MANAGEMENT OF FELINE FIBROSARCOMAS
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Fibrosarcomas are generally considered in the Soft Tissue Sarcoma (STS) group of cancers. Cats are similar to dogs when it comes to STS except for the fact that nerve sheath tumours and synovial cell sarcomas are extremely rare in cats compared to dogs. There are also several unique fibrosarcoma settings in cats. Cats have been reported to suffer from a virally induced multicentric fibrosarcoma; they can develop a vaccine associated fibrosarcoma; and there have been reports of fibrosarcoma developing in the orbit of cats with phthisis bulbi, ocular trauma or ocular foreign bodies.

The cause of nonvirally induced, non–vaccine associated and non-ocular fibrosarcomas is generally not known. These tumours are seen in cats 8 to 12 years of age with no sex or breed predilection. Over 50% of these fibrosarcomas occur on the limbs making limb salvage curative surgery very difficult. These solitary STS’s are slow growing, low grade and can be permanently controlled with properly performed surgery. Wide or radical surgical margins are indicated for the management of these tumours in cats. There are no large studies reporting the efficacy of surgery with adjuvant radiation therapy for these types of STS in cats.

Sarcomas following ocular trauma occur most often in cats 7 to 15 years of age and the latency following trauma averages 5 years. Damage to lens and chronic uveitis may be risk factors. These tumours are often advanced by the time they are diagnosed with extension into the bone of the orbit and the optic nerve. Therefore I recommend removal of the phthisical feline eye or cat eyes that are blind and have been severely traumatized or chronically inflamed.

Feline sarcoma virus (FeSV) are true hybrids and result from the rare recombination of feline leukemia virus (FeLV) DNA provirus with cat proto-oncogenes. Cats that have FeSV are always FeLV positive. It is thought that only 2% of fibrosarcoma of cats are virally induced. The FeSV-induced tumors are multicentric and mostly found in young cats. These tumors are generally very fast growing with metastatic rates reported of 30% or so. Prognosis is very poor in these cats. Although some authors indicate chemotherapy with radiation therapy may be tried, recurrences and progressive disease usually ensues.

Vaccine-associated sarcomas consist of cells that are morphologically and immunohistochemically compatible with fibroblasts and myofibroblasts. The precise pathogenesis of vaccine-associated sarcomas is unknown but may involve stimulation of these cells by highly immunogenic and persistent adjuvants or other vaccine components resulting in inflammation that alone or in association with unidentified carcinogens or oncogenes leads to neoplastic transformation and tumor development. Transition zones from inflammatory granuloma to sarcoma have been identified and strongly suggest that the inflammatory response to vaccination is antecedent to sarcoma development in cats.

Vaccine-associated feline sarcomas are highly invasive and, often, rapidly growing neoplasms that require aggressive treatment, which may include a combination of surgery, radiation therapy, and chemotherapy. Metastases may develop, and the metastatic rate increases with survival time. Because vaccine-associated sarcomas often mimic benign postvaccinal injection site granulomas, differentiating these lesions is critical.

The first meeting of the Feline Vaccine Associated Sarcoma Task Force (VAFSTF) was held Nov 11, 1996. A combined effort of the AVMA, AAHA, AAFP, and VCS, the task force has representatives from each of the sponsoring organizations and from the USDA-APHIS and the Animal Health Institute. The 10-member task force was assembled to address the issue of development of sarcomas at injection sites of commonly used vaccines in cats.

The major reference material for the notes on Feline Vaccine Associated Sarcoma for these notes has been the Feline Vaccine Associated Sarcoma Task Force web page: http://www.avma.org/vafstf/default.asp

Current task force guidelines recommend that masses at vaccine sites that are still evident 3 months after vaccination, are > 2 cm in diameter, or are growing in size 4 weeks after vaccine administration be treated aggressively. (Table 1)

Task force-funded studies have shown the value of computed tomography and magnetic resonance imaging in determining the extent of these tumors before surgery or radiation therapy. These types of diagnostic imaging studies have improved the effectiveness of treatments and the overall outcome. The control rate is higher for lesions located on limbs, presumably because wide surgical margins can be obtained with limb amputation. The best treatment results are associated with aggressive resection at the first surgery; there appears to be minimal opportunity for tumor control if the patient has undergone previous surgeries for the tumor.

