

Case 13

CASE NUMBER IDENTIFICATION OF SLIDE
194266-16 SLIDE 3

CONTRIBUTOR/INSTITUTION
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SIGNALMENT
15 year old female spayed feline Domestic Shorthair

HISTORY
This cat, who is owned by a veterinarian, has a history of two basal cell tumors over the past four years. There is also a history of atopic dermatitis treated initially with prednisolone. Treatment was transitioned to cyclosporine three years ago due to excessive polyphagia. In the last year, all medications were discontinued due to vomiting. Currently there is mild to moderate pruritus. In July 2016, a 2-3mm raised, partially alopecic papule was noted on the neck. Fine needle aspirate cytology was inconclusive. Two additional similar papules were noted on the neck in November 2016. All three papular lesions were surgically excised. The tissue was submitted to Cornell University for histopathologic evaluation. There is no history of lethargy, weight loss, or decreased appetite. Mild kidney disease is currently being monitored.

HISTOLOGIC FINDINGS:
Haired skin, left neck punch and masses (slide 3; 3 sections): All examined sections exhibit similar features. Severe infiltrating the dermis and extending into the subcutis are large numbers of small mature lymphocytes accompanied by smaller numbers of eosinophils. The infiltrate forms a band-like pattern in the superficial dermis with a perivascular to interstitial infiltrate in the deeper portions of the dermis and subcutis. Small numbers of lymphocytes extend into the deeper cutaneous trunci muscle. Multifocally throughout the infiltrate, there are nodular clusters of darker, more densely packed lymphocytes. The majority of lymphocytes are 1.5 times the size of an erythrocyte (small) with distinct cell borders, small amount of cytoplasm, hyperchromatic and occasionally folded nuclei. The lymphocytes forming the dense clusters have scant cytoplasm and darker, more hyperchromatic nuclei. Multifocally there is a Grenz zone along the dermal-epidermal border. However multifocally the lymphocytes infiltrate the epidermis. In general, this infiltrate is small numbers of individual lymphocytes however in some areas there are small clusters and plaques that resemble Pautrier's microabscesses. In the areas where lymphocytes infiltrate, there is fairly pronounced intercellular edema (spongiosis). Pilosebaceous units are present and many hairs are in anagen. Sebaceous glands are not consistently present in all of these units. Rarely, lymphocytes are noted in the outer root sheath of follicles. The lymphocytic infiltrate extends to all the specimen margins.

Immunohistochemistry was performed and the following antibodies were used against Pax-5, CD20, CD45B220, CD3, and IBA1

Pax-5, CD20 and CD45B220 are all markers for feline B cells. There is moderate to strong immunoreactivity present within the clusters of more densely packed hyperchromatic lymphocytes.

CD3 is a marker for T cells. There was moderate to strong immunoreactivity within most of the infiltrating lymphocytes, this included those within the dermis, subcutis and epidermis. The dense clusters multifocally scattered through the dermis and subcutis were not immunoreactive.

IBA1 is a marker for histiocytes. Large numbers of dermal dendritic cells between and among the lymphoid infiltrate show moderate to strong immunoreactivity. There is approximately 1 dendritic cell in a 4-5 cell population.

MORPHOLOGIC/ETIOLOGIC DIAGNOSIS:

Haired skin: Feline cutaneous lymphocytosis

DISCUSSION:

The histologic features and immunophenotyping are most consistent with cutaneous lymphocytosis (CL), sometimes referred to as pseudolymphoma or cutaneous lymphoid hyperplasia. CL is a rare disease in cats characterized by a dense proliferation of small T lymphocytes in the superficial and deep dermis. The cause of this proliferation is unknown, but some believe it to be an inflammatory response to various stimuli such as insect bites, infections, trauma and vaccinations. This theory is based on human cases of pseudolymphoma that have been linked to a variety of immune stimuli. Most human cases, though, are idiopathic. Historical findings in cats are often unremarkable but some cats have weight loss, hyporexia or anorexia, and lethargy. Grossly, the most common lesion is a solitary area of alopecia, erythema and scaling on the thorax. Multiple lesions can also occur, as well as plaques, crusting, nodules (as in this case), and ulcerations. Other locations include the legs, flank, neck (as in this case), abdomen and paw pads. Pruritis is reported in about half of the cases.

Histologic differentiation of CL from a small cell non-epitheliotropic cutaneous lymphoma (NECL) can be a challenge depending on the stage of CL. In contrast to NECL which has a bottom heavy appearance and arises in the deep dermis, CL starts in the superficial dermis, but can extend into the deep dermis. Cellular morphology is frequently similar with small, dense nuclei, compact chromatin and a small to moderate amount of pale cytoplasm. Additional similarities can include low mitotic rate and the presence of a Grenz zone. Some cases of feline CL, including our case, exhibit mild epitheliotropism including small intraepidermal aggregates resembling Pautrier's microabscesses. Immunophenotyping can help support the diagnosis of CL over NECL. The presence of a predominantly T lymphocytes with small aggregates of B lymphocytes is indicative of CL as NECL does not contain nodular aggregates of B cells.

In most cases of feline CL, there is acute development of lesions with slow progression of clinical signs and a stable quality of life. However, because some cats develop internal lesions and systemic signs of disease, feline CL may be an indolent form of T cell lymphoma. It has been proposed that the cutaneous lymphoproliferative diseases, including cutaneous lymphocytosis and cutaneous lymphoma, represent points on a continuum of lymphoproliferative disorders with monoclonal cutaneous lymphoma representing the extreme malignant end of the spectrum and polyclonal cutaneous lymphocytosis the benign end of the spectrum. Evidence supporting this theory includes the finding of clonal expansion of TCR gamma in 14 of 20 cats with CL, as well as five cats with confirmed involvement of multiple internal organs. It is not clear in these cats if the organ involvement develops from the cutaneous lesion or the cutaneous infiltrate is from the organ involvement. Unfortunately, histologic features and immunophenotyping don't aid in predicting which cats will have systemic involvement. The only factor

that seems to correlate with organ involvement is the presence of lethargy, anorexia and weight loss. Cats with these historical signs were more likely to develop involvement of internal organs. Certainly there is a lot more that needs to be learned about this entity in order for diagnostic pathologists to give a confident diagnosis and prognosis to clinicians. While additional cutaneous lesions have developed in this cat, surgical removal of these lesions has been curative for now and the cat is clinically doing well.

REFERENCES:

Gilbert, S. 2004. Clinical, morphologic and immunohistochemical characterization of cutaneous lymphocytosis in 23 cats. *Veterinary Dermatology*. 15: 3-12.

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Pariser, M. 2014. Feline cutaneous lymphocytosis: case report and summary of the literature. *Journal of Feline Medicine and Surgery*. 16: 758-763.