

Pathology In Practice



Figure 1—Photograph of a mass at the tip of the amputated tail of a 6-year-old ferret. The owner reported that the mass on the tail had been present for approximately 6 months and was rapidly increasing in size. On cut surface, the mass is lobulated and mostly composed of firm, translucent tissue admixed with whitish firm areas (resembling cartilaginous and osseous metaplasia) and dark red foci (interpreted as hemorrhage).

History

A 6-year-old neutered male ferret was referred to the University of Georgia Small Animal Teaching Hospital because of a mass at the tip of the tail and 2 slightly raised skin masses (1 on the cranial aspect and 1 on the caudal aspect of the thorax). The owner reported that the mass on the tail had been present for approximately 6 months and was rapidly increasing in size; the other 2 masses were becoming increasingly ulcerated and had likely become pruritic because the ferret frequently attempted to scratch them. With the exception of the 3 masses, the ferret appeared clinically normal.

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Clinical and Gross Findings

At the initial evaluation, the ferret had a $4.5 \times 2.5 \times 2.5$ -cm mass that encompassed the entire tip of the tail. The mass was covered with haired skin, which was partially ulcerated and covered with crusts. Two slightly raised, white, soft skin masses located on the left side of the thorax were also evident; one mass was 0.5 cm in diameter and the other was 1 cm in diameter. A sample of the mass on the tail was collected via fine-needle aspiration and submitted for cytologic evaluation. Based on the clinical appearance and known prevalence in this species, the thoracic masses were presumed to be mast cell tumors. The tail was amputated, and the skin masses were surgically removed. The 3 masses were submitted for histologic examination. On cut surface, the tail mass was firm with a lobular appearance. Translucent areas were admixed with islands of both grossly recognizable cartilage and hard white osseous tissue (Figure 1).

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →

Cytologic and Histopathologic Findings

Cytologic examination of a fine-needle aspirate (stained with modified Wright's stain) obtained from the tail-tip mass revealed numerous, variably sized clusters of physaliphorous cells (foamy cells containing mucoid-laden vacuoles) that were occasionally enmeshed within a pink, fibrillar material. The cells were round to polygonal with an abundant amount of eosinophilic cytoplasm, which was typically obscured by numerous large intracytoplasmic vacuoles. Nuclei were round to ovoid with a coarsely granular chromatin pattern. There was moderate anisocytosis and anisokaryosis within this cell population, and many binucleated and multinucleated cells were detected (Figure 2). Among the clusters of cells, a mucinous matrix was seen, which stained lightly blue with an Alcian blue stain at a pH of 2.5.

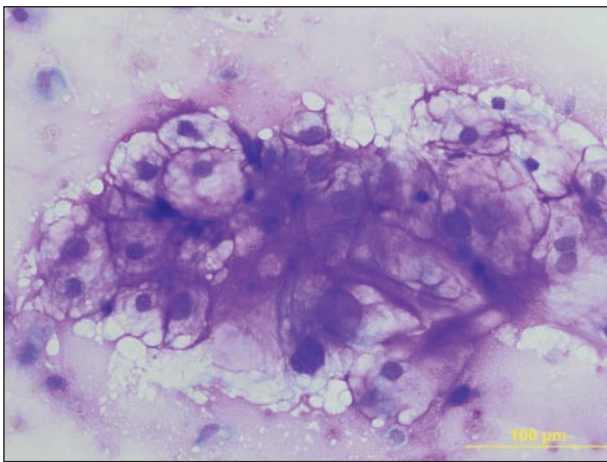


Figure 2—Photomicrograph of a fine-needle aspirate of the mass on the tail tip of the ferret in Figure 1. Notice the tight clusters of round to polygonal cells that contain abundant eosinophilic cytoplasm, which is largely obscured by numerous nonstaining, intracytoplasmic vacuoles (physaliphorous cells). Modified Wright's stain; bar = 100 μ m.

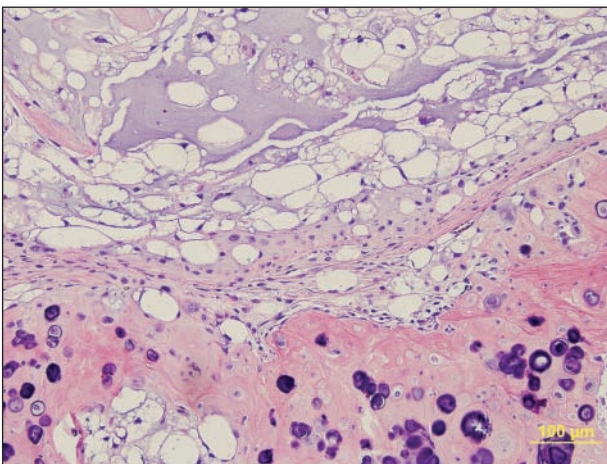


Figure 3—Photomicrograph of a section of the mass on the tail tip of the ferret in Figure 1. Physaliphorous cells (large vacuolated cells) are arranged within lobules that contain amorphous basophilic material (mucin). The lobules are surrounded by spindle cells. At the bottom of the image, chondroid and osseous matrix are observed adjacent to the clusters of physaliphorous cells. H&E stain; bar = 100 μ m.

