Improving Prediction of Canine Lymphoma Disease Status & Prognostication

Timothy M. Fan, DVM, PhD, DACVIM (Oncology, Internal Medicine)
University of Illinois at Urbana–Champaign

In the Literature

Chalfon C, Martini V, Comazzi S, et al. Minimal residual disease in lymph nodes after achievement of complete remission predicts time to relapse in dogs with large B-cell lymphoma. *Vet Comp Oncol*. 2019;17(2):139-146.

FROM THE PAGE …

The sensitive and reproducible detection of cancer is essential for accurate disease diagnosis, monitoring, and prognostication and can collectively elevate the quality of care provided for cancer patients. Molecular techniques (eg, flow cytometry, PCR testing, genome sequencing) can detect minimal residual disease (MRD; ie, low numbers of lymphoma cells) burdens on diagnosis and following definitive therapies. Over the past decade, molecular diagnostics in veterinary medicine have been leveraged for the diagnosis and management of common cancers, including lymphoma, transitional cell carcinoma, and hemangiosarcoma.[1-3] The most significant molecular advancements have been in canine lymphoma with flow cytometry and PCR for antigen receptor rearrangements. Although sufficient evidence supports the use of molecular diagnostics for canine lymphoma diagnosis,[4,5] less information is available regarding

their applicability for lymphoma disease prognostication.[6,7] As such, additional investigations are necessary to define the clinical relevance of lymphoma disease detection by molecular techniques and illustrate how the identification of low numbers of lymphoma cells following systemic treatment may influence time to relapse (TTR).

This prospective study examined the prognostic utility of flow cytometry for identifying MRD (CD21+ lymphoma cells) in affected lymph nodes of dogs with diffuse large B-cell lymphoma after achieving complete clinical remission following treatment with systemic chemotherapy and autologous vaccine therapy. Twenty-two dogs were included for calculating TTR. Lymph node aspirates, peripheral blood, and bone marrow samples were collected from dogs that achieved complete clinical remission after systemic therapies for lymphoma and were subjected to flow cytometric analysis for identifying CD21+-expressing cells (ie, putative residual lymphoma cells). Only lymph node infiltration by CD21+ cells was predictive of TTR; dogs with >0.5% CD21+ cells experienced the shortest time to relapse (118 days). Based on these findings, MRD assessment by flow cytometry on lymph node samples may provide prognostic information regarding TTR in dogs with diffuse large B-cell lymphoma that have achieved complete clinical remission following systemic therapies.

… TO YOUR PATIENTS

Key pearls to put into practice:

1 MRD (ie, low levels of lymphoma cells in the body) is thought to be responsible for lymphoma relapse following systemic therapies.

2 MRD can be detected through sensitive molecular techniques and, for lymphoma, is commonly identified via flow cytometry and/or PCR testing.

3 The presence and extent of MRD detected following systemic therapies can influence overall treatment efficacy, including durability of therapeutic response (ie, TTR).

4 Molecular diagnostics are expected to advance veterinary care for cancer patients through improvements in disease diagnosis, monitoring, and prognostication.

References

1. Mochizuki H, Shapiro SG, Breen M. Detection of BRAF mutation in urine DNA as a molecular diagnostic for canine urothelial and prostatic carcinoma. *PLoS One*. 2015;10(12):e0144170.

2. Burnett RC, Vernau W, Modiano JF, Olver CS, Moore PF, Avery AC. Diagnosis of canine lymphoid neoplasia using clonal rearrangements of antigen receptor genes. *Vet Pathol*. 2003;40(1):32-41.

3. Dowling M, Samuelson J, Fadl-Alla B, et al. Overexpression of prostate specific membrane antigen by canine hemangiosarcoma cells provides opportunity for the molecular detection of disease burdens within hemorrhagic body cavity effusions. *PLoS One*. 2019;14(1):e0210297.

4. Lana SE, Jackson TL, Burnett RC, Morley PS, Avery AC. Utility of polymerase chain reaction for analysis of antigen receptor rearrangement in staging and predicting prognosis in dogs with lymphoma. *J Vet Intern Med*. 2006;20(2):329-334.

5. Thalheim L, Williams LE, Borst LB, Fogle JE, Suter SE. Lymphoma immunophenotype of dogs determined by immunohistochemistry, flow cytometry, and polymerase chain reaction for antigen receptor rearrangements. *J Vet Intern Med*. 2013;27(6):1509-1516.

6. Rao S, Lana S, Eickhoff J, et al. Class II major histocompatibility complex expression and cell size independently predict survival in canine B-cell lymphoma. *J Vet Intern Med*. 2011;25(5):1097-1105.

7. Aresu L, Arico A, Ferraresso S, et al. Minimal residual disease detection by flow cytometry and PARR in lymph node, peripheral blood and bone marrow, following treatment of dogs with diffuse large B-cell lymphoma. *Vet J*. 2014;200(2):318-324.