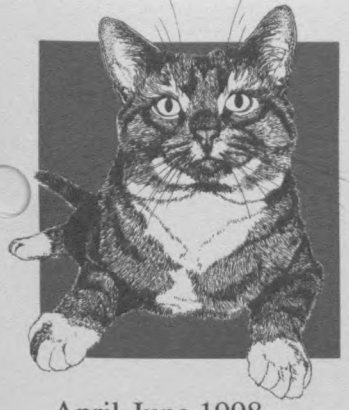

Feline Health Topics

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Feline Cancer Potpourri

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Feline Cutaneous Squamous-Cell Carcinoma

Cutaneous squamous-cell carcinomas (SCC) occur mostly in adult cats especially around the head and neck, and particularly the ears, nose, and eyelids of cats lacking cutaneous pigment. In these locations the tumors are sunlight-induced in the same manner as described for dogs. Siamese cats appear less likely to develop cutaneous squamous-cell carcinoma than other cats.[1] In a series of 90 cats with nasal planum SCC, 66 cats (73%) had some white skin or hair color.[2]

There is a clear clinical progression of lesions on the face and ears of cats lacking cutaneous pigment. Initially the area is erythematous and may have a waxy, dark crust that is easily removed. The lesions appear histologically as either actinic keratosis (precancer) or as carcinoma *in situ* (non-invasive cancer). Ulceration progresses if the lesions are untreated, with subsequent invasion and destruction of surrounding structures.

Inside this issue ...

Actinically induced cutaneous squamous-cell carcinomas in cats rarely, if ever, metastasize. In a series of 90 cats with nasal planum SCC, only six were found to have metastasized to mandibular lymph nodes and one to lungs.[2] Metastasis was more likely to occur late in the course of disease. Regional lymph nodes should be palpated and fine-needle aspiration or biopsy performed if they are enlarged. Thoracic radiographs are not usually indicated for this tumor in cats.

Tumor proliferative fraction, as measured by immunohistochemical detection of Proliferating Cell Nuclear Antigen (PCNA), was found to be of prognostic significance for control of nasal planum SCC in cats treated by radiotherapy. In addition, tumor size was found to be prognostic for tumor control. Cats with smaller tumors (<2 cm maximum diameter) had not reached a median survival (i.e., fewer than half of the cats had tumor recurrence) but the average was 53 months, while larger tumors (>4 cm maximum diameter) were controlled for a median of 9 months.[2]

While the synthetic retinoid 13 cis-retinoic acid has not been shown to reverse preneoplastic changes for cutaneous SCC in cats,[3] newer retinoids such as etretinate have not yet been evaluated in this species. In view of the efficacy of etretinate in dogs, it would seem logical that these newer retinoids may also show efficacy for feline preneoplastic squamous-cell carcinoma.

Resection of the pinna for aural SCC is effective in the majority of cats if adequate resection is achieved. Essentially the entire pinna should be removed. However, these tumors may recur locally, as can SCC of the eyelids and nasal planum.

Actinically induced SCC in the cat is very sensitive to radiation therapy. Precancerous plaques and early lesions may be treated with brachytherapy radiation (e.g., strontium-90) at a single high dose. In a group of 25 cats treated with strontium-90, nearly 90% were free of tumor at one year with an average tumor-free period of 34 months.[4]

Local current-field radiation hyperthermia (50°C for 30 seconds) was very effective in causing tumor regression in superficial SCC of cats.[5] Of 19 cats with SCC, 13 (68%) had complete regression. Tumors that did not extend 2 mm or deeper in tissue responded best. However, duration of response was observed for only 2 to 6 months.

For more advanced lesions, external-beam teletherapy produces long remissions. Ninety cats with SCC of the nasal planum were treated with orthovoltage-radiation therapy to a dose of 40 Gray in 4-Gray fractions.[2] The median control of tumors for these cats was 14 months. However, advanced tumor stage (i.e., larger tumors) affected outcome adversely. Fifteen cats whose tumors recurred were re-irradiated successfully.

Cryotherapy has been recommended as a treatment for SCC of the face in cats. In one study, however, this modality was considerably less effective than either surgery or radiation therapy in achieving local tumor control.[6] Eleven of fifteen cats had local tumor recurrence within a median of six months after cryotherapy. We recently completed a study involving 87 cats with squamous cell carcinomas of the head that were treated with cryotherapy. The median disease free interval was 14 months. Cats that had lesions less than 1 cm in diameter had a much higher probability of having tumors controlled than those with larger tumors. Therefore, it is recommended that tumors larger than 1 cm in diameter be treated with procedures other than cryotherapy.

