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Ultrasonographic nodular appearance of small bowel metastasis from canine mammary carcinoma

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3 1 Ultrasonographic nodular appearance of small bowel metastasis from canine
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10 4 Elisabet Domínguez, Eduard Anadón, Yvonne Espada, Llorenç Grau-Roma,
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12 5 Natàlia Majó, Rosa Novellas.
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16 7 Key words: Mammary carcinoma, intestinal metastasis.
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18 8 Running head: Nodular small bowel metastasis mammary carcinoma
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10 **Abstract**

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

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20 **Signalment, history and clinical findings**

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

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

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

29 Medical treatment was initiated with fluid therapy (Ringer Lactate, B Braun
30 VetCare SA, Rubí, Spain; 15.4ml/h, IV), fenbendazol (Panacur, Intervet
31 International B.V., Salamanca, Spain; 50mg/Kg, PO), and intestinal diet
32 (Prescription Diet™ i/d™ Canine canned, Hill's Pet Nutrition, Inc®/™., USA).
33 Diagnostic imaging exams, including thoracic and abdominal radiographs and
34 ultrasound scan, were performed.

35 **Imaging diagnosis**

36 Abdominal ultrasound was performed using high frequency sectorial (CA123,
37 convex-array, 3-9 MHz) and linear (LA523, linear-array, 4-13 MHz) transducers
38 (MyLab™70 Esaote, Italy). Multiple, oval to rounded, well defined and well
39 margined, hypoechoic nodules, measuring between 0.3 and 0.7cm were
40 observed in the muscularis layer of the jejunal wall (Fig. 1). The nodules did not
41 alter the remaining normal layers of the affected intestinal segment, being the
42 mucosa, submucosa, and serosa clearly identified. In general, the thickness of
43 the jejunal wall was within normal limits (less than 5mm), except where nodules
44 were present. In such areas, the intestinal wall reached 6mm. No significant

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3 45 ultrasonographic abnormalities were detected on the thickness, layering and
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5 46 content of the stomach, duodenum, ileum or colon. Mixed gastrointestinal
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7 47 luminal content with gas, fluid, and mucous patterns was observed, and
8
9 48 gastrointestinal motility of all segments, including the jejunum, was considered
10
11 49 normal. No blood flow signal was detected inside the nodular lesions using
12
13 50 Color Doppler ultrasound as in the rest of the intestinal wall (Fig. 2). No signs of
14
15 51 vascular abnormalities, such as luminal thrombi, were evident in the mesenteric
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17 52 regional vessels.

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21 53 Well defined, hypoechoic nodules of less than 2 cm were also visible in the
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23 54 spleen, cranial pole of the right kidney, adrenal glands, abdominal wall, and
24
25 55 mesentery. A small amount of anechoic peritoneal effusion was observed
26
27 56 between intestinal loops.

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29
30 57 Thoracic radiographs revealed a mixed pulmonary pattern with marked diffuse
31
32 58 bronchointerstitial component, presence of small pulmonary nodules, and
33
34 59 alveolar pattern affecting the caudal portion of the left cranial lung lobe. An
35
36 60 aggressive lytic lesion in the spinous processes of T4 and T5 was also
37
38 61 observed. Abdominal radiographs did not show significant abnormalities.

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41 62 Non-cardiac thoracic ultrasound demonstrated the presence of 0.5-0.9cm
42
43 63 pulmonary nodules in contact with the thoracic wall and consolidation of the left
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45 64 cranial lung lobe.

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47 65 The presumptive imaging diagnosis was a malignant mammary tumor with
48
49 66 multiple metastases to thoracic and abdominal structures. The differential
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51 67 diagnosis for the nodules affecting the muscularis layer of the jejunum included
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53 68 nodular infiltration due to primary intestinal neoplasia (lymphoma, mast cell
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55 69 tumor, disseminated histiocytic sarcoma) or metastatic infiltration. Other
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3 70 differentials such as intestinal smooth muscle tumor, muscular hypertrophy,
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5 71 muscular hyperplasia, hematoma, or granuloma, were considered less likely.¹⁻⁶
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8 **Outcome and pathologic findings**

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10 73 Positive response to medical treatment was observed during the first day of
11
12 74 hospitalization. However, clinical signs worsened the following hours and the
13
14 75 owners elected euthanasia. Complete post-mortem examination was
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16 76 performed.

