

## CASE REPORT

## Sonographic features of peritoneal lymphomatosis in 4 cats

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Email: keaton.morgan@vsg.co.nz**Background:** The metastatic spread of feline lymphoma to the peritoneum ("lymphomatosis") has been rarely reported in the literature. The sonographic features specific to this rare disease manifestation have not been described and have important treatment and prognostic considerations prompting definitive diagnosis.**Objectives:** To describe the ultrasonic features of feline peritoneal lymphomatosis.**Animals:** Four cats with alimentary lymphoma and peritoneal metastasis confirmed using cytology, histology, or both.**Results:** The sonographic features described include either a nonobstructive, focally diffuse, and circumferential intestinal mass, or an eccentric, focally diffuse, gastric mass. The intestinal and gastric lesions exhibited hypo-to-anechoic transmural wall thickening with loss of wall layering in association with discrete-to-coalescing plaques or sheets of thickened, hypoechoic tissue throughout the mesentery or omenta. All cases exhibited only small volumes of anechoic free peritoneal fluid. Three of the 4 cats also had multiple small hypoechoic nodular foci on the parietal and/or visceral peritoneal surfaces. Two cats had bilateral renomegaly because of lymphoma invasion (2/4) and 1 cat had local lymphadenopathy secondary to lymphoma invasion (1/4).**Conclusions and Clinical Importance:** Peritoneal lymphomatosis is a rare manifestation of lymphoma metastasis and to date appears to be associated specifically with B-cell alimentary lymphoma.

## KEYWORDS

lymphoma, mesentery, omentum, peritoneum, ultrasound

## 1 | INTRODUCTION

Lymphoma is the most common neoplasm in cats and is a diverse group that can be classified both anatomically and histologically.<sup>1</sup> Anatomic locations include alimentary, mediastinal, multicentric, nodal, leukemic, and extranodal forms.<sup>1</sup> Despite the prevalence of feline lymphoma, peritoneal dissemination (lymphomatosis) is a rarely reported metastatic manifestation. The peritoneum is devoid of lymphoid tissue; hence, the mechanism of invasion is unknown. In human

medicine seeding through the peritoneal folds and ligaments from alimentary lymphoma or lymphatic dissemination have been suggested.<sup>2</sup> Primary neoplasia arising from the peritoneum is rare as compared to secondary neoplasia, which arises from the transcoelomic spread of a malignancy originating from the epithelial (carcinomatosis), mesenchymal (sarcomatosis), or hematopoietic (lymphomatosis) cell lines.<sup>3</sup>

To the authors' knowledge, 3 cases of peritoneal lymphomatosis in cats have been reported and the sonographic characteristics are yet to be described.<sup>4,5</sup> The purpose of this article is to describe the

**Abbreviations:** ALT, alanine aminotransferase; AST, aspartate aminotransferase; CT, computed tomography; ECVDI, European college of veterinary diagnostic imaging; FeLV, feline leukemia virus; FIP, feline infectious peritonitis; FIV, feline immunodeficiency virus; HGAL, high grade alimentary lymphoma; IGAL, intermediate grade alimentary lymphoma; LGAL, low grade alimentary lymphoma.

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sonographic features of lymphomatosis of the peritoneum in cats and create awareness of this rare manifestation of alimentary lymphoma.

## 2 | MATERIALS AND METHODS

The first 2 cases presented to the Veterinary Imaging Centre, at Perth Veterinary Specialists, Australia and were scanned using a Siemens S200 ultrasound machine with a L14-5 high frequency linear probe. The 3rd and 4th cases presented to Veterinary Diagnostic Imaging Ltd, of the Veterinary Specialist Group in Auckland, New Zealand and were imaged using a Philips IE33 machine with a C8-5 curved array probe. The ultrasound examinations were performed by the same ECVDI board-certified radiologist (DT). Four different board-certified veterinary pathologists examined the samples.