Photodynamic therapy has been shown to be quite effective in controlling SCC in cats. In one study, 7 of 11 feline SCC's of the pinna or nasal planum completely resolved using a chloro-aluminum sulfonated phthalocyanine photosensitizer, and five of these responses lasted 44 weeks or longer.[7] In another trial using aluminum phthalocyanine tetrasulfonate, long-term (3 to 18 months) responses were seen in 12 of 17 patients.[8] However, toxicities, including one fatality, were more prevalent in this study.

Mitoxantrone chemotherapy rarely brings objective response in feline oral SCC, but could be considered as an option for metastatic skin lesions.[10] When combined with external-beam radiation therapy, mitoxantrone has been shown to control oral SCC for a median of 170 days, which is substantially longer than when either modality is used alone.[11]

Regardless of the therapy used, it should be remembered, however, that the cat is still susceptible to acquiring new tumors from sunlight exposure, and

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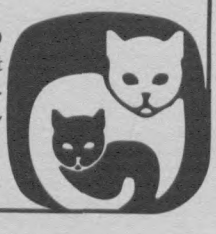

its behavior should be appropriately modified. Preferably cats should be protected from sunlight exposure during the middle part of the day.

Hemangioma-Hemangiosarcoma in Cats

Cutaneous hemangiomas and hemangiosarcomas are rare in cats, and occur mainly in older animals. This tumor is similar to squamous-cell carcinoma in that it is actinic, or sunlight-induced. Cutaneous hemangiosarcoma occurs commonly in cats from areas where actinically induced tumors are common (California, Missouri, Florida), but not in cats from the northeastern United States.[12,13,14]

Feline hemangiomas appear as solitary tumors in the dermis and subcutis without any site predilection. In contrast, feline hemangiosarcomas may have a predilection for the head (ear tips, nasal planum) and also for nonpigmented skin. They are usually solitary.

The prognosis following surgical excision of cutaneous hemangiomas is usually good although local recurrence following surgical excision of cutaneous hemangiosarcoma is frequent. Metastasis appears to be rare. It is therefore appropriate to treat this tumor as a soft-tissue sarcoma in cats, with aggressive initial surgery as the best therapeutic approach.

Round (Discrete) Cell Tumors

This group of tumors may also be called discrete cell tumors, and their appearance on cytologic preparations is that of clumps or individual cells that are round in appearance without obvious attachment to other cells. Round cell tumors include mast cell tumors, histiocytomas, lymphomas, plasmacytomas and transmissible venereal tumors.

Mast Cell Tumors in Cats:

Mast cell tumors (MCT) were the only cutaneous tumor diagnosed in cats younger than one year in one study.[1] In the same study, Siamese cats were three times more likely to develop cutaneous mast cell tumors. Tumors in Siamese cats are usually subcutaneous and composed of "histiocytic" cells. These tumors may regress without therapy.[15]

The most common cutaneous mast cell tumors in cats are single, firm, and circumscribed dermal nodules.[16] Appearance of multiple similar masses is the next most common presentation. These tumors are usually histologically well differentiated and have a benign clinical course. While most cutaneous MCTs in the cat are benign, in some studies, cutaneous tumors are associated with malignant disease evidenced by visceral involvement.[16,17] Lymphoreticular mast-cell tumors are often seen in cats, with marked splenomegaly the most common finding. Diffuse cutaneous disease may occur with this form of MCT. Mastocythemia and bone-marrow involvement are seen in many of these cats, and the presenting signs of vomiting and anorexia are presumably owing to tumor degranulation. Intestinal mast-cell tumors have been described in cats; they are always malignant.

The suspicion of MCT in a chronically vomiting cat with marked splenomegaly can be confirmed by fine-needle aspirate of the spleen. Less frequent sites for lymphoreticular mast cell tumors in cats are the mediastinum (with resultant pleural effusion) and lymph nodes. These cats often have high numbers of circulating mast cells as well as anemia and other cytopenias from bone-marrow infiltration and erythrophagocytosis by malignant cells.

The treatment of choice for cutaneous MCT in cats is surgery; for solitary tumors, a good prognosis can usually be given. Some cats may develop multiple well-differentiated tumors, and these cats may be treated with multiple palliative surgeries or corticosteroids (1 mg/kg prednisone daily). For invasive or incompletely excised MCTs, radiation therapy appears to be a successful adjunct to surgery; however, data regarding tumor control and patient survival are not as well established as for dogs.

