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New Treatment Protocol for Feline Oral Squamous Cell Carcinoma

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Squamous cell carcinoma is the most common oropharyngeal tumor seen in the older cat. This very aggressive disease is treatable by surgery in only about 50 percent of the patients because it involves the tongue or its base. The median survival rate from time of diagnosis is one to three months because the animals are euthanized at that time because of the inability to eat. The tumor is usually not diagnosed until it has progressed substantially. Owners first notice something is amiss when the cat is not grooming itself and is reluctant to eat. This tumor is very similar to advanced head and neck cancer in humans, which too has a very poor prognosis for treatment. Only 15 to 30 percent of patients with advanced head and neck live five years or more after diagnosis.

Dr. Sydney Evans, assistant professor of radiology at the School of Veterinary Medicine, University of Pennsylvania, is investigating a treatment protocol for feline oral squamous cell carcinoma, using a new cell sensitizing drug and radiation treatments. Cats with these tumors, when treated by radiation alone, have a median survival rate of four months. "It has long been suspected that the low success rate of radiation treatment for these tumors has been due to hypoxic tumor cells which are radiation resistant," said Dr. Evans. "Hypoxic cells are oxygen poor and they are not easily killed by radiation. One can make a hypoxic cell more receptive to radiation by administering drugs which change the cells' state of oxygenation." Unfortunately, these drugs, when given in quantity, are neurotoxic and cause damage to central and peripheral nerves. Because this tumor in the cat can represent an animal model for human head and neck cancer, new treatment modes used in animals can provide a great deal of information for new treatment of human patients.

Dr. Evans and her colleagues studied the effects of etanidazole when it is injected directly into the tumor bearing tissue to see whether this method could improve the outcome of radiation therapy.

Eleven cats with measurable oral squamous cell tumors were entered in the clinical study. Thoracic radiographs were performed, as well as blood tests. The tumors were biopsied and staged. Seven of the cats also had skull radiographs while four received an MRI. Each cat received 12 radiation treatments, given three times a week over 16 weeks. Between treatments most of the animals were at home with their owners.

For each treatment the animals were anesthetized so that they would remain still during radiation. Thirty minutes prior to radiation treatment, the tumor, as well as surrounding normal tissue, was injected at 5 mm intervals with etanidazole. The first four cats studied received the drug prior to every other treatment. The fifth cat received the drug injected into the tumor and intravenously on alternate treatments. Because no significant toxicity was observed, the amount of the drug injected was increased for the remaining cats, and the drug was administered prior to each radiation treatment.

In addition, pharmacokinetic studies were conducted in four cats. It was observed that drug levels in the plasma peaked 14 minutes after intratumor injection. Some of the patients developed self-limiting fevers and leukopenia (low white blood cell count). After radiation treatments ended, cats were seen at regular intervals for examination and/or biopsy of the tumor site.

In all cats, tumor regression occurred during the course of therapy. In most cats this correlated with the resolution of anorexia, return of grooming habits and stabilization of weight. "The local tumor response has been encouraging, especially in those cats with tongue squamous cell carcinoma," said Dr. Evans. "For the six cats with the lesion of or under



A squamous cell carcinoma prior to treatment.



The same site after treatment.

the tongue who completed the protocol, the median time to progression and survival as of early September was 122 days. This compares favorably with the data from previous studies in which the median survival rate for cats with tongue squamous cell carcinoma is 31 and 91 days respectively."

Of the 11 cats treated, three remain without

evidence of local tumor progression. Five cats have had local recurrence at 55, 125, 139, 202, and 331 days post treatment and have been euthanized. Three cats died, one due to pulmonary metastases, pulmonary thromboembolism and pneumonia, one due to a tracheal obstruction, and one due to osteonecrosis. This can be compared to previous studies of radiation alone, where the recurrence is reported at 46 to 142 days following diagnosis. Six animals were autopsied and viable and necrotic tumor cells were found at the treatment site.

"We chose to investigate the IT route of drug administration because we expected it to result in an optimal ratio of tumor response to normal tissue toxicity," said Dr. Evans. "The IT route for radiosensitizers was of particular interest in light of previous data which suggested that failure to improve outcome resulted from the inability to achieve adequate tumor drug levels before dose-limiting neurotoxicity."

While this treatment does not offer a cure, it does provide a longer quality life for these feline patients. When the tumor recurs, no further treatment is given and the animal is euthanized. Dr. Evans said that "the present study had encouraged continued technical and dosing modification of IT etanidazole administration in feline squamous cell carcinoma and other animal tumor models. While IT therapy alone is promising as a route of administration in easily accessible, well visualized lesions, it may, in the future, have an even more important role in supplementing systemic administration, particularly of bulky, hypoxic tumor sites." The study was a joint project with the Fox Chase Cancer Institute. In addition to Dr. Evans, Dr. Stuart Helfand and Dr. Thomas Van Winkle, and Deborah Allen, from the Veterinary School worked on the project.

Coping with Loss

It's 3:30 on a Tuesday afternoon, and a small group of sad-looking people are gathered in a room at the School of Veterinary Medicine. There's the young mother who, four weeks ago, had her much-loved dog euthanized; it was leaking urine all over the house; after a week of relief, the woman was dragged down by an overwhelming guilt about her decision, and not giving the dog a proper goodbye. Her husband sits at her side.

There's a woman whose 20-year-old cat screamed every night, for no reason that had ever been diagnosed. The woman, whose apartment echoes with quiet now, still feels badly that she didn't comfort the cat when, riddled with cancer, it was put to sleep; that was several months ago.

There's another woman who cried so hard when her cat died that she burst a blood vessel in her lung and had to be hospitalized. This was the cat that had sustained her when her husband died, 12 years ago; the cat which had sat with her at the dinner table and on the side of the bathtub, which had even accompanied her on a trip to Paris and cruised with her down the Seine.

And what they're all doing is sharing tales about the animals that they loved as dearly as people—and whose deaths have left them with a hole in their lives, and a palpable grief that feels like it just won't let up.

"It's important to talk to people who have animals," says Kathleen Dunn, M.S.W. a psychiatric social worker at the University of Pennsylvania School of Veterinary Medicine. She leads the Pet Bereavement Support Group at the School, one of few such groups in the United States. "Other people will tolerate you for a while, but then will often say

something hurting, like 'It was only an animal; why not get another one?'"

Although often incomprehensible to non-pet owners, a pet's death can be as devastating as the death of an important human being. "People sometimes feel a sadness so terrible that they think they'll never get over it," says Dunn, who is "on call" 24-hours a day for emergency cases.

The reason for this pain is the depth of the bond that's formed between most pet owners and their animal companions. "What happens when you select a pet is that you get very attached," Dunn says, "The relationship consists of lots of love and joy and fun — and, as I hear a lot, the unconditional love you get back from your pet. Because this bond is so deep, the animal becomes a person to you, part of the family — sort of a perennial two-year-old. And if the relationship is threatened by death or illness, it's like a child dying. It doesn't matter that what died was 'only' an animal; a loss is a loss is a loss."

The death of an animal can also stir up the memories of losing an important human being. "Someone in the group might say, 'I'm feeling as bad, or worse, than when my mother died,'" Dunn says. The stages of the mourning and grieving process that a pet owner goes through is analogous to the process made famous by death-and-dying expert Elizabeth Kubler-Ross. Pet owners often experience anger, either at the veterinarian who couldn't "save" their pet, or at themselves for not taking certain steps that might have prevented their animal's demise. At another point they may feel guilty, because they didn't follow their veterinarian's advice exactly, or because they chose to euthanize a failing animal that