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Management of vaccine-associated sarcomas in cats

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Management of vaccine-associated sarcomas in cats

Soft tissue sarcomas (STS) account for 7% to 9% of all malignant skin and subcutaneous tumors in cats.[1] Although the underlying cause is not fully understood, development of some of these tumors in cats has been associated with previous trauma or vaccine-site injection.[2,3,4] These tumors arise from mesenchymal tissues including fibrous connective tissue, cartilage, blood vessels, muscles, nerves, or fat. They are histologically distinct, but share many common clinical features; particularly the propensity for local invasion. Vaccine-associated sarcomas (VAS) can include (but are not limited to) fibrosarcomas, neurofibrosarcomas, nerve sheath tumors, malignant fibrous histiocytoma, leiomyosarcomas, liposarcomas, and myxosarcomas. These sarcomas are characterized by having a "pseudocapsule," poorly defined margins, and fingerlike projections that infiltrate tissue planes (ie, between muscles and layers of connective tissues). As a result, they tend to be difficult to completely excise, making local recurrence common. In addition to local invasion, they can also metastasize via the blood or lymphatics. Because of these characteristics, STS in cats present a significant clinical challenge. The way in which the primary care veterinarian manages the initial phases of diagnosis and treatment can dramatically affect the patient's outcome. Multimodality therapy is usually necessary along with careful preplanning so that diagnostics and early treatment do not ultimately interfere with possible future treatment.

Patients with seemingly small tumors are noted to have more extensive disease on a CT scans.[5]

PATIENT EVALUATION AND PRESUMPTIVE DIAGNOSIS

Presence of a mass – Any mass that develops in a previous injection site should be considered malignant until proven otherwise. A lesion should be fully assessed and aggressively treated if it persists more than 3 months after injection, is larger than 2 cm in diameter, or is increasing in size after 1 month after injection.

History and testing – If a vaccine-associated sarcoma is suspected based on history, clinical presentation, and location of the mass, the following database should be obtained:

- Thoracic radiographs
- Blood analysis to include CBC and serum chemistry panel
- Urinalysis
- Preoperative FeLV and FIV testing
- Abdominal ultrasound
- Biopsy and cytology – Fine needle aspirates can be performed but are not always a reliable indicator of neoplasia. Sarcomas typically do not exfoliate well; therefore, a negative aspirate does not rule out cancer. If malignant cells are seen on cytology, a presumptive diagnosis of cancer can be made. If aspiration cytology provides a presumptive diagnosis of sarcoma, referral for evaluation by an oncologist should be considered before any attempts at surgery.

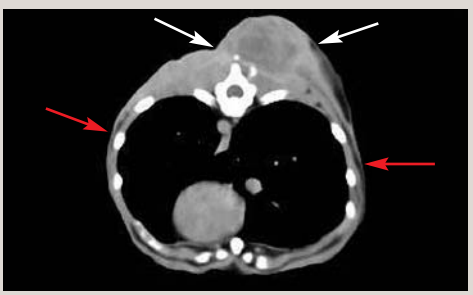
DEFINITIVE DIAGNOSIS

Incisional biopsy: If cytology is unrewarding, an incisional biopsy of the mass should be performed. Taking a small wedge from the tumor or using a Tru-cut® biopsy is preferable to attempting a larger surgery without a definitive diagnosis.

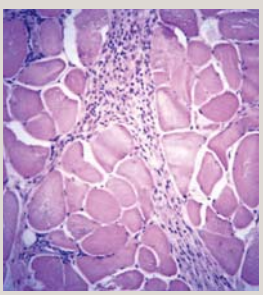
BIOPSY FOR VAS

Incisional biopsy
Small wedge biopsy taken to obtain a tissue diagnosis without jeopardizing future curative intent surgery or radiation.

Needle-core biopsy
An automatic Tru-Cut® biopsy device can also be used to obtain tissue for histopathology.



CT scan of a patient with suspected vaccine-associated sarcoma. White arrows show the borders of what was palpable on physical examination. The red arrows show the true extent of disease based on contrast-enhanced CT. Radiation therapy was advised to cytoreduce the tumor to a more operable size. Following radiation therapy, a curative surgery was possible.



Histopathology of a vaccine-induced tumor shows cords of sarcoma cells infiltrating through muscle tissue, demonstrating the infiltrative, invasive nature of these tumors.

Histology: A histologic diagnosis obtained in this manner helps the surgeon plan appropriate therapy without jeopardizing a future definitive surgical resection or radiation therapy.

Excisional biopsy: If the mass is too small for incisional biopsy, then an excisional biopsy may need to be performed. Wide and deep margins, whenever possible, should be attempted in hopes that the excisional biopsy will be both diagnostic and therapeutic.

Advanced Imaging: When feasible, computed tomography (CT scan) is recommended for all patients with a histologic diagnosis of STS. McEntee, et al showed that the volume of tumor based on the contrast enhanced CT images was on average twice the size of the tumor based on physical examination and caliper measurements, showing the importance of accurate delineation of disease for surgical and/or radiation treatment planning (more often than not, treatment decisions regarding operability change once the CT images are reviewed).[5] Patients with seemingly small tumors that would have been taken to surgery are often noted to have more extensive disease in a CT scan than was anticipated, and warrant undergoing radiation therapy first.

