

Feline (Cancer) Focused Family Feud

Sara Fiocchi, DVM, DipACVIM (Oncology)

Susie Kang, DVM, Practice Limited to Oncology

What are the most common causes of hypercalcemia in cats?

- Idiopathic hypercalcemia
- Chronic renal disease
- Squamous cell carcinoma
- Lymphoma
- Primary hyperparathyroidism

Hypercalcemia in cats is usually an incidental finding. When total calcium is elevated on a routine lab panel, ionized calcium should be evaluated also. In most cases of hypercalcemia, cats will have both elevated total and ionized calcium. In cats with chronic renal failure, their total calcium may be elevated but ionized calcium may be normal, elevated or even decreased. Only the ionized calcium has biologic effect. The severity of hypercalcemia does not predict the cause nor correlate with the presence or absence of clinical signs. An abdominal ultrasound, thoracic radiographs, oral exam, rectal exam and cytology or histopathology of any masses is important to rule out an underlying neoplasm. Evaluating PTH/PTHrP can also be useful, although hypercalcemia of malignancy occasionally occurs in the absence of elevated PTHrP.

Name the 2 most common oral tumors in cats.

- Squamous cell carcinoma (SCC)
- Fibrosarcoma (FSA)

Squamous cell carcinoma

- 70-80% of oral tumors in cats are SCC
- Site predilection: tongue, pharynx, and tonsils
- Bone involvement is common
- Surgery: median survival time (MST) 45 days and 1 year survival <10%
- Radiation therapy: poor response with MST of 90 days
- Best treatment is still combination of surgery and radiation if possible
- Cause of death: usually due to local disease

Fibrosarcoma

- 13-17% of oral tumors in cats are fibrosarcoma
- Site predilection: gingiva
- Distant metastasis is <20%
- Bone involvement common
- Treatment: combination of surgery and radiation if possible, MST depends on the extent of the disease
- Cause of death: usually due to local disease

Which 2 chemotherapy agents should not be used in cats due to serious adverse effects?

- 5-fluorouracil (5-FU)
- Cisplatin

Cisplatin causes fatal pulmonary edema in cats. 5-FU causes fatal neurotoxicity. The cream formulations used to treat skin cancers in humans are also fatal if ingested, even in small doses (such as licking where the owner applied it or if the owner pets the cat and residue is left on the fur and later groomed off). 5-FU can be safely used intravenously in dogs but ingestion is toxic with reported survival rates of 20-25% with aggressive supportive care.

Name prognostic factors for female cats with mammary adenocarcinoma.

- Tumor size
- Lymph node metastases
- Histologic grade
- Lymphatic / vascular invasion
- Siamese breed (versus DSH) in some studies

Mammary adenocarcinoma accounts for ~17% of feline tumors, with the highest risk in intact females. Males may also develop mammary carcinoma but the majority have a history of exposure to progestins. 85-95% of feline mammary tumors are malignant. Tumor size is the most consistent prognostic factor followed by the presence or absence of lymph node metastases. Stage is also prognostic and feline mammary carcinomas are staged according to a four-tier system. Survival time is > 24 months for stage 1, 12-24 months for stage 2 disease, 4-12 months for stage 3 disease and 1 month for stage 4 disease. Chemotherapy is typically recommended for cats with higher stage disease or those with aggressive histologic appearance, though statistical evidence is lacking. DSHs have better outcome than purebreds, Siamese worse than DSH (but in other studies breed was not prognostic).

Stage 1	T1 <2 cm	N0	M0
Stage 2	T2 2-3 cm	N0	M0
Stage 3	T1, T2	N1	M0
	T3 > 3 cm	N0/1	M0
Stage 4	any T	any N	M1

Name some contraindications to prednisolone use in cats.

- Diabetes mellitus
- Congestive heart failure
- Systemic fungal infections
- Gastric ulcers

Prednisolone and other steroids can contribute to diabetes mellitus in predisposed cats as they increase insulin resistance and decrease insulin sensitivity. These cases may be reversible with discontinuation of the drug, but cats may also remain insulin dependent. In cats suspected to be borderline diabetics or those with a history of transient diabetes (achieved remission with insulin therapy and now normoglycemic), budesonide or topical steroids may be more appropriate.

Prednisolone and other corticosteroids, most notably methylprednisolone acetate, are associated with congestive heart failure. This is thought to be due to volume retention as hypertension was not observed in one study. Provided cats survived the initial crisis, hypertrophic changes resolved after stopping methylprednisolone and prolonged survival was reported. In cats with cardiac disease, corticosteroids should be avoided until consultation with a cardiologist suggests otherwise. Dexamethasone may have lesser risk than prednisolone.