## 3 | CLINICAL CASE REPORTS

### 3.1 | Case 1

#### 3.1.1 | Clinical features

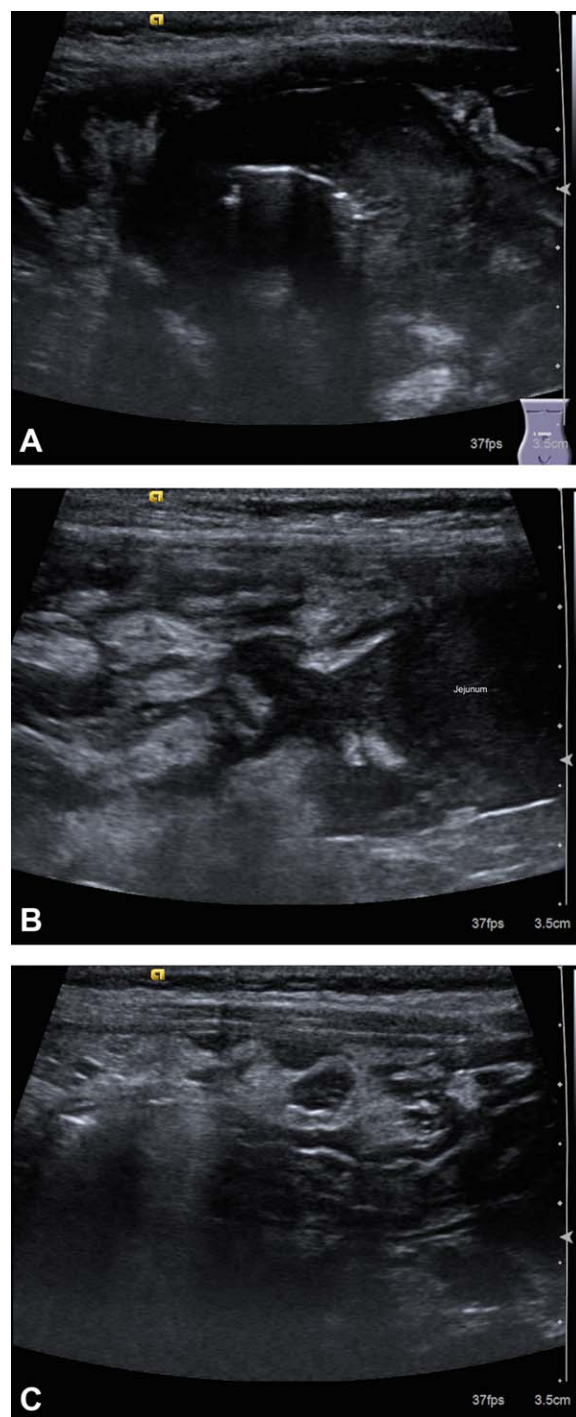
A 5-year-old, neutered male, domestic medium hair presented with a history of acute lethargy. The only abnormality detected on physical examination was a palpable abdominal mass. Hematology and biochemistry revealed nonspecific findings including a mild stress lymphopenia ( $0.37 \times 10^9/L$  [1.5–7]) and mild increase of liver enzyme activities (ALT 96 U/L [6–83] and AST 96 U/L [26–43]).

#### 3.1.2 | Sonographic findings

Within the terminal jejunum and extending into the ileum there was severe, diffuse, symmetrical and concentric transmural thickening (jejunum up to  $\sim 12$  mm thick; normal  $< 2.8$  mm)<sup>6</sup> with effacement of normal wall layering, a generalized reduction in mural echogenicity and localized hypomotility (Figure 1A). The mass did not result in a mechanical obstruction; however, the serosal margin at its mesenteric border was highly irregular and poorly defined, and coalesced with extensive sheets of abnormal thickened hypo-to-anechoic tissue which extended throughout the mesentery (Figure 1B,C). In addition, multiple small discrete-to-coalescing hypoechoic nodules and plaque-like lesions arose from the visceral and parietal peritoneal surfaces. The peritoneal fat was hyperechoic with increased attenuation and a small-to-moderate volume of anechoic free fluid was identified within the dependent aspects of the peritoneal cavity. The mesenteric and ileocolic lymph nodes were mild-to-moderately enlarged (up to  $\sim 12$  mm width; normal  $< 5$  mm)<sup>7</sup> with rounded contours and exhibited a heterogeneous-to-diffuse reduction in echogenicity. The kidneys were moderate-to-severely enlarged (51–56 mm length) with moderately irregular margins and a moderate diffuse but patchy increase in parenchymal echogenicity; the corticomedullary definition was mild-to-moderately reduced bilaterally. No further abdominal abnormalities were noted.

