

Rhabdomyosarcoma in a Ferret (*Mustela putorius furo*)

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ABSTRACT. A 5-year-old spayed male ferret showed a subcutaneous mass in the right lateral thoracic wall. Microscopic examination revealed that the neoplasm had proliferated in the subcutis with infiltration into the surrounding tissues. A packed bundle of large polymorphic neoplastic cells, containing abundant eosinophilic cytoplasm and a round to ovoid, occasionally bizarre nucleus, were arranged interwoven. The neoplasm had metastasized to the right axillary lymph node. The neoplastic cells were intensively positive for vimentin, desmin and myoglobin. Skeletal muscle type creatine phosphokinase-positive granules were detected in the cytoplasm. Ultrastructurally, various amounts of disorganized myofibrils with focal density resembling the Z-band were shown in the cytoplasm of the neoplastic cells. The neoplasia was diagnosed as rhabdomyosarcoma.

KEY WORDS: ferret, rhabdomyosarcoma.

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Since ferrets have been kept as household pets or used as experimental animals, reports of neoplastic diseases in ferrets have increased [1,5]. As to myogenic neoplasms of ferrets, although neoplasms originating from smooth muscles are commonly observed in the reproductive system [1], primary neoplasm originating from striated muscle is very rare [5]. This report describes a spontaneous rhabdomyosarcoma in a ferret.

A 5-year-old spayed male ferret showed a subcutaneous mass in the right lateral thoracic wall. This mass had gradually increased in volume, and reached a size of 7.5 × 4.5 × 4.5 cm after one year. Surgical resection of the mass and the right axillary lymph node was performed. The mass was relatively well demarcated. However, the surrounding muscle was partially affected by the neoplastic growth, thus the neighboring muscle was excised along with the mass. Grossly, the mass appeared fibrous and pale tan on cut surface. An area of necrosis was observed in the center of the mass. The lymph node was firm and lost its original architecture on cut surface. The resected mass and lymph node were fixed in neutral-buffered 10% formalin, embedded in paraffin, cut at 3 µm, and examined after stained with hematoxylin-eosin (HE) and phosphotungstic acid hematoxylin stain (PTAH). Antibodies used for immunostain were directed to the cytokeratin (AE-1/AE-3, prediluted, Dako, Denmark), vimentin (prediluted, Dako), desmin (prediluted, Dako), myoglobin (prediluted, Dako) and skeletal muscle type creatine phosphokinase (mmCPK, 1: 100, Biogenesis, UK). For electron microscopy, formalin-fixed samples were post-fixed in osmium tetroxide and embedded in epoxy resin. Ultra-thin sections were double-stained with uranyl acetate and lead citrate, and examined with a transmission electron microscope (H-8100, Hitachi, Japan).

Microscopic examination revealed that the neoplasm proliferated in the subcutis with invasion into the surrounding muscle and connective tissues. A packed bundle of large round, polygonal, or spindle-shaped neoplastic cells with

abundant eosinophilic cytoplasm were arranged interwoven, and the cytoplasm of some neoplastic cells contained fine fiber (Fig. 1) which were stained blue with PTAH. The nuclei containing one or several large nucleoli, were round to ovoid, occasionally bizarre, and varied in size. Mitoses were rare (<1/High powered field). Some neoplastic cells appeared like a tadpole or to be multinucleated. In the axillary lymph node, there were frequent areas of massive infiltration and proliferation of neoplastic cells, although no apparent invasion of the tumor into the lymphatic vessels was not indicated in the primary site. Immunohistochemically, most of neoplastic cells were strongly positive for vimentin, desmin and myoglobin (Fig. 2A), but negative for cytokeratin. The cells were almost granularly positive for mmCPK in the cytoplasm (Fig. 2B).

Ultrastructurally, the neoplastic cells contained numerous mitochondria and various amounts of parallel-arranged myofibrils (approximately 15 nm in diameter) with focal

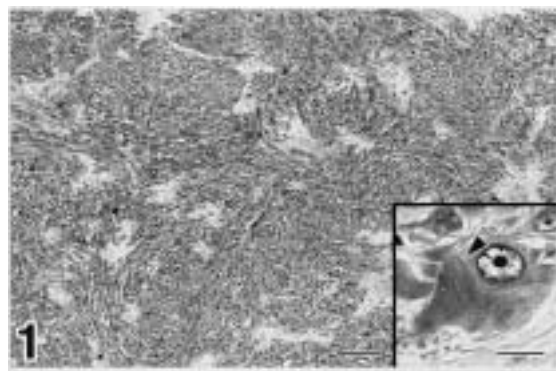


Fig. 1. Histopathology of tumor. Neoplastic cells are arranged in interwoven pattern. HE. Bar=250 µm. Insertion: The polygonal neoplastic cell contains fine fibers (arrowhead) in the cytoplasm. HE. Bar=10 µm.

