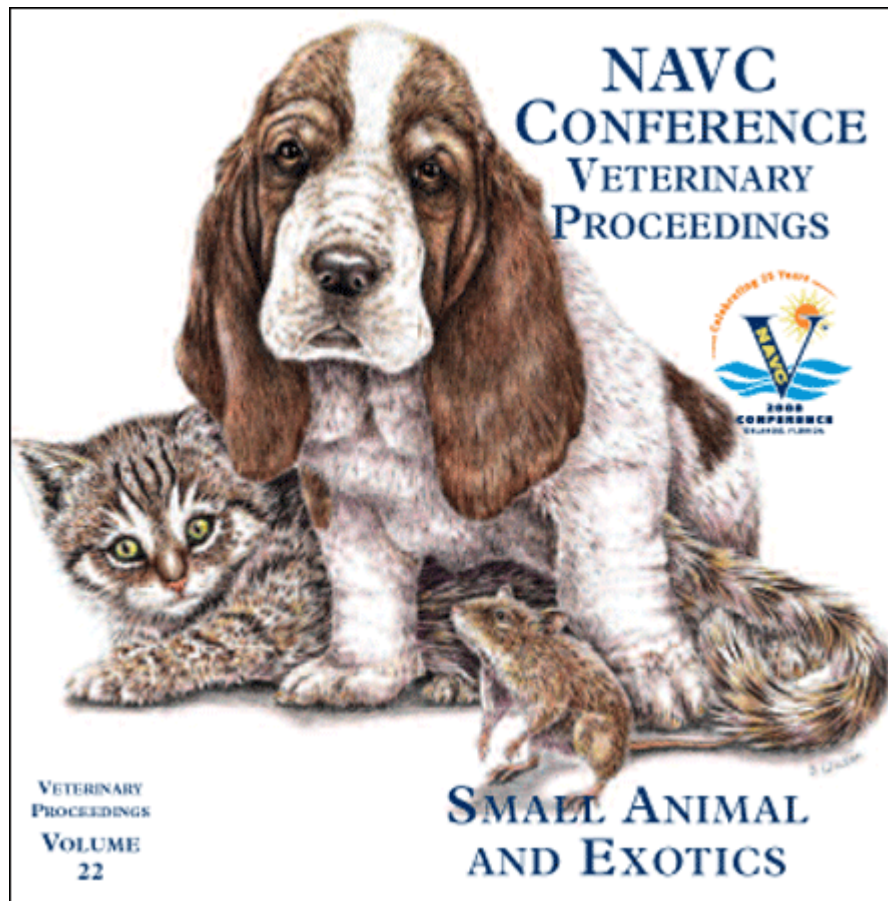


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TUMORS OF THE GI TRACT

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Tumors of the gastrointestinal tract (GI) occur in each of the different anatomic units from the oral cavity through the anus. They are varied histologically and clinical signs relate primarily to location, size, and the degree of compromise of normal function. Some are associated with multifocal localization and some are solitary lesions. Some authors include the liver and pancreas and perianal glands as part of the GI tract. Tumors of the GI tract have generally been adequately covered in a variety of formats. The purpose of this article is to update selected tumor types based on the latest literature available and explore some current controversies.

INFLAMMATORY BOWEL DISEASE (IBD) AND EPITHELIOTROPIC LYMPHOMA IN CATS

Approximately 90% of lymphoma in cats is classified as intermediate- or high-grade based on histologic appearance. High-grade lymphomas are those with large amounts of cytoplasm, large and prominent nucleoli, hyperchromatic chromatin pattern staining, and numerous mitotic figures. Low-grade lymphoma is characterized by the presence of small lymphocytes with round nuclei, enough cytoplasm to result in relatively uniform spacing of nuclei, and mitoses are characteristically absent. High-grade tumors are sometimes referred to as "lymphoblastic" while low-grade tumors are sometimes referred to as "lymphocytic." Intermediate-grade tumors have characteristic between high and low-grade.