#### 3.1.3 | Histologic examination

Humane euthanasia was performed the same day as the ultrasound findings on owners request. Samples were collected at necropsy for



**FIGURE 1** Abdominal ultrasound images of a 5-year-old cat (case 1) with an alimentary mass and peritoneal metastasis. A, severely thickened terminal jejunal segment with transmural loss of layering. B, Diffuse and extensive hypoechoic mesenteric thickening, which coalesces with the abnormally thickened jejunal wall. C, Multiple hypoechoic nodules/plaques arising from the parietal peritoneum

histopathology. The intestinal mass revealed extensive infiltration of the serosa, muscularis, and submucosal lymphoid tissues with multifocal infiltration of the mucosa. The predominant cell type was a round cell, which displayed scant to moderate eosinophilic cytoplasm with ovoid to irregular, large, central nuclei. The nuclei had a finely granular

chromatin pattern and prominent, large central nucleoli. Marked anisocytosis and anisokaryosis were also present, together with a high mitotic rate (>40 per 10 high power field). The mesentery, subcapsular sinusoids of the mesenteric lymph nodes and renal cortex were also densely infiltrated with the same atypical lymphocytes as those seen in the ileum. Immunohistochemical staining of the tissues showed a smattering of CD3-positive T-cells whereas the tumor cells were strongly positive with the B cell marker CD20, consistent with a diagnosis of large B-cell lymphoid neoplasia. The liver and spleen were not involved.

## 3.2 | Case 2

### 3.2.1 | Clinical features

An 11-year-old, female spayed domestic medium hair presented for abdominal ultrasonographic examination because of abnormally quiet behavior, weight loss (body condition score 2.5/9), and recent inappetence. On physical examination, there was increased respiratory rate (44 br/min) and effort, mild dehydration, pale mucous membranes, and abdominal enlargement. In-house retroviral testing revealed a positive FeLV and negative FIV. Hematology revealed moderate anemia (RBC  $3.2 \times 10^{12}/L$  [5–10]) with a moderate regenerative response (1.4% reticulocytes) and a stress lymphopenia ( $0.54 \times 10^9/L$  [1.5–7]). There was also mild hypoproteinemia (57 g/L [60–80]).

### 3.2.2 | Sonographic findings

Within the mid abdomen, there was a single jejunal segment (~30 mm in length), which exhibited diffuse, circumferential, and mildly asymmetrical but concentric transmural thickening (jejunum up to ~16 mm thick). There was a generalized reduction in mural echogenicity and the normal alternating hyperechoic and hypoechoic wall layering pattern was severely distorted but not effaced. There was no evidence of a mechanical obstruction with the gastrointestinal tract both oral and aboral to the mass being predominantly empty of content. There was extensive mesenteric thickening, with coalescing sheets of well vascularized hypoechoic tissue, but no discrete nodular foci or peritoneal (visceral or parietal) lesions. A generalized increase in echogenicity and attenuation of the mesenteric fat and a small volume of anechoic free peritoneal fluid were also noted. No lymphadenopathy or further abdominal abnormalities were identified.

