Canine and feline skin tumors

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Introduction
Due to its complex structure a large variety of tumors may arise in the skin (Table 1), as can secondary (metastatic) tumors. Approximately 2/3 of all canine cutaneous tumors are solitary, benign lesions originating from the epithelium or from adnexal structures, whilst in the cat malignant tumors are more common than benign ones. The etiology of most skin tumors is still unknown, but roles of UVB light exposure, hormonal and viral etiologies are demonstrated in some tumors. This article provides an overview of the more common skin tumors affecting dogs and cats but excludes soft tissue sarcomas.

A presumptive diagnosis of a solitary skin tumor may be made on clinical examination, but multifocal lesions may be harder to distinguish from other dermatological conditions. Fine needle aspiration (FNA) is a quick, minimally invasive and useful technique for assessing any mass within the skin. In some cases (e.g. mast cell tumors, cutaneous lymphoma) cytology may provide a diagnosis, although histological examination of the tumor is still required to grade the lesion. Fine needle aspiration of local lymph nodes is also useful to assess metastatic spread. Skin punch, needle or incisional biopsies are required for a definitive histological diagnosis. Collection of a representative sample of tissue is important and is discussed elsewhere in this issue. Excisional biopsy (local resection of the whole mass) should only be performed after careful consideration; it can have disastrous consequences if used inappropriately and the opportunity for curative treatment may be lost forever. Excisional biopsy is appropriate in cases where prior knowledge of tumor histology/grade would not alter the surgical approach.

KEY POINTS
- The skin is the most common site for neoplasia in dogs and cats.
- A huge number of different tumors may arise in the skin, and the prognosis can vary from excellent to hopeless depending on the tumor type.
- Accurate identification of the tumor is essential to allow for informed treatment options to be considered.

Specific cutaneous tumors
Squamous cell carcinoma
Squamous cell carcinoma (SCC) is one of the more common malignant cutaneous tumors in the dog and the most common in the cat, usually affecting animals > 10 years with no breed predisposition. SCC can occur anywhere in the skin in the dog, whereas lesions are more common on the
Table 1.
Classification of the more common cutaneous and subcutaneous tumors by cell of origin.

<table>
<thead>
<tr>
<th>Origin</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Epithelial tumors</strong></td>
<td></td>
<td></td>
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<tr>
<td>Epidermis</td>
<td>Papilloma - Trichoblastoma (basal cell tumor) - Infundibular keratinizing acanthoma (intracutaneous cornifying epithelioma)</td>
<td>Basal cell carcinoma Squamous cell carcinoma</td>
</tr>
<tr>
<td>Sebaceous gland</td>
<td>Sebaceous gland adenoma Sebaceous epithelioma</td>
<td>Sebaceous gland adenocarcinoma</td>
</tr>
<tr>
<td>Perianal glands</td>
<td>Perianal gland/hepatoid gland adenoma</td>
<td>Perianal gland/hepatoid gland carcinoma</td>
</tr>
<tr>
<td>Apocrine glands</td>
<td>Adenoma/cystadenoma</td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>Hair follicles</td>
<td>Pilomatrixicoma - Trichoepithelioma</td>
<td></td>
</tr>
<tr>
<td><strong>Round cell tumors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mast cells</td>
<td>Mast cell tumors</td>
<td></td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>Cutaneous lymphoma - Epitheliotrophic T-cell lymphoma</td>
<td></td>
</tr>
<tr>
<td>Plasma cells</td>
<td>Plasmacytoma</td>
<td></td>
</tr>
<tr>
<td>Epidermal dendritic cells</td>
<td>Canine cutaneous histiocytaoma</td>
<td></td>
</tr>
<tr>
<td>(Langerhans cells)</td>
<td>Cutaneous histiocytosis</td>
<td></td>
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<tr>
<td>Interstitial and</td>
<td></td>
<td></td>
</tr>
<tr>
<td>interdigitating dendritic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mesenchymal tumors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fibroblasts</td>
<td>Collagenous hamartoma - Acrochordon (skin tag, fibroepithelial polyp) - Fibroma - Myxoma</td>
<td>Fibrosarcoma Myxosarcoma</td>
</tr>
<tr>
<td>Adipocytes</td>
<td>Lipoma</td>
<td>Liposarcoma</td>
</tr>
<tr>
<td>Blood vessel endothelium</td>
<td>Hemangioma</td>
<td>Hemangiosarcoma</td>
</tr>
<tr>
<td>Blood vessel wall</td>
<td>Leiomyoma - Hemangiopericytoma - Myopericytoma - Angioleiomyoma - Angiofibroma</td>
<td>Leiomyosarcoma Angioleiomyosarcoma</td>
</tr>
<tr>
<td>Peripheral nerve</td>
<td>Peripheral nerve sheath tumor (PNST) Schwannoma</td>
<td>Malignant PNST</td>
</tr>
<tr>
<td>Melanocytes</td>
<td>Melanoma</td>
<td>Malignant melanoma</td>
</tr>
<tr>
<td>Unknown origin</td>
<td>Anaplastic sarcoma with giant cells (aka: malignant fibrous histiocytoma, giant cell tumor of soft parts)</td>
<td></td>
</tr>
</tbody>
</table>

