

Ultrasonographic and histopathological findings of gastric adenocarcinoma in a uremic cat

Ultrasonografische en histopathologische bevindingen bij een uremische kat met maagadenocarcinoom

¹M. Esmans, ¹A. LeGarrères, ¹A. Bongartz, ¹F. Carofiglio, ²M. Heimann, ³T. Schwarz

¹Clinique Bongartz et associés, 10 rue Sopers, B-4030 Grivegnée

²Anapet, 269 rue du Faubourg, B-6110 Montigny le Tilleul

³The Royal (Dick) School of Veterinary Studies, The University of Edinburgh, Roslin Midlothian, EH25 9RG, UK

mayaesmans@gmail.com

ABSTRACT

Gastric carcinoma is very rare in cats. In this case report, a gastric adenocarcinoma in a chronically uremic cat is described. The cat presented with vomiting, dysorexia and weight loss. The ultrasound examination demonstrated an ultrasonographic pseudolayering effect on the gastric wall, which is suggested as a specific sign of adenocarcinoma. On histopathology, this adenocarcinoma was organized, and a continuous intralymphatic infiltration line was visible underneath the muscularis mucosae, which might explain the pseudolayering effect.

SAMENVATTING

Een maagcarcinoom is zeer zeldzaam bij katten. In deze casuïstiek wordt een maagcarcinoom bij een chronisch uremische kat beschreven. De kat vertoonde symptomen als braken, gedeeltelijke dysorexie en gewichtsverlies. Op het ultrasonografisch onderzoek bleek dat de maagwand pseudogelaagd was, wat een specifieke indicatie is voor adenocarcinoom. Uit het histopathologisch onderzoek bleek dat dit adenocarcinoom gestructureerd was en dat een doorlopende intralymfatische infiltratielijn zichtbaar was onder de muscularis mucosae. Dit zou de pseudogelaagdheid kunnen verklaren.

INTRODUCTION

Gastrointestinal adenocarcinoma occurs more rarely in cats than in humans and dogs. The stomach is the least frequently reported location. Only four cases of gastric adenocarcinoma have been reported in cats, representing only 1% of all reported gastrointestinal adenocarcinoma in this species (Turk et al., 1981; Rossmeisl et al., 2002; Dennis et al., 2006).

CASE REPORT

History, physical examination, laboratory tests and ultrasonographic findings

A 20-year-old, castrated, male domestic short hair cat was presented for chronic vomiting, dysorexia and progressive weight loss over one year. The cat had

been diagnosed four years previously with chronic nephropathy with increased creatinine and uremia values by the referring veterinarian. This nephropathy had been well-controlled for several years.

On physical examination, the cat was cachectic and had a heart murmur. A hard structure was palpated in the cranial abdomen.

Diagnostic tests including complete blood count, serum biochemical profile, serum total thyroxin (T4) concentration and abdominal ultrasonography were performed. The complete blood count was within normal limits but the serum biochemical profile revealed mild creatinemia of 2 mg/dL (reference range: 0 to 1,8mg/dL) and mild azotemia of 153mg/dL (reference range, 16 to 35mg/dL). The T4 serum concentration was also increased at 5,6 µg/dL (reference range: 1,5 to 4,8 µg/dL).

Abdominal ultrasonography revealed two major abnormalities. The kidneys were normal in size (3.6

cm in length for the left and 3.8 cm for the right kidney), but they had an irregular outlining and a hyperechoic cortex, consistent with the chronic nephropathy previously diagnosed. There was a marked thickening of the gastric wall (up to 12mm, reference range <4mm) (Newell et al., 1999) with loss of normal gastric folds and normal architecture, induced by modified wall layering. The fundus and pyloric antrum had an excessively thick submucosal layer, consistent with pseudolayering (Penninck et al., 1998) and the limit of the serosa could not always be clearly defined. The inner and outer surfaces were mildly irregular (Figure 1). The pyloric antrum showed additional small mass effects involving the muscularis and serosal layers (Figure 2). The stomach was completely immotile and the peripheral fat was mildly hyperechoic. The proximal duodenum was affected by similar wall changes. No gastric lymph nodes were identified but there was a hypoechoic 5mm-large lymph node in the pancreatic area. The liver was enlarged and heterogeneous in echogenicity with multiple small hypoechoic nodules. The spleen was normal in size but contained a 5mm by 9mm-oval, mildly hypoechoic zone in the hilus (Figure 3). There was no abdominal free fluid.

