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Cutaneous Epitheliotropic Lymphoma In A Baboon (*Papio spp.*): A Case Report And A Brief Literature Review

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Abstract

Cutaneous epitheliotropic lymphoma (CEL) has not been reported in non-human primates. We report the first case of CEL in a 9 year old baboon. The phenotype of the neoplastic cells in this baboon is similar to CEL in humans (CD3+, CD4+, CD8-), and different from dogs (CD3+, CD4-, CD8+).

Keywords

Skin; Mycoses Fungoides; T-Lymphocytes; Monkey; Primate

INTRODUCTION

Cutaneous epitheliotropic lymphoma (CEL) is a rare neoplasm of T-cell lymphocytes with a tropism for epidermis and adnexal components [1–4]. CEL, or epidermotropic lymphoma [5, 6] was first reported in humans as a condition called mycosis fungoides (MF) [7]. CEL is extremely rare in non-canid species [4]; there have been no reports of CEL in non-human primates (NHPs). We present a case of CEL in a 9 year old baboon and present a brief review of CEL in veterinary literature.

CASE REPORT

The 9-year-old, female baboon (*Papio spp.*) was maintained at the Southwest National Primate Research Center and presented with raised pruritic lesions on the right forearm skin. The animal was treated with cephalexin (538.5mg, PO BID, Lupin Pharmaceuticals) for one week. The lesion persisted and, following the results of a skin punch biopsy, the animal was

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euthanized two months later. All animal care and procedures were approved by the Texas Biomedical Research Institute Institutional Animal Care and Use Committee.

A complete necropsy was performed; except for the skin and axillary lymph node (enlarged), the rest of the organs were grossly within normal limits. Skin (biopsy and necropsy specimens) and axillary lymph node samples were fixed in 10% neutral buffered formalin, processed conventionally, embedded in paraffin, cut at 5 microns, stained with hematoxylin and eosin, and evaluated by board-certified veterinary pathologists. Additional sections were prepared for immunohistochemical labeling for CD3, CD4, CD8, CD20, and CD68 markers using standardized protocols. The specific dilutions and details of the antibodies are shown in Table 1. Paraffin scrolls were submitted for qualitative ultrasensitive QPCR for detection for Human T-cell lymphotropic viruses (HTLV) and Simian T-cell lymphotropic viruses (STLV) specifically: HTLV-I, HTLV-II, STLV-I, STLV-II, STLV-III, STLV-PH969, and STLV-pp1664 to a commercial laboratory (Zoologix Inc. Chatsworth, CA).

Histological examination revealed the dermis, adnexal structures, and perivascular spaces were diffusely expanded and replaced by a poorly demarcated, infiltrative, neoplasm composed of sheets of round cells consistent with intermediate-sized lymphocytes (Figure 1A). The cells had distinct cell borders, indistinct cytoplasm, and oval to indented nuclei with dense to coarsely stippled chromatin (Figure 1B and C). Mitoses averaged 1 per 40x field; there was moderate anisokaryosis. Scattered eosinophils (Figure 1C), macrophages and rare multinucleated giant cells were present within the neoplasm. Neoplastic cells multifocally infiltrated into the epidermis and adnexal structures (hair follicles) (Figure 1B, 1D, E, F). The findings in the lymph node were consistent with lymphoid hyperplasia; no metastasis was noted. Immunohistochemically, in the skin, over 90% of the neoplastic cells were CD3+ (Figure 1D, E, F), CD4+ (Figure 1G), and uniformly CD8- (not shown). There were few clusters of CD20 expressing lymphocytes (less than 5%, Figure 1H) and scattered CD68+ macrophages (Figure 1I). The skin samples tested negative for HTLV-I, HTLV-II, STLV-I, STLV-II, STLV-III, STLV-PH969, and STLV-pp1664 by ultrasensitive qualitative QPCR.

The Texas Biomedical Northrup Library Collections were used to perform literature searches of printed books, eBooks, journals, conference proceedings, institutional repositories, and additional online databases including PubMed, Scopus, Web of Science, and Primate Lit.

