**Ultrasonographic nodular appearance of small bowel metastasis from canine mammary carcinoma**

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Ultrasonographic nodular appearance of small bowel metastasis from canine mammary carcinoma


Key words: Mammary carcinoma, intestinal metastasis.

Running head: Nodular small bowel metastasis mammary carcinoma
Abstract

A 10 year-old entire female Beagle dog was evaluated for an acute history of lethargy, anorexia, and diarrhea. Mammary tumors were detected during physical examination. Ultrasonographic scan revealed the presence of a unique pattern of multiple, well defined and well marginated hypoechoic nodules in the muscularis layer of the jejunum. These nodules were not associated with changes in the rest of the normal intestinal layering and were not causing signs of intestinal obstruction. Mammary carcinoma metastases to intestinal muscularis layer were diagnosed on histopathological examination.
Signalment, history and clinical findings

A ten-year-old entire female Beagle dog presented with a three days history of anorexia, lethargy, and diarrhea.

On physical exam, the dog presented mammary tumors on the right M4 and M5 mammary glands, and multiple cutaneous nodules in the abdominal wall and the thoracic epaxial soft tissues.

Complete blood work revealed mild normocytic, normochromic, non-regenerative anemia, moderate left shift neutrophilic leukocytosis, moderate hypercalcemia, and decreased sodium and chloride.

Medical treatment was initiated with fluid therapy (Ringer Lactate, B Braun VetCare SA, Rubí, Spain; 15.4ml/h, IV), fenbendazol (Panacur, Intervet International B.V., Salamanca, Spain; 50mg/Kg, PO), and intestinal diet (Prescription Diet™ i/d™ Canine canned, Hill’s Pet Nutrition, Inc®/™, USA).

Diagnostic imaging exams, including thoracic and abdominal radiographs and ultrasound scan, were performed.

Imaging diagnosis

Abdominal ultrasound was performed using high frequency sectorial (CA123, convex-array, 3-9 MHz) and linear (LA523, linear-array, 4-13 MHz) transducers (MyLab™70 Esaote, Italy). Multiple, oval to rounded, well defined and well marginated, hypoechoic nodules, measuring between 0.3 and 0.7cm were observed in the muscularis layer of the jejunal wall (Fig. 1). The nodules did not alter the remaining normal layers of the affected intestinal segment, being the mucosa, submucosa, and serosa clearly identified. In general, the thickness of the jejunal wall was within normal limits (less than 5mm), except where nodules were present. In such areas, the intestinal wall reached 6mm. No significant
ultrasonographic abnormalities were detected on the thickness, layering and content of the stomach, duodenum, ileum or colon. Mixed gastrointestinal luminal content with gas, fluid, and mucous patterns was observed, and gastrointestinal motility of all segments, including the jejunum, was considered normal. No blood flow signal was detected inside the nodular lesions using Color Doppler ultrasound as in the rest of the intestinal wall (Fig. 2). No signs of vascular abnormalities, such as luminal thrombi, were evident in the mesenteric regional vessels. Well defined, hypoechoic nodules of less than 2 cm were also visible in the spleen, cranial pole of the right kidney, adrenal glands, abdominal wall, and mesentery. A small amount of anechoic peritoneal effusion was observed between intestinal loops. Thoracic radiographs revealed a mixed pulmonary pattern with marked diffuse bronchointerstitial component, presence of small pulmonary nodules, and alveolar pattern affecting the caudal portion of the left cranial lung lobe. An aggressive lytic lesion in the spinous processes of T4 and T5 was also observed. Abdominal radiographs did not show significant abnormalities. Non-cardiac thoracic ultrasound demonstrated the presence of 0.5-0.9cm pulmonary nodules in contact with the thoracic wall and consolidation of the left cranial lung lobe. The presumptive imaging diagnosis was a malignant mammary tumor with multiple metastases to thoracic and abdominal structures. The differential diagnosis for the nodules affecting the muscularis layer of the jejunum included nodular infiltration due to primary intestinal neoplasia (lymphoma, mast cell tumor, disseminated histiocytic sarcoma) or metastatic infiltration. Other
differentials such as intestinal smooth muscle tumor, muscular hypertrophy, muscular hyperplasia, hematoma, or granuloma, were considered less likely.¹⁻⁶

**Outcome and pathologic findings**

Positive response to medical treatment was observed during the first day of hospitalization. However, clinical signs worsened the following hours and the owners elected euthanasia. Complete post-mortem examination was performed.