Considering the poor prognosis associated with these findings, the owner elected euthanasia and a complete postmortem examination was performed.

Anatomic and histopathologic findings

On macroscopic examination, the stomach had a thickened and firm wall with loss of elasticity. Sessile to polypoid nodules were present on the serosal surface, some of which were associated with engorged lymph vessels (Figure 4A). At the opening of the stomach, a coarsely nodular fundic mucosa was identified (Figure 4B) and multiple, randomly distributed nodular, sessile masses ranging from 3 mm to 25 mm in diameter were noted. The largest mass had a granular appearance (Figure 4B). On transverse sections, the level of thickening was variable and was limited to the mucosa in most areas with foci of transmural thickening and loss of architecture within the fundus and pyloric antrum. The pancreatic lymph node was hyperplastic, circular and of increased, firm consistency. The mesentery showed numerous miliary nodules (Figure 4C). The spleen showed stromal invasion by continuity, developing from a local mesenteric metastasis (Figure 3).

Microscopic examination of the stomach wall revealed multifocal areas of neoplastic proliferation. In general, the neoplastic growth pattern was of the intestinal tubular type (Figure 5) but in a few areas, above the tubular areas, within the fundus, foci of diffuse solid carcinoma with signet ring cells could be observed. In the tubular pattern, the nuclei were large with irregular contour, contained a reticular vesiculous chromatin and a prominent eosinophilic nucleoli. The

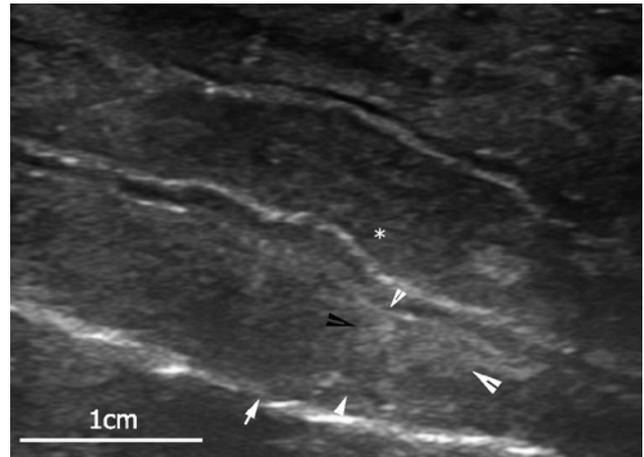


Figure 1. Ultrasonographic image showing severe thickening of the gastric fundus wall (10mm) with a thick echoic central proliferation and loss of normal layering (8mm, between white arrowheads). Within the echoic proliferation islands of particular hyperechogenicity are visible (between black arrowheads). * Lumen, arrow: serosa.

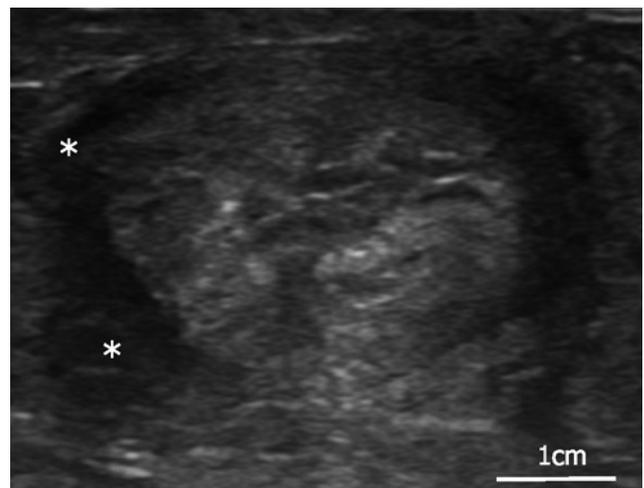


Figure 2. Ultrasonographic image showing a thickened pyloric antrum wall with muscular and serosal nodular proliferations (*).