### 3.2.3 | Cytologic and histologic examination

Fine needle aspirates acquired under ultrasound guidance of the intestinal lesion revealed a moderately dense eosinophilic background with abundant lymphoglandular bodies and a mixed lymphoid population consisting of predominantly medium-sized lymphoid cells (67%; 1.5–2.5  $\times$  RBC diameter) with a small to moderate amount of basophilic cytoplasm, round to slightly cleaved nuclei, coarse to clumped chromatin and large variably prominent nucleoli. Occasional mitoses were also seen. Based on this atypical lymphoid population, lymphoma was suspected. The cat deteriorated over the following days and humane euthanasia and necropsy were performed. Histopathology of the intestinal mass revealed extensive infiltration of the serosa, muscularis, and submucosal lymphoid tissues with diffuse infiltration of the lamina

propria. The predominant cell type was a uniform population of small lymphocytes with scant eosinophilic cytoplasm and hyperchromatic nuclei. Similar atypical small lymphocytes extended into the mesentery insinuating between the adipocytes. Immunohistochemical staining of the tissues showed the diffuse small cell population to stain negative with CD3 and show moderate cytoplasmic staining with CD20, consistent with a diagnosis of B-cell lymphoid neoplasia. Histopathological examination of the mesenteric lymph nodes revealed a benign hyperplastic response and the liver and spleen were not involved.

## 3.3 | Case 3

### 3.3.1 | Clinical features

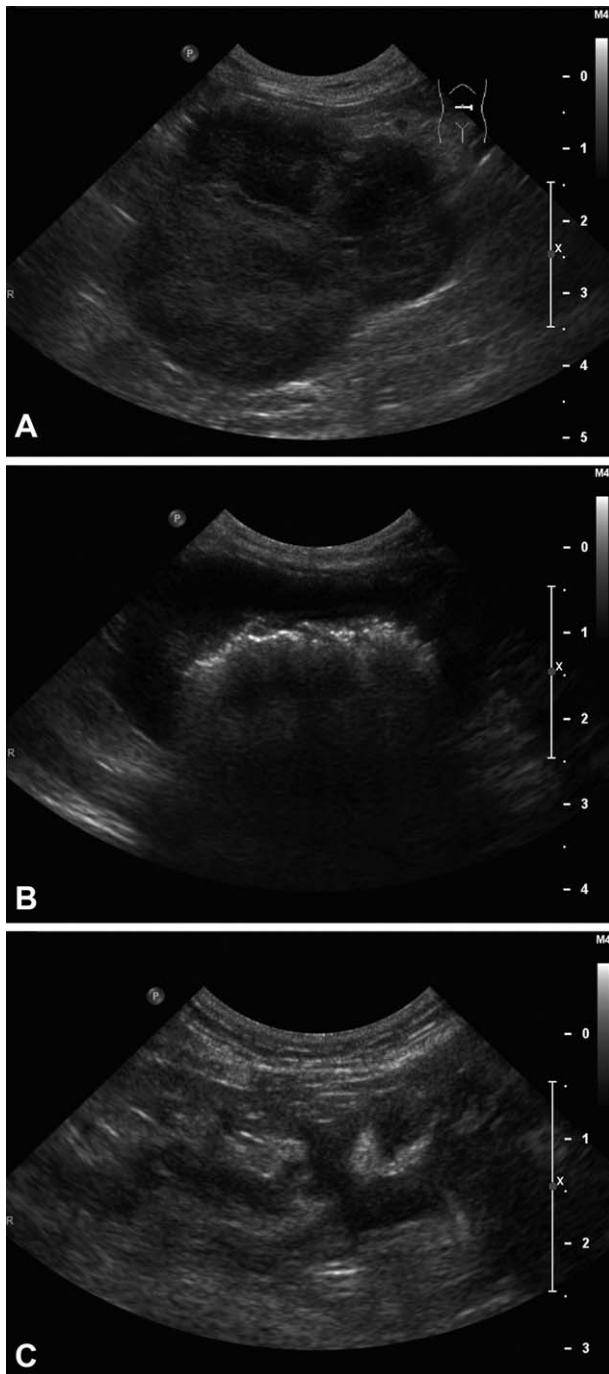
A 6-year-old, neutered male, Maine coon was presented for abdominal ultrasonographic examination after a 1-month history of chronic diarrhea since being quarantined after importation to New Zealand from Malaysia. Additionally, during this time, the owner reported intermittent inappetence and subjective weight loss. Physical examination revealed multiple small palpable abdominal masses and a low body condition score (3/9). Remaining physical examination was unremarkable. Hematology revealed mild anemia (PCV 24%) and a stress leukogram with mild neutrophilia ( $10.40 \times 10^9/L$  [1.48 – 10.29]) and mild lymphopenia ( $0.81 \times 10^9/L$  [0.92 – 6.88]).

