Cancer ABCs: Early Diagnosis and Treatment of Skin and Subcutaneous Masses through Aspirates, Biopsies, and Cytology Sue Ettinger, DVM, DACVIM (Oncology)
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When a pet presents with a dermal or subcutaneous mass, the owner is often told, "Keep an eye on it." But what does that mean? Keep an eye on it for how long? How much should a mass grow before it is investigated? As a cancer specialist, I hear all too often that a mass does not "look" or "feel" malignant. The truth is that even an experienced cancer specialist like me cannot look at or feel a mass and know what it is. It is well documented that cytologic and histologic evaluations are important diagnostic tools in veterinary oncology and that obtaining a preliminary diagnosis optimizes treatment planning. It is also recommended to evaluate masses that are growing, changing in appearance, or irritating to the patient. However, currently, no specific guidelines exist for determining when to aspirate, biopsy, or monitor canine and feline skin and subcutaneous masses.

Without guidelines to increase both public and professional awareness, superficial masses may be monitored for too long. Allowing a tumor to grow can turn what might have been a simple surgical removal into a much more complicated procedure. Surgical excision of larger masses may result in less than adequate surgical margins (narrow or incomplete), leading to recurrence and additional costly therapy (more aggressive local surgery, radiation therapy, and/or chemotherapy). Even worse, the tumor may become too big or advanced to be removed or treated at all. I see this all the time. These are often the most frustrating and heartbreaking cases. In veterinary medicine, most skin and subcutaneous tumors can be cured with surgery alone if diagnosed early when they are small.

There are three things we can do for skin and subcutaneous masses in dogs and cats:

- 1. Be proactive with lumps and bumps.
- 2. Know what a mass is before you remove it.
- 3. Make the first surgery the only surgery.

1. BE PROACTIVE WITH LUMPS AND BUMPS

See something: If a dog or cat has a mass that is the size of a pea (1 cm) and has been there 1 month, **Do something**: Aspirate or biopsy; and treat appropriately!

See Something, Do Something. Why Wait? Aspirate.® (SSDS) is a lumps and bumps cancer awareness program that provides guidelines for evaluating superficial masses in dogs and cats. Obtaining a definitive diagnosis with cytology or biopsy *early and before excision* will lead to improved patient outcomes for superficial masses. When smaller, superficial tumors are detected early, surgery is likely curative, especially for benign lesions and tumors that are only locally invasive with a low probability of metastasis. If a tumor is removed with complete surgical margins, the prognosis is often good with no additional treatments needed. Although the See Something, Do Something guidelines specify a 1 cm mass, smaller masses may also be aspirated or biopsied. However, they should not be allowed to grow larger than 1 cm without investigation. Practitioners should measure and document the size of the initial mass for comparison to see growth and educate clients about the "pea" size requirement to encourage them to have masses evaluated.

- Visual monitoring is not enough.
- Pet owners need to be aware of the "pea" size requirement to have masses evaluated.
- Veterinarians must measure and document the size of the mass to compare growth.
- If > 1 cm (or size of large pea) and present for a month, the mass should be aspirated or biopsied.
- Knowing the tumor type prior to the FIRST surgery will increase success of a curative-intent surgery.

2. KNOW WHAT A MASS IS BEFORE YOU REMOVE IT

Aspiration and Cytology

Diagnosis of many skin and subcutaneous masses can be achieved with fine needle aspiration (FNA) and cytology. FNA and cytology provide a diagnosis for many dermal and subcutaneous masses, especially those that that exfoliate well. FNA is useful to distinguish neoplasia from inflammation and benign masses, including lipomas and sebaceous adenomas. Cellular morphology may also allow the determination of benign or malignant phenotype. For malignant tumors, cytology provides information that assists in formulating diagnostic and treatment plans. Advantages of cytology include minimally invasive approach, low risk, low cost, and results that are available more quickly than biopsy results. The disadvantages are that results may be nondiagnostic or equivocal because of a small number of cells in the sample, poor exfoliation of the cells, or poor sample quality. In these cases, histopathologic confirmation may be required for definitive diagnosis.

FNA may be accomplished using one of two techniques: aspiration or fenestration. During aspiration, the needle and syringe are attached, and vacuum is maintained. In fenestration, the needle alone is inserted into the mass percutaneously. Fenestration is done without aspiration, often yields more cellular material, and causes less hemorrhage. I personally prefer and start with fenestration as I find it easier and consistently get diagnostic samples. Aspiration is more useful for fluid-filled masses. Unless the sample is composed exclusively of fat, clear cystic fluid, or acellular debris, it should be submitted to a trained cytopathologist. When in doubt, send it out. Including an adequate history helps the pathologist make an accurate diagnosis.