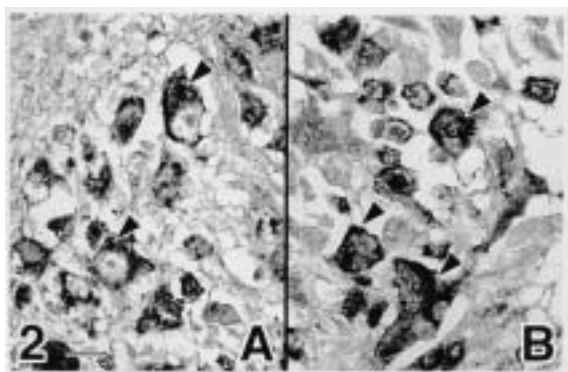


Fig. 2. Immunohistochemistry for myoglobin (A) and mmCPK (B). In both, positive reactions (arrowheads) are observed in the cytoplasm of neoplastic cells. Bar=10 μ m.

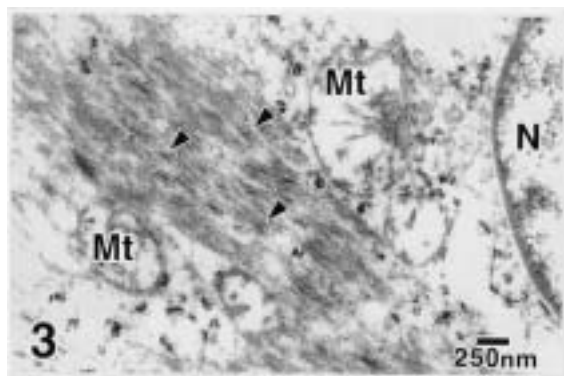


Fig. 3. Ultrastructures of the neoplastic cell. Note abundant myofibrils in parallel arrangement with focal density resembling the Z-band (arrowheads). Mt: Mitochondria, N: Nucleus, Bar=250 nm.

density resembling the Z-band in the cytoplasm (Fig. 3).

We diagnosed the case as rhabdomyosarcoma based on the histological, immunohistochemical and ultrastructural features. There have been a few previous reports of rhabdomyosarcoma in ferrets but no detailed descriptions were available for histological features, immunohistochemistry, or ultrastructures of the tumor. In a previous report, rhabdomyosarcoma of a ferret developed in the lateral thoracic subcutis [4] similar to our case, thus the thoracic subcutis

may be a common site for this tumor. However, further investigations should be required to define the prevailed site of this tumor occurrence in ferret.

The neoplastic cells in the present case had abundant cytoplasm and distinct myofibrils with focal density resembling the Z-band on the observation with electron microscope. In addition, mitosis was uncommon. Therefore, the case may be relatively well-differentiated muscle tumor. Although it was necessary to distinguish the present case from rhabdomyoma because of its low mitotic index, in canine rhabdomyosarcomas the mitotic index varies from low to very high [2], moreover, severe cellular atypia, infiltrative growth and neighboring lymphatic metastasis were observed in the present case. Based on these observations, we diagnosed this case as rhabdomyosarcoma.

Rhabdomyosarcoma is rare in domestic animals and humans; however, misdiagnosis is sometimes unavoidable because of its histological variety [2]. Immunohistochemical techniques and electron microscopic observation have been used to accurately identify the origin of neoplasm, especially sarcoma in soft tissues including rhabdomyosarcoma [2]. In human rhabdomyosarcoma, myoglobin was detected in 30% of embryonic and in 67% of alveolar types, respectively. These are higher percentages than those diagnosed by the presence of cross-striations with a light microscope. The mmCPK antibody was slightly more sensitive than the antibody for myoglobin, and a 60% positive percentage was obtained when both specificities were used [3]. Examinations of cytoplasmic myofibrils and immunoreactivities of desmin, myoglobin, and mmCPK will be recommendable to confirm the diagnosis of rhabdomyosarcoma, in ferrets as well as in other animals.

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