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BRIEF COMMUNICATIONS and CASE REPORTS

Cutaneous Lymphoma in a Ferret (*Mustela putorius furo*)

X. LI, J. G. FOX, S. E. ERDMAN, AND D. G. ASPROS

Key words: Ferrets; lymphoma; skin.

Ferrets (*Mustela putorius furo*) have been increasingly used as laboratory animals for biomedical research and are becoming popular as pets. Consequently, the biology, diseases, and tumor incidence of ferrets are being described more frequently.^{1,4,5,10} From 1950, when the first neoplasm was reported in ferrets, to 1979, approximately 20 cases of different types of neoplasms were documented in ferrets.¹ To date, of the more than 250 cases of various neoplasms reported in ferrets, about 20% of them are lymphomas.^{1,4,5,10} Lymphomas appear to be common in ferrets, and a viral etiology has been suspected.^{4,5} However, cutaneous lymphoma in ferrets has not been well documented. In this report, we describe a spontaneous case of cutaneous lymphoma in a 5-year-old male neutered fitch ferret.

The ferret was born in 1988 and was one of three pet ferrets in a household, all of which were vaccinated regularly against canine distemper and rabies. The other two ferrets were asymptomatic, one of which was a littermate of the ferret described in this report. In September 1992, the ferret had slight weight loss and a reduction in the quantity and quality of the hair coat. By January 1993, a 1.5-cm-diameter raised cutaneous plaque was noted over the lumbar spine. A fine-needle biopsy of the plaque established a presumptive diagnosis of cutaneous lymphoma. A blood sample was taken via jugular vein using manual restraint, and a complete blood cell count revealed a low normal count of lymphocytes (945/ μ l).⁵ Analysis of serum chemistry indicated an increased level of blood glucose (369 mg/dl); other parameters, such as total protein (5.4 g/dl), albumin (2.7 g/dl), and globulin (2.7 g/dl), were all within normal limits.⁵ Radiography of the abdomen revealed the cutaneous plaques as a soft tissue mass at the level of the 4th lumbar vertebra, and thoracic radiographs depicted a generalized cardiomegaly. One month later, another 1-cm-diameter cutaneous nodule was noticed adjacent to but slightly caudal to the initial plaque. Physical examination and radiography revealed no evidence of metastasis to or involvement in any other tissues or organs.

The cutaneous masses were excised, fixed in 10% neutral buffered formalin, processed by routine methods, cut in 5- μ m-thick sections, and stained with hematoxylin and eosin (HE). A staging system that was developed for canine lymphomas has been utilized for ferret lymphomas.^{2,4} According to this system, stage I lymphomas involve a single site only, stage II involves multiple noncontiguous sites on the same side of the diaphragm, stage III involves spleen and lymph node only on both sides of the diaphragm, and stage IV involves

multiple sites on both sides of the diaphragm. Grades and histopathology of this case utilized a working formulation for the non-Hodgkin's lymphomas established by the National Cancer Institute.^{4,8} The formulation separates the non-Hodgkin's lymphomas into 10 major types and three grades based on morphologic criteria. Types A-C are low-grade, D-G are intermediate-grade, and H-J are high-grade malignancies.

Histologically, the cutaneous plaque and nodule consisted of predominantly large and occasionally small to medium-sized lymphoid cells with little stroma located primarily in the deep dermis and subcutis (Fig. 1). The cells were arranged in diffuse compact cellular sheets or lobules with multifocal compressing, entrapping, or dissecting the adjacent adnexal structures, adipose tissues, and collagen bundles. The cells were round to oval, with scant (often a narrow rim) amphophilic to basophilic cytoplasm. The nuclei were large and round to oval (i.e., noncleaved), with a slight to moderate variation in size; euchromatic chromatin was coarsely clumped. The nucleoli were prominent, distinctive, one to multiple, and mostly eosinophilic and sometimes were located adjacent to the nuclear membrane on the short axis of the oval nuclei. There was a very high mitotic index, up to 20 mitotic figures/high-power field (400 \times). There was mild multifocal necrosis of individual or clusters of the lymphoid cells within the compact cellular sheets or lobules. There was multifocal invasion of the lymphoid cells into the subjacent skeletal muscle and the superficial dermis. The overlying epidermis was thin, one to three cell layers, with little keratin debris on the surface.

