Ocular Neoplasia

What’s Common?
What’s New?

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Anatomic Distribution of Canine Primary Ocular Neoplasia
(n = 6110)

- Globe: 3225 (53%)
- Conjunctiva: 1192 (19%)
- Eyelid: 1408 (23%)
- Orbit: 288 (6%)
Canine Primary Tumors of the Globe (n = 3225)

- Tumors of the globe make up 3225 out of 6110 total neoplasms = 53%.
Canine Primary Conjunctival Tumors
(n = 1192)

Peripheral Nerve Sheath Tumor 11
Viral Papilloma 39
Mast Cell Tumor 52
Squamous Cell Carcinoma 85
Squamous Papilloma 110
Tumor of the Third Eyelid Gland 182
Hemangiosarcoma 186
Hemangioma 163
Melanoma 204
Reactive Papilloma 220

Tumors of the conjunctiva make up 1192 out of 6110 total neoplasms = 20%.
Tumors of the eyelid make up 1408 out of 6110 total neoplasms = 23%.
Tumors of the orbit make up 285 out of 6110 total neoplasms = 5%.
2135/5722 Canine Melanocytic Tumors

- Outside the Globe: 264
  - Conjunctival: 159
  - Eye Lid: 72
  - Skin: 33
- Affecting the Globe: 1871
  - Anterior Uveal Melanocytoma: 1245
  - Anterior Uveal Malignant Melanoma: 312
  - Limbal Melanocytoma: 213
  - Choroidal: 86 Melanocytoma and 11 malignant Melanoma
  - Metastatic Melanoma: 15
Anterior Uveal Melanocytoma
1245 Cases

Many cases are arising from within ocular melanosis or heavily pigmented globes
Heavily pigmented Round cells and Heavily pigmented Spindle cells
Limbal (Epibulbar) Melanocytoma
213 Cases
German Shepherds are over-represented
Canine Limbal Melanocytoma
Typical Limbal Melanocytoma

Atypical
Round cells dominate

Electron Micrograph
Melanocytes
Anterior Uveal Malignant Melanoma
312 Cases

Many Cases are Arising from Melanocytoma or Melanosis
Malignant Uveal Melanoma
Malignant Uveal Melanoma
Malignant Uveal Melanoma
Choroidal Melanocytic Tumors
86 Benign & 11 Malignant
After 4 years the dog developed neurologic disease
Presumed to be secondary to invasion of the optic foramen
Conjunctival Melanoma

- 159 cases
- Most are malignant by morphologic criteria
- Most recur elsewhere on the conjunctiva when removed
- They seldom metastasize
- Those on the palpebral conjunctiva are more likely to metastasize
Conjunctival Melanoma
Conjunctival Melanoma
Conjunctival Melanoma
Conjunctival Melanoma
Canine Iridociliary Epithelial Tumors
717 Cases
116 are Adenocarcinoma
10 Cases of Malignant Adenocarcinoma with features of Pleomorphic Adenocarcinoma
Pigmented Iridociliary Adenoma
Iridociliary Adenoma
Basement Membranes
Immunohistochemistry of Canine Iridociliary Epithelial Tumors

- Vimentin+
- Cytokeratin- (Malignant tumors tend to become +)
- S100+
Non-uveoinvasive (n = 7)

Vimentin

100% positive

Pancytokeratin

14% positive

Adeno-CA (n = 7)

Vimentin

100% positive

Pancytokeratin

57% positive
Pleomorphic adenocarcinoma

16 cases
Pleomorphic adenocarcinoma
Pleomorphic adenocarcinoma

Vimentin: 100% positive (n = 16)

Pancytokeratin: 75% positive (n = 16)
Pleomorphic adenocarcinoma

- Four (25%) dogs received an intraocular gentamicin injection 2-10 mo (ave 4.25 mo) prior to diagnosis
- 7 (44%) dogs had a history of chronic eye disease of at least one year
Pleomorphic adenocarcinoma—survival and outcome of 16 cases

