

Evaluation of Serum Thymidine Kinase Type 1 as a Diagnostic Biomarker in the Differentiation of Feline Lymphoma from Inflammatory Bowel Disease

VDI Laboratory



Introduction

Feline lymphosarcoma (LSA) often presents similarly to that of inflammatory bowel disease (IBD) making for a difficult diagnosis and subsequent treatment decisions.

VDI-TK measures thymidine kinase (TK) type 1 activity, which is involved in the synthesis of DNA precursors and is only expressed in S-G2 cells. In human and canine studies, serum TK levels correlate to the proliferative activity of tumor disease. The purpose of this study was to evaluate its effectiveness in cats to assist in the differential diagnosis of LSA from IBD.

Objectives

To compare serum thymidine kinase type 1 (TK) activity among cats with various forms of LSA, IBD, and healthy controls and to evaluate the use of TK for the diagnosis of various forms of LSA in cats.

Materials & Methods

VDI-TK Assay

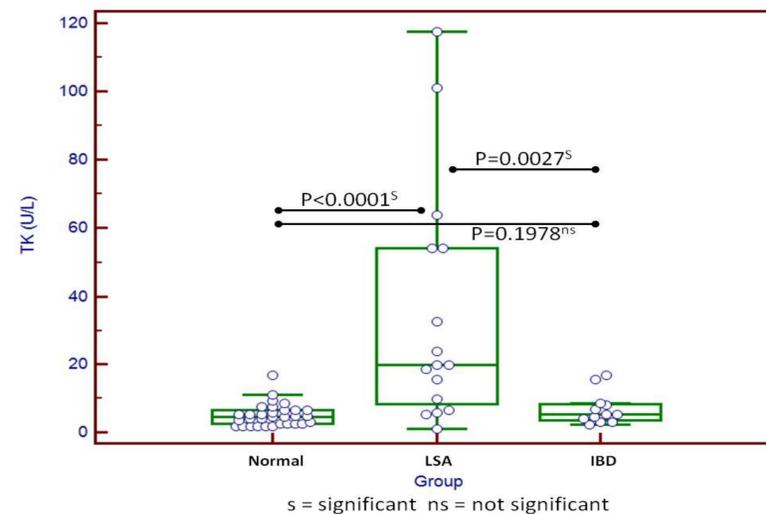
Serum TK was evaluated by Veterinary Diagnostics Institute. The assay is a competitive chemiluminescence immunoassay specific for cytosolic (TK1) isoenzyme. All samples were tested double-blinded.

LSA and IBD Groups

Cats that presented to various partner facilities between July 2010 to March 2011 were eligible for inclusion. Cats had to have confirmed disease by biopsy or other standard diagnostic regimen and prior to any medication.

Control Group

Cats obtained from Tufts and University of Missouri were enrolled as a control group. All cats were required to have an unremarkable physical examination, CBC, and biochemical profile.



Results

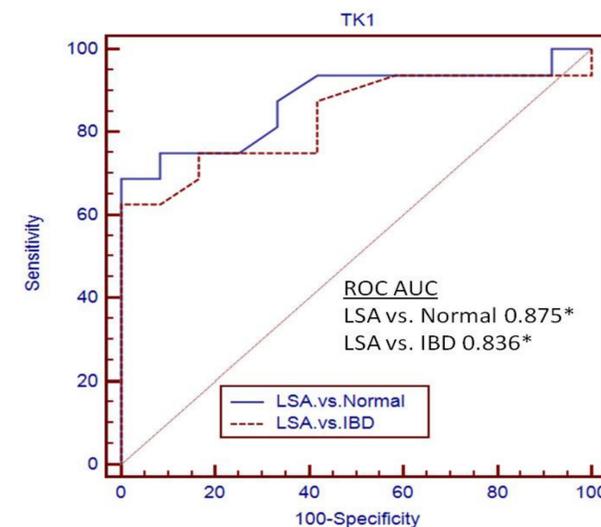
Study Population

A total of 59 cats met the criteria and were enrolled in this study, including 28 cats with disease (LSA n=16; IBD n=12) and 31 healthy control cats.

Comparison of Serum TK Among Groups

Serum TK concentration was significantly greater in the LSA group (median, Q1, Q3: 19.8, 8.1, 54.1 U/L) compared with the IBD (5.2, 3.5, 8.1 U/L) and healthy control groups (4.4, 2.6, 6.6 U/L). There was no significant difference in TK concentration between the IBD and healthy control groups.