17
18 77 Macroscopically, three well-defined nodules, measuring 0.5-1cm diameter, were
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21 78 present in the distal jejunum. Nodules were solid and whitish on cross-section
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23 79 and did not disrupt the intestinal mucosa or serosa (Fig. 3). Similar nodular
24
25 80 lesions were detected in the mammary glands, inguinal superficial lymph nodes,
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27 81 abdominal wall, thoracic epaxial muscles, and in other thoracic and abdominal
28
29 82 viscera-including the lungs, heart, spleen, liver, kidneys, and adrenal glands.

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31 83 Microscopically, all the nodules showed a similar histological pattern. In the
32
33 84 intestine, macroscopic nodules corresponded to a non-encapsulated and poorly
34
35 85 demarcated neoplastic proliferation that severely infiltrated the tunica
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37 86 muscularis and submucosa of the intestinal wall (Fig. 4). Neoplastic cells were
38
39 87 organized in small acini or solid nests, within a fine fibrovascular stroma.
40
41 88 Neoplastic cells were epithelial, polygonal to cylindrical-shaped, medium in size
42
43 89 (15-30 μm in diameter) and showed indistinct borders. They showed a
44
45 90 moderate amount of pale eosinophilic, and often vacuolated, cytoplasm and a
46
47 91 central, rounded to oval big nucleus, with finely stippled chromatin and mainly
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49 92 one prominent eosinophilic nucleolus. A moderate degree of pleomorphism,
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51 93 anisocytosis, and anisokaryosis was evident, and a moderate to large number
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53 94 of mitosis (2 to 6 per 40x HPF) were present. Within the tumour, several
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3 95 extensive areas of coagulative necrosis, fibrin and haemorrhage were
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5 96 observed. Presence of neoplastic emboli was detected in the lymphatic vessels
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7 97 of the intestinal submucosa.
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10 98 **Discussion**

11 99 The ultrasonographic appearance of canine primary intestinal neoplasia,
12
13 100 including carcinoma, lymphoma, and smooth muscle tumors has been well
14
15 101 characterized.^{2, 7-13} Primary intestinal neoplasms are uncommon in dogs, being
16
17 102 adenocarcinoma and lymphoma the most frequent primary canine
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19 103 gastrointestinal tumors. Other described malignancies include leiomyosarcoma,
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21 104 fibrosarcoma, poorly differentiated sarcoma, mast cell tumors, carcinoid,
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23 105 hemangioma, and osteosarcoma. Benign tumors include polyps and
24
25 106 leiomyomas.^{7,14-16} The most common ultrasonographic findings in canine
26
27 107 intestinal carcinomas are transmural thickening of the intestinal wall, which is
28
29 108 usually focal with complete loss of the normal intestinal layering, changes in the
30
31 109 normal wall echogenicity, decreased focal intestinal motility with or without signs
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33 110 of intestinal obstruction, regional lymphadenopathy and/or nodules at the
34
35 111 mesentery/omentum.^{2,9,11} Alimentary lymphoma in dogs can be diffuse or can
36
37 112 appear as a solitary hypoechoic intestinal mass with transmural thickening and
38
39 113 loss of wall layering. It is the most common neoplastic cause of diffuse
40
41 114 infiltration and wall thickening in dogs. Lymphoma may cause partial stenosis of
42
43 115 the intestinal lumen, but it usually does not cause complete obstruction.
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45 116 Regional lymphadenopathy with enlarged, rounded, and hypoechoic lymph
46
47 117 nodes is common. Other reported findings are reduced wall echogenicity and
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49 118 decreased motility.^{2,9,17} Leiomyosarcomas are malignant smooth-muscle
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51 119 tumors that originate from the muscularis layer of the bowel wall. They are often
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3 120 large, heterogeneous, mixed echogenic intramural lesions with eccentric
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5 121 growing pattern.^{2,10,18} Leiomyomas tend to be small, and appear as focal
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7 122 intramural hypoechoic thickening with loss of wall layering.⁹
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10 123 Canine mammary gland tumor is one of the most common neoplasia,
11
12 124 accounting for approximately 50% of all tumors in intact female dogs.¹⁹
13

