

## Duodenal peripapillary adenocarcinoma causing extrahepatic biliary obstruction and icterus in a cat

*Duodenaal peripapillair adenocarcinoom leidend tot extrahepatische galobstructie en icterus bij een kat*

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### ABSTRACT

A six-year-old, female, neutered domestic shorthair cat was presented with chronic weight loss and a two-day history of partial anorexia and lethargy. Abdominal ultrasonography revealed a regional thickening of the duodenal wall with loss of normal layering, a normally walled segmentally dilated distal aspect of the common bile duct containing slightly hyperechoic bile, and a mild to moderately enlarged major duodenal papilla. Based on the ultrasound examination, the primary differential diagnosis was a peripapillary duodenal neoplastic or less likely, an inflammatory or infectious process with secondary extrahepatic biliary obstruction. Postmortem examination revealed a duodenal, peripapillary adenocarcinoma with metastasis into the liver and lymph nodes, and external compressive obstruction of cystic- and common bile duct.

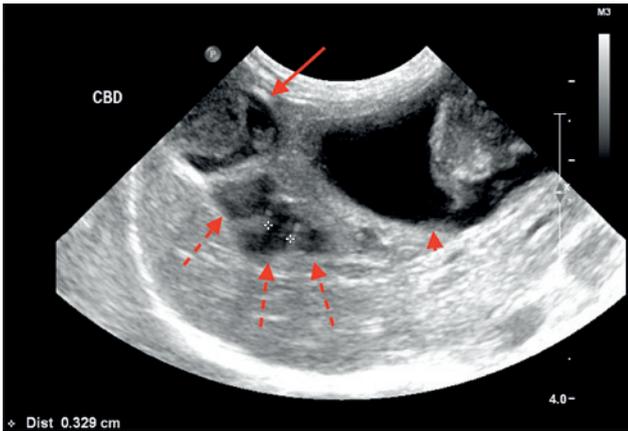
### SAMENVATTING

Een zes jaar oude, vrouwelijke, gesteriliseerde Europese korthaar werd aangeboden voor chronisch vermageren, en partiële anorexie en lethargie die reeds twee dagen aanwezig waren. Op abdominale echografie was er een focale verdikking van de wand van het duodenum met verlies van het normale patroon van de lagen. De gemeenschappelijke galafvoergang was focaal gedilateerd en bevatte echogene gal. De papilla duodenalis was mild tot matig gedilateerd. Op basis van het echografisch onderzoek was de meest waarschijnlijke diagnose een peripapillaire duodenale neoplasie, of minder waarschijnlijk, een inflammatoir of infectieus proces, met secundaire extrahepatische galgangobstructie. Tijdens autopsie werden een duodenaal peripapillair adenocarcinoom met metastasen in de lever en regionale lymfeknopen, en een obstructie van de extrahepatische galgangen gediagnosticeerd.

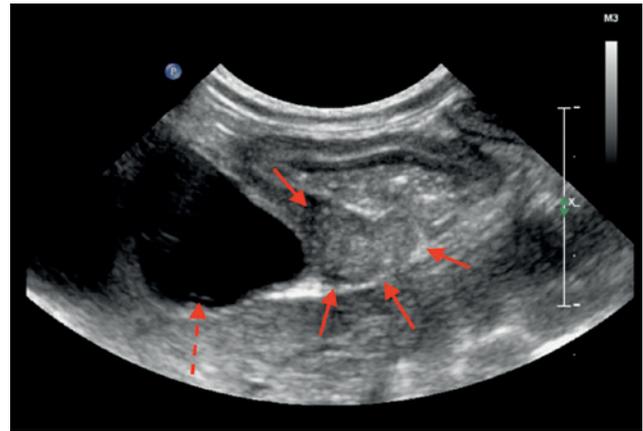
### INTRODUCTION

Extrahepatic biliary obstruction is a well-known complication in feline veterinary medicine and can be caused by mural thickening, luminal obstruction or extraluminal compression. There are some reports in cats, including inflammatory and parasitic infectious diseases (common bile duct, liver, pancreas or duodenum), neoplastic processes (originating from the common bile duct, the liver, the pancreas or the major duo-