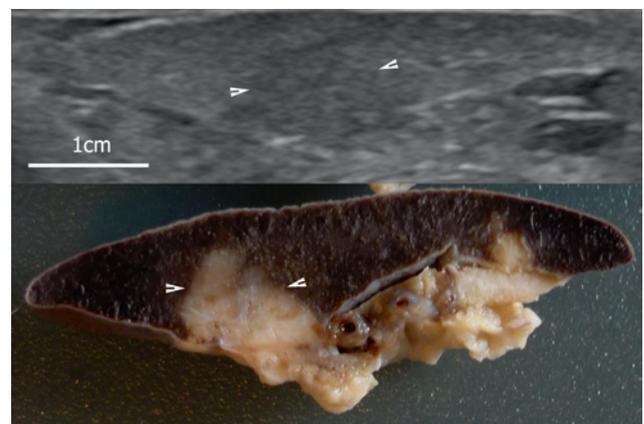


Figure 3. Ultrasonographic image and post-mortem image of the corresponding cut surface of the spleen. There is a stromal infiltration at the hilus (between arrowheads).

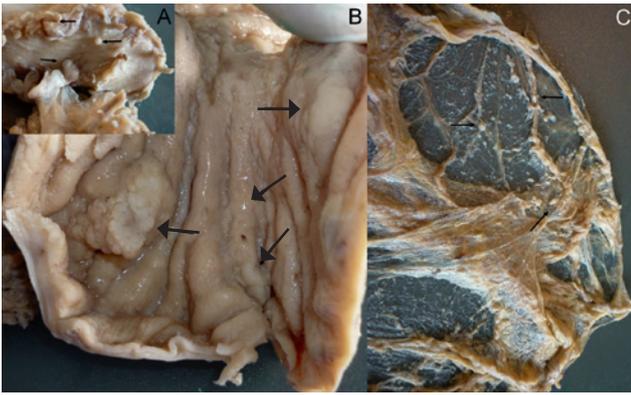


Figure 4. Macroscopic aspect of the stomach wall after formalin fixation. The serosal surface reveals numerous nodules (quadrant A arrow) and dilated invaded lymph vessels. The quadrant B illustrates the mucosal surface of the stomach. The plicae are thickened, and numerous randomly distributed sessile lesions are seen ranging from 3 to 25 mm (black arrows). The white arrow points to the largest lesion with a granular surface. The mesentery shows numerous miliary nodules (quadrant C, arrows).

mitotic activity was of 24 mitosis per 10 high power field (2 /10hpf within the normal mucosa). The fibrosis accompanying the carcinoma within the mucosa was minimal and not desmoplastic. The surrounding non-neoplastic mucosa demonstrated mild to moderate multifocal inflammatory reaction. This inflammation was superficial or deep, mainly lymphocytic with mild epitheliotropism. Occasional foci of nuclear atypia could be seen in different types of cells, and were associated to occasional tubular structure formation among the fundic glands. In some areas, the gastric pits were slightly elongated and tortuous. No specific organism was observed. Within the submucosa, a continuous, intralymphatic line of neoplastic infiltration was present, running underneath the muscularis mucosae (Figure 5). In the more severely involved areas, the deep submucosa, the muscularis up to the serosa, were full of neoplastic infiltration associated with severe desmoplastic fibrosis and inflammation. The mesentery and splenic parenchyma revealed a tubular neoplastic infiltration associated with desmoplasia. Occasional papillary projections could be seen within vessels or on the serosal surfaces. These infiltrates had the cytological atypia of the most aggressive foci of the gastric wall. Microscopically, the pancreas was within normal limits.