Use with caution in cases of renal insufficiency.

Use in pancreatitis is controversial although not necessarily contraindicated.

Name some implicated/possible iatrogenic causes of Feline Injection Site Sarcomas.

- Rabies vaccine
- FeLV vaccine
- Any vaccine is possible
- Long acting shots such as long acting penicillin, methylprednisolone, lufenuron (Program)

Much like trauma induced sarcomas in the lens of the eye, it is suspected that inflammation leads to fibroblast and myofibroblast proliferation and eventual tumor formation in the region of the injection.

It can take 4 weeks to 10 years to develop a tumor.

No single manufacturer or vaccine type has a higher or lower association. Also needle gauge, syringe reuse, shaking multi-dose vials, mixing vaccines in a single syringe, and syringe type did not play a role.

Rate is 3.6/10,000 for injection site sarcomas, other soft tissue sarcomas is 20/100,000

Other reported associations: microchip, non-absorbable suture (nylon), retained surgical sponge.

There is no specific evidence that we are aware of that Convenia causes injection site sarcomas.

What treatment and management options are available for feline hyperthyroidism?

- Radioactive I-131
- Methimazole
- Surgery
- Hill's y/d diet
- External beam radiation therapy (for non-functional tumors)
- Percutaneous radiofrequency ablation

Consumption of commercially prepared canned foods, indoor residence, use of cat litter, and exposure to herbicides, fertilizers and topical flea products are implicated.

Siamese and Himalayan breeds are at a DECREASED risk.

I-131 (2-6mCi) with benign disease: 98% cure rate. Can re-treat if needed to achieve cure.

I-131 (20-30mCi) with thyroid carcinoma: may be better if combined with thyroidectomy, survival greater than 1 year in most cases (MST 20 months).

Methimazole: Only helps with stopping thyroid hormone production, does nothing for the underlying disease.

Which tumors in cats are most commonly treated with Sr-90?

- Squamous Cell Carcinoma (of the nasal planum and head - solar induced)
- Mast cell tumor (MCT)

Cutaneous SCC: 1 and 3 year control: 89 and 82%

Nasal Planum SCC (superficial lesions): one fraction results in a 98% response (88% complete response) with a progression-free survival (PFS) of 1710 days and MST of 3076 days.

MCT: 98% control rate (remember, this is for cats, not dogs)

Also used on eyelid tumors, corneal tumors, basal cell tumors and can be used in a palliative protocol for sublingual SCC in very select cases.

What are the most common feline nasal tumors?

- Nasal lymphoma
- Epithelial tumors (carcinoma, adenocarcinoma, SCC)
- Sarcoma
- Nasopharyngeal polyps

Can also see mast cell tumor, melanoma and plasmacytoma.

90% are malignant. Low metastatic rate.

Definitive radiation therapy for non-lymphoma: MST 12mo (n=16). 1yr: 44-63%, 2yr 16%.

How does the biologic behavior of nasal lymphoma in cats differ from other forms of lymphoma in cats?

- Usually localized disease
- Radiation therapy often used as sole treatment modality
- Majority are B cell
- Prognosis

Unlike most other forms of lymphoma, feline nasal lymphoma is often a localized disease. Hence, radiation therapy can be considered as a sole treatment modality. Full staging (thoracic radiographs, abdominal ultrasound) are needed prior to radiation therapy to look for evidence of systemic disease. Cats treated with definitive radiation have a median survival of 15+ months; 75-95% CR; MST 1.5-3yr. Cats treated with more conservative radiation protocols (< 32 Gy total dose) are reported to have shorter survival times. Approximately 15-20% of cats will relapse systemically, thus if feasible systemic chemotherapy (typically a CHOP protocol) is recommended in addition to radiation therapy. Chemotherapy as the sole treatment modality is associated with shorter survival times (versus radiation therapy alone). With CHOP/COP, 75% achieve a clinical remission (CR) and for those who achieve CR the median survival time (MST) is 2yr.

What are the most common types of bladder tumors in cats?

- Transitional cell carcinoma (55%)
- Sarcoma (18%)
- Benign mass/polyp (18%)
- Lymphoma (7%)

Bladder tumors are less common in cats than in dogs. When tumors occur, the most common tumor type is transitional cell carcinoma (TCC). There is less data on prognosis in cats compared to dogs. One study in cats reported ~20% of cats with TCC had pulmonary metastasis at the time of diagnosis and ~5% had regional lymph node metastasis. Like in dogs, urinary tract infections were common in this patient population (30-75%), so routine screening for infection should be done. There is limited data on survival times with treatment; one study reported an overall median survival time of 8.5 months and included cats treated with one or more of the following treatments: surgery, piroxicam, chemotherapy. A second study reported 90% of cats showed clinical improvement when treated with meloxicam and a median survival of ~ 10 months with meloxicam +/- surgery.