denal papilla) and reports describing extrahepatic biliary obstruction secondary to internal occlusion such as plugs, cholelithiasis or foreign bodies. Extrahepatic biliary obstruction has also been described secondary to congenital malformations, diaphragmatic hernia, liver fluke infestation and cysts. Non-obstructive dilation of the common bile duct has been reported as well and can be caused by segmental dilation or choledochal cysts (D'Anjou and Penninck, 2015; Gaillet et al., 2007; Head and Daniel, 2005; Lawrence et



**Figure 1.** Long axis ultrasound image of the gallbladder (long arrow), the non-dilated, tortuous common bile duct (dashed arrow) and the segmental dilatation of the common bile duct (short arrow). Note the severe segmental dilatation of the distal common bile duct compared to the middle part.



**Figure 2.** Long axis image of the duodenum in the region of the major duodenal papilla. The papilla is moderately enlarged (solid arrows) and there is segmental dilatation of the distal common bile duct adjacent to it (dashed arrow).

al., 1992; Mayhew et al., 2002; Neer, 1992; Gaschen, 2011; Kelly et al., 1975; Mayhew and Weisse, 2008; Barsanti et al., 1976; Haines et al., 1996; Brioschi et al., 2014; Naus and Jones 1978; Della Santa et al., 2007; Spain et al., 2017; Grand et al., 2018).

Extrahepatic biliary obstruction can be challenging to diagnose since the history and clinical signs are often nonspecific, including icterus, nausea, decreased appetite and vomiting. Blood examination often reveals hyperbilirubinemia and a marked increase in serum alkaline phosphatase activity but does not lead to final conclusions (Head and Daniel, 2005). Ultrasonography is considered to be the modality of choice for the diagnosis of extrahepatic biliary obstruction in veterinary medicine. However, the detection of specific lesion arrangement, such as focal mass or the distinction between obstructive or non-obstructive dilation of the common bile duct can be challenging (Gaillot et al., 2007). In a study by Gaillot et al. (2007), describing thirty cats with extrahepatic biliary obstruction, the pancreatic origin of the triggering mass was identified in 55 % of the cats; in just 18 % of these masses the dignity was accurately recognized by ultrasound (Fahle et al., 1995; Leveille et al., 1996; Gaillot et al., 2007; Brioschi et al., 2014; Spain et al., 2017).

In human medicine, the most common causes of extrahepatic biliary obstruction are choledocholithiasis and pancreatic carcinoma (Materne et al., 2000). Assessment of human partial or complete obstruction is based on clinical, laboratory, ultrasonographic and endoscopic parameters (Bakaen et al., 2000; Kim et al., 2001). To the authors' best knowledge, this is the first report describing the imaging findings in an extrahepatic biliary obstruction caused by a duodenal peripapillary adenocarcinoma in a cat.

## CASE DESCRIPTION

A six-year-old, female, neutered domestic short-hair cat was presented with weight loss for already a few months and a two-day history of partial anorexia and lethargy. The clinical examination was characterized by a reduced body condition score of 2/9, mild discomfort at abdominal palpation and jaundice. Hematogenous examination revealed the following abnormal blood values: hyperbilirubinemia 12.8 mg/dL (reference range < 0.40 mg/dL), elevated aspartate transaminase 116 U/L (reference range < 83 U/L), alanine transaminase 328 U/L (reference range < 91 U/L), gamma glutamyltransferase 42 U/L (reference range < 10 U/L) and alkaline phosphatase 217 U/L (reference range 17-63 U/L). At this point, neoplasm with hepatobiliary origin, inflammation and/or infection affecting the bile duct system were hypothesized. Abdominal ultrasonography was performed using an 8-5 MHz broadband curved array transducer and a 12-5 MHz linear array transducer (iU22 Philips, Bothell, WA). Ultrasonographic examination revealed irregular, thickened and diffusely hyperechoic mesenteric fat in the cranial abdomen. The liver was subjectively enlarged and demonstrated a heterogeneous, slightly hyperechoic parenchyma. Multiple, small, anechoic tubes with hyperechoic wall and absent Doppler signal corresponding to dilated intrahepatic bile ducts were detected. The gallbladder was moderately filled with bile and a moderate to large amount of organized, hyperechoic material attached to the dependent wall. The common bile duct demonstrated a tortuous course with mild amount of intraluminal sludge but still had a normal luminal diameter (3.4 mm). Proximal to the major duodenal papilla, there was a focal, fluid filled, segmental dilatation of the distal aspect of the common bile duct present (2.2 x 3.0 cm; height x length) (Fig-