### 3.3.2 | Sonographic findings

A large (~47  $\times$  36 mm), well defined, heterogeneously hypoechoic mass with ill-defined anechoic regions was identified within the dorsal mid abdomen and surrounded/engulfed the cranial mesenteric artery (Figure 2A). In addition, a short jejunal segment (~50 mm length) located within the caudal right abdominal quadrant exhibited severe diffuse, symmetrical, and concentric transmural thickening (up to ~13.3 mm thick) with complete effacement of wall layering and a diffusely anechoic appearance (Figure 2B). The mucosal margin of the affected segment was irregular, with dissecting intramural gas foci consistent with ulceration. There was no evidence of a mechanical obstruction. The mesenteric fat was moderately hyperechoic and contained extensive thickened sheets of abnormal hypoechoic tissue and smaller numbers of discrete-to-coalescing nodular foci (Figure 2C). Plaque-like regions of hypoechoic tissue were also present on the visceral peritoneum of the spleen. There was a minute volume of anechoic free peritoneal fluid. No lymphadenopathy or further abdominal abnormalities were noted.

### 3.3.3 | Cytological examination

Fine needle aspirates acquired under ultrasound guidance from the mesentery consisted predominantly (~70%) of large lymphocytes which were larger than a neutrophil and had round to irregular nuclei with granular chromatin, indistinct nucleoli and a small amount of basophilic granular cytoplasm which often contained several small clear vacuoles. Occasional mitotic figures were observed and the background contained numerous lymphoglandular bodies. Cytology of the jejunal mass consisted more of mixed population of lymphocytes with scattered plasma cells; however, large lymphocytes also appear to predominate in these samples and were similar to those described in the



**FIGURE 2** Abdominal ultrasound images of a 6-year-old cat (case 3) with an alimentary mass and peritoneal metastasis. A, Well-defined heterogeneous mass lesion infiltrating the root of the mesentery and encasing the mesenteric vessels. B, Diffusely thickened jejunal wall with effacement of wall layering and mucosal ulceration. C, Extensive hypoechoic mesenteric thickening mesentery. Histopathology and immunohistochemistry were not performed in this case.

### 3.3.4 | Follow-up

This case was lost to follow-up 3-months after ultrasound diagnosis. It was being treated with the COP chemotherapeutic protocol<sup>1</sup> during these 3 months and on last follow-up was clinically normal. The owners

declined further chemotherapy because of the associated stress on the cat travelling in and out of hospital.

## 3.4 | Case 4

### 3.4.1 | Clinical features

A 9-year-old, neutered male, Chinchilla cat presented for abdominal ultrasonographic examination after acute lethargy and anorexia of less than 24 hours duration. Physical examination revealed bilateral enlarged and irregular kidneys and a cranial abdominal mass. In-house biochemistry revealed a mild increase in BUN (11.3 mmol/L [3.6–10.7]) and mild decrease in sodium (140 mmol/L [142–164]). Packed cell volume and total protein concentrations were normal at 25% and 80 g/L (24%–40% and 58–80 g/L). In-house complete blood count revealed a stress leukogram with a mild neutrophilia ( $15.36 \times 10^9/L$  [1.48–10.29]), mild lymphopenia ( $0.73 \times 10^9/L$  [0.92–6.88]), mild monocytosis ( $15.36 \times 10^9/L$  [1.48–10.29]), and mild eosinophilia ( $0.01 \times 10^9/L$  [0.17–1.57]).