Inflammatory bowel disease in cats is associated with a lymphocytic (and often plasmacytic infiltration) of small reactive T lymphocytes. There has been speculation by pathologists and clinicians that lymphocytic-plasmacytic IBD in cats may actually represent a low-grade intraepithelial T-cell lymphoma and not a reactive infiltration by T cells. Epitheliotropism in the context of alimentary lymphoma refers to the characteristic homing of neoplastic T cells to the mucosal epithelium of the intestinal tract. This form of lymphoma has been reported in both dogs and cats. With this variant of lymphoma the involved area is mostly infiltrated with small, and to a lesser extent a population of intermediate-size malignant lymphocytes, rather than larger lymphoblasts. Immunophenotyping will generally confirm the small lymphocytes as T cells in both epitheliotropic lymphoma and IBD. Without the ability to perform clonal analysis, on the basis of morphology alone (which is all that routine H&E stained histopathology specimens can allow the pathologist to evaluate) it can be impossible to distinguish IBD from epitheliotropic lymphoma. Clinicians need to be aware of this potential for confusion and for a misdiagnosis of IBD when in fact the clinical disorder is a rare variant of lymphoma. Because of this confusion, treatment for IBD

will often precede the definitive diagnosis of lymphoma by many months. Cats with epitheliotropic intestinal lymphoma usually have a predominance of duodenal lesions and have a prolonged clinical course.

The basis for the apparent relationship between IBD and lymphoma is unclear, but the presumption is that the IBD is the antecedent event leading to malignant transformation. There is abundant literature in human and veterinary medicine linking the effects of chronic inflammation to the development of cancer. In cats such inflammatory events as post-vaccination granuloma, eye trauma, and sunlight will precede malignant cancer in some individuals. Likewise in dogs, chronic wounds and chemical exposure may lead to cancer as well.

Perhaps the most widely accepted example of chronic inflammation preceding tumor development at the same site is found with chronic *Helicobacter* infection and gastric carcinoma. People that are colonized with *Helicobacter* are at dramatically higher risk for gastric cancer development than are uninfected people. Both dogs and cats with *Helicobacter* infections have been proposed as models of gastric tumor development in humans.

Non-epitheliotropic lymphoma of the GI tract in cats is more often categorized as being high-grade. With high-grade lymphoma of the GI tract there may be associated mesenteric lymphadenomegaly, splenomegaly and/or hepatomegaly in addition to a specific intestinal localization. Non-epitheliotropic intestinal lymphoma in cats is variably reported as being primary T-cell type and in other reports as primarily B-cell type and almost all will be FeLV test negative.

LARGE GRANULAR LYMPHOCYTE (LGL) LYMPHOMA

Large granular lymphocyte lymphoma is characterized by the presence of a morphologically distinct subset of lymphocytes that contain intracytoplasmic azurophilic granules. These cells are a normal, though minor, population of peripheral blood lymphocytes, but represent a large subset of intraepithelial lymphocytes in the intestinal tract. Most LGL lymphomas reported in dogs and cats are intestinal. In cats they are consistently found in the small intestine with a predominance of jejunal lesions. This disorder has a very aggressive clinical behavior and is usually of T-cell or non-B type origin; probably most consistent with natural killer (NK) cells. Interestingly, some cats that are diagnosed with LGL intestinal lymphoma have a history of a prior diagnosis (working or definitive) of IBD.

Some cats with LGL intestinal lymphoma will have nonspecific clinical signs such as anorexia, weight loss, vomiting and diarrhea. They frequently also have a palpable abdominal mass. Cats will also often have a circulating LGL lymphocytosis. Dogs with LGL intestinal lymphoma are often asymptomatic to paucisymptomatic when diagnosed with LGL malignant disease. In cats an associated leukemia with LGL lymphocytes is often reported. There are reports that alimentary lymphoma of all types in cats may be increasing in prevalence.

MAST CELL TUMORS OF THE GI TRACT

Mast cell tumors of the skin are very common but GI mast cells are far less common. Their full clinical characterization is also unclear. Miniature breeds of dogs, especially Maltese, appear to be most frequently affected. Affected individuals tend to be older (9.7 + 2.6 years) and no sex differences are apparent. The most common localization is the upper GI tract and the lumen of the associated gut is often narrowed.

