

## Case Report

# Adenocarcinoma of the Dorsal Glands in 2 European Ground Squirrels (*Spermophilus citellus*)

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Olfactory communication is an important aspect of the biology of ground squirrels; accordingly, some of their integumentary glands are associated with scent-marking behavior. Although reports of neoplasms in ground squirrels are limited, the literature on tumors in this family of rodents is extensive, with hepatocellular carcinomas in woodchucks and fibromas in squirrels being the 2 most common neoplasms. Apocrine gland tumors occur frequently in domestic animals such as cats and dogs but to our knowledge have not previously been reported in squirrels. Here we describe 2 cases of adenocarcinoma of the dorsal glands in privately owned European ground squirrels (*Spermophilus citellus*). The skin nodules were characterized histologically by proliferation of epithelial cells, which were arranged in a tubuloacinar pattern with neoplastic emboli within the blood vessels. Adenocarcinoma of the dorsal glands was diagnosed in light of the anatomic localization, immunohistochemistry results, and histochemistry findings.

Olfactory communication is an important aspect of the biology of most ground squirrels;<sup>10,12</sup> accordingly, some of their integumentary glands are associated with scent-marking behavior.<sup>5,10</sup> Squirrels have 3 glandular anatomic areas: the oral–cheek area, dorsal area, and the anal area.<sup>10</sup> The dorsal gland field in the skin extends from the scapular region caudally and from the scapular region anterioventrally to the ear.<sup>9,10</sup> Approximately 60 individual oval-shaped sudoriparous glands comprise the dorsal gland field. Individual dorsal glands are composed of a tightly coiled and branched fundus, a large sinus, and a singular duct, which opens on the free surface of the skin.<sup>9,10</sup> The strong-smelling oil secreted by the glands probably is released on vegetation and serves as a source of information to other members of the species.<sup>9</sup> These glands seem to be more active during spring and summer than during winter. They are stimulated by excitement, present in both sexes, and larger in adult male squirrels.<sup>10</sup> Here we describe 2 cases of neoplasia of the dorsal glands in 2 privately owned European ground squirrels (*Spermophilus citellus*; Sciuridae).

### Case report

The first case was a 2-y-old, intact female squirrel that developed a solitary mass measuring 1 cm in diameter at the base of the neck. The mass was firm and haired, with distinct borders. Neither ulceration nor hemorrhage was observed. The other case was a 3-y-old, intact female squirrel that presented with multiple masses on her back. The nodules, ranged from 0.3 to 1.5 cm in diameter, were round, firm, and haired. The largest ulcerated mass was excised and submitted for histologic examination.

On physical examination, the squirrels had no clinical evidence of local or systemic lymph node involvement. Surgery was performed to excise the single mass from the first squirrel and the largest ulcerated mass from the second. For both surgeries, anesthesia was induced by using intramuscular medetomidine (30 µg) and ketamine (15 mg) and maintained, after intubation, by using 2% isoflurane. At 2 mo after surgery, both squirrels were still in good clinical condition.

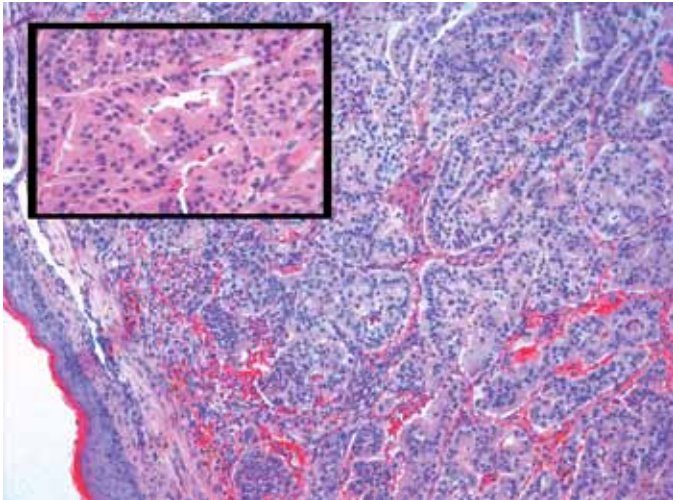
On gross examination, both nodules had a gray to whitish cut surface. Representative samples from the masses were fixed in 10% neutral buffered formalin, routinely processed for histology, and stained with hematoxylin and eosin. Additional sections underwent periodic acid–Schiff staining and immunohistochemistry.