Macroscopically, three well-defined nodules, measuring 0.5-1cm diameter, were present in the distal jejunum. Nodules were solid and whitish on cross-section and did not disrupt the intestinal mucosa or serosa (Fig. 3). Similar nodular lesions were detected in the mammary glands, inguinal superficial lymph nodes, abdominal wall, thoracic epaxial muscles, and in other thoracic and abdominal viscera-including the lungs, heart, spleen, liver, kidneys, and adrenal glands.

Microscopically, all the nodules showed a similar histological pattern. In the intestine, macroscopic nodules corresponded to a non-encapsulated and poorly demarcated neoplastic proliferation that severely infiltrated the tunica muscularis and submucosa of the intestinal wall (Fig. 4). Neoplastic cells were organized in small acini or solid nests, within a fine fibrovascular stroma.

Neoplastic cells were epithelial, polygonal to cylindrical-shaped, medium in size (15-30 µm in diameter) and showed indistinct borders. They showed a moderate amount of pale eosinophilic, and often vacuolated, cytoplasm and a central, rounded to oval big nucleus, with finely stippled chromatin and mainly one prominent eosinophilic nucleolus. A moderate degree of pleomorphism, anisocytosis, and anisokaryosis was evident, and a moderate to large number of mitosis (2 to 6 per 40x HPF) were present. Within the tumour, several
extensive areas of coagulative necrosis, fibrin and haemorrhage were observed. Presence of neoplastic emboli was detected in the lymphatic vessels of the intestinal submucosa.

Discussion

The ultrasonographic appearance of canine primary intestinal neoplasia, including carcinoma, lymphoma, and smooth muscle tumors has been well characterized.\textsuperscript{2, 7-13} Primary intestinal neoplasms are uncommon in dogs, being adenocarcinoma and lymphoma the most frequent primary canine gastrointestinal tumors. Other described malignancies include leiomyosarcoma, fibrosarcoma, poorly differentiated sarcoma, mast cell tumors, carcinoid, hemangioma, and osteosarcoma. Benign tumors include polyps and leiomyomas.\textsuperscript{7,14-16} The most common ultrasonographic findings in canine intestinal carcinomas are transmural thickening of the intestinal wall, which is usually focal with complete loss of the normal intestinal layering, changes in the normal wall echogenicity, decreased focal intestinal motility with or without signs of intestinal obstruction, regional lymphadenopathy and/or nodules at the mesentery/omentum.\textsuperscript{2,9,11} Alimentary lymphoma in dogs can be diffuse or can appear as a solitary hypoechoic intestinal mass with transmural thickening and loss of wall layering. It is the most common neoplastic cause of diffuse infiltration and wall thickening in dogs. Lymphoma may cause partial stenosis of the intestinal lumen, but it usually does not cause complete obstruction. Regional lymphadenopathy with enlarged, rounded, and hypoechoic lymph nodes is common. Other reported findings are reduced wall echogenicity and decreased motility.\textsuperscript{2,9,17} Leiomyosarcomas are malignant smooth-muscle tumors that originate from the muscularis layer of the bowel wall. They are often
large, heterogeneous, mixed echogenic intramural lesions with eccentric growing pattern. Leiomyomas tend to be small, and appear as focal intramural hypoechoic thickening with loss of wall layering.

Canine mammary gland tumor is one of the most common neoplasia, accounting for approximately 50% of all tumors in intact female dogs. Malignant canine mammary tumors have the potential to metastasize. In general, malignant epithelial mammary tumors metastasize via lymphatic vessels to regional lymph nodes and the lungs. However, more distant metastases sites, including the liver, spleen, bone, and brain have been described. Intestinal metastases have rarely been reported in dogs, without specification of which intestinal layer was affected. Skeletal and cardiac muscle metastatic infiltration from mammary tumors has also been reported.