The tumor was strongly positive for cytokeratin 7, negative for cytokeratin 5/6, showed a sporadic positivity for cytokeratin 20, and was negative for gastrin and chromogranin. The mitotic index evaluated with Ki67 was of 28%. Various organ sections served as external control.

Following the macro- and microscopic examinations, this gastric carcinoma was classified as a type I, nodular to polypoid form.

DISCUSSION

The normal ultrasonographic appearance of the gastric wall has been reported in cats (Newell et al., 1999; Couturier et al., 2012), but there is only one report to date describing the ultrasonographic appearance of a gastric carcinoma in the cat (Rossmesl et al., 2002). One other study described the ultrasonographic appearance of intestinal adenocarcinoma in five cats (Rivers et al., 1997a). Gastrointestinal lymphoma is considered the most common gastric neoplasia in cats. Ultrasonographically gastrointestinal lymphoma appears as wall thickening with loss of layering and/or proliferation of the muscularis layer (Barrs and Beatty, 2012; Zwingenberger et al., 2010; Daniaux et al., 2013).

Gastric wall thickening with loss of normal layering is suggestive but not pathognomonic for neoplasia (Lorentzen et al., 1993; Kaser-Hotz et al., 1996; Rivers et al., 1997b; Penninck et al., 1998; Lamb and Grierson, 1999; Beck et al., 2001; Swann and Holt, 2002). This feature has also been described with severe gastritis, ulceration (Penninck et al., 1997), eosinophilic granulomatous gastroenteritis (Rodriguez et al., 1995; Brellou et al., 2006), chronic hypertrophic pyloric gastropathy (Biller et al., 1994) and uremic gastropathy (Grooters et al., 1994) in dogs. Modified wall layering with pseudolayering has been described in dogs but not in cats with adenocarcinoma (Penninck et al., 1998; Beck et al., 2001). Pseudolayering consists of a poorly echogenic lining on the innermost and/or outermost portions of the gastric wall separated by a more echogenic central zone and has been suggested to be specific for gastric carcinoma in dogs (Penninck et al., 1998).

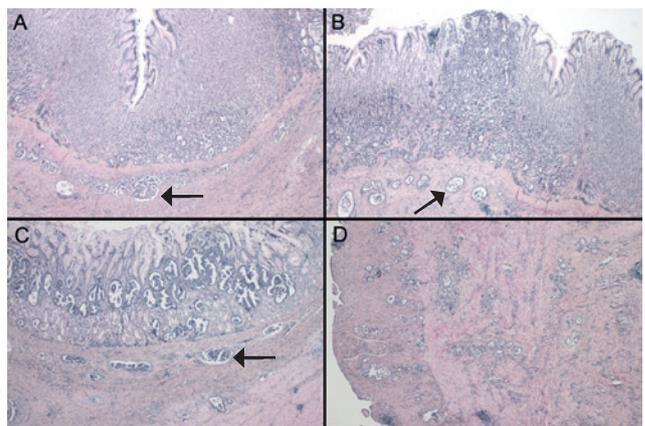


Figure 5. Histopathology of the stomach wall (HE, x 40). The quadrants A and B show sections at the level of the fundus and the quadrant C at the level of the pyloric antrum. The arrows point to lymphatic cell invasion. The lymphatic infiltration is surrounded by a band of fibrosis, which matches the echographic observation. The quadrant D illustrates the severe fibrosis and tumoral infiltration in the subserosal and muscular layer.

In the present case, some anatomic findings were easy to identify by ultrasound as the loss of motility/elasticity, the irregular nodular appearance on the serosal layer and the regional adenopathy. Some other ultrasonographic findings were not as clear. The macroscopic invasion of the spleen was really evident, whereas the ultrasonographic findings were only subtle. Ultrasonographically, the mesenteric fat was brighter than normal but the military nodules could not be identified, and the gastric wall thickness was variable in size but the nodules on the mucosal surface were not identifiable, maybe because of the normally folded nature of the stomach.

