent to least: diffuse iris, limbal, and atypical. There is good correlation between malignancy and location within the eye. Diffuse iris melanomas are considered to be indolent and malignant. Limbal melanocytomas are much more common in dogs and are benign and well-differentiated in both dogs and cats. Feline atypical melanoma arises focally or multifocally within the uveal tract, most often in the ciliary body or choroid. Despite its benign morphology, post-enucleation follow-up in cases of atypical melanoma suggested a malignant potential.<sup>5</sup> Masses in the posterior uvea are less likely to be noticed clinically so that compared to FDIM, atypical melanomas generally grow to a larger size and are more likely to extend outside the sclera before diagnosis.<sup>5</sup>

As the single most common intra-ocular tumor of cats, the recognition and management of feline diffuse iris melanoma (FDIM) has considerable importance to clinicians and pathologists. FDIM has a characteristic clinical presentation of progressive iris pigmentation, iris thickening and/or dyscoria. FDIM is a common cause of glaucoma in cats, which occurs once the neoplastic cells have infiltrated into the iridocorneal angle. Histopathologically, a previously described grading system for FDIM uses the qualifiers “early”, “moderate” and “advanced” and prognosis is affected by extent of disease at the time of enucleation.<sup>6</sup> Feline diffuse iris melanoma (FDIM) develops gradually, typically over several years, such that there is much debate regarding the appropriate time of enucleation. Some clinicians choose onset of glaucoma as an end point to determine time of enucleation. More conservatively, some clinicians choose to enucleate when there is an increased rate of change of iris pigmentation, which usually correlates histologically with early infiltration of neoplastic cells into the uveal stroma. When it occurs, metastasis has been most frequently reported in the liver.<sup>2,4</sup> The enucleated globe was graded as “advanced” in all cases of metastatic FDIM that were confirmed by our lab. In these cases, metastatic tumors occurred in the kidney and/or liver, suggesting that abdominal ultrasound may be the most appropriate procedure in staging cats with FDIM.

### ***Feline Ocular Post-Traumatic Sarcoma (FOPTS)***

In most cases of FOPTS, there is a documented history of ocular trauma to the affected eye. The span of time from initial ocular trauma to detection of the neoplasm ranges from many months to 10 years.<sup>7</sup> Clinically affected eyes most often show a white opacity without apparent pain or discomfort. The neoplastic cells characteristically migrate to cover the inner circumference of the globe, eventually occupying much of the intraocular space and frequently extending outside the globe at either the optic nerve head or the limbus. In nearly all cases, the lens is destroyed, often with intraocular inflammation. There is a reported case of hematogenous metastasis with local invasion to the level of the optic chiasm.<sup>7</sup>

Although all behave similarly, there are three histologic subtypes of FOPTS, in order of frequency: spindle cell variant (148 in the database), round cell variant (64) and osteo/chondrosarcoma (33). These variants cannot be differentiated clinically or grossly. The spindle cell variant FOPTS are negative for S-100 and thought to arise from a neoplastic transformation of lens epithelial cells, and may share some characteristics with vaccine-associated sarcomas in cats.<sup>7,8</sup> The osteo/chondrosarcoma variant FOPTS is the least common and is characterized by malignant mesenchymal cells that produce cartilage and/or osteoid matrix. The cell of origin is unknown.

The round cell variant FOPTS was characterized recently and neoplastic lymphocytes are believed to be the cell of origin.<sup>9</sup> Preliminary results from this report showed that the neoplastic cells stain with both T and B lymphocyte markers by immunohistochemistry.

### ***Iridociliary epithelial tumors***

Iridociliary epithelial tumors (IET) are the third most common intra-ocular tumor of cats. Compared to canine IET, they are more uniform, tending to be solid, non-pigmented and non-invasive.<sup>10</sup> The neoplastic cells are supported by a very fine vascular stroma that frequently gives rise to variably blood-filled cavitations within the solid mass. Immunohistochemical staining of neoplastic cells, like the native iridociliary epithelium, is generally positive for neuron specific enolase (NSE) and vimentin, while negative for cytokeratin. However there is frequent loss of vimentin immunoreactivity and/or co-expression of vimentin and cytokeratin. Individual cells or clusters of cells are supported by thin periodic acid Schiff (PAS)-positive basement membranes although the PAS reaction is often less distinct compared to the canine IET. Osseous metaplasia is also a common feature of feline IET.