Name the 3 most common intestinal tumors in cats.

- Lymphoma (55%)
- Intestinal carcinoma
- Mast cell tumor

What are some differences between large cell vs small cell intestinal lymphoma (LSA)?

- Duration of clinical signs
- Sonographic findings
- Prognosis
- Treatment plan

Lymphoblastic (large cell) lymphoma (25% of GI LSA cases)

- History: acute history of vomiting, diarrhea, inappetence, weight loss
- Usually associated with a large mass in the intestines (may or may not have lymphadenopathy)
- 18% complete remission with CHOP protocol with MST of less than 6 months
- May want to do surgery depending on the size of the mass or presence of obstruction but no survival benefit has been shown vs chemo alone

Small cell LSA (75% of GI LSA cases)

- History: chronic history of vomiting, diarrhea, weight loss or inappetence
- Slow to progress
- Sometimes difficult to differentiate from inflammatory bowel disease
- Diffuse thickening of the muscularis layer (may or may not have lymphadenopathy)
- 69% complete response with prednisolone and chlorambucil with MST of 2 years or more

What are some important prognostic factors for cats with lymphoma?

- Grade
- Anemia (cats with lower PCV tend to do worse)
- FeLV status (positive = worse)
- Response to therapy
- Location (e.g. nasal better, mediastinal worse unless Siamese)

If Siamese and FeLV neg: 90% of cats w/mediastinal respond to treatment, MST 9months.

If CNS involvement: <50% response rate, MST 1-2mo.

Pure hepatic = worse prognosis

Exposure to tobacco smoke increases relative risk. Any exposure: 2.4 RR. 5+yr exposure: 3.2 RR.

Name 5 cutaneous neoplasms in cats.

- Basal cell tumor (19.5%)
- MCT (17.4%)
- Fibrosarcoma (17.4%)
- SCC (11.4%)
- Sebaceous hyperplasia/adenoma (3.1%)

- Basal cell tumor (19.5% of cases)
 - Usually solitary and well circumscribed, found on the head, neck and shoulders
 - Usually benign, grow slowly
 - Surgical excision carries a good prognosis. One study: 124 cases in cats treated with surgical excision: none of the tumors recurred or metastasized.
- Mast cell tumor (17.4%)
 - Surgery is the treatment of choice and most of these lesions are behaviorally benign and wide surgical margins may not be as critical as in the dog
 - Most of these tumors occur on the head
 - Local recurrence rates range from 0-24% after surgical excision
 - Incidence of systemic spread after surgical excision varies from 0-22%
- Fibrosarcoma (17.4%)
 - Surgery, radiation +/- chemotherapy
- Squamous cell carcinoma (11.4%)
 - Most common locations: sparsely haired areas of the nasal planum, eyelids and pinnae
 - Surgery, cryosurgery, radiation, strontium are the mainstays of treatment
 - Outcome is generally good if treated early
 - Surgical excision of lesions of the pinnae resulted in long term control (> 1.5 years in most)
 - Radiation therapy: 93% response rate, MST of 946 days
 - Strontium provided long term control in 25 cats with early superficial lesions
- Sebaceous hyperplasia/adenoma (3.1%)
 - Usually a single solitary lesion, often on the head
 - Recurrence has not been reported after excision

What are some lab or clinical abnormalities noted in cats with multiple myeloma?

- Hyperglobulinemia (94%)
- Marrow plasmacytosis (>10% is the cutoff in cats) (50-97%)
- Proteinuria (71%) (Bence Jones protein 40-59%)
- Hypercalcemia (10-25%)
- Bone lysis (5-45%)
- CBC abnormalities (anemia 50-64%, thrombocytopenia 50%, neutropenia 37%, circulating plasma cells 5-25%)
- Hyperviscosity syndrome (35-44%)
- Azotemia (22-40%)

Treatment options: Melphalan, CHOP

Prognosis: 60% of cats transiently respond to chemo but overall prognosis is poor and *most* succumb to the disease within 4 months.

Name four negative prognostic indicators for feline pulmonary adenocarcinoma.