DISCUSSION

We present the first report of CEL in a baboon (*Papio spp.*) which presented with gross lesions on forearm skin. CEL is a subgroup of epitheliotropic lymphoma which is a rare neoplasm of T cells with tropism to epidermis and adnexal structures [3, 4, 8]. CEL is characterized by [5, 9, 10] an abundance of CD3+ T-cells and their migration into the epidermis and adnexal structures of the skin [4, 11, 12], with the presence of infiltrates such as plasma cells, eosinophils, histiocytes, [5, 12–14] and frequent clustering of T lymphocytes around the dendritic cells forming Pautrier's microabscesses (not present in this case) [4, 11, 13, 15, 16]. In several studies analyzing CELs, canid species have been shown to

illustrate the CD3+CD4-CD8+ phenotype [4, 12, 17]. In contrast, human tissues with MF commonly react as CD3+CD4+CD8- [4, 12, 18]. Feline CEL frequently presents with the CD3+CD4-CD8- phenotype [19, 20]. In the present case CD3+CD4+CD8- reactivity in this baboon is similar to human patients with MF [12, 18]. The differences in the cellular phenotypes of the neoplastic cells may be clinically significant. In dogs with CD8+ CEL, the prognosis is usually poor, with mean survival time ranging from few months to 2 years [13, 21]. In contrast, in humans with CD4+ CEL have a favorable outcome (5 year survival > 75 %) [13, 22], compared to CD8+ CEL with much lower survival rates [22]. The etiology of the CEL and epitheliotropic lymphoma is unknown; however, HTLV and STLV have been implicated in human and NHP cases of T-cell lymphomas [23–25]. In the present case, the paraffin embedded skin samples were negative for the tested strains of STLV and HTLVs.

We performed an extensive literature review of the CEL cases in veterinary literature. CEL has been widely reported in dogs [13, 17, 26, 27] and cats [1]. However, reports of CEL in other species are rare and include cows [28–30], hamsters [31, 32], mice [6, 33], and single reports in a rat [5], ferret [34], squirrel [35], coati [12], cuscus [36], chipmunk [16], zebrafish [37], hedgehog [38], Tasmanian devil [39], opossum [14], marsh rice rat [4], and alpaca [40]. There are currently no reports of CEL in NHPs. In contrast, lymphosarcoma is one of the more common neoplasms reported in the NHP literature, including cases in rhesus macaques [41], owl monkeys [42, 43], marmosets [42], vervet monkeys [23], and baboons [44]. Although rare, CEL can occur in baboons (NHPs) and should be in the differential when evaluating skin lesions in NHPs. The present case demonstrates that CEL in NHPs may be antigenically more similar to human CEL than to CEL in other species such as dogs, and perhaps a more useful model of the disease.

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Figure 1.

A-I. Cutaneous epitheliotropic lymphoma in a baboon.

A) Skin. Neoplasm composed of sheets of round cells consistent with intermediate-sized lymphocytes with distinct cell borders, oval to indented nuclei with dense to coarsely stippled chromatin. H&E.

B) Rare areas of lymphocytes infiltrating the epidermis. H&E.

C) Scattered eosinophils are present admixed with the neoplastic cells. H&E.

D) Immunohistochemistry for CD3. Over 90% of the neoplastic cells are CD3+. DAB.

E) Immunohistochemistry for CD3. Note the tropism to epidermis and adnexal structures (hair follicle epithelium). DAB.

F) Immunohistochemistry for CD3. Note hair follicles surrounded and infiltrated by neoplastic cells. DAB.

G) Immunohistochemistry for CD4. Over 90% of the neoplastic cells are CD4+. DAB.

H) Immunohistochemistry for CD20. Note clusters of few (less than 5%) CD20+ lymphocytes. DAB. Inset: Higher magnification of CD20+ cells.

I) Immunohistochemistry for CD68. Note few (less than 5%) CD68+ macrophages. DAB. Inset: Higher magnification of CD68+ cells.

Table 1.

Immunohistochemistry antibody dilutions and clone information

Target Protein	Primary Antibody	Dilution	Clone
CD3	Rabbit anti-human, Polyclonal antibody	1:100	Polyclonal
CD4	Mouse anti-human, IgG ₁ Monoclonal antibody	Pre-diluted	4B12
CD8	Mouse anti-human, IgG _{2b} Monoclonal antibody	Pre-diluted	4B11
CD20	Mouse anti-human, Monoclonal antibody	1:200	L26
CD68	Mouse anti-human, IgG ₁ Monoclonal antibody	1:400	3F103