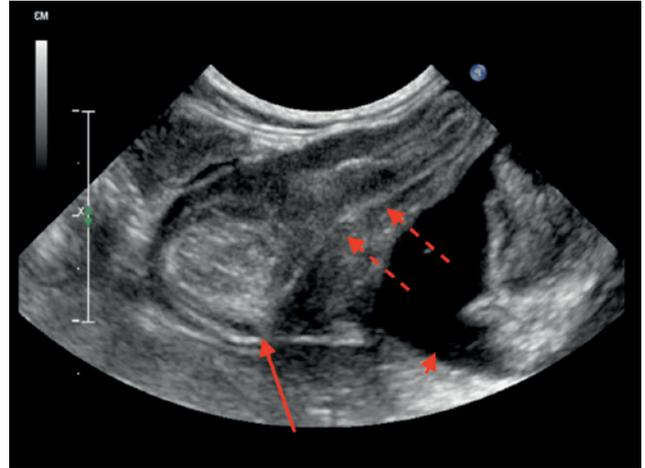
ure 1). The wall of the common bile duct was folded and partially protruded into the luminal widening. The major duodenal papilla was mildly to moderately enlarged (11.0 mm in diameter) (Figure 2). The adjacent portion of the duodenum presented a focal, moderate transmural thickening of the wall (9.4 mm), with diffuse pseudolayering and a concurrent hypoechoic, ill-defined focal asymmetric thickening of the muscularis layer proximal to the duodenal papilla (16 mm) (Figure 3). There was no peristalsis detected in this portion of the duodenum. The stomach was moderately filled with food, although the cat had not been fed during the last eight hours. The pancreas was subjectively normal in size with well-defined demarcation towards the duodenum and showed a hypoechoic parenchyma with a moderate dilation of the pancreatic duct (diameter of 2.5 mm). The gastric and pancreaticoduodenal lymph nodes were mildly enlarged (6 mm), preserving normal echogenicity and shape.

Based on the ultrasound findings, the clinical presentation and laboratory test results, the remaining differential diagnosis included extrahepatic biliary tract obstruction secondary to a duodenal and papillary infiltrate of inflammatory or neoplastic origin with lymphatic metastasis or reactive adenitis, regional steatitis and gastroduodenal subobstruction. Ultrasound guided fine-needle aspiration of the pancreaticoduodenal lymph nodes showed low cellularity; the nodes were not diagnostic. Surgical exploration and sampling of the lesion were advised with potential medical or surgical treatment in form of a choledochoduodenostomy and stent placement. Based on financial concerns and the suspicion of a neoplastic process, the owner declined any further examinations and the cat was euthanized and submitted for necropsy.

Postmortem examination grossly revealed a diffuse segmental dilation of the bile duct filled with increased viscous bile. Surrounding the major papilla, the duodenal wall was irregularly thickened over a length of 4 cm and was subjectively firm on palpation (Figure 4). The duodenal mucosa showed few ulcerations. The regional lymph nodes were moderately enlarged. Furthermore, within the hepatic parenchyma, there were two well-circumscribed whitish nodular areas within the left caudal (1.0 cm in diameter) and right cranial lobe (0.5 cm in diameter) detectable.

