ADVANCED VETERINARY MEDICINE OF MIAMI

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FELINE VACCINE-ASSOCIATED SARCOMA – MYTH OR REALITY???

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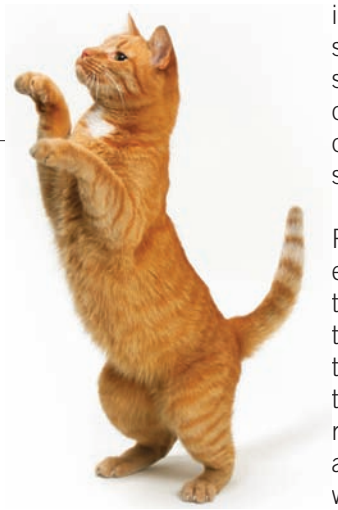

Vaccination has generally been considered to be a benign procedure in veterinary medicine. Unfortunately, soft tissue sarcoma development subsequent to vaccination (vaccine-associated sarcoma; VAS) in cats has dramatically changed this view within our profession over the last twenty years.

The vaccines generally associated with this disease to date have been the adjuvanted rabies and feline leukemia virus vaccines, however, association with non-adjuvanted FVRC-P vaccines have been occasionally reported. The potential role of inflammation as a necessary antecedent to the development of this disease has been previously published and seems highly plausible based on the aforementioned association with adjuvanted vaccinations. Newer non-adjuvanted vaccines are likely a step in the right direction for the prevention of this disease, and we eagerly await longer-term results on the incidence of tumors with these vaccines.

Currently, VAFSTF (Vaccine-Associated fibrosarcoma Task Force) in concert with the AVMA and AAFP recommend that: 1) use of vaccines packaged in single-dose vials is strongly encouraged, 2) occurrences of VAS or other adverse reactions be reported to the vaccine manufacturer (the United States Pharmacopoeia no longer accepts these reports), 3) vaccination protocols be standardized within practices so that location, type, manufacturer and serial number is entered into the permanent medical record, 4) vaccines limited to pan-leukopenia, herpesvirus and calicivirus should be administered on the right shoulder, 5) rabies vaccines should be administered as distally as possible on the right rear limb, preferably below the knee, 6) feline leukemia virus vaccines should be administered as distally as possible on the left rear limb, preferably below the knee, and 7) injection sites of ALL other medications be recorded in the permanent medical record. This information can also be accessed at www.avma.org by following the link for the VAFSTF.

If you suspect you are dealing with a VAS in a cat, the appropriate staging diagnostics should include full physical examination, bloodwork/urinalysis, retroviral testing and 3-view chest radiographs. Retroviral testing is recommended to ensure that FeLV is not acting as a helper virus for the production of a feline sarcoma virus-associated sarcoma. Radiography for the evaluation of metastasis is performed since it appears that approximately 5% of cats with VAS have metastasis at presentation, whereas approximately 25-30% have metastasis at necropsy. Confirmation of the suspected diagnosis should be performed by obtaining an incisional biopsy with a Tru-Cut biopsy instrument (or similar incisional biopsy instrument), or small wedge biopsy. The tumor should NOT be removed until a complete diagnosis is made and a consultation with an oncologist or surgeon has been performed.

Recent studies document that RADICAL first excision of VAS is essential for an extended period of time without recurrence. In addition, recent studies also document that the practice of vaccination of the distal portions of the limbs for rabies and/or FeLV vaccinations appears appropriate since patients with VAS of the distal limbs can undergo radical surgical extirpation via amputation which appears to allow for longer survival. Unfortunately, even with aggressive surgery alone in non-distal limb locations, relatively few cats with VAS are cured. Due to poor cure rates with surgery alone, the additional use of adjuvant radiation therapy and/or chemotherapy has been under investigation at multiple veterinary cancer centers for the last few years. It is presently unknown whether it is better to perform radiation therapy prior to radical surgery, or perform radical surgery and then post-operative radiation therapy. However, the combination of radical surgery and radiation therapy in recent studies appears to have a median survival time of 600-800 days, suggesting that additional therapies is worthwhile in the treatment of this disease. Similarly, the use of chemotherapy has been reported by multiple investigators to have efficacy

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against gross feline VAS. When given to cats with grossly palpable VAS, carboplatin or a combination of doxorubicin and cyclophosphamide resulted in a 50-60% response rate. Feline non-VAS would be expected to have a 5-10% response rate to these forms of chemotherapy, thereby suggesting that feline VAS is a remarkably different tumor than non-VAS. The use of radical surgery, radiation therapy and chemotherapy as tri-modality therapy in feline VAS is likely the best form of therapy for cats with VAS (> 3 yr median survival time for VAS cats treated with tri-modality therapy).