14 125 Malignant canine mammary tumors have the potential to metastasize. In
15
16 126 general, malignant epithelial mammary tumors metastasize via lymphatic
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18 127 vessels to regional lymph nodes and the lungs. However, more distant
19
20 128 metastases sites, including the liver, spleen, bone, and brain have been
21
22 129 described. Intestinal metastases have rarely been reported in dogs, without
23
24 130 specification of which intestinal layer was affected.²⁰ Skeletal and cardiac
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26 131 muscle metastatic infiltration from mammary tumors has also been reported.²¹⁻²⁵
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29 132 However, no references about intestinal smooth muscle metastasis have been
30
31 133 found.
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34 134 In women, breast carcinoma is the most common neoplasm.²⁶ Metastatic breast
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36 135 disease usually affects the lungs, liver, bones, soft tissue, brain, and adrenal
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38 136 glands. As it occurs in dogs, gastrointestinal involvement is uncommon and it
39
40 137 mainly affects the stomach, colon and rectum, with direct invasion of lymphatic
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42 138 vessels as the proposed mechanism.²⁷ Metastases to the duodenum, jejunum,
43
44 139 and ileum are rare and usually associated with peritoneal carcinomatosis.²⁷
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47 140 Common imaging findings of intestinal metastases are diffuse mural thickening
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49 141 of the intestinal wall -often associated to mucosal ulceration-, regional
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51 142 lymphadenopathy, peritonitis, and the presence of single or multiple sites of
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53 143 intestinal obstruction secondary to intestinal masses or strictures.²⁷⁻²⁹
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56 144 Gastrointestinal breast cancer metastases are recognized at necropsies, but the
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3 145 presence of clinical signs is uncommon.^{28,29} Patients can show abdominal pain,
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5 146 diarrhea, vomiting, fatigue, anemia, inappetence, hyporexia, and signs of
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7 147 intestinal obstruction, mimicking other disorders such as Crohn's disease.²⁹⁻³⁰
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10 148 In the case presented here, a paraneoplastic syndrome is the most likely
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12 149 explanation for most of the presenting clinical signs (anorexia, lethargy, and
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14 150 diarrhea). Diarrhea is one of the clinical signs observed in human cancer
15
16 151 patients.³¹ Although diarrhea secondary to small intestine neoplastic affection is
17
18 152 usually seen in dogs with jejunal or ileal tumors³², the small size and muscular
19
20 153 location of the nodules and the fact that the intestinal mucosa was intact, makes
21
22 154 direct effect of the neoplasia less likely. Inappetence and weakness may have
23
24 155 been exacerbated in this dog by the presence of hypercalcemia, which has
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26 156 been associated with several tumor types, including mammary gland carcinoma
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28 157 and adenocarcinoma.^{33,34}
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32 158 The unique ultrasonographic appearance of the intestinal metastases in this
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34 159 case -described as nodular, well defined hypoechoic nodules affecting the
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36 160 muscularis layer- has not been described in other intestinal neoplasms. Thus, it
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38 161 may be considered as a pattern of intestinal metastases.
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258 **Figures**

- 49 259 Fig.1. A. B-Mode ultrasonographic image of the jejunum. A well-defined
50
51 260 hypoechoic nodule is located in the muscularis layer of the intestinal wall
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53 261 causing mild thickening of the affected segment. The submucosa and serosa
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3 262 layers show normal ultrasonographic appearance. B. Schematic image of the
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5 263 parietal nodule (arrows).
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7 264 Fig. 2. Color Doppler image of another segment of the distal jejunum. A well-
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9 265 marginated hypoechoic nodule is present in the muscularis layer of the
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11 266 intestinal wall. No abnormal flow signal was detected inside the nodular lesion
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13 267 as in the rest of the intestinal wall.
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16 268 Fig. 3. Macroscopic image of the jejunum. A well-defined, solid nodule,
17
18 269 measuring 0.5-1cm diameter, is visible in the distal jejunum (arrow). The nodule
19
20 270 did not disrupt the intestinal mucosa or serosa.
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22

