Diagnostic Exercise
From The Davis-Thompson Foundation*

Case #: **197**; Month: **September**; Year: **2022**
Answer Sheet

Title: Chordoma in a Ferret (*Mustela putorius furo)*

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Clinical History: A 5-year-old, entire male domestic ferret (*Mustela putorius furo)* was presented to the clinic for excisional removal of a 1.5 cm mass on the distal aspect of the tail.

Gross Findings: The sample is comprised of a 3 cm x 2 cm x 1 cm segment of haired skin, previously cut, with 2 cm diameter nodular firm white mass (representative sections were taken) (Figures 1A and1B).

Gross Images:

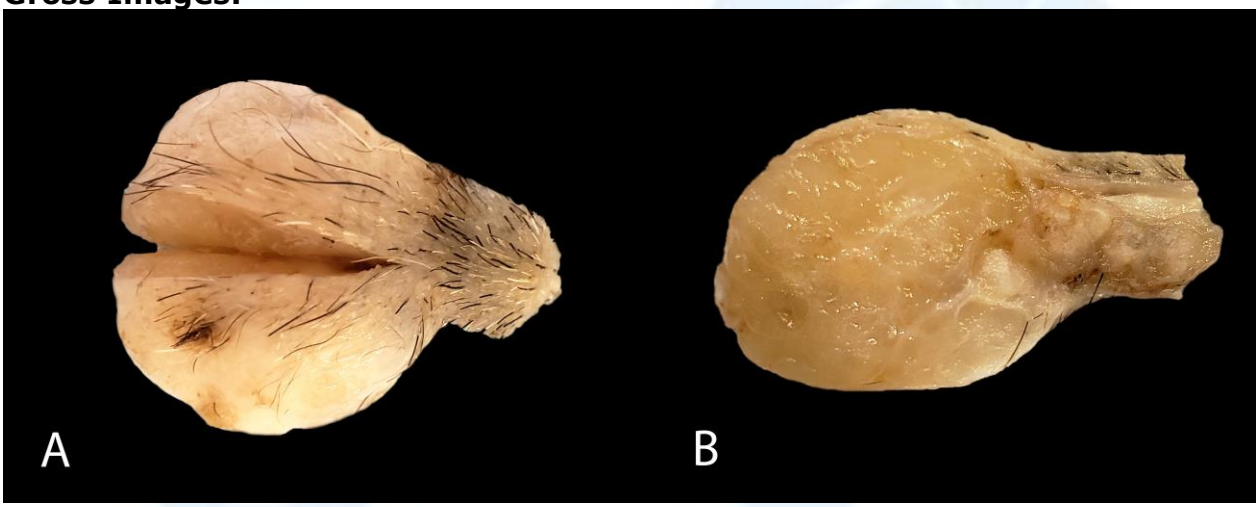

Figure 1

Microscopic Images:

