Latin Comparative Pathology Group
The Latin Subdivision of the CL Davis Foundation
Diagnostic Exercise

Case #: 54 Month: March Year: 2015

Answer Sheet

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Clinical History: A 1-year-old, spayed female, Domestic Shorthair cat was presented for acute lethargy and labored breathing. Findings at the physical examination included icterus, enlarged liver and spleen, and a palpable mass in the central abdomen. Due to poor prognosis, the animal was euthanatized.

Necropsy Findings: See gross images.

Gross images:

Figure 1 and 2

Follow-up questions: Gross description; Morphologic diagnosis; Differential diagnosis

Diagnosis:

1) Gross description: An 8 cm x 2 cm, pale yellow, well-vascularized, soft mass was present in the central abdominal cavity, encompassing the ileocecal junction (Figure 1). The distal-most aspect of the ileum was mildly to moderately dilated. The spleen was markedly enlarged, measuring 15 cm x 5 cm x 1.5 cm. Dozens of 0.1 to 1.5 cm diameter slightly raised nodules were disseminated throughout the splenic parenchyma (Figure 2). On cut section, these nodules were white, soft, and homogenous.

   Other gross findings in this case: Both kidneys had 10-20 raised, tan to white, 1 mm to 6 mm diameter nodules that extended from the capsular surface into the parenchyma. The liver was diffusely pale red, had rounded edges and was friable. The mediastinum was expanded by a 4 cm x 1 cm mass with the same characteristics as the mass encompassing the ileocecal junction. The left tonsil was enlarged, measuring 1 cm in diameter, whereas the right tonsil was unremarkable, measuring 7 mm x 1 mm.

2) Morphologic Diagnosis: Disseminated lymphoma.

3) Differential Diagnosis: Multisystemic granulomatous inflammation, metastatic neoplasia.

Microscopic findings:

The mass in the central abdomen was histologically consistent with a mesenteric lymph node, the parenchyma of which was extensively effaced and expanded by sheets of round to polygonal intermediate-sized neoplastic round cells with distinct cell borders and scant eosinophilic cytoplasm. The nuclei of these cells were round with densely stippled chromatin and indistinct nucleoli. Moderate anisokaryosis was present, and the mitotic index was low (2 mitoses per 10 high power fields). Neoplastic cells extensively infiltrated the ileum at the ileocecal junction, extending from the serosa through the tunica muscularis and submucosa focally into the mucosa. The spleen had multifocal to coalescing nodular aggregates of cells that were similar to those described for the mesenteric lymph node. A similar population of neoplastic cells also extensively infiltrated the kidney, liver (Figure 3), adrenal cortex, mediastinum, and tonsil. Neoplastic cells were negative by immunohistochemistry for CD3 (T-cell marker) and positive for CD 20 (B-cell marker) (Figure 4), consistent with the diagnosis of B-cell lymphoma.

