

# Eccrine adenocarcinoma of the footpads in 2 cats

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**Abstract** — Adenocarcinoma of sweat glands of the footpads was diagnosed in 2 cats. Clinical signs included lameness and swelling of multiple digits. Pulmonary metastasis was detected in one case. Diagnosis was based on histopathological and immunohistochemical findings. Eccrine adenocarcinoma should be included in the differential diagnosis of footpads lesions in aged cats.

**Résumé** — Adénocarcinome des glandes eccrines des coussinets plantaires chez 2 chats. Un adénocarcinome des glandes sudoripares des coussinets plantaires a été diagnostiqué chez 2 chats. Les signes cliniques comprenaient de la boiterie et de l'enflure de plusieurs doigts. Des métastases pulmonaires ont été détectées dans un cas. Le diagnostic s'est basé sur des observations histopathologiques et immunohistochimiques. Les adénocarcinomes des glandes eccrines devraient faire partie du diagnostic différentiel des lésions des coussinets plantaires chez les chats âgés.

(Traduit par docteur André Blouin)

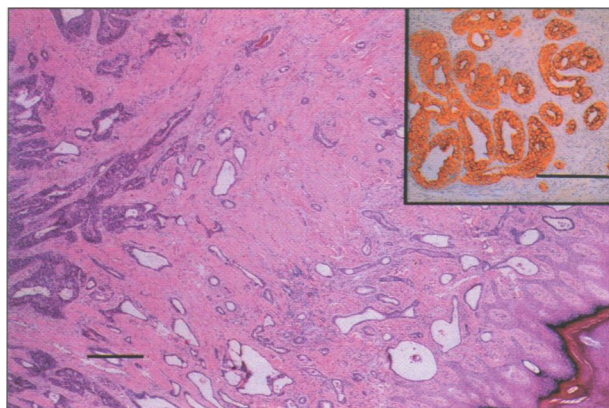
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## Case 1

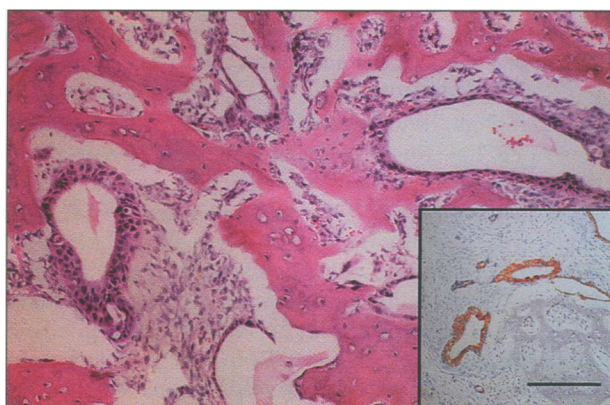
An 11-year-old, male, domestic shorthair cat was first seen with the presenting complaint of left hindlimb lameness of 2 weeks' duration. On physical examination, the paw was painful and radiographs showed a fracture of the 3rd phalanx (PIII) in the 3rd digit. The digit was amputated, but histological examination was not performed. A month later, the cat was presented again, due to limping on the right hind limb. A physical examination revealed a painful paw and radiographs showed a degenerating/moth eaten appearance of the distal portion of PIII on the 1st digit. The toe was amputated and submitted for histopathological examination. Ten days later, the cat was euthanized because of progressive weight loss. Postmortem examination revealed an off-white firm nodule, measuring 1 cm in diameter, in the cranioventral lobe of the lung. Gross examination of the cut surface of the decalcified toe revealed a tan, soft-tissue mass extending from the foot pad into the bone. On microscopic examination, neoplastic cells were seen to be arranged in tubules, clusters, and acini. These cells infiltrated the dermis (Figure 1) and extended into the phalangeal bone. Tumor cells were ovoid with a round, prominent nucleus and ill-defined cytoplasmic borders. Squamous metaplasia was observed in some areas and mitotic figures were numerous (> 5 per 40X field). Histological examination of the lung revealed neoplastic cells of similar characteristics to those seen in the footpad. Neoplastic cells were not seen in the other tissues examined, including regional lymph nodes. A diagnosis of eccrine adenocarcinoma of sweat glands of the footpads with metastasis to the lung was made.