## **Primary Tumors of the Conjunctiva**

### ***Squamous cell carcinoma***

Squamous cell carcinoma (SCC) is the most common primary conjunctival/eyelid tumor in the cat. These tumors present as ulcerated or exophytic lesions from the bulbar or palpebral conjunctiva, which may invade deep into orbital tissues and are multifocal in rare cases.<sup>4</sup> A recent study found a higher incidence of SCC in white cats and older cats as compared to cats with other tumors.<sup>11</sup>

### ***Conjunctival melanocytic tumors***

Unlike benign limbal melanocytomas that may involve the episcleral conjunctiva, other conjunctival

melanocytic tumors in cats are generally malignant. Although conjunctival malignant melanomas are locally aggressive and may recur after surgical excision, they do not tend to metastasize.<sup>12</sup>

### ***Conjunctival Surface Adenocarcinoma***

Conjunctival Surface adenocarcinoma is a rare neoplasm particular to cats, which is papillary and arises from the conjunctival epithelium to protrude from the surface of the third eyelid and/or bulbar conjunctiva. Some neoplastic cells have secretory material that is suggestive of goblet cells of the conjunctival epithelium. Complete surgical excision may not be possible due to infiltrative behavior, and pulmonary metastasis has been documented.<sup>13</sup>

## **Primary Tumors of the Eyelids**

### ***Hidrocystoma***

Hidrocystoma is reported most frequently in Persian cats; and although benign, hidrocystomas may demonstrate recurrence or new lesions may appear elsewhere in the conjunctiva after surgical excision.<sup>11,14,15</sup> Grossly, these are multifocal, pigmented, nodular lesions on the eyelids. Histologically, glandular epithelium forms unilocular or multilocular cysts with histiocytic inflammatory cells and cysts contain light brown, amorphous pigment that has not been characterized. Although some overlap may exist, hidrocystoma can be differentiated from cystic apocrine adenoma of the eyelid, which arises sporadically in cats of various breeds and is generally solitary, non-pigmented, and cured by excision.

### ***Peripheral nerve sheath tumor***

In a recent survey of feline peripheral nerve sheath tumor (PNST), 6 of 59 (10.2%) were associated with the eye.<sup>16</sup> Of ocular PNST, the eyelid is the most common site in cats and dogs, although other reported sites include the uveal tract, retina, conjunctiva and orbit of dogs and cats.<sup>16,17</sup> The upper lid is more commonly affected than the lower and recurrence after excision occurs in nearly all cases.<sup>11,17</sup> In one study, 7% of all feline eyelid tumors were PNST, considerably lower than the proportion reported in our database (27.9%).<sup>11</sup>

### ***Mast Cell tumor***

A previous study reported mast cell tumors as 25.6% of all feline eyelid tumors and reported a tendency for mast cell tumors to occur in young cats.<sup>11</sup> Mast cell tumors are not as common in our database (12.6% of eyelid tumors), and young cats are not over-represented. Mast cell tumors in the eyelid of cats are morphologically similar to the majority of feline cutaneous mast cell tumors, with uniformly well-differentiated cells.

## **Primary Tumors of the Orbit**

### ***Feline restrictive orbital fibroblastic sarcoma***

Several primary tumors occur with low frequency in the orbit of cats. Feline restrictive orbital myofibroblastic sarcoma (FROMS) was the most frequently diagnosed orbital tumor in cats in this study. This tumor was described recently and the name FROMS was proposed to replace the term feline orbital pseudotumor.<sup>18</sup> FROMS is an aggressive, infiltrative neoplasm composed of dense myofibroblastic tissue. It is progressive and locally infiltrative, with a tendency to spread to the contralateral eye, surrounding skin and/or

oral cavity. Although it is classified as an orbital tumor, involvement of the eyelids is common and thick eyelids with restricted movement may be the first clinical sign the disease. The COPLOW database contains no similar tumors in dogs, although there is a recent report of two canine cases of inflammatory myofibroblastic tumor, one of which was orbital.<sup>19</sup>

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