head of the cat, affecting the nasal planum (Figures 1,2), pinnae, eyelids and lips. SCC may be productive, forming a friable, papillary growth, or erosive, forming an ulcerated lesion, and must be distinguished from inflammatory or infective lesions.

**Etiology**

Prolonged exposure to UVB light is recognized to be an important factor of actinic solar dermatitis, carcinoma in situ and eventually invasive SCC, but some may be caused by papilloma viruses, thermal injury or chronic inflammation.

**Behavior, treatment and prognosis**

Actinic keratosis is a pre-invasive lesion which may develop to pre-malignant carcinoma and then SCC. These are locally invasive tumors that infiltrate the underlying dermal and subcutaneous tissue. They are usually differentiated and metastasis (usually slow) tends to be via the lymphatic route, but the incidence is variable at other sites, e.g. in the nail-bed of the digit (Figure 3) it can behave much more aggressively. Canine tumors of the nasal planum are locally aggressive and frequently metastasize to the draining lymph nodes.
Wide local surgical excision is the treatment of choice and if achieved, the prognosis is favorable. SCC is moderately radiosensitive and radiotherapy may be indicated as an alternative or adjunctive treatment in cases where adequate surgical resection is not possible. Locally applied Strontium 90 has been reported for treatment of superficial lesions (1). Photodynamic therapy (PDT) has been used successfully for treatment of early, superficial lesions of the nasal planum in cats and provides a good alternative to surgery and radiotherapy (2).

A multicentric SCC in situ has been described in cats (3). Biologically this is a premalignant lesion which is histologically similar to Bowen’s disease in humans (sometimes referred to as Bowenoid carcinoma). This tends to affect middle aged to older mixed breed cats with lesions developing in haired, pigmented regions of the skin. A papilloma virus may be implicated in the etiology, and the lesion can progress to invasive SCC.

SCC of the nail-bed region of the canine digit is an aggressive tumor and invasion and destruction of the distal phalanx is common. Amputation of the affected digit(s) is the treatment of choice but these tumors may metastasize to the local and regional lymph nodes and distantly; the prognosis is guarded. A phenomenon of SCC affecting several digits has been reported in large breed, black dogs e.g. standard poodles, giant schnauzers (4). These tumors appear to have a lesser tendency for metastasis but may affect multiple digits on different feet.

**Melanoma**

Melanocytic tumors are relatively uncommon. In dogs, cutaneous melanoma principally affects older animals and is most common in breeds with heavily pigmented skin, e.g. the Scottish terrier. Older cats are also affected but there is no sex or breed predisposition. Grossly, tumors may appear as flat, plaque-like to domed masses, up to 2 cm in diameter, sited within the dermis. They are usually dark brown to black and quite well defined. Malignant tumors may attain larger size, contain less pigment and frequently ulcerate. In the cat cutaneous melanoma must be distinguished from the more common pigmented basal cell tumor.

**Behavior, treatment and prognosis**

Tumor site seems to be an important factor governing the behavior of cutaneous melanoma. Most melanocytic tumors of the canine skin are slow-growing and benign. Tumors arising on the digits and at mucocutaneous junctions (e.g. eyelids and lips) are more aggressive with a higher incidence of metastasis to local lymph nodes, the lungs and other organs.