However, no references about intestinal smooth muscle metastasis have been found.

In women, breast carcinoma is the most common neoplasm. Metastatic breast disease usually affects the lungs, liver, bones, soft tissue, brain, and adrenal glands. As it occurs in dogs, gastrointestinal involvement is uncommon and it mainly affects the stomach, colon and rectum, with direct invasion of lymphatic vessels as the proposed mechanism. Metastases to the duodenum, jejunum, and ileum are rare and usually associated with peritoneal carcinomatosis.

Common imaging findings of intestinal metastases are diffuse mural thickening of the intestinal wall -often associated to mucosal ulceration-, regional lymphadenopathy, peritonitis, and the presence of single or multiple sites of intestinal obstruction secondary to intestinal masses or strictures. Gastrointestinal breast cancer metastases are recognized at necropsies, but the
presence of clinical signs is uncommon.\textsuperscript{28,29} Patients can show abdominal pain, diarrhea, vomiting, fatigue, anemia, inappetence, hyporexia, and signs of intestinal obstruction, mimicking other disorders such as Crohn's disease.\textsuperscript{29-30} In the case presented here, a paraneoplastic syndrome is the most likely explanation for most of the presenting clinical signs (anorexia, lethargy, and diarrhea). Diarrhea is one of the clinical signs observed in human cancer patients.\textsuperscript{31} Although diarrhea secondary to small intestine neoplastic affection is usually seen in dogs with jejunal or ileal tumors\textsuperscript{32}, the small size and muscular location of the nodules and the fact that the intestinal mucosa was intact, makes direct effect of the neoplasia less likely. Inappetence and weakness may have been exacerbated in this dog by the presence of hypercalcemia, which has been associated with several tumor types, including mammary gland carcinoma and adenocarcinoma.\textsuperscript{33,34} The unique ultrasonographic appearance of the intestinal metastases in this case - described as nodular, well defined hypoechoic nodules affecting the muscularis layer- has not been described in other intestinal neoplasms. Thus, it may be considered as a pattern of intestinal metastases.
References


**Figures**

Fig.1. A. B-Mode ultrasonographic image of the jejunum. A well-defined hypoechoic nodule is located in the muscularis layer of the intestinal wall causing mild thickening of the affected segment. The submucosa and serosa
layers show normal ultrasonographic appearance. B. Schematic image of the parietal nodule (arrows).

Fig. 2. Color Doppler image of another segment of the distal jejunum. A well-margined hypoechoic nodule is present in the muscularis layer of the intestinal wall. No abnormal flow signal was detected inside the nodular lesion as in the rest of the intestinal wall.

Fig. 3. Macroscopic image of the jejunum. A well-defined, solid nodule, measuring 0.5-1cm diameter, is visible in the distal jejunum (arrow). The nodule did not disrupt the intestinal mucosa or serosa.

Fig. 4. Microscopic image of the metastasis of mammary carcinoma infiltrating the intestinal submucosa and tunica muscularis. Inset: high power magnification image showing the cytological characteristics of the neoplastic cells. Mitosis are numerous (arrowheads).
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209x81mm (300 x 300 DPI)
Fig. 2. Color Doppler image of another segment of the distal jejunum. A well-marginated hypoechoic nodule is present in the muscularis layer of the intestinal wall. No abnormal flow signal was detected inside the nodular lesion as in the rest of the intestinal wall.

167x130mm (96 x 96 DPI)
Fig. 3. Macroscopic image of the jejunum. A well-defined, solid nodule, measuring 0.5-1cm diameter, is visible in the distal jejunum (arrow). The nodule did not disrupt the intestinal mucosa or serosa.
Fig. 4. Microscopic image of the metastasis of mammary carcinoma infiltrating the intestinal submucosa and tunica muscularis. Inset: high power magnification image showing the cytological characteristics of the neoplastic cells. Mitosis are numerous (arrowheads).

86x108mm (300 x 300 DPI)