Through the support of VAFSTF, there have been a number of research studies which have been completed throughout the country to elucidate the etiopathogenesis, epidemiology, treatment and prevention of this disease (reader is referred to www.avma.org and the VAFSTF link). Unfortunately, the AVMA pulled its continued funding of VAFSTF which precipitated its sunsetting in 2005, even though we continue to see many cases of VAS. It is easy to see that even with aggressive therapies, we many times lose the battle against this remarkable tumor. The key to this disease is a better understanding of what causes this tumor, so that we may determine ways to vaccinate our feline friends without inducing extremely malignant tumors. >>>>>

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The KEY FACTS to know in feline vaccine-associated sarcoma are:

1. Best to prevent this disease, not treat it after it has occurred!!
2. Staging should include full PE, bloodwork/UA/FeLV/FIV and 3 view chest films (consider AbdUS)
    A. Approximately 5% have metastases at time of presentation
    B. Approximately 25-35% have metastases at time of death
3. Strong considerations should be made to perform CT or MRI to delineate the resectability of the VAS. These images are also helpful for RT planning and dosimetry.
4. Very few cats with VAS are cured with treatment because it is so aggressive, recurrent and potentially metastatic
    A. Aggressive tumors need to be treated aggressively
    B. Single modality treatment invariably fails
5. Treatment options
    A. Surgery only
        1. Minimal excision
            A. Reduced time to recurrence; average survival time 6-8 months
            B. Reduced ability to potentially cure the cat
            C. Sets cat up for serial debulkings unfortunately
        2. Radical excision
            A. Increased time to recurrence vs. minimal excision
            B. Likely will still be recurrent due to dirty margins or second primary tumor
            C. Should NOT be used as sole treatment of VAS (Follow with radiation approximately two-three weeks after surgery)
                1. CONTROVERSY
                    A. What if one obtains clean margins with radical excision VAS?
                    B. Most oncologists still follow with radiation to the site
                    C. One exception would be distal limb VAS treated with surgery alone
                        1. Recent paper shows that the only VAS cases potentially cured with sx were cats with distal limb VAS treated with radical surgical extirpation (ie limb amputation)
    B. Radiation only
        1. Not presently recommended for VAS
        2. Palliative radiation (ie 3-6 larger dose) may be useful to slow tumor down
            A. Average survival time likely 3-4 months
        3. Usually combined with surgery and/or chemotherapy
    C. Chemotherapy only
        1. Chemotherapy appears to be useful for VAS
        2. Chemotherapy for non-vaccine-associated sarcomas is generally not helpful
        3. Agents shown to be of benefit with gross VAS (40-60% response rates)
            A. Carboplatin
            B. Adriamycin (doxorubicin) + cytoxan (cyclophosphamide)
        4. Usefulness in gross VAS argues for use with minimal disease situations such as encountered after surgery and/or radiation, instead of waiting for gross disease recurrence or metastasis to appear
    D. Multi-modality
        1. Appears to be best way of treating VAS
        2. Surgery & Radiation
            A. Average survival time approximately 18 months
            B. CONTROVERSY
                1. Sequence of Rx modality
                2. Better to do sx then RT or RT then sx?? Presently unknown
                3. Author believes RT then sx
                    A. Sx then RT involves huge RT field
                    B. RT then sx results in smaller, less difficult RT field and sx complications of irradiated tissues in cats appears to be minimal
        3. Tri-modality therapy
            A. RT/Sx/Chemotherapy
            B. Average survival time appears to be ~ 2-3 years
            C. Sequence of RT & Sx still problematic, but follow with chemotherapy
            D. See chemo only area above for chemotherapy types found to be useful
            E. Studies performed to date evaluating the usefulness of adjuvant chemo in the treatment of microscopic VAS after surgery and/or RT have found chemo to be of limited to no benefit; however, these studies have routinely not had enough statistical power to be able to delineate a survival advantage conferred by adjuvant chemotherapy use. The NCSU paper (Kobayashi et al) has shown that the median survival time of cats with VAS treated with RT, then sx then carboplatin is > 3 years, suggesting tri-modality therapy is optimal.

References available on request.

CLINICAL UPDATE ON CYCAD PALM INTOXICATION IN DOGS

By: Jeffrey Toll, VMD, DACVIM

Palms in the Cycad family (including Sago, False Sago, Cardboard, and Coontie) are common ornamental plants in South Florida. Canine ingestion of these plants, especially the seeds, often results in serious or fatal intoxication. Hepatic, renal, and GI necrosis and failure are generally seen as acute or subacute phenomena. These toxicities have historically been difficult to manage once absorption of the toxic principle (cycasin) has occurred since it is believed that cycasin undergoes enterohepatic recycling. Based on this theory and in collaboration with practitioners in Miami-Dade and Broward Counties, we have begun to administer cholestyramine (Questran®) along with other standard treatments to patients with known or suspected cycad intoxication. Cholestyramine is an ion exchange resin which is not systemically absorbed and which binds to and results in subsequent fecal excretion of bile salts. We theorize that cycasin is similarly bound to and subsequently excreted with cholestyramine. Extrapolating dosages from the human literature, our preliminary clinical impressions have been very favorable. We are in the process of reaching out to the ACVIM Liver Study Group to develop a research project evaluating selected aspects of cycad intoxication and therapies including cholestyramine. Feel free to contact Dr. Toll for more information on updates on this project and assistance with the management of these patients.

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Specializing in veterinary internal medicine, our mobile consultancy brings sophisticated and interdisciplinary services and expertise to a network of practices throughout our community. Our goal is to develop the best possible relationships with our clients based on communication and integrity. We provide veterinary specialty services that benefit veterinary practices, pets, and their owners.

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- On-site results and recommendations
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