Immunohistochemistry was performed on 4-µm tissue sections by using an automated Bond immunostainer (maXTM, A Menarini Diagnostics, Florence, Italy) and primary antibodies against pan-cytokeratins (dilution 1:75; clone AE1/AE, DakoCytomation, Carpinteria, CA), calponin (dilution 1:30,000; clone hCP, Sigma, St Louis, MI) and human factor VIII-related antigen (no additional dilution; Diagnostic BioSystems, Pleasanton, CA). The Bond Polymer Refine detection system (Leica Biosystems, Newcastle, UK), which contains a peroxide block and the chromogen 3,3'-diaminobenzidine tetrahydrochloride was used. All sections were counterstained with Mayer hematoxylin. To verify the specificity of the primary antibodies, positive internal controls, consisting of epidermis, skin annexes, and remaining normal glandular tissue, were used. Negative controls were included in each run.

Histologically, both lesions consisted of a well-demarcated, unencapsulated neoplastic nodule involving the superficial dermis in the first squirrel and the subcutis and underlying muscular layer in the second. Both neoplasms were composed of epithelial cells arranged in anastomosing tubules, irregular acini and focally in solid sheets intermingled with fine collagenous stroma (Figure 1). The neoplastic cells were columnar in shape, with distinct cell

Received: 20 Oct 2011. Revision requested: 23 Nov 2011. Accepted: 04 Jan 2012.  
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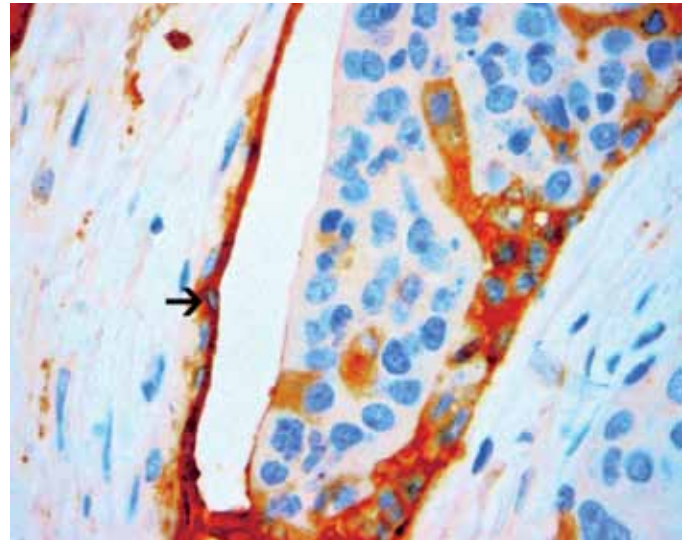


**Figure 1.** Neoplastic proliferation of pleomorphic cells, which are arranged in tubules, acini, and sheets. Infiltrates of numerous neutrophils and cellular debris are evident within the glandular lumen. The inset highlights the almost perfect acinar structure of the lesion. Hematoxylin and eosin stain; magnification, 100 $\times$ .

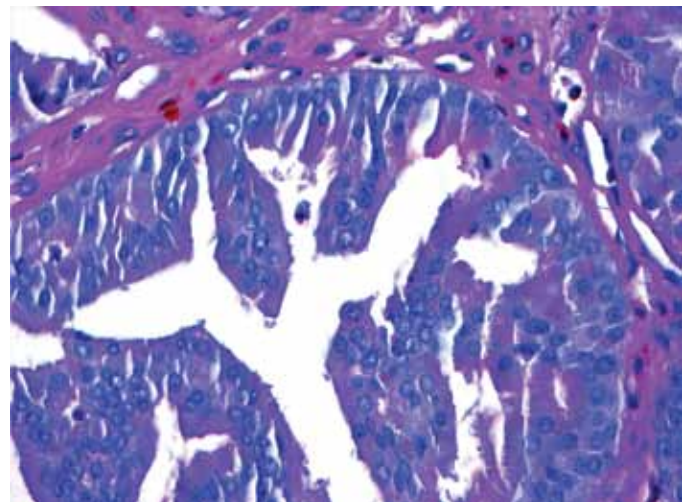
borders, abundant eosinophilic cytoplasm, and ovoid to round vesicular nuclei with prominent single or multiple nucleoli. Anisocytosis and anisokaryosis were remarkable, and the mitotic activity was high: 48 mitoses per 10 high-power fields in the first squirrel and 17 mitoses per 10 high-power fields in the second. In both cases, neoplastic emboli were present in the lumen of the surrounding vessels (Figure 2), marked by human factor VIII-related antigen. In both lesions, neutrophils and necrotic debris were present within the lumen of the neoplastic tubules. The presence of crusted and purulent ulceration of the skin overlying the lesion may explain, at least in case 2, the intraluminal inflammatory process. Neoplastic cells showed strong diffuse cytoplasmic positivity for pan-cytokeratins, confirming the epithelial origin of the neoplasia. Spindle cells positive for calponin, which were present close to the basement membrane of the glands and in the intertubular stroma, confirmed the presence of a myoepithelial component, which seems likely to play a major role in the release of exudates.<sup>9</sup> Periodic acid-Schiff staining showed a brilliant pink granular positivity encountered in the apical aspects of the cytoplasm of the acinar cells and within the lumen of the tubules and confirmed the glandular mucous origin of the neoplasia (Figure 3). In both cases, diagnoses of adenocarcinoma of the dorsal glands were made in light of the clinical presentation and localization of the lesions, as supported by histopathologic, immunohistochemical, and histochemical features.