Radiation therapy when combined with surgery increases tumor control. Radiation therapy has been shown to be beneficial if given before or after definitive surgery. Despite the combination of aggressive surgery and radiation therapy, however, treatment will fail in many patients. Vaccine-associated feline sarcomas are somewhat sensitive to a variety of chemotherapeutic agents such as doxorubicin, carboplatin, mitoxantrone, and cyclophosphamide. However, the addition of chemotherapy to radiation therapy and surgery has only modestly prolonged disease-free intervals. The unfortunate truth is that there are no good treatment options for cats with these tumors, further emphasizing the importance of tumor prevention.

The FVASTF has developed a recommended protocol for vaccine administration. (Table 2)

Vaccination should be viewed as a medical procedure to be performed only after careful assessment of the needs of the patient, rather than as an automatic act dictated by the calendar. Each veterinarian and cat owner must determine the relative risk of disease for individual cats and make appropriate decisions regarding vaccination. Rabies vaccination recommendations should follow state and local regulations.

The AAFP and Academy of Feline Medicine Advisory Panel on Feline Vaccines has stressed the importance of vaccinating the largest number of cats possible within a population, vaccinating each individual cat no more frequently than necessary, and vaccinating only against infectious disease agents to which individuals have a realistic risk of exposure and subsequent disease. The panel concluded that annual revaccination is not always needed and may increase the risk that sarcomas will develop at vaccination sites.

The VAFSTF and AAFP guidelines for vaccination of cats stress standardization of vaccination sites. These guidelines
for vaccination sites have been adopted by many of the schools and colleges of veterinary medicine in North America and by the US Army.

Vaccination is a medical procedure that should be undertaken with the same thoughtful consideration as any other medical procedure in veterinary practice. As with most aspects of medical practice, there are benefits and risks to vaccination. Accordingly, vaccination protocols should be individualized to the patient, with consideration given to the medical importance and zoonotic potential of the infectious agent, the patient's risk of exposure, and germane legal requirements.

Vaccine-associated feline sarcomas are a conundrum for the veterinary medical profession. We do not understand the attributes of the feline immune system and genome that make cats susceptible to VAFS, yet we must continue to vaccinate cats against key infectious diseases. Vaccination was once considered an essential routine medical procedure with minimal risk. In the past decade, we have recognized that vaccination protocols must include assessment of the risk of sarcoma development. Until more is known about the epidemiology and pathogenesis of VAFS, we can only limit vaccination to the minimum required for optimal health. As new vaccines and technologies are developed, their potential advantages and limitations should be evaluated. The VAFSTF recommends that previously issued guidelines on standardization of vaccination and injection sites, diagnosis and management of VAFS, and reporting of adverse events be followed.

Billions of dollars have been spent to understand the causes of and find cures for cancers in humans. In comparison, our efforts to understand and cure vaccine-associated sarcomas in cats are just beginning. There is still much to be done. Further research into the epidemiology, causes, treatment, and prevention of vaccine-associated sarcomas is essential to solving this problem.

Table 1. Protocol for diagnosis and treatment of suspected vaccine-associated sarcomas in cats

The following recommendations from the Vaccine-Associated Feline Sarcoma Task Force are based on information available as of April 1999 and are subject to revision as new information becomes available.

**Diagnosis**

1. Record anatomic location, shape, and size (measured by caliper in 3 dimensions) of all masses that develop at the site of an injection.
2. Treat any mass that develops at an injection site as if it were malignant until proven otherwise. A mass should be fully assessed and aggressively treated if it
   - Persists > 3 months after injection,
   - Is > 2 cm in diameter, or
   - Is increasing in size 1 month after injection.

If a mass meets 1 or more of these criteria, a diagnostic biopsy should be performed prior to surgical excision. A cutting needle biopsy or incisional wedge biopsy is preferred. Cutting needle biopsy should be done in such a way that any subsequent surgical procedure to remove the mass can readily include the entire needle tract. Incisional wedge biopsy should be performed in such a way that any subsequent surgical procedure to remove the mass can also remove all tissue affected by the biopsy. Cytologic evaluation of fine-needle aspirates is considered unreliable for the diagnosis of vaccine-associated feline sarcomas and is not recommended.

