Cytologic Evaluation of Lymph Nodes in Dogs and Cats

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Fine-needle aspiration cytology of lymph nodes is a valuable aid in achieving a diagnosis or in guiding additional testing. Indications for aspirating lymph nodes include unexplained enlargement of a single lymph node or generalized lymphadenopathy. Regional lymph nodes may be aspirated as part of the staging process for certain neoplasms. Mandibular lymph nodes drain the oropharynx and typically have some degree of reactivity. It is best to avoid these nodes unless only they are enlarged. Also avoid very large lymph nodes and the center of any large node where necrosis may be present. Regarding internal lymph nodes, mesenteric nodes drain the gastrointestinal tract and often are reactive, a fact to consider when evaluating aspirates from this location.

Large lymphocytes/lymphoblasts are fragile cells, and proper preparation of slides is critical to avoid lysing cells. Aspirated material should not be allowed to dry on a slide as the sample will be too thick. The sample may be spread using another slide held at an angle, or another slide can be placed on top of the sample and the 2 slides gently pulled apart. Be gentle and apply only minimal pressure. If the nodules are surrounded by fat, and if slides contain only perinodal fat and very few cells, do not attempt to evaluate it. When aspirating mandibular lymph nodes, submandibular salivary gland may be aspirated and consists of cohesive clusters of glandular cells. If this occurs, sampling a different lymph node may be indicated.

Quick stains, such as Diff-Quik®, are good stains if well maintained and not contaminated with material from other slides and if proper staining procedures are followed. Quick stains typically are good nuclear stains, but sometimes cytoplasmic features, such as mast cell granules, do not stain well.

NORMAL LYMPH NODE

In normal lymph nodes small lymphocytes, about 7-10 µm in diameter and smaller than neutrophils, comprise 75-95% of the cells. Medium-sized lymphocytes or prolymphocytes (9-15 µm) and large lymphocytes/lymphoblasts (>15 µm) comprise the remaining lymphocytes. A few plasma cells, macrophages, mast cells, neutrophils, and eosinophils may be present. Lymph node size is important, because even if cells are present in normal proportions, lymphoid hyperplasia must be present if a lymph node has doubled in size.

REACTIVE LYMPHOID HYPERPLASIA

In reactive nodes, small lymphocytes comprise >50% of the lymphoid cells, but lymphoblasts and plasma cells are increased. Plasmacytosis may be more prominent that the increase in lymphoblasts in animals with fungal infections, such as with nasal aspergillosis. If the node is draining a tumor, lymphoblasts may be more prominent than plasma cells. Macrophages and mast cells also are increased in reactive nodes. If hyperplasia is present in a single lymph node, the site being drained should be examined for a lesion. If present in multiple lymph nodes, then systemic causes, eg, systemic infections or immune-mediated diseases, should be considered. Free nuclei and cytoplasmic fragments frequently are seen in lymph node aspirates containing increased large lymphocytes. In cats, syndromes involving lymph node hyperplasia include idiopathic lymphadenopathy of young cats, which may mimic lymphoma because medium-sized and large lymphoid cells comprise the majority of cells. In these cats, lymph nodes typically regress spontaneously within 4 months. Some cases are associated with FIV infection. Other causes of generalized lymphadenopathy with reactive hyperplasia in cats include bartonellosis and FIV infection.

LYMPHADENITIS

Inflammatory cells may drain into lymph nodes or nodes may be the site of inflammation. In neutrophilic lymphadenitis, neutrophils comprise >5% of cells when the node is draining a lesion and often >20% when the node is a site of inflammation. Causes include bacterial infection, necrosis within the node, and certain metastatic tumors, eg, squamous cell carcinoma. If eosinophils are >3%, consider hypersensitivity disorders, including parasitic infections, and tumors sometimes associated with eosinophilic infiltrates (eg, mast cell tumor, lymphoma). In cats with hypereosinophilic syndrome widespread infiltration of tissues, including lymph nodes, may occur. In dogs, we have noted an increase in eosinophils in irradiated nodes. Histiocytic lymphadenitis is characterized by an increase in macrophages, and sometimes inflammatory giant cells are noted. If both neutrophils and macrophages are increased, the term “pyogranulomatous” is used. Granulomas, however, are a histologic, rather than a cytologic, feature. Macrophages sometimes appear like epithelial cells with large round nuclei and abundant cyto-
plasm that does not contain phagolysosomes; these cells are termed epithelioid macrophages. Cause of histiocytic and pyogranulomatous inflammation include infections with fungi, higher bacteria, such as Actinomyces, Mycobacterium, protozoal organisms, such as Leishmania, Neorickettsia, and Prototheca. Often, elements of reactive lymphoid hyperplasia, particularly plasmacytosis, accompany histiocytic or pyogranulomatous lymphadenitis.

LYMPHOID NEOPLASIA

In dogs, the most frequent form of lymphoma is multicentric lymphoma, characterized by generalized lymphadenopathy. Lymph node aspirates often are diagnostic and typically large lymphocytes with prominent nucleoli and basophilic cytoplasm comprise the majority of cells. Lymphomas composed of medium-sized lymphocytes are more challenging to diagnose cytologically, and small cell lymphomas require histopathologic examination or other tests for confirmation. In cases where the diagnosis cannot be made cytologically, confirmatory tests include histopathologic examination, immunophenotyping, and PCR tests for clonality. In cats, the most frequent form of lymphoma seen in the US is the alimentary form, and cats are negative for FeLV. However, multicentric lymphoma does occur. A particularly aggressive form of lymphoma in cats is large granular lymphocyte (LGL) lymphoma. These tumors typically arise in the GI tract or intra-abdominal lymph nodes and metastasize to liver and spleen. The granules in LGLs, which are either natural killer (NK) cells or cytotoxic T cells, contain highly toxic substances, such as perforins, and the prognosis for this aggressive tumor is poor. Recently, a Hodgkin’s-type lymphoma has been identified in cats.

METASTATIC NEOPLASIA

Metastatic disease is diagnosed cytologically by finding tissue cells that are not normally found in a lymph node. Lymph nodes with metastatic tumors are not always enlarged. The lack of tumor cells in a cytologic sample also does not rule out metastasis, which may be focal. The easiest metastatic tumors to identify are carcinomas and adenocarcinomas because of the large size of the cells and the formation of cohesive clusters. Unless there are high numbers of sarcoma cells present, these tumors are more difficult to detect, and biopsy often is needed. Metastatic melanoma can be diagnosed if a pleomorphic population of melanin-containing melanoblasts is identified. However, care must be taken not to confuse macrophages containing melanin (melanophages) or hemosiderin (hemosiderophages) with tumor cells. Likewise, because mast cells may be increased in reactive lymphoid hyperplasia, the finding of increased mast cells in a node from an animal with a mast cell tumor does not necessarily signify metastasis. Large aggregates of mast cells, effacement of the node by mast cells, or atypical mast cell morphology should be identified to diagnose metastasis. Finally, round cell tumors, including some forms of histiocytic sarcoma and hemic neoplasms, can be found in lymph nodes. Round cell tumors are typically easy to identify in lymph nodes; however, identifying the specific type of round cell tumor may require immunocyto/histochmistry.

ADDITIONAL READING


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