<table>
<thead>
<tr>
<th>Outcome</th>
<th># cases</th>
<th>Site of confirmed or suspected metastasis (#cases)</th>
<th>Survival (months)</th>
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<tbody>
<tr>
<td>Documented metastasis</td>
<td>2</td>
<td>Lung (2), kidney (1)</td>
<td>9, 30</td>
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<tr>
<td>Suspected metastatic disease</td>
<td>4</td>
<td>Lung (2), liver (1), abdominal mass (1)</td>
<td>4, 4, 7, 10</td>
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<tr>
<td>Dead for unknown reason</td>
<td>6</td>
<td>N/A</td>
<td>2, 3, 10, 22, 24, 39</td>
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<tr>
<td>Alive</td>
<td>2</td>
<td>N/A</td>
<td>2, 41</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>2</td>
<td>N/A</td>
<td>N/A</td>
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</tbody>
</table>

Survival times in red are dogs that received gentamicin
Malignant Variant of Iridociliary Epithelial Tumor (Pleomorphic Adenocarcinoma)

Cytokeratin

Vimentin

Lung Metastasis
Spindle Cell Tumors of Blue Eyed Dogs
70 cases
Spindle Cell Tumor of Blue Eyed Dogs

- Median age=8.3 years
- Gender equal
- Laterality equal
- Siberian Huskies, Australian Shepherd, Border Collie and other breeds with blue or partly blue eye
Spindle Cell Tumor of Blue Eyed Dogs
GFAP

Stains Schwann cells of non-myelinating nerve fibers
Distribution of GFAP+ Cells in the Uvea of Blue Eyed Dogs
Distribution of GFAP+ Cells in the Uvea of Pigmented Dog Eyes
Anatomic distribution of feline primary ocular neoplasia (n = 2599)

- Globe: 82%
- Conjunctiva: 12.3%
- Eyelid: 4.4%
- Orbit: 1.15%
Feline tumors of the Globe (n=2136)

- Other: 13
- FOPTS, Osteo/Chondrosarcoma: 33
- FOPTS, Round Cell Variant: 64
- Iridociliary Epithelial Tumor: 124
- FOPTS, Spindle Cell Variant: 148
- Melanoma: 1754
Feline Conjunctival Tumors (n=319)

- Squamous Cell Carcinoma: 190
- Melanoma: 50
- Tumor of the 3rd Eyelid Gland: 26
- Hemangiosarcoma: 16
- Hemangioma: 14
- Mucopidermoid Carcinoma: 13
- Other: 10
Feline Eyelid Tumors
(n = 114)

- Other: 11
- Spindle Cell Tumor: 16
- Melanoma: 12
- Mast Cell tumor: 14
- Apocrine Gland Tumor: 30
- Peripheral Nerve Sheath Tumor: 31
Feline Tumors of the Orbit (n = 30)

- Other: 2
- Liposarcoma: 2
- Chondroma: 2
- Meningioma: 2
- Lacrimal Adenocarcinoma: 3
- Osteosarcoma: 4
- Anaplastic Sarcoma: 6
- Fibrosarcoma: 9
Feline Melanocytic Ocular Tumors: 2766

- Melanoma: 1510
  - Diffuse Iris Melanoma...1340 (263 Early)
  - “Atypical” ...27
  - Limbal...46
  - Conjunctival...27
  - 70 mostly DIM improperly labeled
Ages of Cats with Melanosis, Early Melanoma, Melanoma, and Extensive Melanoma

Progression of Feline DIM

Melanosis n = 84
Ages of Cats with Melanosis, Early Melanoma, Melanoma, and Extensive Melanoma

Progression of Feline DIM

Early Melanoma n = 325
Ages of Cats with Melanosis, Early Melanoma, Melanoma, and Extensive Melanoma

Melanoma (not extensive)  n = 1242
Ages of Cats with Melanosis, Early Melanoma, Melanoma, and Extensive Melanoma

Progression of Feline DIM

Extensive Melanoma n = 272
Metastatic Potential of Feline Diffuse Iris Melanoma
Early Stages of Feline Diffuse Iris Melanoma

Early Melanoma
Melanosis
Melanosis
Early FDIM
Tumor confined to the iris
Feline Iridociliary Epithelial Tumors