Mitoxantrone caused a partial response in a feline mast cell tumor, but the drug has not been further evaluated for the treatment of this disease.[10]

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The treatment of choice for lymphoreticular MCTs in cats is splenectomy; long-term survival occurs in many cats receiving no other therapy. Response to splenectomy seems greater than would be explained by simple tumor mass reduction, as hematologic and other organ involvement apparently resolve. It is possible that splenic suppressor-cell activity may be reduced after splenectomy allowing for some control by the cat's immune system. For this reason the use of postoperative corticosteroids in these cats is controversial.[18,19]

Mammary Adenocarcinoma

Owners frequently present their cat with a mammary mass for a "skin condition on the underside". When a cat with a mammary mass is presented, a malignancy must be considered. At least 70-90% of feline mammary tumors are malignant. Mammary tumors are regarded to be the third most frequently occurring tumor in the cat, following hematopoietic neoplasms and skin tumors. Although there is no proven breed-associated predilection for mammary tumors, some investigators have suggested that domestic shorthaired and Siamese cats have higher incidence rates than other cats. Siamese cats may have twice the risk of any other breed of developing mammary tumors.

Mammary neoplasia has been reported to occur in cats from nine months to 23 years of age, with a mean age of occurrence of 10 to 12 years. One study suggests that the disease occurs at an earlier age in Siamese cats and the incidence reaches a plateau at about nine years of age. The majority of affected cats are intact females, however the disease is occasionally seen in spayed females and rarely in male cats. More than 80% of the feline mammary tumors are histologically classified as adenocarcinomas. The frequency of diagnosis of the specific type of adenocarcinomas differs slightly among pathologists, but most agree that tubular, papillary, and solid carcinomas are the most common. The majority of adenocarcinomas have a combination of tissue types in each tumor. Sarcomas, mucinous carcinomas, duct papillomas, adenosquamous carcinomas and adenomas are rarely seen.

Cats with mammary tumors are often presented to the veterinarian at least five months after they were initially noted, and thus are often in an advanced stage of development. The mammary tumor often appears as a locally invasive mass that may adhere to the overlying skin but rarely to the underlying abdominal wall. The tumor is usually firm and nodular. At least one-quarter of affected patients have ulcerated masses.

The infiltration of lymphatics may be clinically apparent as subcutaneous linear, beaded chains. Swelling due to tumor thrombi or decreased vascular return can cause discomfort, edema, and a change in the temperature in the pelvic limbs. The involved nipples are red and swollen and may exude a tan or yellow fluid. The tumor may involve any or all mammary glands and is noted equally in the left and right sides. A slightly higher incidence has been noted in the cranial two glands by some investigators. More than half of the affected cats have multiple-gland involvement. These tumors can be associated with chronic mastitis, uterine disease, and other unrelated tumors, as well as anemia, osteoporosis, ascites, and leukocytosis.

Before any diagnostic or therapeutic steps are taken, the health status of the cat must be fully assessed. A chemical screen, urinalysis, and a complete blood count should be done to identify any presurgical abnormalities. In several studies, more than 80% of the cats with a mammary malignancy had metastases to one or more of the following organs at the time of euthanasia: lymph nodes, lungs, pleura, liver, diaphragm, adrenal glands, and kidneys.[20] Thoracic radiographs in both the right and left lateral and ventrodorsal planes should be made to search for pulmonary, lymph node, and pleural metastases. Mammary tumor pulmonary metastases appear radiographically as interstitial densities. They range from those that are faintly seen, to those that are several centimeters in diameter, to miliary pleural lesions that can produce significant effusion. Sternal lymphadenopathy is occasionally seen. Whenever regional lymph nodes can be evaluated they should

be assessed by fine needle aspiration cytology or biopsy. Aging changes in the lungs and pleura as well as inactive inflammatory lesions may stimulate metastatic disease; treatment should not be withheld because of equivocal radiographic findings.

Because of the high frequency of malignancy, an aggressive approach should be taken to confirm the diagnosis. A preliminary biopsy is not recommended unless it will change either the owner's willingness to treat or the surgical procedure. Tissue for histopathology is taken at the time of mastectomy and should include the regional lymph nodes. If pleural fluid is removed from a cat with a mammary gland lesion, cytologic examination of the fluid should be performed to search for malignant cells.