### 3.4.2 | Sonographic findings

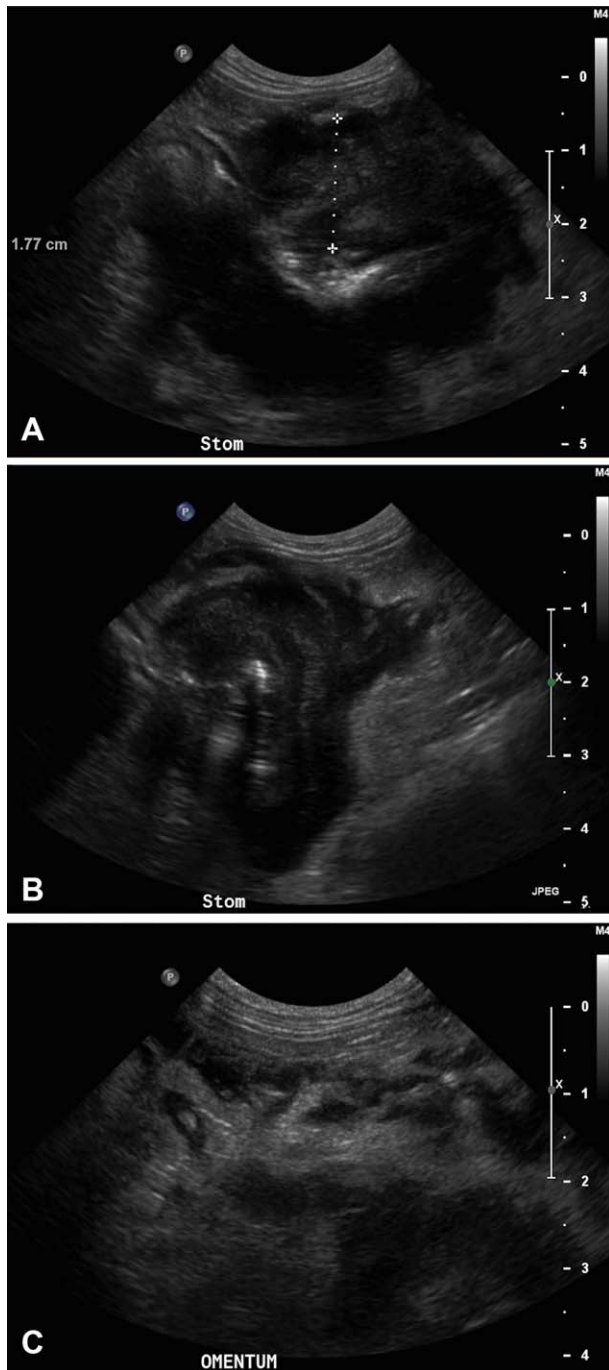
The fundus of the stomach exhibited severe diffuse but eccentric, hypo-to-anechoic, transmural wall thickening with complete effacement of normal wall layering and an irregular/ulcerated mucosal margin (Figure 3A). Abnormal hypo-to-anechoic tissue extended into the omentum from the serosal surface of the gastric mass (Figure 3B) and numerous discrete-to-confluent, plaque-like/nodular foci were evident throughout the mesentery of the cranial-to-mid abdomen (Figure 3C); multiple similar anechoic plaques were noted on the visceral peritoneum of the liver. There was also a moderate generalized increase in echogenicity of the peritoneal fat and a minute volume of anechoic free peritoneal fluid. The kidneys were moderately enlarged (~54–56 mm length) and moderately hyperechoic with an anechoic subcapsular rim bilaterally. No lymphadenopathy or further abdominal abnormalities were noted.