- 102/2766 neoplastic cases
- Tend to be non-pigmented
- Solid
- Cavitated
- About half have metaplastic bone
- Vimentin+, Cytokeratin-
Feline Iridociliary Adenoma
Feline Iridociliary Adenoma
Feline Iridociliary Adenoma
Spindle Cells
Feline Iridociliary Epithelial Tumors
Immunohistochemistry

Vimentin 34%

Cytokeratin 20%
Not related to tumor type

NSE 100%
Feline Post-traumatic Sarcoma
234/2766

- Spindle cell variant
  - 149 cases
  - Lens epithelial origin
- Round cell variant
  - 54 cases
  - Variant of lymphoma
- Osteosarcoma/Chondrosarcoma
  - 26 OSA/5 Chondrosarcoma cases
  - Unknown cell of origin
Reasons to believe PTS is related to trauma

• Lens capsule rupture
• History of trauma or abnormal eye
• Time between trauma and tumor
  – Between 2 months and 15 years
Early Spindle Cell Variant PTS
Feline Post-traumatic Sarcoma
Feline Post-traumatic Sarcoma
Cellular Features of Spindle Cell PTS

Collagen 4

Vimentin

αA Crystallin
Feline Post-traumatic Sarcoma
Follow-up Spindle Cell Variant

- Cases which have extended beyond the sclera have a bad prognosis
  - Local recurrence
  - Extension towards the brain
- Cases removed within the sclera have a good prognosis
- 8% of traumatized globes removed prophylactically have early PTS
Round Cell Variant PTS
Round Cell Variant PTS
Round Cell Variant PTS
Feline PTS Osteosarcoma
Feline Restrictive Orbital Myofibroblastic Sarcoma
FROMS
(Feline Orbital Pseudotumor)
Signalment—14 cases of FROMS

- **Breed:**
  - 9 DSH
  - 3 DLH
  - 1 Maine Coon
  - 1 unknown

- **Gender**
  - MN = 5  FS = 9

- **Age**
  - Mean = 10.5 years, Median = 10 years
  - Range = 4 - 16 years

- **Unilateral = 13**   **Bilateral = 1**

- **Oral lesions = 1**
Clinical Characteristics

- Restricted mobility of globe and eyelids
- Thickened and distorted eyelids
- Profound corneal disease
Clinical Characteristics

- Thickening +/- ulceration of lips
- Proliferative gingival lesions (neoplastic?)
• Local Extension to adjacent tissues
• Thickening and effacement along fascial planes
Feline Restrictive Orbital Myofibroblastic Sarcoma

- Severe corneal disease
- Dense, fibrous orbital tissues
- Globe spared
Feline Restrictive Orbital Myofibroblastic Sarcoma
Feline Restrictive Orbital Myofibroblastic Sarcoma

Lymphocytic Foci
Subepithelial neoplastic cells

Smooth Muscle Actin (SMA)
Second orbit from necropsy specimen
• Spindle cells in irregular short bundles with collagenous matrix
• Bland nuclear profile
• Mitotic activity virtually absent
## FROMS Immunohistochemistry

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>+</th>
<th>-</th>
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<tbody>
<tr>
<td>Vimentin</td>
<td>8</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>S 100</td>
<td>8</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>SMA</td>
<td>8</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Melan A</td>
<td>2</td>
<td>0</td>
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</table>
Clinical Progression & Survival

• 9 of 10 cases with adequate follow-up had spread to the contralateral eye and/or oral cavity/lips

• All cats (5) that were confirmed deceased were euthanized due to progressive disease

• Of 3 cats currently living, 2 have signs of progressive disease
Feline Restrictive Orbital Myofibroblastic Sarcoma: Summary

- Behavior is locally invasive and severely restricts the mobility of globe, eyelids and lips
- Morphology suggests an infiltrative myofibrosarcoma, seldom forms a mass lesion, lacks cellular atypia
- Diagnosis requires histopathology plus clinical picture
- Distribution and extent in the oral cavity and elsewhere in the head is under investigation
FROMS DDx
Squamous Cell Carcinoma