Histologically, the tail-tip mass was well circumscribed, nonencapsulated, and arranged in multiple irregular lobules that were separated by spindle-shaped immature mesenchymal cells. The lobules were composed of large vacuolated, polygonal cells with oval, pleomorphic, eccentric nuclei (physaliphorous cells). These cells were often bi- or trinucleated and embedded in a basophilic mucinous matrix. Within some lobules, islands of chondrocytes with a central core of trabecular bone were observed (Figure 3). Mitotic figures were not present. The mass expanded the deep dermis and subcutaneous tissues and compressed the associated adnexa. The overlying epidermis had moderate orthokeratotic hyperkeratosis and contained focally extensive crusts that were composed of degenerate neutrophils and necrotic debris.

Immunohistochemical staining of sections of the tail-tip mass with antibody against vimentin^a revealed strong expression of that protein in the cytoplasm of physaliphorous and chondrocytic cells and in the osseous matrix. Immunohistochemical staining was also performed with antibody against cytokeratin.^b Expression of cytokeratin was limited to the cytoplasm of physaliphorous cells and typically restricted to a thin peripheral rim, whereas vimentin was distributed more diffusely within the cells. Histologic examination of the 2 thoracic masses confirmed the suspicion of well-differentiated mast cell tumors.

Morphologic Diagnosis

Chordoma (chondroid variant).

Comments

Chordoma is a neoplasm that originates from remnants of the notochord.¹ The notochord, which is believed to originate from primitive mesoderm, extends the entire length of the developing embryo along the midline, ventral to the developing neural tube. It delineates the cranial-caudal axis of the embryo, induces the formation of the head and CNS, and has a central role in the development of the vertebral bodies and the basal portions of the sphenoid and occipital bones. As the vertebral column develops, it surrounds the notochord, resulting in segmentation and virtual obliteration of this embryonic structure. The notochord persists between the vertebrae and expands to form the nucleus pulposus of each intervertebral disk. This is believed to be the only derivative of notochordal tissue in adult animals, although remnants can persist in any location from the sphenoid-occipital region to the tail tip.²

Histologically, chordomas consist of lobules of physaliphorous cells that are separated from adjacent normal tissues by a thin fibrovascular stroma. These cells are usually closely packed, variably sized polygonal cells that have distinct borders and multiple large nonstaining, intracytoplasmic vacuoles. At the margin of these masses, chordoma cells often appear as smaller stellate cells with a granular to microvacuolated eosinophilic cytoplasm. Nuclei are typically round to ovoid with stippled chromatin and occasional distinct nucleoli. Physaliphorous cells are often surrounded by a mucinous extracellular matrix that stains with Alcian blue stain.^{2,3}

In various species, chordomas generally have both epithelial and mesenchymal characteristics, as indicated by the dual expression of cytokeratin and vimentin intermediate filaments. Dual expression of cytokeratin and vimentin is not unique to chordomas and has been detected in mesothelium, endothelium, granulosa and rete ovary cells, Sertoli cells, endometrial epithelium, thyroid gland epithelium, kidney epithelium, choroid plexus, meninges, umbilical cord, and synovium.^{2,4} In chordomas, S-100 protein and neuron-specific enolase may be present; in a study² of chordomas in 20 ferrets, 15 (75%) were positive for S-100 protein and 17 (85%) were positive for neuron-specific enolase. A positive result for S-100 is believed to be related to glycosaminoglycans within the chordoma stroma, whereas neuron-specific enolase is present in cells with features of high metabolic activity.⁴

In domestic ferrets, chordomas are the fifth most common tumor (detected in 2.2% of tumor-bearing ferrets) and the most common musculoskeletal tumor (detected in 54% of ferrets with a musculoskeletal tumor).⁵ Chordomas typically develop on the tip of the tail² but may also develop in the cervical⁶ and thoracic vertebral column⁵ and in the coccygeal region.⁷ Other less frequently reported neoplasms of the tail tip in domestic ferrets include sebaceous gland carcinomas, sweat gland carcinomas, and papillary cystadenomas.³ In ferrets, chordomas are generally considered to be locally aggressive, with little metastatic potential, although there are rare reported cases of both local and distant skin metastases.^{6,7} Whether males or females are more predominately affected has not been definitively established.

In addition to ferrets, chordomas in humans,⁸ rats,^{8,9} mink,¹ dogs,^{4,10,11} and rarely in cats^{12,13} have been reported. Chordomas in humans are typically slow-growing and locally invasive, and the recurrence rate following surgical removal is high.¹⁰ It is estimated that approximately 30% of chordomas in humans metastasize, often following a long clinical course. Most commonly, the tumors metastasize to the lungs, skeleton, and liver.⁷ In humans, chordomas are classified as a classic, dedifferentiated, or chondroid variant. The presence of a chondromatous component and spindle cells differentiate the chondroid variant from the classic form.¹⁰ This distinction is important because the survival rate of humans with chondroid chordomas is 3 times as great as the survival rate for humans with classic chordomas.⁷ Chordomas in ferrets and mink are

typically chondroid variants,^{1,2} whereas those in rats are histologically most similar to classic chordomas and are commonly highly malignant.⁸

Given the frequency with which this tumor type develops at the tip of the tail in ferrets, chordoma should be a primary differential diagnosis for a tail-tip mass in this species. Detection of physaliphorous cells admixed with a mucinous background via cytologic and histologic examinations is generally diagnostic. Immunophenotyping of the neoplastic tissue yields positive results for both cytokeratin and vimentin, along with variable expression of S-100 protein and neuron-specific enolase. Although cutaneous metastasis of chordomas in ferrets has been reported rarely,^{6,7} mass excision is typically curative.

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- a. Anti-vimentin antibody (clone V9), Biogenex, San Ramon, Calif.
 b. Anti-cytokeratin AE1/AE3 antibody, Biogenex, San Ramon, Calif.
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