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**Figure 1.** Footpad, Case 1. Neoplastic proliferation of moderately anaplastic epithelial cells arranged in variably sized tubular structures that readily infiltrate the underlying tissues; bar = 300 µm. Inset: Positive staining of tumor cells with AE1/AE3 immunoperoxidase stain; bar = 100 µm.



**Figure 2.** Third phalanx, Case 2. Neoplastic infiltration of the marrow spaces. Inset: Positive staining of tumor cells with CAM 5.2 immunoperoxidase stain; bar = 100 µm.

## Case 2

The 3rd and 4th digits from the right hind limb of a 8-year-old, male, domestic shorthair cat were submitted for histological examination. The cat was presented

with a complaint of a 1-week-long lameness in the right hind limb. On physical examination, the 3rd and 4th digits of the right hind limb were swollen. Bacterial pododermatitis was suspected and the cat was administered 22.7 mg of enrofloxacin, q12h for 8 d. Five days after the beginning of the treatment, the owners indicated that there had been no improvement and that the disease was apparently spreading. Three days later, the cat was examined and the 2nd and 3rd digits on left hind foot, and 2nd digit on both front feet were swollen and painful. Due to the rapid progression of the condition and absence of infectious etiologic agents, as evidenced by negative impression smears and aspirates, an autoimmune disease was suspected and the cat was given prednisone in a decreasing and alternate dose regime (5.7 mg, q12h for 5 d, then 5.7 mg, q24h for 5 d, and then every other day for 5 d). After 12 d of steroid therapy, there was no improvement, the cat was unable to walk, and the owners elected euthanasia. Permission for necropsy examination was refused, but the 3rd and 4th right hind digits were submitted for histological examination. The decalcified sections of digits exhibited neoplastic proliferation of highly anaplastic epithelial cells, arranged in irregularly shaped tubules embedded in a prominent fibrous connective tissue stroma. Neoplastic tubules readily infiltrated the underlying tissues, including bone (Figure 2). Tubular structures contained occasional cellular debris and were lined by 2 or more layers of cuboidal to columnar pleomorphic epithelial cells. Neoplastic cells had large, round to oval, euchromatic nuclei (up to 3-fold anisokaryosis), prominent nucleoli, and a moderate amount of pale basophilic cytoplasm with indistinct cell borders. Mitotic figures were common. A diagnosis of eccrine adenocarcinoma of sweat glands of the footpads was made.

Paraffin-embedded tissues from the affected digits in both cases and the neoplasm detected in the lung in Case 1 were submitted for immunohistochemical examination to confirm the histological diagnosis. Immunoperoxidase staining by the avidin-biotin complex method (1) revealed that the neoplastic cells in the digits (Figure 1, inset) and in the lung stained positive with a cocktail of 2 monoclonal antibodies AE1/AE3 (Hybritech Inc., San Diego, California, USA), which detects both low and high molecular weight cytokeratins. A wide variety of epithelial structures in the skin, including apocrine glands, stratified squamous epithelial cells, and inner root sheaths, are stained by AE1/AE3 (2). Tissues were also stained with a monoclonal antibody CAM 5.2 (Becton Dickinson, Franklin Lakes, New Jersey, USA), which recognizes the simple epithelia expressing the cytokeratin pair 8/18 or 19 w. Neoplastic cells stained positive with CAM 5.2 (Figure 2, inset). Both apocrine glands and the inner root sheath of hair follicles are stained by CAM 5.2 (2). Thus, in order to distinguish inner root sheath from apocrine glands, an antibody that detects cytokeratin pairs 1/5 and 10/11 (34BE12, Enzo Biochem, Farmingdale, New York, USA) was used (2). There was faint staining in some areas of the tumor, specifically within the cells lining neoplastic ducts, whereas the inner root sheath and stratified squamous epithelial cells stained darkly. The location and the histological and immunocytochemical characteristics of the tumor in

these 2 cases are consistent with a diagnosis of adenocarcinoma arising from the eccrine sweat glands of footpads.