Histologic evaluation of the duodenum showed a multi-lobulated neoplasm transmurally affecting the duodenal wall with focal infiltration of the major duodenal papilla. The neoplastic cells formed multifocal acini and tubuli lined by cuboidal cells with large, round, centrally located nuclei and moderate amount of eosinophilic cytoplasm. Some acini contained mucous material. A large amount of fibrovascular stroma was supporting the neoplastic cells. Multifocal areas of necrosis and ulceration accompanied those areas, and neoplasm was seen at the mucosal epithelium. The mitotic figure was one per high power field of 40x. Histologic evaluation of the hepatic nodules and

enlarged lymph nodes revealed infiltrative secondary neoplastic tissue representing the same characteristics as the aforementioned duodenal neoplasm (consistent with metastasis). Within portal areas, bile duct proliferation, fibrosis and inflammation (lymphoplasmacytic) were present. In some areas, the fibrosis extended in between the hepatocytes (dissecting fibrosis).



**Figure 3.** Ultrasound image in oblique axis of the transition zone between abnormal and normal duodenal tissue. Proximal is to the left. There is mild luminal dilation present in the proximal aspect (solid arrow) and loss of normal wall layering distal to it (dashed arrows). There is normalization of the duodenal wall layering in the distal aspect on the left of the image. The segmental dilation of the common bile duct is adjacent to it (arrowhead).



**Figure 4.** Postmortem images at the time of necropsy. The duodenum is irregularly thickened (solid arrow) proximal to the entrance of the common bile duct (dashed arrow). The segmental dilation of the distal common bile duct close to the duodenal papilla is depicted (arrowhead). The yellow gross appearance of the surrounding mesenteric fat is explained by mild steatitis and saponification. The grossly visible zonal pattern of the liver is a normal finding in cats and might reflect fat storage (star).

As morphological diagnosis, a duodenal adenocarcinoma with local metastasis to liver and lymph nodes and external compressive obstruction of the common bile- and pancreatic duct, causing jaundice and biliary fibrosis was stated.

## DISCUSSION

In the present case, the history, clinical presentation and the laboratory results match the reports previously published in cats with extrahepatic biliary obstruction (Head and Daniel, 2005; Mayhew et al., 2002; Buote et al., 2006). The main ultrasonographic finding leading to suspicion of extrahepatic biliary obstruction is a common bile duct diameter of  $> 5$  mm, reported in 97 % of cats with extrahepatic biliary obstruction and intra hepatic dilatation of the bile duct (Gaillot et al., 2007). In a recent report, feline segmental dilations or choledochal cysts of the common bile duct have been described in four cats with chronic gastrointestinal clinical signs (Spain et al., 2017). Although the etiology of choledochal cysts is most likely multifactorial, it is unclear. Congenital and acquired etiologies have been reported (Grand et al., 2010). An abnormal pancreaticobiliary junction is the most common formulated hypothesis for the development of acquired choledochal cysts in human medicine (Stringer, 2018). The distinction of a choledochal cyst from an extrahepatic biliary obstruction is challenging and can be even more difficult with comorbid conditions, like in the present case (Spain et al., 2017). In this case, the common bile duct demonstrated a segmental dilatation proximal to the duodenal papilla and presented otherwise within normal limits. It is possible that a choledochal cyst developed secondary to the papillary neoplastic infiltration. However, a primary choledochal cyst cannot be excluded. Focal thickening of the intestinal wall can be caused by neoplastic and non-neoplastic disorders. Inflammatory changes usually lead to transmural thickening with preserved wall layering. However, in some instances, the wall layering can be altered (Gaschen, 2011). Intestinal neoplasia and infectious diseases often cause intestinal masses with loss of normal wall layering (Gaschen, 2011). The ultrasonographic differential diagnoses of duodenal neoplastic, infectious or inflammatory infiltration as underlying cause in the present case were based on those assumptions.