Biopsy

If cytology is non-diagnostic, a pretreatment biopsy is recommended before complete tumor removal. This biopsy will help determine the optimal treatment plan. A practical recommendation in these cases is if the lesion fits in an 8 mm biopsy punch, **punch it out**. If the mass is larger than an 8 mm biopsy punch, an incisional biopsy (wedge, Tru-cut, punch) is required for diagnostic confirmation before tumor removal. Staging diagnostics are also often indicated before curative-intent surgery. Consultation with a veterinary oncologist is recommended to help in these diagnostic decisions.

3. MAKE THE FIRST SURGERY THE ONLY SURGERY

It is tempting to remove a mass right away, and owners often say they want it removed as soon as possible. An excisional biopsy establishes a diagnosis and removes the tumor at the same time. However, this approach is not recommended for undiagnosed skin and superficial masses because surgical approaches vary with tumor type. For benign masses, marginal excision may be adequate for long-term control. In contrast, malignant tumors often require 2 to 3 cm margins. When an excisional biopsy (or debulking surgery) leads to incomplete margins for malignant tumors, more treatment, more morbidity, and more expense ensue. Thus, removing the mass entirely is not recommended without a cellular diagnosis before definitive excision. Research confirms that the first surgery is the best chance for a cure.

WHAT ARE THE MOST COMMON TUMORS?

Primary skin and subcutaneous tumors are common in dogs and cats. While the overall incidence is difficult to determine, approximately 25% to 43% of submitted canine and feline biopsy samples are of the skin. Of submitted samples, 20% to 40% are reported to be malignant. The most common malignant skin tumors in **dogs** are mast cell tumors, soft tissue sarcomas, and squamous cell carcinomas (**Table 1**). The most common benign canine skin and subcutaneous benign tumors include lipomas, histiocytomas, and perianal gland adenomas. In **cats**, the most common superficial tumors are basal cell tumors, mast cell tumors, squamous cell carcinomas, and fibrosarcomas. These 4 tumor types make up about 70% of all skin tumors in cats. Sebaceous gland adenomas are much less common. If basal cell tumors are excluded, the percentage of malignant skin tumors in cats is higher than in dogs, with studies reporting 70% to 80%.

Table 1. Most Common Skin Tumors in Dogs and Cats

Dogs		Cats	
Malignant	Benign	Malignant	Benign
MCT: 10%-17%	Lipomas: 8%	MCT: 13%-	Basal cell tumors:
SCC: 2%-6%	Histiocytomas: 8%–12%	21%	15%–26%

STS:	Perianal gland adenomas:	SCC: 10%-	Sebaceous gland
FSA: 2%-6%	8%–12%	15%	adenomas: 2%–
Malignant nerve	Sebaceous gland	FSA: 15%-	4%
sheath tumors:	adenomas/hyperplasia: 4%-	17%	
4%–7%	6%		
	Trichoepitheliomas: 4%		
	Papillomas: 3%		
	Basal cell tumors: 4%–5%		

CYTOLOGY OF CANCER

Neoplasia is characterized by the presence of a homogeneous population of cells that come from the same tissue of origin. With cytology, we try to then determine 1) what is the tissue of origin, and 2) is the mass is benign or malignant. Primary nuclear characteristics can be used to determine whether the cell population is benign or malignant. In benign masses, the cells have a more uniform appearance, including the nuclear and cytoplasmic size, shape N:C ratio. In benign cells the nucleoli are more consistent in size, shape, and number between cells.

Malignant cells have: 1) anisokaryosis, 2) pleomorphism, 3) high or variable N:C ratio, 4) increase mitotic activity, 5) variability of nucleoli, 6) coarse chromatin, 7) nuclear molding, 8) multinucleation Cytology can also be useful to determine the tissue of origin:

- 1. Epithelial neoplasms exfoliate in sheets and clumps, and cells are often clustered. Cells are round to polygonal. Malignancies are termed carcinoma if they are non-glandular and adenocarcinoma if they are glandular. Examples include TCC, basal cell tumors, and perianal adenomas.
- 2. Mesenchymal neoplasms are often less cellular aspirates and cells are more individual. CSells are spindle, oval, elongated and wispy. Malignancies are called sarcomas. Examples include hemangiosarcoma, osteosarcoma, and soft tissue sarcomas.
- 3. Round cell neoplasms exfoliate well, and cytology is often helpful and definitive. Cells are often round to oval and cell borders are more discrete then the clustered carcinoma cells. Common types include histiocytic tumors, MCT, lymphoma, melanoma, plasma cell tumors, and TVT.
- 4. Endocrine/neuroendocrine neoplasms are also known as naked or free nuclei. These are tumors of chemoreceptors or endocrine glands such as thyroid, parathyroid, and pancreas. Of this category, canine thyroid tumors are most evaluated with cytology.

Even the most experienced veterinarian or oncologist cannot look at or palpate a mass and know whether it is malignant or not. Cancer is a cellular diagnosis. It is always recommended to evaluate masses that are growing, changing in appearance, or irritating to the patient. But these guidelines are not enough. All skin and SQ masses that are >1 cm and have been present for 1 month should be aspirated for cytologic evaluation. Biopsy is indicated if cytology does not provide a diagnosis.