**Management**

If a mass that develops at a vaccination site is confirmed to be malignant, the following procedures should be followed:

1. Routine thoracic radiography and preoperative laboratory analyses should be performed.
2. When feasible, computed tomography or magnetic resonance imaging should be performed. Soft-tissue sarcomas often spread along fascial planes, and these local extensions of the tumor may be undetectable visually during the early stages of tumor growth. Results of advanced diagnostic imaging may be useful in determining the extent of surgery and the size of the radiation field that will be needed to maximize the chances for successful treatment.
3. Prior to initiating any treatment, consult a veterinary oncologist for current treatment options, which may include radiation therapy, chemotherapy, surgery, and other modalities.
4. Never "shell out" a sarcoma. Incomplete surgical removal of a sarcoma is the most common cause of treatment failure. Use standard oncologic surgical techniques to avoid seeding malignant cells. Remove at least a 2-cm margin of normal-appearing tissue around all sides of the mass, including the deep side. In some instances, reconstruction of the body wall, removal of bone, and other advanced surgical techniques will be required.
5. Submit the entire excised specimen for histologic evaluation. Mark the excised mass with India ink or suture tags to provide anatomic references to facilitate subsequent treatment.

After a vaccine-associated sarcoma has been removed, the patient should be rechecked and a physical examination performed monthly for the first 3 months after surgery, then at least every 3 months for 1 year. Additional diagnostic procedures should be performed as appropriate for the abnormalities detected.

Table 2. Protocol for administration of vaccines to cats

The issue of vaccine-associated sarcomas is clearly complex, and complete answers are expected only after the expenditure of considerable effort. In the interim, veterinarians and cat owners alike can make decisions that may reduce the possibility of sarcoma development and improve the chances of successful treatment. More complete recommendations will be made as information from the task force is generated, but on the basis of material from the American Association of Feline Practitioners, the Academy of Feline Medicine, and the California Veterinary Medical Association, the task force presents the following guidelines:
1. The manufacturer's label recommendation is the only official item veterinarians currently have to demonstrate the basis for vaccination.

2. Alternative vaccination routes (e.g., nasal or topical) should be considered if and when feasible.

3. Use of vaccines packaged in single-dose vials should be encouraged.

4. Vaccination is a medical procedure, and customized vaccination protocols should be developed for individual patients. No vaccine should be administered until the medical importance and zoonotic potential of the infectious agent, the patient's risk of exposure, and the germane legal requirements have been considered.

5. Any vaccine-associated sarcomas and other adverse reactions should be reported to the vaccine manufacturer and the United States Pharmacopeia. Information about the United States Pharmacopeia's Veterinary Practitioners' Reporting Program can be obtained by calling 1-800-4-USP-PRN. Submission of forms by diagnostic laboratories will be facilitated if the laboratories include a report form for each instance of a vaccine-associated sarcoma. The report form should include vaccine type, serial number, and vaccination site; this information should also be incorporated in the patient's permanent medical record.

6. To further characterize the causal link between vaccination and development of sarcomas and to facilitate treatment of vaccine-associated sarcomas, the following general guidelines for administration of vaccines and other injectable products are suggested:

   a. Veterinarians should standardize the sites for administration of vaccines and other injectable products in their practices and document the location of each injection, the type of vaccine or other injectable product administered, and the manufacturer and serial number of any vaccine given in the patient's medical record.

   b. The following sites for administration of vaccines are recommended.*

      i. Vaccines containing antigens limited to panleukopenia virus, feline herpesvirus type-1, and feline calicivirus, with or without *Chlamydia* antigens, should be administered on the right shoulder, according to the manufacturer's recommendations.

      ii. Vaccines containing rabies virus antigen, with or without any other antigen, should be administered on the right hind limb, as distally as possible, according to the manufacturer's recommendations.

      iii. Vaccines containing FeLV antigen, with or without any other antigen except rabies virus antigen, should be administered on the left hind limb, as distally as possible, according to the manufacturer's recommendations.

__*Initial recommendations of the Vaccine-Associated Feline Sarcoma Task Force distributed in November 1996. These recommendations vary slightly from the 2000 American Association of Feline Practitioners and Academy of Feline Medicine guidelines.*__