A variety of nonmalignant lesions must be considered in a differential diagnosis of mammary neoplasia. The most common benign growths are classified as cysts, papillary cystic hyperplasia, lobular hyperplasia, and mastitis. Fibroepithelial hyperplasia is a common benign lesion involving one or more glands and is frequently seen one to two weeks following estrus in young, intact females. The gland may be so large that the patient may walk with an abnormal gait and the skin overlying the mass may be discolored, edematous, and painful. The signs are similar to those seen with most malignant tumors. Because the benign masses closely resemble malignant neoplasms, they are often mistakenly treated as malignancies.

In the last 20 years, little progress has been made in extending the survival time of feline mammary tumor patients. Because stromal invasion is almost always present and metastases are frequently present at the time of surgery, a guarded to poor prognosis should always be given. Sixty-six percent of the cats that have had their tumors surgically excised have a recurrence at the surgical site. Most studies state that the time from tumor detection to the death of the cat is rarely over 12 months. The most significant prognostic factors influencing tumor recurrence and survival for cats with malignant mammary neoplasia are tumor size, the extent of surgery needed to remove the tumors, and histologic grading of the tumors.

Tumor size is the most important of these prognostic factors.[21] Following surgery, the median for survival for cats with tumors > 3 cm in diameter is six months; for cats with tumors 2 to 3 cm in diameter, the median for survival following surgery is two years; and for cats with tumors < 2 cm in diameter, the median for survival after surgery is approximately three years. Radical surgery, when compared with regional "lumpectomy", has been shown to reduce local tumor recurrence but not to increase the overall time of survival. Cats with well-differentiated tumors with few mitotic figures per high-power field live longer compared with those with tumors that are not as well differentiated histopathologically. The one-year survival rate was high in cats with a tumor that did not show lymphatic infiltration. There is a good correlation between the grade of malignancy, method of growth, and prognosis. Patients with pulmonary metastatic disease rarely survive longer than two months.

Mammary neoplasms in the cat have been treated in a variety of ways, however surgery is the most widely used treatment. There have been no reports documenting the efficacy of radiation therapy or commercially available biological response modifiers for the treatment of this disease. The biological response modifier, liposome-encapsulated muramyltripeptide phosphatidyethanolamine (L-MTP-PE) may not be effective when used in combination with surgery or chemotherapy.

The success of surgery is hindered by the invasive nature of the disease and its tendency for early metastasis. Radical mastectomy (i.e. removal of all glands on the affected side) is the surgical method of choice because it significantly reduces the chance of local tumor recurrence. This procedure is frequently utilized regardless of the size of the tumor.

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Several surgical principles are observed when performing a mastectomy on feline mammary tumor patients. During or prior to surgery, bacterial culture and antibiotic sensitivity testing may be indicated because approximately one fourth of mammary carcinomas are ulcerated. An *en bloc* resection is often employed in such a way that the tumor and draining nodes and vessels are removed by wide surgical excision and a partial or complete resection of the underlying tissue is performed. If bilateral mastectomy is indicated, the affected glands and their associated lymph nodes are removed and a second surgery is performed 10 to 14 days later; the interim allows the skin to stretch for a complete closure at the second surgery. Early vessel ligation is essential; one study noted that two-thirds of the cases examined had tumor invasion of lymphatics and veins. Gentle handling of all tissue is essential. Copious flushing of the surgery area after the tumor is removed helps eliminate exfoliated neoplastic cells. Although spaying has been shown not to decrease the incidence of recurrence, some believe that it is warranted because of the occasionally seen coexisting ovarian and uterine disease.[22]

If the mammary mass is due to a benign condition such as fibroepithelial hyperplasia, spaying often results in regression of the hyperplastic tissue. Although regression may take up to five months, this condition often resolves spontaneously within a few weeks of diagnosis even without performing an oophorectomy.

Radiation therapy is not used routinely to treat feline mammary tumors. Presently, there are no major claims that radiation dramatically increases the survival rate of feline mammary tumor patients, however it may reduce local recurrence rates.