Histologic features of this disorder are important to the clinician because confusion with GI lymphoma is possible. Mast cell tumors and lymphoma are both classified as round cell tumors. When mast cells have abundant cytoplasmic granules and are well differentiated confusion with lymphoma is unlikely. However, cases of T-cell GI lymphoma in dogs and GI mast cell tumors with very similar histologic features are reported. Tumor cells of lymphoma are characterized by round nuclei with dense chromatin, scanty cytoplasm and large distinct nucleoli. Mast cell tumors of the intestine have moderate to abundant cytoplasm with round to ovoid nuclei with sparsely scattered granules showing metachromasia. These granules, usually abundant in cutaneous mast cell tumors, are the hall mark of these cells but in intestinal tumors the granules may not be seen with routine H&E sections. These morphologic characteristics are very similar to those of moderate to large T-cell lymphoma of intestinal origin. In addition, variable eosinophilic infiltrations can be present in both lymphoma and mast cell tumors involving the gut. The use of immunohistochemistry, special stains like toluidine blue and alcian blue, plus the mast cell marker known as c-kit is vital for correct diagnosis.

There are limited reports of treatment of intestinal mast cell tumors. One reported dog was treated with lomustine (80 mg/m² orally every 3 weeks), prednisone (30mg/m² once daily x 7 days, then 20 mg/m² once daily x 7 days, then 20 mg/m² every other day). Supportive treatment with sucralfate and omeprazole were also given. This particular dog remained in partial remission for 7 months. In other reports, surgery followed in some cases by prednisone, vincristine, and/or cyclophosphamide resulted in very short periods of control (1 to 2 months at most).

INTESTINAL CHORISTOMA

A choristoma is a mass of histologically normal tissue that is found in an abnormal location. They are often classified by the predominant tissue within the lesion and further described by the location where the tissue is found. *Gastrointestinal choristoma* is the term for heterotrophic gastrointestinal tract tissue while *gastric choristoma* and *intestinal choristoma* refer specifically to lesions with only one type of epithelium. Choristomas are rare but they have been reported to involve the skin and subcutaneous tissues. They form following failure of separation between the notochord and a portion of the underlying endoderm during embryonic development. They typically are diagnosed in young animals.

REFERENCES

1. Darbès J, Majzoub M, Breuer W, et al. Large granular lymphocyte leukemia/lymphoma in six cats. *Vet Pathol.* 1998; 35; 370-379.
2. Roccabinaca P, Vernau, W, Caniatti M, et al. Feline large granular lymphocyte (LGL) lymphoma with secondary leukemia: primary intestinal origin with predominance of CD3/CD8α phenotype. *Vet Pathol.* 2006; 43:15-28.
3. Louwerens M, London CA, Pedersen NC, et al. Feline lymphoma in the post-feline leukemia virus era. *J Vet Intern Med.* 2005; 19:329-335.
4. Carreras JK, Goldschmidt M, Lamb M, et al: Feline epitheliotrophic intestinal malignant lymphoma: 10 cases (1997-2000). *J Vet Intern Med.* 2003; 17:326-331.
5. Ozaki K, Yamagami T, Nomura K, et al. Mast cell tumors of the gastrointestinal tract in 39 dogs. *Vet Pathol.* 2002; 39:557-564.
6. Ozaki K, Yamagami T, Nomura K, et al. T-cell lymphoma with eosinophilic infiltration involving the intestinal tract in 11 dogs. *Vet Pathol.* 2006; 43:339-344.
7. Baldi A, Colloca E, Spugnini EP. Lomustine for the treatment of gastrointestinal mast cell tumor in a dog. *J Small Anim Pract.* 2006; 47:465-468.
8. Whitten KA, Belote DA, McLeod CG. Intestinal choristoma in the subcutis of a dog. *Vet Pathol.* 2006; 43:356-357.
9. Bentley AM, Goldschmidt MH, Bennett RA. Intestinal choristoma in the midcervical region of a dog. *J Am Anim Hosp Assoc.* 2006; 42:223-225.