Wide surgical excision is the treatment of choice for benign dermal melanoma and the prognosis
following complete surgical excision is good. Surgical excision is also indicated for local control of malignant tumors but the prognosis in such cases is guarded to poor because of the risk of metastasis. There is no proven role for chemotherapeutics in the control of malignant melanoma. Investigations into the canine melanoma vaccine, using human tyrosinase, are still ongoing (5).

**Mast cell tumors**
The presentation and behavior of mast cell tumors (MCT) differs between the cat and dog.

**Canine MCT**
These are one of the most common cutaneous neoplasms, representing up to 20% of all canine skin tumors (6). They tend to affect older animals (mean age 8 years) but may occur at any age. Several breeds of dog including the boxer, Staffordshire bull terrier, and possibly the Labrador and golden retriever appear to be predisposed. The tumors show tremendous diversity in gross appearance, clinical behavior, rate of metastasis and response to treatment, as a result of which they present considerable prognostic and therapeutic problems. The following is a short review; readers are advised to refer to the extensive literature available.

**Presentation/clinical signs**
The gross appearance can mimic any other cutaneous tumor (Figures 4, 5). Low grade, well-differentiated tumors usually present as a solitary slowly growing, dermal nodule. Some tumors ulcerate through the skin and in some cases local release of histamine from tumor cells may cause the lesion to fluctuate in size and become red and ‘angry’ looking. More aggressive MCTs may present as large, ill-defined soft tissue masses and some may be surrounded by satellite nodules as the tumor spreads through surrounding cutaneous lymphatic vessels (Figure 6).

**Behavior**
MCTs can vary in behavior, from slowly growing, low grade tumors which follow a benign course to rapidly growing, invasive, highly malignant tumors. Histological grading based upon the degree of cellular differentiation, the mitotic index and invasion of adjacent tissue has been shown to be of prognostic value (7-9). Behavior, suggested treatments and prognosis of MCTs are discussed in Table 2.

Malignant MCTs may metastasize either by the lymphatic route or via the blood. In most cases the first sign of metastasis is enlargement of the local lymph node. Discrete pulmonary metastases are rare; disseminated MCTs more commonly metastasize to the spleen, liver, kidneys and the skin.
Table 2.
Prognosis and suggested treatments for canine MCT based on histopathological grade.

<table>
<thead>
<tr>
<th>Origin</th>
<th>Description</th>
<th>Mitotic index (Mitoses/10hpf)</th>
<th>Metastatic potential</th>
<th>Recommended treatment</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>Well differentiated</td>
<td>Low (&lt; 10%)</td>
<td>Surgical excision</td>
<td>Good</td>
<td></td>
</tr>
<tr>
<td>Grade II</td>
<td>Intermediate in histological appearance and behavior. Prognosis is harder to predict.</td>
<td>&lt; 5-7*</td>
<td>Variable (&lt; 20%)</td>
<td>Surgical excision +/- radiotherapy if complete resection not possible.</td>
<td>Fair</td>
</tr>
<tr>
<td>Grade II</td>
<td>&gt; 5-7*</td>
<td>Variable (&lt; 50%)</td>
<td>Surgical excision +/- radiotherapy if complete resection not possible. Adjunctive chemotherapy should be considered.</td>
<td>Guarded</td>
<td></td>
</tr>
<tr>
<td>Grade III</td>
<td>Poorly differentiated and rapidly growing.</td>
<td>High (&gt; 80%)</td>
<td>Chemotherapy (traditional or tyrosine kinase inhibitors). Multimodal therapy including surgery + radiotherapy should be considered.</td>
<td>Poor</td>
<td></td>
</tr>
</tbody>
</table>

*The best cut-off has not been established for MI, with different authors favoring 5 or 7 mitoses/10 hpf.

**Paraneoplastic Syndromes**
Both solitary and metastatic MCTs can have local or systemic effects via the release of histamine and other vasoactive amines from the tumor cells. This can cause local edema and erythema of the adjacent tissues and distant gastro-duodenal ulceration leading to anorexia, vomiting, melena, anemia and, in some cases, perforation.

**Diagnostic Investigations**
Hematological assessment may indicate anemia due to blood loss from a bleeding intestinal ulcer. Circulating mast cells (mastocytosis) are rare but eosinophilia may be present.

Mast cells can be readily identified by FNA cytology and this simple technique should be performed prior to surgical removal of any cutaneous lesion. MCT cannot be graded accurately on cytology alone, although some indication of the degree of differentiation of the tumor cells may be possible. Excisional samples should therefore be submitted for histological grading and assessment of the margins of excision.