1. Stage (lymph nodes, digits)
2. Poorly differentiated tumor
3. Clinical signs (coughing, dyspnea)
4. Pleural effusion at time of diagnosis

Pulmonary adenocarcinoma is a more aggressive disease in cats than in dogs. Many cats have advanced disease at the time of diagnosis. Advanced tumor stage, poorly differentiated histology, and presence of pleural effusion and/or dyspnea are associated with a poor prognosis (T1N0M0 – MST 6 months, all others MST 3 days). In one small study of 20 cats, 50% of cats did not survive the peri-operative period, likely due to advanced stage of disease. Cats with moderately or well differentiated tumors and those without clinical signs at presentation have a better prognosis with median survival times reported between 19-24 months. Chemotherapy is often recommended due to the aggressive nature of the disease though data is limited. Commonly used drugs in the adjuvant setting include doxorubicin and carboplatin.

Describe the biologic behavior of feline osteosarcoma.

- Metastatic risk 5-10%
- Most common feline primary bone tumor
- Amputation alone results in survival times of over 1-4 years
- Appendicular tumors have better prognosis than axial tumors

Primary bone tumors are rare in cats but osteosarcoma is most common. It is much less aggressive than in dogs. Approximately 70% of feline osteosarcomas occur in the appendicular skeleton and no site predilection is reported. The radiographic appearance is similar to what is seen in dogs. The metastatic rate is very low and amputation is associated with long term survival. Axial tumors are associated with a shorter median survival time (6 months), presumably due to difficulty attaining local control.

How is the Feline Interleukin 2 Immunomodulator (Merial's new fibrosarcoma vaccine) given?

6 times (once one week pre-op, then weekly for four weeks beginning one week post-op, and finally two weeks later)

5 sites (pre-op 5 sites equidistant around the tumor; post-op in a 5cm square around the scar and one in the center of the scar)

SC injections (typically while anesthetized)

0.2mL per site

In a live canarypox vector

Feline IL-2 Immunomodulator is conditionally licensed. The IL-2 cytokine can cause up-regulation of the post-surgical local immune response to feline FSA. In one published study and one unpublished field study, an IL-2 vaccine decreased the post-surgery and radiation therapy (RT) recurrence rate from ~60% to ~30% (at 24months in the field study) in adult cats with stage I disease. It is our assumption that surgery + vaccine *without* RT would not achieve these same results (one cat with microscopic disease was treated at VCG with vaccine alone (no radiation therapy) and the disease quickly regrew). Early, aggressive surgery, and in most cases adjuvant RT, remains standard of care for the treatment of feline fibrosarcomas.

Feline acromegaly is characterized by:

- Pituitary tumor (pars distalis adenoma)
- Excess growth hormone
- Physical changes (enlarged feet, broadening of the face, protrusion of the mandible, hepatomegaly, heart murmur)
- Elevated insulin-like growth factor-1
- Insulin-resistant diabetes mellitus
- Weight gain despite poor diabetic control

Feline acromegaly is caused by a pituitary tumor, most commonly an adenoma in the pars distalis, secreting excessive growth hormone. The disease is thought to be rare, but may be significantly underdiagnosed. It is thought to be more common in male cats. The most common clinical concern is development of insulin-resistant diabetes mellitus, caused by GH-induced defect in how insulin acts on the target cells. The unusual feature noted in these diabetics is WEIGHT GAIN despite poor diabetic control, due to elevated GH levels. In one study of ~160 cats with insulin-resistant DM 32% had significantly elevated IGF-1 levels (downstream hormone induced by GH, 84% sensitive/ 92% specific for acromegaly); 18 cats had CT scans and the diagnosis was confirmed in 17/18 cats. Other physical changes seen, as described above, occur due to excess GH. Radiation therapy is the primary treatment for this disease, and leads to improved diabetic control in 93% of patients. Medical therapy with somatostatin analogs (octreotide) that suppress GH release have been evaluated, but due to short duration of action of the standard forms these have not been widely used. There is limited data on survival with radiation, though several small studies of cats with pituitary tumors (some of which were acromegalics) reported a median survival of ~ 18 months. Stereotactic radiation therapy is being used in these patients as well in an effort to provide better tumor control while minimizing the number of anesthetics required due to the high anesthetic risk in this patient population.

What are the most commonly encountered brain tumors in cats?

- Meningioma
- Glioma
- Olfactory neuroblastoma
- Choroid plexus tumors

Meningioma by far are the most common brain tumor in cats (>50%). Meningiomas in cats can be multiple and are usually much more amenable to surgery. Radiation therapy (palliative or definitive) may also be a viable option if the client is not able to do surgery, if the tumor reoccurs, or is not completely excised.