23 271 Fig. 4. Microscopic image of the metastasis of mammary carcinoma infiltrating
24
25 272 the intestinal submucosa and tunica muscularis. Inset: high power magnification
26
27 273 image showing the cytological characteristics of the neoplastic cells. Mitosis are
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29 274 numerous (arrowheads).
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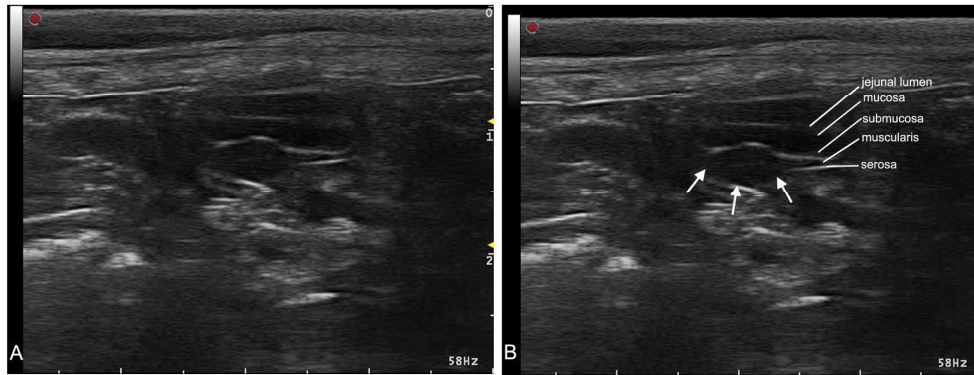


Fig.1. A. B-Mode ultrasonographic image of the jejunum. A well-defined hypoechoic nodule is located in the muscularis layer of the intestinal wall causing mild thickening of the affected segment. The submucosa and serosa layers show normal ultrasonographic appearance. B. Schematic image of the parietal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

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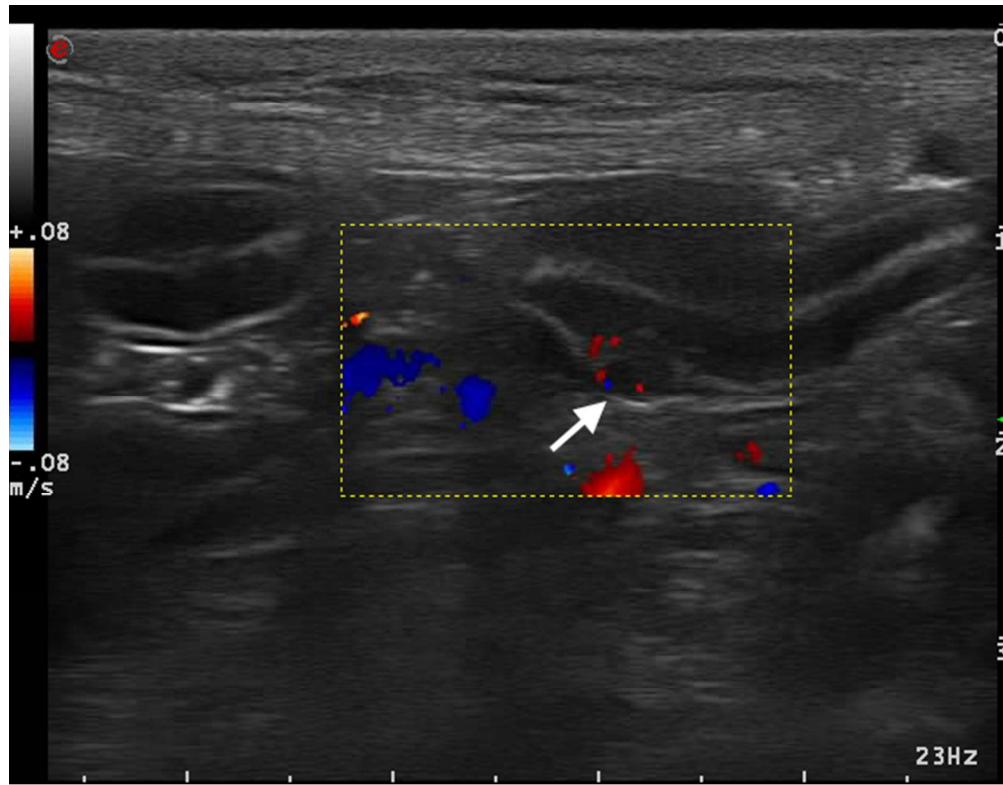