AFTER THE ASPIRATE/BIOPSY

Benign tumors may not need to be removed. A variety of factors, including mass location should be considered. Surgery should be recommended when a benign tumor is causing pain, irritation, bleeding, or infection. Surgery should also be recommended if an increase in growth would prevent a surgery in the future. Alternatively, if removing the tumor requires a complicated surgery (i.e., near a joint, on the distal limb with minimal surrounding tissue for reconstruction) or the pet has other pre-exiting issues, you and the pet owner may make an educated decision as to whether proceeding to surgical removal is warranted. **Pets with masses not removed should be monitored (via measurement) by the veterinarian every 3 to 6 months.** If surgery is performed, most **benign** masses require smaller surgeries, as wide margins are typically not needed.

If the aspirate/biopsy reveals **malignancy**, consult with veterinary oncologist for appropriate staging recommendations. For malignant tumors, the first surgery should be a wide excisional surgery. If wide excisional surgery is not possible due to the size or anatomic location of the mass, consultation with a veterinary oncologist or board-certified surgeon is indicated. Surgeons may be able to perform specialized surgeries such as axial pattern flaps to remove the tumor completely.

Debulking (cytoreductive) surgery should not be recommended, as this will not obtain margins, and additional post-operative treatments such as radiation will be required to prevent recurrence. In some cases, cytoreductive surgery may be performed for palliation, or with an understanding that adjunctive therapy such as radiation therapy will follow the procedure.

After surgery:

- Review the histopathology report tumor type, grade, vascular and lymphatic invasion.
- Consult with a veterinary oncologist for additional therapeutic considerations for malignant tumors.
- Assess the QUANTITY of surgical margins in consideration of tumor type and biologic behavior.
 (One mm margins for a malignant tumor may be called "clean" on a biopsy report, but size of margins must be considered considering tumor histology.)
- If margins are inadequate, recommend adjunctive treatment before tumor recurrence for optimum patient outcome. Post-operative options include scar revision (second surgery), radiation to prevent regrowth, or chemotherapy which may slow recurrence in some cases.
- It is important to consult a board-certified surgeon before attempting scar revision.
- Monitor for local tumor recurrence and metastasis as indicated by the histologic diagnosis and margin assessment.

RECURRENCE AND MONITORING

Patients with reported complete surgical margins can potentially suffer tumor recurrence due to microscopic cancer extension that is not seen in the evaluated sections. Therefore, it is essential to monitor for local regrowth, and to recruit the pet owner to monitor the surgical scar as well, to identify early relapse. For malignant tumors with wide, clean margins and low metastatic potential, follow-up rechecks are recommended every two to three months after the surgery for as much as one year of follow up. Early detection is key to addressing recurrence and metastasis to ensure the highest possible chance of success.

Owners are encouraged to check their pets regularly at home for new masses.

- Owners should check their pet monthly for superficial masses by noting their location and size.
- Create a "body map" with size and location of superficial masses recorded, along with fine needle
 aspiration cytology results. This body map can serve as an objective medical record document and
 owner guide to follow masses longitudinally, and to allow for identification of new masses over time.
- All masses should be aspirated and submitted for cytology. Masses that do not need cytologic assessment include lipomas, cysts, and those containing acellular debris.
- If cytology is non-diagnostic, discuss repeating the aspirate, or proceed to biopsy.
- Know the tumor type prior to surgery. The first surgery is your patient's best chance for cure.

SURGERY MAY BE ALL THAT IS NEEDED

We all must be proactive to advocate for early cancer detection. Visual monitoring of superficial masses is not enough. Obtaining a definitive diagnosis via either cytology or biopsy *early and before excision* <u>will</u> lead to improved patient outcomes for superficial masses. Surgery is likely curative for the majority of these cases, especially for benign masses and those locally invasive malignancies that are non-metastatic. If tumors are detected and removed earlier – when they are small and with clean margins, the prognosis is often good, and the patient may not require additional therapy.

IN SUMMARY

Visual monitoring of superficial masses is not enough. Cancer is a cellular diagnosis. It is always recommended to evaluate masses that are growing, changing in appearance, or irritating to the patient, but these guidelines are not enough. All skin and subcutaneous masses that are >1 cm and have been present for 1 month should be aspirated for cytologic evaluation. Biopsy is indicated if cytology does not provide a diagnosis. Veterinary professionals and pet owners all must be proactive to advocate for early cancer detection. If tumors are detected and removed earlier—when they are small and with clean margins—the prognosis is often good, and the patient may not require additional therapy. See something, do something! See Something: When a skin mass is the size of a pea (1 cm) and has been present for 1 month, Do Something: Aspirate or biopsy and treat appropriately! Early detection saves lives. Why wait? Aspirate.®

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