Local and regional lymph nodes should always be evaluated by palpation, radiography/ultrasound (as appropriate) and cytology. Ultrasound evaluation of liver, spleen and kidneys is also valuable. Pulmonary metastasis is rare but skin is a common site for MCT metastasis and skin nodules should be investigated by FNA or biopsy. Dogs presenting with multiple low/intermediate grade MCT have separate de novo tumor development rather than metastatic disease, and each should be dealt with as a separate tumor. Survival time in these animals is not less than dogs with a single MCT (10).

**Treatment**
Surgical resection is undoubtedly the treatment of choice for any well differentiated MCT. Wide surgical resection is not as important as previously thought and 2 cm margins should be adequate for all grade I & II tumors < 5 cm diameter, but not the most aggressive tumors (11). The most common cause of treatment failure is poorly executed or planned surgery, leading to inadequate resection of the primary tumor and subsequent local recurrence. The first surgical attempt stands most chance of success and cure rates for subsequent surgical excisions or adjunctive therapies are low. It is vitally important to identify a MCT (cytologically or histopathologically) prior to any attempt at treatment so that appropriate surgical margins can be planned and achieved at the first attempt.

Radiotherapy may be beneficial as a post-surgical treatment in cases of intermediate tumors where complete surgical resection is not feasible (12).
and, on occasions, may be used in conjunction with chemotherapy for the treatment of tumors which cannot be surgically excised due to their site (13). There is no good evidence for the use of radiotherapy as a sole treatment.

For grade II tumors with a high mitotic index and grade III tumors chemotherapy is used to prevent or slow metastatic spread (14). Short term responses have been achieved with protocols involving vinblastine, chlorambucil and prednisone, or lomustine (CCNU). Two tyrosine kinase inhibitors, masitinib and toceranib, are licensed in some countries for use in unresectable or recurrent intermediate and high grade canine MCT; although experience is lacking, they show promising efficacy (15,16). It should be remembered that surgery is still the treatment of choice and a judgment of unresectable should be made by a specialist surgeon.

Patients with systemic and/or gastrointestinal signs must be treated appropriately with agents such as H2 antagonists, cimetidine or ranitidine. Sucralfate is also of benefit.

**Feline MCT**

In the cat MCTs are less common than in the dog and also less of a diagnostic problem. Two forms are recognized: cutaneous and visceral. Most cutaneous MCTs are benign solitary cutaneous/dermal nodules. Uncommonly, a cat may be affected by multiple skin nodules, or a solitary lesion may be invasive. Histological grading of feline cutaneous MCTs has not been shown to be clinically useful. Surgical resection is the treatment of choice and the prognosis is usually good (17). In cats with multiple tumors corticosteroids may be of palliative value. Invasive or incompletely excised tumors may be treated with adjunctive radiotherapy.

A variant of feline MCT has been reported mostly affecting Siamese cats (18). This tumor, which may be multicentric, is characterized histologically by sheets of histiocyte-like mast cells with scattered lymphoid aggregates and eosinophils. These tumors may regress spontaneously without therapy.

**Plasmacytoma**

Plasmacytomas are common in dogs but rare in cats. They typically affect older dogs with no breed predilection and usually present as a solitary skin or mucocutaneous tumor; the oral cavity (including gingiva), feet, trunk and ears are the most common sites. The gross appearance is usually of a raised red or ulcerated, quite well-defined mass, rarely more than 2-5 cm in size. Plasma cells are derived from B-lymphocytes; histological diagnosis can be difficult if the tumor cells are lacking clear differentiation, and special staining techniques may be required to differentiate plasmacytoma from poorly differentiated sarcoma and other round cell tumors. Potentially a plasmacytoma could represent a metastasis from the systemic form of plasma cell malignancy, multiple myeloma; this has been reported in the cat but not the dog (19). Both cutaneous and oral forms of plasmacytoma are usually benign and are rarely associated with systemic signs. Surgical resection is usually curative and prognosis is good.