## Discussion

Literature on tumors in the rodent family Sciuridae is extensive, particularly for woodchuck hepatocellular carcinomas<sup>11</sup> and squirrel fibromas,<sup>1,3,8</sup> which are the 2 most common neoplasms. The neoplasms that have been identified in ground squirrels thus far include skin cancers, accessory lachrymal gland cancers, mammary cancers, and virus-induced tumors (Figure 4). Apocrine gland tumors occur frequently in domestic animals, such as cats and dogs but, to our knowledge, have not previously been reported to occur in squirrels. The clinical presentation, including nodular intradermal and subcutaneous masses, and



**Figure 2.** Neoplastic emboli, in which the acinar architecture is preserved, are present within a blood vessel. Immunohistochemical staining for factor VIII strongly highlights the endothelium (arrow). Immunohistochemistry with DAB chromogen and hematoxylin counterstain; magnification, 630 $\times$ .



**Figure 3.** Granular intracytoplasmic substance, mostly present in the apical aspects of the acinar cells, is strongly positive by periodic acid-Schiff staining, thus confirming the apocrine origin of the neoplasia. Periodic acid-Schiff stain; magnification, 400 $\times$ .

the microscopic features of the dorsal gland adenocarcinomas in squirrels that we describe here are analogous to those of apocrine glands reported in other animal species.<sup>4</sup>

No data are available about the biologic behavior of apocrine gland tumors in squirrels. However, the rapid and locally invasive growth of the current tumors and the presence of neoplastic emboli in blood vessels suggest a poor long-term prognosis in these squirrels, as has been reported for apocrine gland adenocarcinoma of other species such as the dog and cat.<sup>4</sup> The 2 cases of adenocarcinoma of dorsal glands we described here occurred in 2- and 3-y-old squirrels, therefore basically at the end of their life expectancy in the wild.<sup>12</sup> Therefore, we speculate that such tumors may be reported more frequently in the future, due to

Common name	Species	Type of tumor and site	Living conditions	No. of cases reported	Reference(s)
Beechey ground squirrel	<i>Spermophilus beecheyi</i>	Harderian gland neoplasm (third eyelid)	wild-caught, captive-housed	18	15
Chipmunk	<i>Tamias sibiricus</i>	Tubular adenocarcinoma (mammary gland)	privately owned	1	13
Chipmunk	<i>Tamias striatus</i>	Cutaneous epitheliotropic lymphoma with liver dissemination	privately owned	1	14
Gray squirrel	<i>Sciurus carolinensis</i>	Mammary carcinosarcoma (mammary gland)	privately owned	1	17
Squirrel	<i>Sciurus</i> sp.	Epitheliotropic lymphoma (left caudolateral thorax)	privately owned	1	7
Thirteen-lined ground squirrel	<i>Spermophilus tridecemlineatus</i>	Malignant melanoma (subcutaneous)	not reported	1	2
Richardson's ground squirrel	<i>Spermophilus richardsonii</i>	Multicentric mast cell tumor (skin of the middle of the tail and lumbosacral region)	privately owned	1	6
California ground squirrel	<i>Spermophilus beecheyi</i>	Squamous cell carcinoma (anterior right leg)	privately owned	1	18
Eastern gray squirrel	<i>Sciurus carolinensis</i>	Multiple virus-induced cutaneous and systemic fibromas	wild	2	1, 3, 5

**Figure 4.** Tumors reported in different species of ground squirrel.

the increasing lifespan of pet and laboratory squirrels.<sup>16</sup> Moreover, factors associated with captivity, including altered photoperiod, disturbed hibernation periods, and access to a commercial rather than a natural diet, may contribute to tumor development. Knowledge of the specific anatomic structures and age of the animal involved may facilitate the clinical and histologic diagnosis of dorsal gland carcinomas.

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