According to the history and the cytologic, hematologic, radiographic, and histologic findings, a stage I cutaneous lymphoma of diffuse large noncleaved cells (type G, intermediate grade) was diagnosed in this case. One could argue that this case might represent a cutaneous manifestation of a multicentric lymphoma or a lymphoproliferative disease associated with Aleutian disease virus (ADV).^{4,5,7,9,11} However, the cutaneous involvement without evidence of multicentric neoplastic development and a normal level of serum globulins in this case do not support that alternative. Elevated serum globulin, a hallmark of the ADV-associated disease in ferrets, was not observed in this case.⁹ Increased blood glucose has been associated with many diseases or physiologic perturbations, but the exact cause in this case is unknown.³

Lymphomas are common in humans and many animal

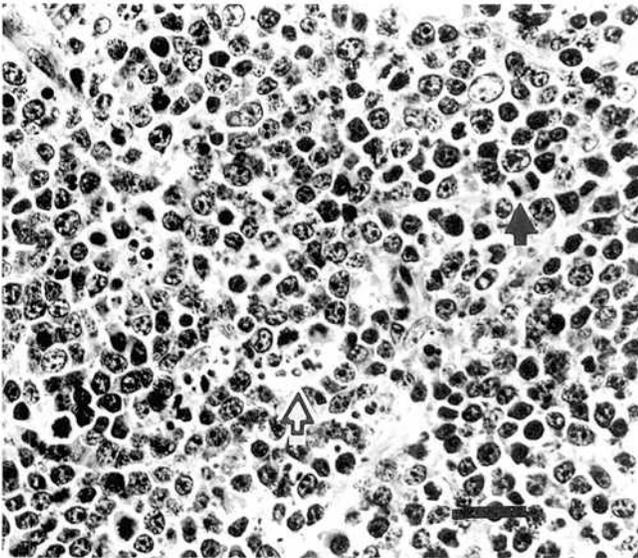


Fig. 1. Skin; ferret. Cutaneous lymphoma consists of a compact cellular sheet of predominantly large round to oval lymphoid cells mixed with some necrotic cells (open arrow). The cytoplasm is scant and amphophilic to basophilic. The nuclei are round to oval (noncleaved), with coarsely clumped to euchromatic chromatin and high mitotic index (solid arrow). The nucleoli, one to multiple, are prominent, round to oval, and distinctive. HE. Bar = 54 μ m.

species, but cutaneous manifestations are uncommon.^{1,4-7,11} In humans, the cutaneous lymphomas are mostly classified as the Sezary syndrome and epidermotropic lymphoma (mycosis fungoides).¹¹ The Sezary syndrome is a hairy T-cell leukemia with a prominent cutaneous involvement. In epidermotropic lymphoma, individuals or clusters of atypical T-lymphocytes invade primarily the epidermis and the epidermis-dermis junction of skin of humans and animal species such as dogs, cats, and hamsters.^{6,7} In this ferret, the neoplastic cells with round nuclei were present in the dermis and subcutis and absent from the epidermis. In bovine species, anatomic locations of the lymphomas correlate with the epidemiologic features of the disease; this correlation has not been shown in ferrets or other species.⁷ Cutaneous lymphomas occur mostly in young adult cattle and progress eventually into multicentric forms and vice versa.⁷ A lymphoma involving the prepuce and inguinal lymph node in a ferret was briefly mentioned in a tabulated series of ferret cutaneous tumors, but details were not provided.¹⁰

Lymphomas in ferrets have been reviewed, and in some cases have been staged, graded, and histologically classified.^{1,4,5} Peripubescent ferrets tend to have rapidly progressive stage IV high-grade immunoblastic lymphomas and small noncleaved cell types, whereas adult ferrets tend to have stage II or IV low-grade lymphomas of diffuse small cell type and stage IV high-grade lymphomas of small noncleaved or polymorphic cell type.⁴ The polymorphic cell lymphomas in fer-

rets were morphologically similar to certain lymphoid hyperplasia and lymphomas associated with virus infections in humans and other animals.⁴ In this adult ferret, the lymphoma appeared to be a stage I intermediate grade and large noncleaved cell type. At present, a retrovirus etiology is suspected for certain ferret lymphomas.⁴

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