Neoplasms of eccrine sweat glands are extremely rare in dogs and cats (3,4). Eccrine adenomas and adenocarcinomas have been observed in dogs, whereas eccrine sweat gland tumors are usually malignant in cats (3). The scarcity of eccrine neoplasms in dogs and cats can be explained by the fact that eccrine sweat glands are few in number compared with apocrine sweat glands. In contrast, eccrine sweat glands are abundant in humans, in whom more than 15 categories of eccrine tumors have been described (4). In cats, eccrine sweat glands are small and tightly coiled and are found only in the footpads (5). They consist of a layer of cuboidal to columnar epithelial cells and a layer of fusiform myoepithelial cells; the excretory duct opens directly into the surface of the footpad (6). These glands secrete when the cat is hot or frightened, causing damp footprints (7). In contrast, apocrine sweat glands are distributed throughout the haired skin, they are located deep to the sebaceous glands and open through excretory ducts into the canal of the hair follicle, superficial to the opening of the sebaceous duct (6). Apocrine glands are present in the interdigital spaces but not in the footpads or the planum nasale (6).

Eccrine carcinoma appears as a poorly defined swelling of the footpad and digit. Lesions may affect multiple toes and ulceration is common (3,4). Lysis of phalangeal bone, such as that seen in Case 1, is generally observed radiographically (4). Eccrine carcinomas are highly aggressive; although rapid metastasis to lymph nodes has been mentioned as a common outcome (3,4), examination of regional lymph nodes in Case 1 did not reveal metastasis.

Differential diagnoses of eccrine adenocarcinoma include nail bed squamous cell carcinoma and keratoacanthoma (4). Melanoma, mast cell tumors, osteosarcoma, lymphosarcoma, and hemangiosarcoma can also occur in the digits (3). Additionally, squamous cell carcinoma affecting more than one digit (7) and metastases of primary lung tumors to the digits have been reported in cats (8–11). Specific types of primary lung tumors capable of producing metastases to the footpads have been identified as squamous cell carcinoma (8), bronchial gland adenocarcinoma (10), and bronchial carcinoma (11).

The possibility of a primary lung tumor with metastasis to the digits was considered in Case 1, but no evidence of a respiratory origin was detected in the neoplastic cells by using routine histological or immunohistochemical procedures. Pseudostratified ciliated epithelium has been demonstrated in the digits and within the lumina of digital arterioles in cases of primary bronchial carcinoma, supporting the assumption that the neoplasm originated in the lungs and metastasized via direct arterial embolism to the digits and other sites (11). The presence of metastases of primary pulmonary malignant tumors in the digits has been interpreted as a reflection of the substantial vascularity of the feline foot pads that is required to facilitate heat loss (9). An interesting feature of some cases of primary pulmonary neoplasm with metastasis to the digits is that the cats are

presented with a complaint of lameness, multiple digital swelling, or fixed exsheathment of the claws, before the appearance of signs related to the lung lesion (9,11).

The morphological characteristics of the neoplastic cells in the digits in the cases described here were consistent with those of eccrine adenocarcinoma; however, the definitive diagnosis was achieved by using immunocytochemical techniques. Immunohistochemical detection of carcinoembryonic antigen, which is normally present in eccrine duct and luminal cuticle, can also be used to distinguish eccrine adenocarcinoma from squamous cell carcinoma (4). The faint staining of the cells lining neoplastic ducts obtained by using antibody 34BE12 may be due to the fact that this antibody stains the duct-lining cells, whereas other epithelial cells remain unstained (12). It is also possible that there are slight differences in the immunoreactivity of eccrine glands compared with apocrine glands. Although both apocrine and eccrine glands function by merocrine secretion (6), they have a different embryologic origin. Eccrine sweat glands develop in fetal life from cords of cells that grow downward from the epithelium of the dermal ridges, whereas apocrine sweat glands arise as an epithelial bud growing from the side of a hair follicle (6).

Due to the rapid progression of the disease, neoplasia was not suspected in either case described here. Both cats were presented with a complaint of lameness in one limb, and within less than a month, multiple digits were swollen and painful, and the cats were unable to walk, which prompted their owners to request euthanasia.

Neoplastic disease, including pulmonary and eccrine gland carcinomas, although not common, should be included in the differential diagnosis in middle-aged and aged cats presented with lameness and painful swelling of multiple digits. In addition to histopathologic examination, immunohistochemical techniques are often necessary to differentiate between primary eccrine ade-

nocarcinomas of the foot pads and metastatic pulmonary carcinomas.

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