### 3.4.3 | Cytological examination

Fine needle aspirates of the gastric mass, omenta, and kidneys were acquired under ultrasound guidance. The gastric mass consisted of large round, discrete mononuclear cells (4–6 $\times$  RBC) with lightly vacuolated basophilic cytoplasm and round to irregular nuclei containing stippled chromatin. Smears of the omentum revealed large numbers of large round cells, similar to those described in the gastric mass, admixed with cellular debris, non-degenerate neutrophils and occasional monocytes and eosinophils. Similar large atypical round cells were also present within the sample from the left kidney. Histopathology and immunohistochemistry were not performed in this case but a diagnosis of metastatic large cell lymphoma was given.

### 3.4.4 | Follow-up

This cat died from progressive renal failure from lymphoma invasion complicated by clinical cardiac disease (hypertrophic cardiomyopathy diagnosed on echocardiogram) 3-days after ultrasound diagnosis.



**FIGURE 3** Abdominal ultrasound images of a 9-year-old cat (case 4) with a gastric mass and peritoneal metastasis. A, Severe transmural gastric wall thickening with effacement of wall layering. B, Abnormal hypoechoic tissue extending from the serosal surface of the gastric mass into the adjacent omentum. C, Multiple discrete-to-coalescing hypoechoic nodules and plaques within the omentum

#### 4 | DISCUSSION

This is a sonographic description specific to peritoneal lymphomatosis in cats. The common findings included an alimentary mural mass lesion with loss of wall layering in association with thickened, hypoechoic plaques, or sheets of abnormal tissue spreading throughout the mesentery

(intestinal mass) or omentum (gastric mass) and a small volume of peritoneal effusion. The 3 intestinal masses described were nonobstructive, focally diffuse, and circumferential, whilst the gastric mass was focally diffuse and eccentric. These findings can serve as a reference for ultrasound examinations with similar presentations.

One report of 14 cases of feline secondary peritoneal malignancies included 11 carcinomatosis, 2 lymphomatosis, and 1 sarcomatosis.<sup>5</sup> All 3 forms were grouped together and referred to solely as “carcinomatosis.” The sonographic findings were also reported together and included connecting peritoneal masses (small hypoechoic round masses throughout peritoneum of the omentum or mesentery), variably sized peritoneal effusions in all cases, lymphadenopathy in 6 cases, parietal masses in 2 cases and a single case of visceral peritoneal masses. In addition, 11 cases had extranodal masses detected in abdominal organs. It is difficult to compare these findings with this case report without clear differentiation between each case. However, there was a commonality in that the 2 lymphoma cases were alimentary: 1 gastric and 1 duodenal.

Alimentary lymphoma is the most common anatomical form of lymphoma in cats and makes up 55% of all intestinal neoplasms.<sup>8,9</sup> The 3 previously reported cases of lymphomatosis were associated with alimentary lymphoma.<sup>4,5</sup> Therefore with inclusion of the 4 cases described in this article, all reported peritoneal lymphomatosis cases have originated from an alimentary lymphoma. The histopathological forms of alimentary lymphoma range from low grade (LGAL), bearing a good prognosis with treatment, to intermediate (IGAL) and high grade (HGAL), which carry a poor prognosis.<sup>9</sup> B-cell lymphoma is associated with IGAL and HGAL and has been recognized as the most common alimentary lymphoma to develop peritoneal malignancies in human medicine.<sup>10</sup> This mirrors the results of the 2 cats described in this case series that had immunohistochemically confirmed B-cell lymphoma. Therefore, feline B-cell alimentary lymphoma may be associated with the manifestation of peritoneal lymphomatosis. This trend cannot be confirmed from this small sample population however.