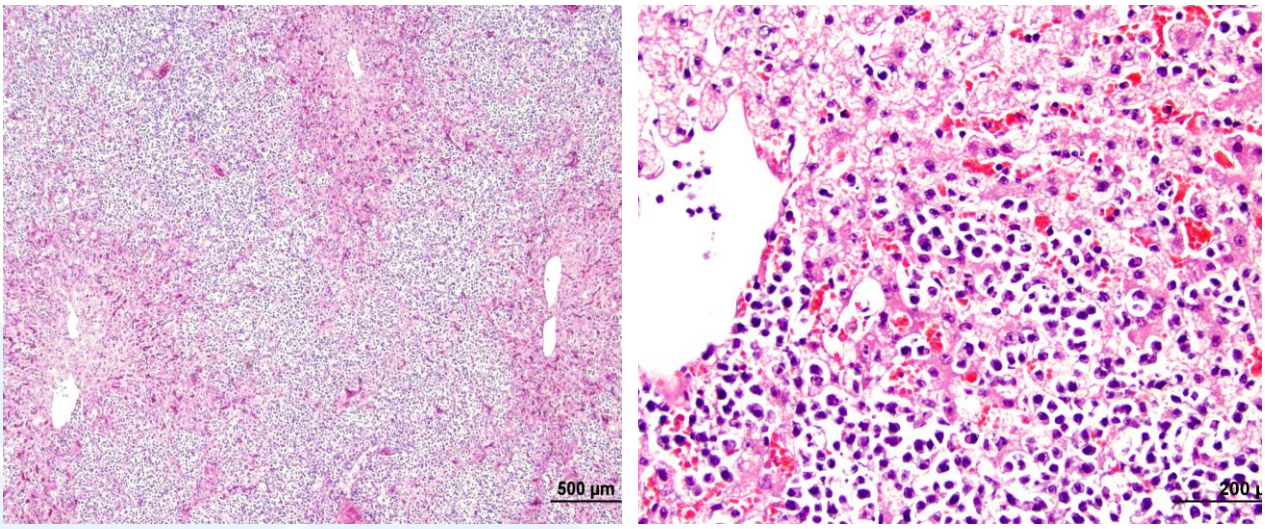

Figure 3A and B

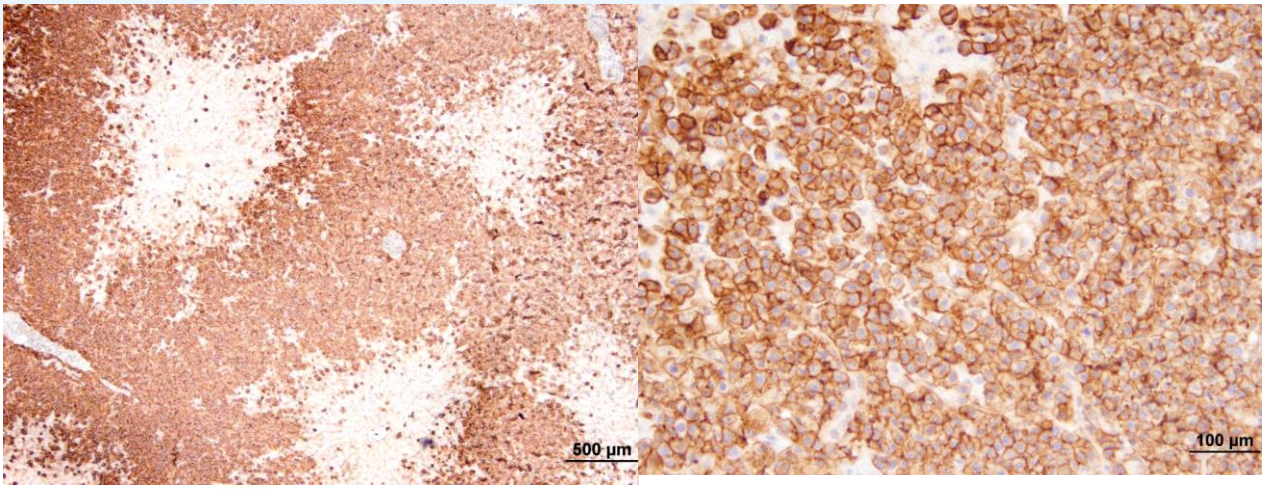

Figure 4A and B

Discussion:

Mesenteric lymph node enlargement can be caused by local or disseminated infection. In cats, viral infection is one of the most important causes of lymphadenopathy. Feline Immunodeficiency Virus (FIV) is well known for causing lymphadenopathy of mesenteric and other lymph nodes. Feline Infectious Peritonitis (FIP), caused by a mutated form of Feline Coronavirus, can also cause enlargement of mesenteric lymph nodes. Infections with bacteria such as *Mycobacterium avium,* causes lymph node enlargement as well, mainly of the mesenteric nodes; however, this rarely occurs in cats because they are naturally resistant to this microorganism. Inflammatory reactions in the

intestine, caused by chronic infection by bacteria, fungi or helminthic parasites, can also lead to reactive response of the regional lymph nodes, resulting in their enlargement. Another frequent cause of enlarged lymph nodes is neoplasia, most commonly lymphoma, as in this case, although metastases of other neoplasms need to be considered as well.