SURGERY

Surgery is the mainstay of treatment for STS and offers the best chance for a cure, but appropriate preoperative decision making and planning are critical for the best possible outcome. It has been said that surgical oncologists should be both good technicians and dedicated tumor biologists.[6] A thorough understanding of the biologic behavior of this cancer will help in the decision-making process. Basic principles of oncologic surgery should always be employed, and implementation of these principles starts long before the surgery is performed. In fact, it starts with obtaining the initial presumptive diagnosis. Any aspiration or biopsy tract that is made needs to be obtained from a site in the tumor where excision of the tract can be done at the time of subsequent definitive surgery.

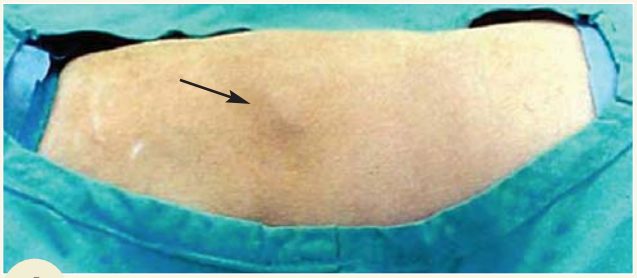
RADIATION AND CHEMOTHERAPY

A multimodal approach appears to be superior to any one modality alone, except for radical complete surgical excision with 5 cm margins and 2 fascial planes below the tumor.[7] Time-to-recurrence and survival times are more favorable when a combination of surgery and radiation therapy are used.[8]

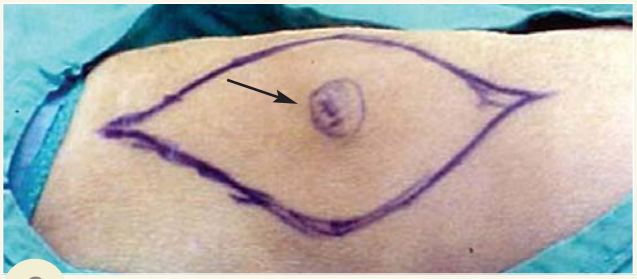
Surgical oncologists should be both technicians and dedicated tumor biologists.

Several chemotherapy agents have been used in cats with vaccine-associated sarcomas including carboplatin, doxorubicin, liposome encapsulated doxorubicin, mitoxantrone, and cyclophosphamide to name a few. One study failed to show a survival advantage when comparing cats treated with surgery, radiation, and chemotherapy to cats treated with surgery and radiation and no chemotherapy.[9] Other studies have suggested a benefit for chemotherapy when partial responses were observed in patients with nonresectable disease.[10,11] Chemotherapy as a sole modality is not adequate for definitive therapy, but may be valuable for palliation of large, unresectable tumors.

SURGERY FOR AN INJECTION-SITE SARCOMA



1 Arrow points to a 1.5 cm subcutaneous mass in the interscapular space – the presumptive diagnosis was vaccine-associated sarcoma.



2 Purple marks show the extent of palpable mass (in circle) and planned surgical borders in an attempt to obtain tumor-free margins. Lateral skin margins of up to 5 cm and 2 fascial planes below the tumor have been suggested for curative-intent resections.[7]

3 Appearance of surgical site postoperatively. The mass and its invasive "fingers" were completely excised.

AUTHOR TIPS FOR VAS SURGERY

- Do not attempt a marginal surgery for VAS.
- Never "shell" or "peel" out a tumor because it appears encapsulated (note that these tumors are characterized as having a "pseudocapsule"). This approach will invariably lead to incomplete excisions and a poorer outcome.
- Always think ahead to what may be needed as follow-up treatment. For example, if a mass is clearly too large to obtain tumor-free margins, don't do surgery first – refer to an oncologist for evaluation and for possible preoperative radiation therapy.
- If a mass appears operable clinically and CT is not available, plan as wide and deep a surgery as the location will allow, keeping in mind that "dirty" margins are often the "deep" margins.
- Remember that amputation may be the best alternative for sarcomas occurring on the limbs.

Patient with aggressive vaccine-associated fibrosarcoma was presented clinic for evaluation and possible surgery, radiation, and chemotherapy.

Patient had undergone multiple incomplete excisions and each time the tumor returned, it would occupy a larger, more extensive area. Because the incision lines cover such a great extent of the body, the field needed to treat with curative therapy causes unacceptable early and late radiation side effects.

Patient treated with surgery and adjuvant radiation therapy for a large vaccine-associated sarcoma. Hair is oftentimes lost during therapy and when it returns, color changes are common.

REDUCING THE RISK OF INJECTION-SITE SARCOMAS

These tumors may be one of the most serious vaccine-associated adverse event reported in cats, although the precise cause of injection-site sarcomas is not currently known. They were first recognized with the transition to killed rabies vaccines and the introduction of feline leukemia virus vaccines – each contained an aluminum adjuvant. A study published in 1993[12] provided epidemiological evidence of a casual relationship between vaccinating with rabies and FeLV vaccines containing aluminum and several studies have implicated vaccine-adjuvant–induced inflammation at the injection site as the potential cause.[13,14,15] Chronic inflammation can contribute to oncogenesis in many species. Cats with a history of ocular trauma and leakage of lens material can develop ocular sarcomas.[4] It is believed that reducing inflammation may reduce the risk of sarcoma development.[13] In one study, four different adjuvant-free vaccines containing modified-live virus and a vectored component were compared to saline controls. None of the tested vaccine combinations produced detectable inflammation. Microscopically, the sites were similar to saline control injection sites at 21 days.[16] The American Association of Feline Practitioners' (AAFP) Advisory Panel has suggested that veterinarians use less inflammatory vaccine products whenever possible.[17]

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