Cytology of the spleen: basic and advanced cases

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Fine-needle aspiration (FNA) cytology of splenic masses/nodules and enlarged spleens is a valuable diagnostic aid. Indications for splenic aspiration include an unexplained nodule or mass, unexplained splenomegaly, and staging of certain neoplasms. Echogenic patterns may suggest a pathologic process, and spleens containing multiple lesions of different patterns are more likely to be associated with malignancy. Cytologic evaluation may provide a specific diagnosis or guide additional testing or approaches, such as surgical exploration. Advantages to FNA are ease of sampling, rapidity of results, evaluation of individual cellular detail, and identification of organisms. Detailed morphologic examination of individual cells is particularly helpful in evaluating hemolymphatic cells. However, tissue architecture is not preserved, and histologic evaluation may be required for a definitive diagnosis. In a study examining the correlation between cytologic and histologic diagnoses of splenic lesions in dogs and cats, in 84% of the cases cytologic evaluation was either diagnostic (61%) or included the diagnosis in the differential (23%). Splenic aspirates may be obtained with minimal risk using 22g or smaller needles under ultrasound guidance and when the hemostatic system is intact. Hemorrhage rarely occurs, even in thrombocytopenic animals.

NORMAL ELEMENTS

Splenic tissue consists of white pulp (lymphoid tissue) and red pulp and marginal zones, where erythrocytes and other blood cells, hematopoietic cells (eg, megakaryocytes and erythroid precursors), macrophages, and mast cells are found. The hematocrit of splenic red pulp is very high (>80%), and aspirates typically contain numerous erythrocytes. Senescent red blood cells are removed from circulation by the spleen, and a small amount of hemosiderin is typically found in normal spleens. Stromal cells and mesothelial cells (which the serosal surface) may be found in any aspirate of the spleen.

HYPERPLASTIC OR REACTIVE CONDITIONS

Reactive splenic conditions include generalized hyperplasia with lymphoid hyperplasia and increased hematopoietic precursors, mast cells, stromal cells, macrophages, and hemosiderin. Lymphoid nodules often have a cytologic appearance similar to other sites of lymphoid reactivity (mostly small lymphocytes and increased numbers of lymphoblasts and plasma cells). Large granular lymphocytes (LGLs) may be seen in small numbers. Occasionally, reactive nodules contain mostly large lymphoid cells with visible nucleoli, making the distinction between a hyperplastic lymphoid nodule and lymphoma challenging. Typically, splenic lymphoma results in diffuse splenomegaly rather than the formation of a discrete nodule. Evaluating all clinical information is important in interpreting these lesions. If reactivity and lymphoma cannot be distinguished, histologic examination, immunocyto/histochemical assays, and/or PCR assays for lymphocyte clonality should be performed. Neoplastic lymphocytes are typically monoclonal, whereas hyperplastic lymphocytes will be polyclonal.

Proliferation of splenic macrophages occurs in response to inflammation and hemolysis. If RBCs are hemolysed in the spleen, as occurs in immune-mediated, oxidative, or hemoparasitic hemolysis, macrophages will be increased. Erythrophagia by macrophages is typically prominent, and hemosiderin is abundant. Excessive hemosiderin in the spleen (hemosiderosis) may occur in hemolytic anemia or may be seen with hematoma or blood-filled spaces associated with hemangioma/hemangiosarcoma.

Splenic extramedullary hematopoiesis (EMH), or the production of hematopoietic cells outside bone marrow, is common. Sometimes small splenic nodules are composed entirely of hematopoietic precursors. This may be an incidental finding, may be found in association with other splenic diseases, or may be a response to bone marrow failure. Evaluation of a complete blood count (CBC) is essential to the correct interpretation of splenic EMH. Finally, in hyperplastic conditions of the spleen, mast cells may increase and appear in small aggregates. It is important not to misdiagnose a splenic mast cell tumor in these cases.

INFLAMMATORY LESIONS (septic and nonseptic)

Splenitis is characterized by the type of inflammatory cells that are present. Bacterial infections with E. coli or Clostridium spp result in neutrophilic inflammation. Necrotic lesions within the spleen also may be accompanied by numerous neutrophils. Fungal infections with yeast, such as Histoplasma spp., or hyphae, such as Aspergillus spp, may induce histiocytic or pyogranulomatous inflammation, as can protozoal organisms, such as Cytauxzoon and Leishmania. If eosinophils are increased, systemic eosinophilic inflammation should be considered. Paraneoplastic
eosinophilic infiltrates may be present in some tumors, such as lymphoma and mast cell tumor. If leukocytes found in circulation, such as neutrophils and eosinophils, are increased in splenic aspirates, evaluate a CBC to ascertain if these cells are circulating in high numbers and, therefore, traveling though the spleen.

**NONINFLAMMATORY, NON-NEOPLASTIC CONDITIONS**

Splenic hematomas, infarcts, torsions, and passive congestion cannot be diagnosed cytologically. In most cases, blood is obtained and cannot be distinguished from high hematocrit blood from a normal spleen.

**SPLENIC NEOPLASIA**

Neoplasms in the spleen may be primary or metastatic. Primary neoplasms or those that are part of a multicentric neoplasm include lymphoma, plasma cell tumor, mast cell tumor, hemolymphatic neoplasia (eg, leukemias), hemangioma and hemangiosarcoma, histiocytic sarcoma and malignant histiocytosis, leiomyoma and leiomyosarcoma, and myelolipoma. Metastatic tumors include carcinomas, including neuroendocrine tumors such as insulinoma, and a variety of sarcomas. Except for mesenchymal or connective tissue tumors (sarcomas), cells from many of these tumors exfoliate well. In hemolymphatic tumors, cytologic evaluation is important because morphologic detail of individual cells can be ascertained.

Tumors of cells normally found in spleen must be distinguished from hyperplastic conditions. The distinction between reactive lymphoid hyperplasia and lymphoma is discussed above. LGL lymphoma is easier to diagnose because lymphocytes contain prominent magenta granules. One type of lymphoma that originates in the spleen is gamma/delta hepatosplenic lymphoma. Splenic plasmacytosis also may be reactive or neoplastic. Clinical information and other diagnostic testing may help distinguish these conditions when plasma cells have a normal appearance. Mast cells may be increased in reactive conditions and even form small aggregates.

Therefore, a cytologic diagnosis of metastatic mast cell tumor depends on the presence of mast cells in very high numbers with effacement of other splenic elements or on the presence of increased mast cells with an atypical morphologic appearance. In feline splenic mastocytosis well-granulated mast cells proliferate, effacing the splenic architecture and resulting in massive splenomegaly. Erythrophagia by mast cells in the spleen may be noted. These cats typically have bone marrow mastocytosis and mastocythemia. Splenectomy alone may result in long remissions. In acute or chronic leukemias, neoplastic cells typically invade the spleen. Diagnosis usually is made by examining peripheral blood and bone marrow and immunophenotyping the cells.

Cells from hemangiosarcoma may not exfoliate well, but if present are a pleomorphic population of fusiform cells. The spleen is a common site for histiocytic sarcoma/malignant histiocytosis in certain breeds, such as Bernese mountain dogs, Rottweilers, and some retrievers. The cells are highly pleomorphic with marked anisocytosis, anisokaryosis, and multinuclearity. Some cells may be phagocytic. In some tumors of macrophages, the cells have a normal morphology, and reactive hemophagocytic syndromes must be distinguished from a neoplasm of phagocytic macrophages.

**ADDITIONAL READING**


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