Lymphoma is the most common hematopoietic neoplasm in cats. Feline Leukemia Virus (FeLV) was considered a common cause of lymphoma in cats in the past. FIV also increases the risk of lymphoma formation in cats, but less so when compared with FeLV. Cats with FeLV infection are more likely to develop mediastinal and multicentric neoplastic disease at a younger age when compared with FeLV-negative cats. Lymphoma not associated with FeLV is more common in older cats, with a median age of 7 to 12 years. In this case, the 1-year-old cat was reportedly up to date on vaccines and had previously tested negative for both FeLV and FIV. It is important to remember, however, that a negative test for this virus (may it be by IFA, ELISA or PCR) does not entirely rule out FeLV as the cause of the disease.

Lymphoma can be classified based on the anatomic distribution as multicentric, alimentary, mediastinal and extranodal. In the multicentric form, the animal generally has solitary or generalized lymphadenopathy possibly followed by hepatosplenomegaly. The affected lymph nodes are enlarged to 5-15 times normal size. Occasionally, the animal can present with non-specific weight loss, anorexia and lethargy. The alimentary form is the most common, affecting primarily older cats. The cat with this type of lymphoma usually shows gastrointestinal signs such as weight loss, vomiting, diarrhea, and palpably enlarged lymph nodes. The alimentary T-cell lymphoma in cats closely resembles the human entity known as enteropathy-associated T-cell lymphoma. This condition is thought to arise from clonal transformation of intestinal intraepithelial lymphocytes after chronic antigenic stimulation, is therefore characterized by epitheliotropism of neoplastic cells and is largely confined to the small intestine. In contrast, alimentary B-cell lymphoma in cats appears to originate from the gut-associated lymphoid tissue and affects predominantly the stomach and ileo-ceco-colic junction. Organs other than the gastrointestinal tract can also be affected in the alimentary form of lymphoma, including the spleen and kidney. The mediastinal form is associated with respiratory and gastrointestinal signs, such as dyspnea, cough and regurgitation, associated with compression of the trachea and esophagus by the enlarged anterior mediastinal lymph nodes. The extranodal form presents variable clinical signs depending on the affected organ.

Immunophenotyping can be used to help classify the neoplastic lymphoid population as T-cell or B-cell in origin, which is helpful to estimate prognosis and guide possible treatment options. In general, T-cell lymphomas have a poorer prognosis than B-cell lymphomas, and aggressive treatment should be used. Chemotherapy is the treatment of choice for lymphoma in cats. The most common chemotherapy protocols use a combination of cyclophosphamide, vincristine and prednisone (COP protocol) or cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP protocol). Nonetheless, the wide variation of anatomic forms of feline lymphoma makes prognostication more difficult in cats than in dogs with lymphoma. Based on organ involvement and immunophenotype of the neoplastic cells, the cat in this case was believed to have had the alimentary B-cell form of lymphoma. Considering the overall extent of organ involvement, prognosis was considered poor.

References and Recommended literature:

Barrs VR, Beatty JA. Feline alimentary lymphoma: 1. Classification, risk factors, clinical signs and non-invasive diagnostics. J Feline Med Surg. 2012 Mar;14(3):182-90.

Barrs VR, Beatty JA. Feline alimentary lymphoma: 2. Further diagnostics, therapy and prognosis. J Feline Med Surg. 2012 Mar;14(3):191-201.

Greene CE (Ed.). Infectious diseases of the dog and cat. Philadelphia, PA: Elsevier. 2006, 3rd ed. 1387 p.

Moore PF, Rodriguez-Bertos A, Kass PH. Feline gastrointestinal lymphoma: mucosal architecture, immunophenotype, and molecular clonality. Vet Pathol. 2012 Jul;49(4):658-68.

Waite AH, et al. Lymphoma in cats treated with a weekly cyclophosphamide-, vincristine-, and prednisone-based protocol: 114 cases (1998-2008). J Am Vet Med Assoc. 2013 Apr 15;242(8):1104-9.

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A final document containing this material with answers and a brief discussion will be posted on the C. L. Davis website by the end of the current month (http://www.cldavis.org/lcpg_english.html).