In human medicine, the most common cause of impaired bile excretion is choledocholithiasis and pancreatic carcinoma (Materne et al., 2000); diagnostics are based on sonographic, endosonographic, intraductal sonographic techniques and cross-sectional imaging modalities, like magnetic resonance tomography (MRT), computed tomography (CT) and PET-CT (Materne et al., 2000; Bakaeen et al., 2000). Endoscopic retrograde cholangiopancreatography has been established in human medicine to identify the location and cause of obstruction. Endoscopic ultrasono-

graphy is considered an alternative imaging method for determining extrahepatic cholestasis (Materne et al., 2000). MR tomography with MR cholangiopancreatography is a reliable procedure for the evaluation of the pancreas and the biliary system (Materne et al., 2000). In feline medicine, abdominal ultrasonography is the most commonly used diagnostic modality for imaging of the cholangiopancreatic area (Leveille et al., 1996; Gaillot et al., 2007) and was the main modality in the present case. Promising publications deal with the use of endosonography as diagnostic tool in veterinary medicine (Schweighauser et al., 2009). By positioning the endoscopic transducer within the lumen of the stomach or duodenum, the general visualization of the pancreas and the surrounding tissues has been improved compared to traditional transcutaneous ultrasound (Schweighauser et al., 2009). In the recent literature, MRT and MR cholangiography also provide promising additional imaging information in patients, in which the pancreas cannot be fully visualized ultrasonographically (Marolf et al., 2012). The cat in the present case report was euthanized due to guarded prognosis and financial concerns before reaching final diagnosis. Endoscopic, endosonographic or surgical exploration would potentially have provided more information and should be considered in similar cases. The potential palliative treatment options would have been of surgical or conservative nature depending on the degree of obstruction. Surgical considerations included biliary-enteric anastomosis or a biliary stent in case of complete obstruction (Mayhew et al., 2002). Duodenal adenocarcinoma was identified in this presented case after gross and histopathologic examination as underlying cause of the development of biliary obstruction. In different reports, feline intestinal adenocarcinoma makes up 0.4 % - 3.0 % of all feline tumors and 7 % - 27 % of all alimentary tumors (Kosovsky et al., 1988; Cribb et al., 1988; Mayhew et al., 2002; Gaillot et al., 2007; Gaschen et al., 2011; Risetto et al., 2011). In 20 % - 61.5 % of cases, adenocarcinoma occurs in the small intestines compared to the large intestines (Risetto et al., 2011). During postmortem examination in the present case, metastasis of the adenocarcinoma to the regional lymph nodes and the liver were identified. In accordance with the findings in the present case, metastatic spread of feline small intestinal adenocarcinoma has been seen in approximately 75 % of the cases into regional lymphnodes, liver and spleen (Kosovsky et al., 1988; Cribb et al., 1988).

In human medicine, primary duodenal adenocarcinoma is also a rare condition, representing approximately 0.3 % of all gastrointestinal tract carcinomas (Spira et al., 1977). Peripapillary tumors (duodenum, distal bile duct) are associated with a worse prognosis than primary tumors of the major duodenal papilla (Kim et al., 2001). Peripapillary tumors represent more than half of the duodenal adenocarcinomas (Bakaeen et al., 2000), and clinical obstructive jaundice is a common complication associated with

primary duodenal adenocarcinoma with an incidence ranging from 18 % to 54 % (Hung et al., 2007). Obstructive jaundice is considered a poor prognostic factor for patients with primary duodenal adenocarcinoma (Hung et al., 2007).

In conclusion, duodenal peripapillary adenocarcinoma should be considered as a rare, but potential cause of extrahepatic biliary obstruction in cats. With ultrasonography, it was possible to satisfactorily detect the location and cause of the obstruction. However, the differentiation between a papillary and a peripapillary origin remains challenging. With endosonography, the visualization would have been improved and would possibly have provided more information before euthanasia and so, more specific treatment options could have been discussed.

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