Chemotherapy, alone or in combination with surgery, is not as successful for feline mammary tumors as it is for other feline tumors such as lymphoma. Cyclophosphamide has been used alone or in combination with other chemotherapeutic agents and has not consistently helped the feline mammary tumor patient. The combination therapy of doxorubicin and cyclophosphamide has been shown to induce short-term partial and complete responses in 50% of cats with metastatic or nonresectable local disease. This chemotherapeutic protocol has been shown to be toxic in some cats and does not prolong survival. Other drugs that may be used include mitoxantrone and taxol. The role of the latter two drugs is still being elucidated, however both have some efficacy in cats with malignant neoplasia. Further studies are necessary to quantify the benefit of adjunctive therapy for mammary neoplasia in cats. Chemotherapy should be used by practitioners who are familiar with the use of these drugs and their side effects. ■

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This article is adapted from Dr. Ogilvie's presentation at the 90th Annual Conference for Veterinarians on March 20-22 at the College of Veterinary Medicine, Cornell University in Ithaca, New York. Dr. Ogilvie serves in the Comparative Oncology Unit, Colorado State University, College of Veterinary Medicine and Biomedical Sciences.

Is the FIP-specific ELISA test specific?

For several years, the role of the 7b gene in virulence of feline coronaviruses (FCoVs) has been studied. The absence of the 7b gene is generally consistent with reduced virulence and a decreased likelihood for the development of feline infectious peritonitis (FIP). The presence of the 7b gene has been associated with virulent strains of the virus that may cause FIP. But, the 7b gene is also present in some enteric strains of FCoVs that are not associated with the development of FIP. Indeed, the "...UCD [avirulent strain of feline enteric coronavirus (FECV)] contains an intact 7b gene indicating that [the absence of this gene is] not a universal distinguishing property of the feline enteric coronaviruses" (Herrewegh, Vennema, Horzinek, et al. 1995. Virology 212, 622-631. Therefore, our concern is that the presence of antibody to the 7b gene of avirulent (FECV) forms is not always consistent with development of FIP. It appears that the 7b gene-correlate of virulence is not an all or none phenomenon.

Recently, it has been purported that the 7b gene product is always associated with the virulent form of the virus. It is also purported that the 7b gene is not present in cats with avirulent FECVs. On this basis, a commercial laboratory is offering a "FIP-specific ELISA test" that detects antibody to the product of the 7b gene. If the test result is positive at 1:160, the laboratory concludes that the cat has a virulent form of the virus; alternatively, "cats testing negative are expected to be free of FIPV" according to their newsletter.

Can we be certain that cats having antibody to the 7b gene product will develop FIP? Presently, there are insufficient data to draw this conclusion. Can we be certain that a positive test result for antibody to the 7b gene product always infers that the virus strain responsible is a virulent FIPV? No - avirulent FECV of the UCD strain can harbor the gene. We urge caution in drawing conclusions about test results from the so-called FIP-specific assay until more data are acquired to assure that the assay will properly classify animals as to their FIP status. The preliminary data are encouraging, but the assay is not yet fully validated. ■

Research Briefs

Prevalence and Risk Factors For Odontoclastic Resorptive Lesions in Cats

(Authors— E.M. Lund, L.K. Bohacek, J.L. Dahlke, et al.)—145 cats more than one year of age were evaluated under anesthesia for odontoclastic resorptive lesions These lesions were graded using a published classification system. Clients completed a standardized survey on signalment, indoor-outdoor status, medications, diet during the past year, number of daily feedings, treat feeding, source of water, and oral hygiene practices.

Forty-eight percent of cats had resorptive lesions. These lesions were most commonly mandibular, and premolars were more often affected. Compared with cats without oral lesions, cats with oral lesions were more likely to be older, female, taking medications, drinking city (vs. well) water, and playing less often with toys. In addition, cats without oral lesions were more likely to have owners who cleaned their teeth daily or twice a week and to be fed diets with higher magnesium, calcium, phosphorus, and potassium contents. Frequency of teeth cleaning was inversely related to the development of odontoclastic resportive lesions. Variables significantly associated with oral lesions were age and magnesium content of diet. Older cats should be examined closely for odontoclastic resorptive lesions. Clients should be advised on methods and frequency of teeth cleaning in cats to prevent lesions. Dietary nutrients may play a role in the development of odontoclastic resorptive lesions in cats. *(Resource: J Am Vet Med Assoc* 212:392-395, 1998)

Other Research Articles of Interest

Elliott J and Barber PJ: Feline chronic renal failure: clinical findings in 80 cases diagnosed between 1992 and 1995. J Small Anim Pract 39:78-85, 1998.

Vennema H, Poland A, Foley J, et al: Feline infectious peritonitis viruses arise by mutation from endemic feline enteric coronaviruses. Virology 243:150-157, 1998. ■

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