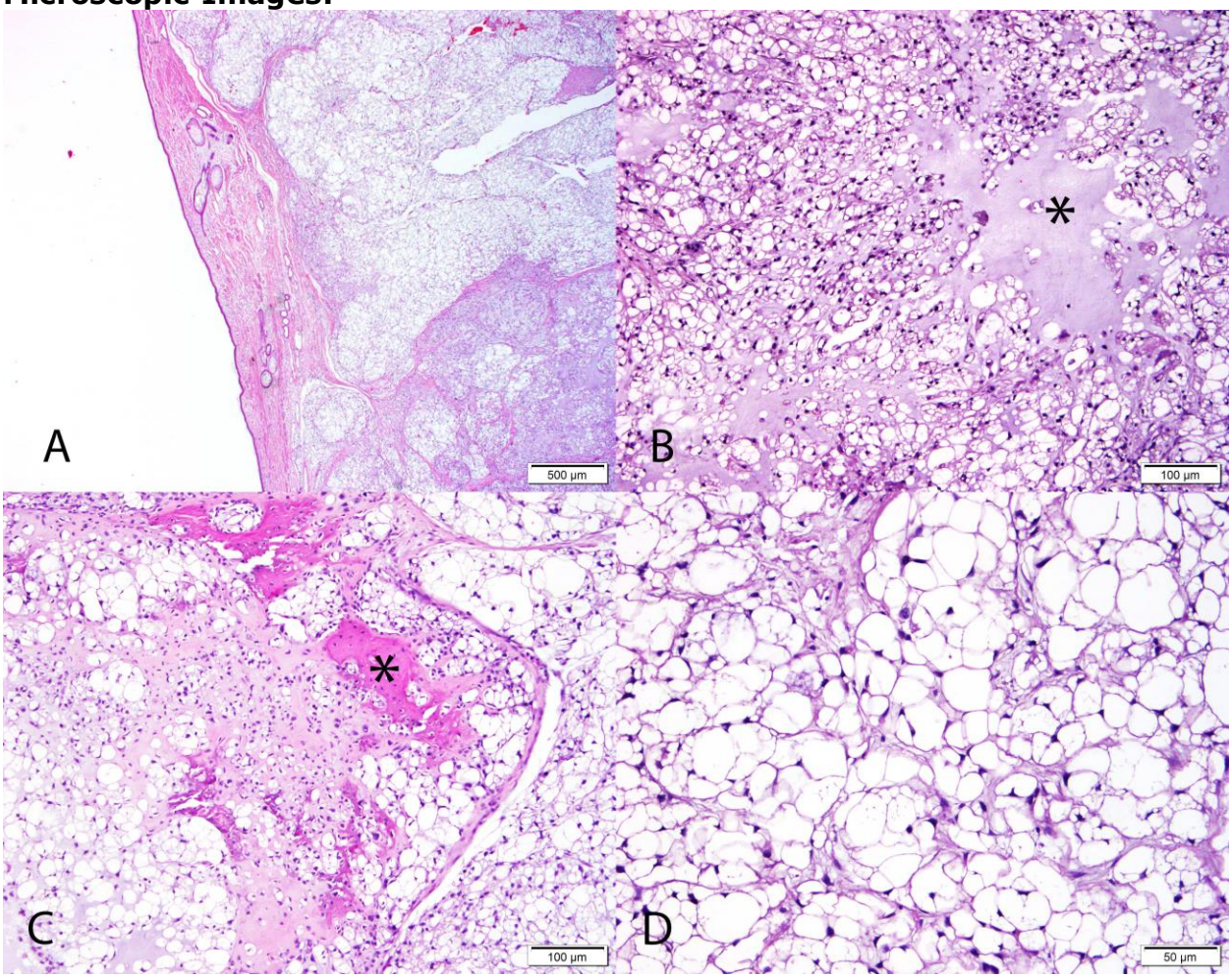

Figure 2. Chordoma, haired skin (tail), ferret. **A.** There is a nodular neoplastic proliferation in the dermis extending to the subcutis. H&E, 20X. **B.** Neoplastic cells form densely packed clusters separated by fibrous trabeculae, within an abundant myxoid matrix (asterisk). H&E, 100X. **C.** There are multiple bone islands surrounded by the myxoid matrix (asterisk). H&E, 100X. **D.** The neoplastic cells are round to polyhedral, with distinct cell borders, vacuolated cytoplasm (physaliferous cells), and a hyperchromatic eccentric nucleus. H&E, 200X.

Morphologic Diagnosis: Haired skin, tip of the tail: Chordoma.

Typical Gross Findings:
Anatomic localization: Tip of the tail (most frequently) and cervical, thoracic, coccygeal (base of the tail) spinal region.
Firm, lobulated, nodular, and often ulcerated mass.

Typical Microscopic Findings:
Lobules of vacuolated cells (physaliferous cells), surrounding cartilage with a central core of bone in a myxoid matrix.

Discussion:

Chordomas are tumors arising from the intraosseous embryonic remnants of the notochord tissue (1,2,4,5,6,7,8). Chordomas have a low incidence in human beings and animals (5 9). Notochord is a rodlike aggregate of cells extending in the entire length of the embryo and defines the cranial-caudal axis of the embryo (1,4,8). It induces the formation of the head and the central nervous system (1,4,8), and it is an organizing center for the development of the vertebral bodies and the basal portion of the occipital and sphenoid bones (4). Histologically, the tumor is comprised by the vacuolated cells known as physaliferous cells arranged in a lobular pattern (1,5,8). In ferrets, chordomas have the unique feature of physaliferous cells surrounding cartilage with a central core of bone (5).