**Histiocytic skin conditions**

Several reactive and malignant neoplastic histiocytic diseases have been described. The most common is canine cutaneous histiocytoma (CCH), a benign cutaneous tumor unique to the skin of the dog and representing up to 10% of all canine cutaneous tumors. CCH is most common in young dogs with 50% occurring in animals < 2 years old. The tumor typically arises on the head, the limbs, feet or trunk, and presents as a rapidly growing, intradermal lesion. The surface may become alopecic and ulcerated. The boxer, dachshund and the flat-coated retriever are reported to be predisposed to CCH. Histological sections show infiltration of the epidermis and dermis by neoplastic histiocytic cells; numerous mitotic figures and an indistinct boundary give this lesion the appearance of a highly malignant neoplasm. However, CCH is a benign tumor which usually regresses spontaneously. Regression is associated with infiltration of the tumor by cytotoxic T-cells and lymphocytic infiltration is often described in histological reports. Surgical excision - if necessary - is usually curative and the prognosis is good.

**Multifocal/diffuse cutaneous neoplasia**

Although MCT and metastases from both carcinomas and sarcomas can present as multiple nodular skin lesions, the tumors most commonly
Cutaneous Lymphoma

Usually of T-cell origin, primary cutaneous lymphoma may be classified as either epitheliotrophic (epidermal) or non-epitheliotrophic (dermal) on histology.

Epitheliotrophic lymphoma (Mycosis fungoides) is more common in dogs. Histological sections show a diffuse infiltration of the epidermis by neoplastic memory T-lymphocytes and other inflammatory cells, Pautrier’s microabscesses and a tropism for adnexal structures (Figure 7). In the advanced stages of the disease the tumor cells invade into deeper layers of the dermis, heralding systemic dissemination.

In the early stage a dog may present with an erythematous, exfoliative or seborrhoeic skin condition, which is often very pruritic; lesions can heal in one region and then erupt in another. This gradually progresses with the development of plaques, nodules and ulceration of the skin. At mucocutaneous junctions infiltration, depigmentation, and ulceration are typical. Terminally there is rapid progression, culminating in widespread dissemination to other organs. The mucous membranes of the mouth, eyes and genitalia may be affected at all stages (Figure 8).

Non-epitheliotrophic lymphoma is a very aggressive tumor that usually presents with multiple cutaneous nodules, plaques or erythroderma. Histologically there is an infiltration of the dermis and subcutis with malignant lymphoid cells, usually of T-cell origin. The disease usually has a rapid course and quickly disseminates to involve other organs such as the liver, spleen and bone marrow. This form of cutaneous lymphoma is more common (although still rare) in the cat.

The prognosis for non-epitheliotrophic lymphoma is poor, with a rapid course and survival times rarely exceeding 2-3 months. Epitheliotrophic lymphoma carries a longer disease course and treatment may be more successful. Response of the lesions to systemic chemotherapy is variable but some improvement can be achieved. Single agent Lomustine (CCNU) has reportedly good but often short-lived remission rates (80%) whilst retinoids, L-asparaginase and Interferon alpha, as well as radiotherapy, have been tried and show some efficacy (20). Topical treatment with nitrogen mustard is not recommended.

Secondary cutaneous lymphoma

Systemic lymphoma can disseminate to the skin. This is more commonly of β-cell origin, reflecting the original tumor. Prognosis is poor as these animals have frequently received extensive chemotherapy and have multi-drug resistance. Radiotherapy may assist with treatment of problematic lesions.

Metastatic cutaneous tumors

Cutaneous metastases may be seen with any
malignancy. Lesions can be very variable in appearance, but usually the presence of a primary malignancy will be known. Biopsy or FNA is usually diagnostic and the prognosis is typically grave. Worthy of particular mention is the lung-digit syndrome seen in cats; this is characterized by metastatic tumors of the digits attributable to a primary lung tumor (SCC, bronchogenic carcinoma, pulmonary carcinoma). Affected cats are typically lame, with pain due to swelling and ulceration of one or more digits; the nail may be lost (21). Prognosis is hopeless.

**Conclusion**

Tumors of the skin are a daily occurrence in small animal practice and whilst the majority of such lesion in dogs are benign and carry a favorable prognosis, it is important to be familiar with the more common malignant tumors in order that they be diagnosed and managed appropriately. This article has sought to provide an overview of the more common skin tumors of the cat and dog for this purpose. The reader is referred to further literature as the subject of cutaneous neoplasia is a vast and complex issue to cover comprehensively.

**REFERENCES**