Fig. 2. Color Doppler image of another segment of the distal jejunum. A well-margined hypoechoic nodule is present in the muscularis layer of the intestinal wall. No abnormal flow signal was detected inside the nodular lesion as in the rest of the intestinal wall.
167x130mm (96 x 96 DPI)

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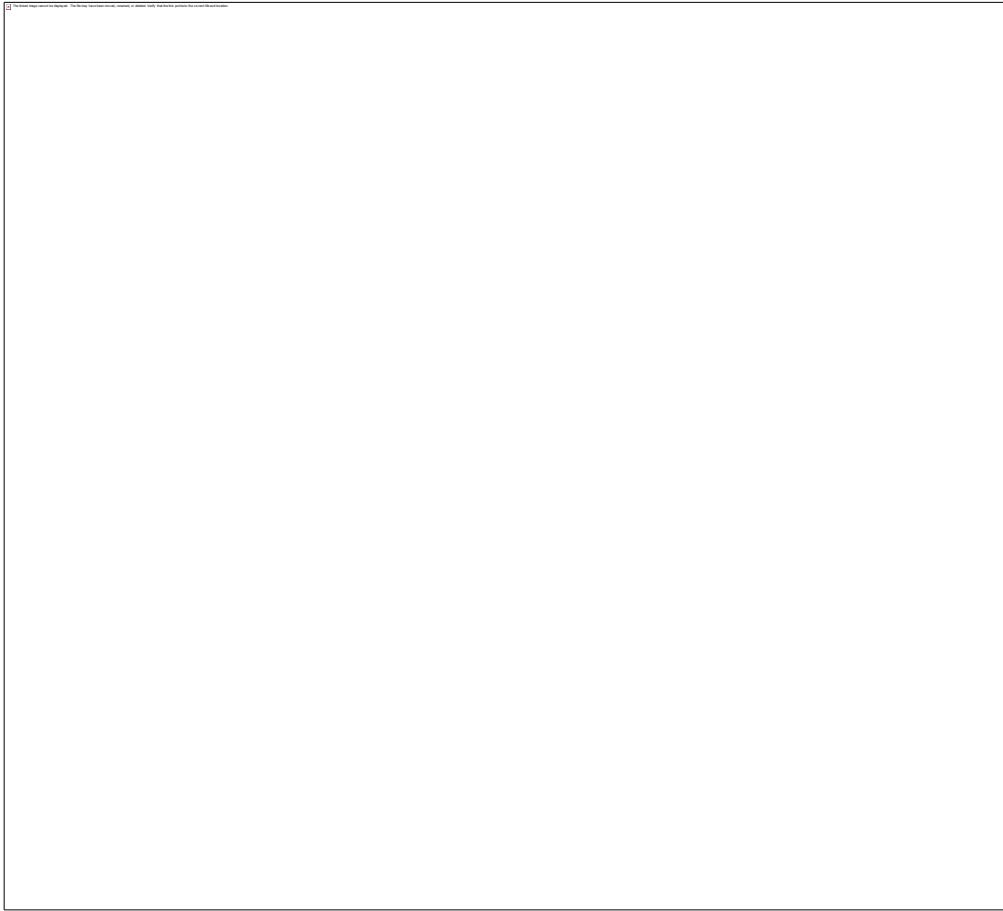


Fig. 3. Macroscopic image of the jejunum. A well-defined, solid nodule, measuring 0.5-1cm diameter, is visible in the distal jejunum (arrow). The nodule did not disrupt the intestinal mucosa or serosa.
87x79mm (300 x 300 DPI)