On histopathology, the continuous intralymphatic line of neoplastic infiltration running underneath the muscularis mucosae could be part of the pseudolayering effect seen on ultrasound, described as a poorly echogenic lining on the innermost and/or outermost portions of the wall separated by a more echogenic central zone (Penninck et al., 1998). Ultrasonographic pseudolayering is thought to be an effect of hemorrhagic neoplastic infiltration. A well-organized neoplastic architecture had already been described previously (Penninck et al. 1998). The line in this case is irregular and often triangular in shape and matches the hyperechoic areas in the central echoic line of the pseudolayering. The more echoic appearance of this zone can be explained by an increased scattering of ultrasound waves secondary to the irregular margins and increased cellular content of the mass lesion (Kremkau, 2011).

The most common clinical signs reported with gastric neoplasia are vomiting, partial anorexia and weight loss (Penninck et al., 1998; Swann and Holt, 2002). Those signs are not specific, and could be seen in numerous conditions. In this case, those signs were also compatible with uremic gastropathy (Grooters et al., 1994), which could have been suspected in this case and hence might have been a limiting factor for clinical detection of gastric carcinoma in cats. This demonstrates the importance of a thorough clinical examination and good differential diagnosis, particularly in case of uncontrolled chronic renalopathy in cats.

Atrophic gastritis and intestinal metaplasia are well accepted precancerous conditions for gastric cancer in humans and hamsters (Sipponen and Marshall, 2000; Peek and Blaser, 2002; Nambiar et al., 2005). This atrophic gastritis is characterized by a loss of normal mucosal glands and can be found also in dogs with uremic gastropathy (Cheville, 1979; Grooters et al., 1994; Peters et al., 2005). There are no reports of uremic gastropathy and atrophic gastritis in cats to date, but it is interesting to note that all reported cats with gastric adenocarcinoma were older animals and three of the four cases had additional gastric conditions, such as uremia (one case) (Rossmesl et al., 2002), gastric parasites (two cases) (Dennis et al. 2006), whereas in the remaining case additional pathology was not reviewed (Turk et al., 1981). On the other hand, chronic nephropathy is a very common condi-

tion in older cats, cancer preferentially occurs at an advanced age, and particularly, gastric carcinoma are very rare in cats. Therefore, the nephropathy and the gastric cancer development may have been independent events in the cat of the present case.

In conclusion, this report is the first description of a feline gastric carcinoma, which bears many similarities to gastric carcinoma in other species. Gastric carcinoma should be considered in cats with gastric wall lesion and be differentiated from more common forms of gastric neoplasia such as lymphoma.

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Uit het verleden

28 FIESIETEN VOOR EEN CRUPEL PEERT (1784)

Een rekening in 1784 opgemaakt door de Brugse 'peerdemeester' Van Ende voor de verzorging ('miestere') van een kreupel paard (Reeks 'Vliegende bladen' - Ephemera I - V15 van de Gentse universiteitsbibliotheek) geeft een indruk van hoe het er in die tijd in dergelijke gevallen kon aan toe gaan.

Het 'crupel peert' van een klaarblijkelijk kapitaalkrachtige eigenaar vergde een langdurige en dure behandeling, met zalven en poeders en niet minder dan 28 bezoeken ter plaatse ('visiten', hier fiesieten geschreven, in het begin twee of zelfs drie per dag). Daarvoor werd in totaal 4 pond, 19 schellingen en 2 groot Vlaams aangerekend (omgezet: 1190 groot). Per visite: 2 schelling, 2 groot (14 groot of 7 stuivers). Om een idee te geven van wat dat betekende, vergelijken we met lonen in het bouwvak in die tijd. Het dagloon van een diender bedroeg toen zowat 24 groot. De hele behandeling kwam neer op ongeveer 50 dergelijke lonen.

L. Devriese