A receiver operating characteristic (ROC) curve was used to determine the area under the curve (AUC). The AUC for TK1 in differentiating LSA from the healthy control group was 0.875 (95% CI, 0.741 – 1.000). The AUC for TK1 in differentiating LSA from the IBD group was 0.836 (95% CI, 0.683 – 0.989). This difference was not significant. The optimum cutoff value that maximized Youden's J statistic (sensitivity + specificity-1) was 9.2 U/L with a sensitivity of 75% and specificity of 91%.



Interval Likelihood Ratios

TK Interval (U/L)	Positive	Negative	Likelihood Ratio	Sensitivity	Specificity
0 – 5	1	23	0.117	1.00	0.00
5 – 9	3	15	0.537	0.91	0.58
9 – 15.4	2	3	1.792	0.75	0.91
15.5 – 24	4	2	5.375	0.68	0.95
24+	6	0	∞	0.63	1.00
TOTAL	16	43			

Discussion

In this investigation, we found that TK with a sensitivity of 75% and specificity of 91% is an effective biomarker in detecting feline lymphoma. Given the high specificity it is particularly good as a “rule-in” diagnostic for lymphoma.

The differential diagnosis of feline LSA versus IBD is a challenging diagnostic workup usually requiring an invasive procedure. More and more pet owners are seeking alternatives due to both cost and potential harm to their pet. For those willing pet-owners, the decision to pursue biopsy is made easier when greater evidence points to cancer as being the more likely cause of the illness. The use of a simple blood diagnostic test is attractive as its non-invasiveness and low cost provide veterinarians an alternative.

Additional investigations are needed to confirm these findings and to examine a wide range of medical conditions and their effects on TK concentrations.

References

- Hall, E J. (2009) “Inflammatory bowel disease in dogs and cats.” Hills’s Pet Nutrition. <https://protrain.hs.llnwd.net/e1/.../GI%20technical%20booklet.pdf>.
- Kiupel, M. et al. “Diagnostic Algorithm to Differentiate Lymphoma From Inflammation in Feline Small Intestinal Biopsy Samples.” *Vet Pathol.* (2011). 48: 212.
- Little, S (2002) “Feline Inflammatory Bowel Disease.” The Winn Feline Foundation. http://www.winnfelinehealth.org/Pages/Feline_IBD_Web.pdf.
- Scott, K., Zoran, D., Mansell, J., Norby, B. and Willard, M. (2011), Utility of Endoscopic Biopsies of the Duodenum and Ileum for Diagnosis of Inflammatory Bowel Disease and Small Cell Lymphoma in Cats. *Journal of Veterinary Internal Medicine*, 25: 1253–1257. doi: 10.1111/j.1939-1676.2011.00831.x
- Tams, Todd R. “Inflammatory Bowel Disease and Intestinal Lymphoma in Cats.” Presented at Atlantic Coast Veterinary Conference. (2001). <http://www.vin.com/vindbpub/searchpb/proceedings/pr05000/pr00427.htm>
- Washabau, R., et al. The WSAVA International Gastrointestinal Standardization Group. (2010). Endoscopic, Biopsy, and Histopathologic Guidelines for the Evaluation of Gastrointestinal Inflammation in Companion Animals. *Journal of Veterinary Internal Medicine*, 24: 10–26. doi: 10.1111/j.1939-1676.2009.0443.x
- Zwingenberger, A. L. et al. “Ultrasonographic Evaluation of the Muscularis Propria in Cats with Diffuse Small Intestinal Lymphoma or Inflammatory Bowel Disease.” *J Vet Intern Med* (2010) 24: 289-292.

Acknowledgments

Special thanks to our contributing institutions:

- Southern California Veterinary Specialty Hospital, Irvine, CA
- Cummings School of Veterinary Medicine at Tufts University, North Grafton, MA
- College of Veterinary Medicine, University of Missouri, Columbia, MO
- Burnt Hills Veterinary Hospital, Burnt Hills, NY
- Guilderland Animal Hospital, Altamont, NY
- Cats on Call Hospital, Scarborough, ME
- Serenity Animal Hospital, Sterling Heights, MI
- Cat Clinic North, Grand Rapids, MI
- Animal Specialty of Cook County, Des Plaines, IL