

Making Sense of Lymphoma Diagnostics in Small Animal Patients



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KEYWORDS

- Lymphoma • Cytology • Immunophenotyping • Flow cytometry
- PCR for clonal antigen receptor gene rearrangement (PARR)
- Immunohistochemistry/immunocytochemistry

KEY POINTS

- Cytologic assessment is diagnostic in most cases of diffuse large B-cell and diffuse lymphoblastic lymphoma in dogs.
- The cytologic diagnosis of lymphoma is more challenging in cats than in dogs.
- Although cytology is useful for staging lymphoma, histopathology is necessary for classification and grading.
- Immunophenotyping by flow cytometry allows evaluation of lymphocyte populations using a panel of antibodies, and serves as an adjunctive tool for both diagnosis and prognosis.
- Polymerase chain reaction (PCR) to detect clonal antigen receptor gene rearrangement (PARR) is a relatively new test in veterinary medicine that has strong potential for supporting the diagnosis of lymphoma. However, false-positive and false-negative results may confound the diagnosis, and PARR is less sensitive in cats than in dogs.
- Immunohistochemistry and immunocytochemistry should not be used as stand-alone diagnostic techniques, nor should an interpretation be based on a single antibody label.

INTRODUCTION

Lymphoma is the most common hemolymphatic malignancy in dogs and cats and, similar to lymphoma in people, is a heterogeneous disease with variable clinical signs and response to therapy.¹ Patient genetics, immunocompetence, location, and morphologic subtype all contribute to the heterogeneity of the disease and prognosis (**Box 1**).

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Box 1

Clinical evaluation of lymphoma

Several options are available for the diagnosis and characterization of lymphoma. This review helps in choosing the best test or tests for the patient.

Anatomically, lymphoma can be characterized as multicentric, alimentary, mediastinal, or extranodal. In dogs, multicentric lymphoma accounts for 80% to 85% of reported cases, and diffuse large B-cell lymphoma is the most common histomorphologic variant.² However, other types of B-cell lymphomas as well as T-cell lymphomas also are frequently diagnosed. The prognosis of lymphoma variants in dogs depends not only on the type of neoplastic lymphocyte but also on the location, characteristics of the cells, and the stage of disease. In cats, the diagnosis is more challenging because lymphoma more commonly affects extranodal sites, particularly the alimentary and upper respiratory tract.^{3,4} Lymphoma affecting the gastrointestinal tract is common but particularly challenging to diagnose, owing to the relative inaccessibility for sampling and potential progression from lymphocytic inflammation to neoplasia. Other types of lymphoma in cats often contain a heterogeneous population of neoplastic lymphocytes plus reactive lymphocytes, plasma cells, and other inflammatory cells.

The diagnosis of lymphoma classically depended on morphologic characteristics identified by cytology and/or histopathology. In recent years, additional assays such as immunocytochemistry (ICC), immunohistochemistry (IHC), immunophenotyping by flow cytometry, and polymerase chain reaction (PCR) to detect clonal antigen receptor gene rearrangement (PARR) have been used to assist in the diagnosis of lymphoma and to classify lymphoma for prognostic purposes. Diagnostic tests are not perfectly sensitive or specific; therefore multiple assays are often used in conjunction or in sequence to enhance the accuracy of diagnosis and assist with prognosis. This article considers the utility and pitfalls of each diagnostic tool (**Box 2**).

CYTOLOGY

Cytologic examination of blood films and samples obtained by fine-needle aspiration (FNA) of tissues or fluids is commonly used in the diagnosis of lymphoma in dogs and cats. Advantages of cytology are that sample collection and slide examination are rapid and can be performed in-house with the minimal resources of glass slides, a Romanowsky stain such as Diff Quick or Wright Giemsa, and a high-quality microscope. Limitations of FNA in comparison with an incisional or excisional biopsy are that FNA does not allow assessment of tissue architecture, and material for additional studies (eg, IHC) is unavailable. Blood sampling and aspiration of superficial masses

Box 2

Tools available for the diagnosis and characterization of lymphoma

Cytology

Histopathology

Immunocytochemistry and immunohistochemistry

Phenotyping by flow cytometry

Polymerase chain reaction to detect clonal antigen receptor gene rearrangement (PARR)

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