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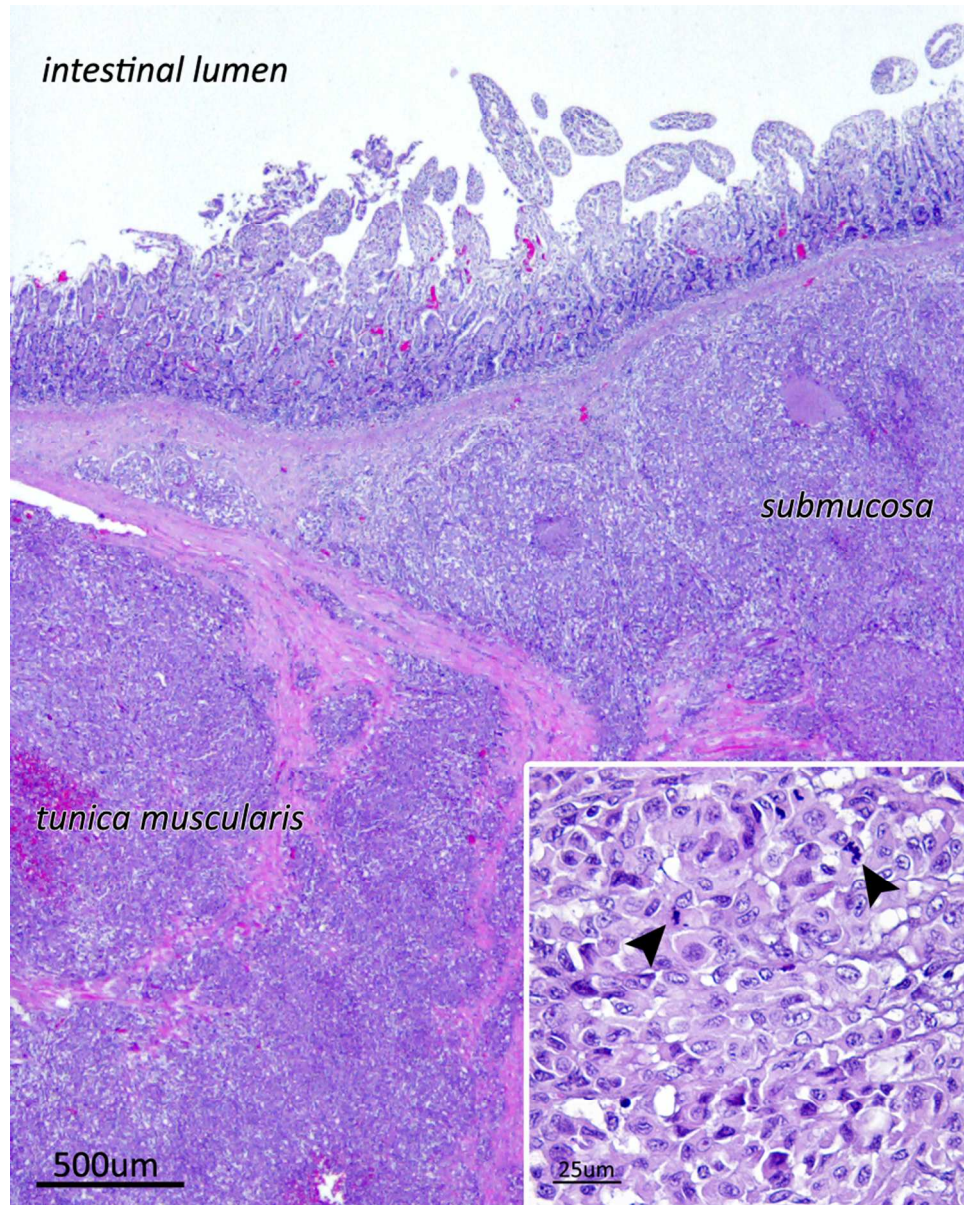


Fig. 4. Microscopic image of the metastasis of mammary carcinoma infiltrating the intestinal submucosa and tunica muscularis. Inset: high power magnification image showing the cytological characteristics of the neoplastic cells. Mitosis are numerous (arrowheads).
86x108mm (300 x 300 DPI)