Differential diagnoses based on the sonographic findings described include peritoneal carcinomatosis and granulomatous peritonitis secondary to feline infectious peritonitis (FIP); however, carcinomatosis would be considered most likely because of a similar signalment and more common disease manifestation. Other less likely differentials include sarcomatosis, primary neoplasia of the peritoneum (eg, mesothelioma), pancreatitis, chronic peritonitis, or traumatic scar tissue.<sup>5</sup> Abdominal carcinomatosis is the peritoneal spread of adenocarcinoma, most commonly located in the gastrointestinal tract, pancreas, or ovaries.<sup>11</sup> Alimentary adenocarcinoma has sonographic findings distinct from alimentary lymphoma and is typically seen as a solitary, eccentric/asymmetric or annular stenosing intestinal lesion, or gastric wall thickening with pseudo-layering.<sup>12-16</sup> When associated with carcinomatosis, hypoechoic nodular foci are seen throughout the mesentery.<sup>5,17</sup> Additional potential differentiators include renal involvement in cases of lymphoma, as this is not typically seen with alimentary carcinoma.<sup>5</sup> FIP with intestinal involvement has been described in 2 reports with a prevalence of 17%-19%.<sup>18,19</sup> The 2 reports had vastly different findings including solitary mural intestinal masses within the colon or at the ileoceocolic junction, or diffuse intestinal wall thickening.<sup>18,19</sup> Specific

peritoneal sonographic features have not been well described in FIP, however, in the author's experience (DT), abnormal hypoechoic tissue, which typically appears as contiguous thickened sheets, can be seen dissecting throughout the mesentery and lining peritoneal surfaces. This material is thought to correspond to the histologically reported fibrinous serositis/peritonitis described with FIP.<sup>20,21</sup> Carcinomatosis and FIP have similar mesenteric sonographic findings to lymphomatosis, however, the index of suspicion for lymphomatosis should increase in the presence of either a focally diffuse nonobstructive intestinal mass or focally diffuse eccentric gastric mass with loss of wall layering. Another variable to consider is the mean age at diagnosis. In this case series, the cats were middle-aged with a mean of 7.8 years whereas the mean reported age of carcinomatosis and FIP is 12.7 years and 3–16 months, respectively.<sup>5,22</sup>

It is important to differentiate between the alimentary forms of lymphoma versus adenocarcinoma for treatment and prognostic reasons. The treatment of B-cell alimentary lymphoma involves chemotherapy and the prognosis is generally poor.<sup>1</sup> Whereas alimentary adenocarcinoma treated with surgical excision is reported to have an average survival time of 365 days even in the presence of carcinomatosis.<sup>23</sup> Therefore, it is important to obtain a definitive diagnosis in cases with similar ultrasound findings of an intestinal mass and peritoneal involvement.

Ultrasound is the mainstay for diagnosing intestinal diseases in dogs and cats, whereas human medicine relies heavily on computed tomography (CT).<sup>17,24</sup> The differences between the CT appearance of the 3 peritoneal secondary malignancies in humans has been described and includes multiple small nodules with local lymphadenopathy in carcinomatosis, bulky heterogeneous masses in sarcomatosis and bulky homogenous masses with diffuse lymphadenopathy in lymphomatosis.<sup>3</sup> Additionally, carcinomatosis was generally associated with larger quantities of free abdominal fluid than lymphomatosis.<sup>3</sup> Overlapping features existed, however, and patterns of peritoneal lymphomatosis can be indistinguishable from peritoneal carcinomatosis and sarcomatosis which warrants consideration.<sup>3</sup> The CT appearance of lymphomatosis in cats has not been described.

In this case report, diagnosis of alimentary lymphoma with peritoneal lymphomatosis was achieved with histopathology of the alimentary mass and abnormal peritoneal tissue in 2 of the 4 cases. The 3rd and 4th cases were diagnosed with cytological analysis of the mass and abnormal peritoneum. The lack of histopathological diagnosis and immunohistochemistry in these cases represents a study limitation, however, the cytological diagnosis of lymphoma in conjunction with typical ultrasound findings is often considered sufficient for diagnosis.<sup>1</sup>

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#### CONFLICT OF INTEREST DECLARATION

The authors declare that they have no conflict of interest with the contents of this article.

#### OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

#### INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

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