In animals, chordomas have been reported most commonly in ferrets, and less frequently in dogs, rats, cats, minks, zebrafish (*Danio rerio*), Perdido Key Beach mouse (*Peromyscus polionotus trissyllepsis*), degus (*Octodon degus*), and tiger (8, 9). This tumor has also been reported in children (9).

Anatomic locations are related to the distribution of notochordal remnants. In ferrets, the most common anatomic localization is the tip of the tail (1,2,5,6,7,8). Also, chordomas have been reported less frequently in the cervical, thoracic, and coccygeal (base of the tail) spinal region (1,2,5,6,7,8). In humans, chordomas are located most commonly at the cranial and caudal extremities of the axial skeleton (7). In rodents, the location of the tumor is wider (cranial, cervical thoracic, lumbar, sacral, and coccygeal segments of the axial skeleton) (4,9). In zebrafish, chordomas has been reported in atypical extra-skeletal location, the intestine (3).

Grossly, in ferrets, the tumors located in the tip of the tail are firm, round, lobulated, and often ulcerated (4,6). Cervical chordomas can be associated with signs of tetraparesis and ataxia, depending on the site of the lesion (6). Chordomas are locally aggressive and with high local recurrence after surgical removal (4,9). In ferrets, metastasis has only been reported twice in the skin and once in the lung (5, 9). However, chordomas are considered benign tumors due to infrequent metastases, slow growth rate and easy surgical excision (tip of the tail) (5). There are no reports of metastasis associated with chordomas arising at the tip of the tail (9).

Histologically chordomas can resemble chondrosarcomas (6). Additional differential diagnoses include myxosarcoma, myxoid liposarcoma, mucinous adenocarcinoma, sebaceous carcinoma, and signet ring cell carcinoma (1,2 7,9).

In humans chordomas are classified within the histologic subtypes: classic, chondroid, and dedifferentiated (with a malignant spindle cell component) (4,9) and each one has a prognostic significance. These classification schemes are not adapted to animals, but most of the chordomas in ferrets are reminiscent of the human chondroid subtype (1,5,9).

Immunohistochemically, chordomas are positive for vimentin, cytokeratin, S100, and NSE (neuron-specific enolase) (1,2,4,7). The immunohistochemical marker brachyury (nuclear T-box transcription factor) has been used to differentiate chordoma from parachordoma in humans (3). It has also been used for the diagnosis of chordomas in Perdido Key Beach mice and zebrafish (3, 10). Brachyury is a regulator of the embryonic notochord formation (3). Additionally, cytokeratin (CK) AEI/AE3, CK 7, and CK 8/18 has been used too (3).

References and Recommended Literature:

1. Camus MS et al. Pathology in Practice: chordoma (chondroid variant). JAVMA 2009;235 (8): 949-951.
2. Cho ES et al. Chordoma in the tail of a ferret. Lab Anim Res 2011;27(1): 53-57.
3. Cooper TK et al. Primary intestinal and vertebral chordomas in laboratory zebrafish (*Danio rerio*). Vet Pathol 2015;52(2): 388-392.
4. Dunn DG et al. A histomorphologic and immunohistochemical study of chordoma in twenty ferrets (*Mustela putorius furo*). Vet Pathol 1991;28: 467-473.
5. Frohlich JR and Donovan TA. Cervical chordoma in a domestic ferret (*Mustela putorius furo*) with pulmonary metastasis. J Vet Diagn Invest 2015;27(5): 656-659.
6. Mullen HS and Beeber NL. Miscellaneous surgeries in ferrets. Vet Clin of North Am 2000;3(3): 663-671.
7. Munday JS et al. Suspected metastasis coccygeal chordoma in a ferret (*Mustela putorius furo*). J Vet Diagn Invest 2004;16: 454-458.
8. Pease AP et al. Radiographic, computed tomographic and histopathologic appearance of a presumed spinal chordoma in a dog. Vet Rad & Ultras 2002;43(4): 338-342.
9. Sautier L et al. Coccygeal chordoma in a degu: case report and review of the literature. J Vet Diagn Invest 2019;31(1): 142-145.
10. Taylor KR et al. Chordomas at high prevalence in the captive population of the endangered Perdido Key beach mouse (*Peromyscus polionous trissyllepsis).* Vet Path 2016;53(1): 163-169.

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