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Pancreatic adenocarcinoma with atypical imaging features mimicking chronic pancreatitis in a dog

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Abstract: An 11-year-old intact female Pomeranian dog was referred for jaundice, anorexia, and vomiting. The blood analysis revealed increased alanine aminotransferase, alkaline phosphatase, and gamma-glutamyl transpeptidase. The serum canine pancreatic lipase immunoreactivity was within the normal reference range. The radiography revealed no significant findings. On ultrasound, the gallbladder was enlarged with a markedly distended common bile duct (CBD) measuring up to 6 mm in diameter. The pancreas had an irregular contour, a hypoechoic peripheral rim, multiple hyperechoic foci with acoustic shadowing, and showed increased echogenicity of the adjacent mesentery. Based on these results, an extrahepatic biliary obstruction secondary to the presumed chronic pancreatitis was diagnosed. The computed tomography (CT) images showed a hypoattenuating pancreatic parenchyma compared to the liver in the early phase, as well as multiple calcifications. A laparotomy was performed to reserve the patency of the CBD. The histopathological examination of the pancreas revealed exocrine pancreatic adenocarcinoma. While various appearances of exocrine pancreatic adenocarcinoma on CT have been reported in humans, CT features of pancreatic adenocarcinoma have not been well-established in dogs. The purpose of this report is to describe the atypical imaging features of pancreatic adenocarcinoma that are similar to those of chronic pancreatitis in a dog.

Keywords: computed tomography; exocrine pancreatic adenocarcinoma; pancreatitis; ultrasound

Exocrine pancreatic adenocarcinoma is the most common exocrine tumour affecting the pancreas, but is rare in dogs and cats, with an incidence of less than 0.5% of all cancers (Selmic 2019). Older female dogs are at higher risk of pancreatic adenocarcinoma (Selmic 2019). The history and clinical symptoms of pancreatic adenocarcinoma are nonspecific and include vomiting, abdominal

pain, lethargy, anorexia, and diarrhoea (Bennett 2017; Selmic 2019).

Various diagnostic imaging modalities are used to identify pancreatic adenocarcinoma, including radiography, abdominal ultrasonography (US), and computed tomography (CT) (Bennett 2017). The final diagnosis can be made through a histopathological examination.

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On the other hand, canine pancreatitis is relatively common. Clinical symptoms are nonspecific as in pancreatic adenocarcinoma, and ultrasonography and serum canine pancreatic lipase immunoreactivity play important roles in the diagnosis of canine pancreatitis (Cordner et al. 2015; Mattoon et al. 2020). The diagnosis of canine pancreatitis in veterinary fields has been restricted to performing cytology or a biopsy due to concerns about iatrogenic injury and lack of data regarding the probability of obtaining a diagnostic sample (Cordner et al. 2015).

Although classic imaging features of exocrine pancreatic adenocarcinoma and canine pancreatitis are well described in human and veterinary medicine (Prokesch et al. 2002; Kalra et al. 2003; Francis 2007; Choi et al. 2008; Bertolini 2017; Wolske et al. 2019; Mattoon et al. 2020), both these pancreatic diseases are often indistinguishable on imaging diagnoses. This report describes a pancreatic adenocarcinoma with atypical imaging features that was misdiagnosed as chronic pancreatitis in a female Pomeranian dog.

Case description

An 11-year-old, 3.32 kg, intact female Pomeranian dog was referred for jaundice, anorexia, and vomiting. A complete blood count revealed leucocytosis [$31.5 \times 10^9/l$, reference interval (RI) $6\text{--}12 \times 10^9/l$]

with monocytosis ($1.3 \times 10^9/l$, RI $0\text{--}0.5 \times 10^9/l$), granulocytosis (27.4 , RI $3\text{--}10 \times 10^9/l$), eosinophilia ($1.4 \times 10^9/l$, RI $0\text{--}0.6 \times 10^9/l$), and thrombocytosis ($638 \times 10^9/l$, RI $200\text{--}460 \times 10^9/l$). The serum biochemical profile showed increased alanine aminotransferase ($34.9 \mu\text{kat/l}$, RI $1.7 \times 10^{-1}\text{--}10^7 \mu\text{kat/l}$), alkaline phosphatase ($6.9 \mu\text{kat/l}$, RI $0\text{--}1.9 \mu\text{kat/l}$) and gamma-glutamyl transpeptidase ($6.3 \mu\text{kat/l}$, RI $0\text{--}0.2 \mu\text{kat/l}$). The C-reactive protein level was also increased (32.4 mg/l , RI $0\text{--}7.6 \text{ mg/l}$). The serum canine pancreatic lipase immunoreactivity was within the normal reference range.

The patient underwent thoracic and abdominal radiography, but no significant findings were detected. On the US (Figure 1), the gallbladder was enlarged with a markedly distended common bile duct (CBD) measuring up to 6 mm in diameter. The parenchyma of the pancreas had a hypoechoic peripheral rim and a hyperechoic central region. Additionally, the pancreas had an irregular contour and multiple hyperechoic foci with acoustic shadowing. An increased echogenicity of the adjacent mesentery was present.

A CT scan (Asteion; Toshiba, Ohtawara, Japan) was performed. For this, propofol (6 mg/kg , i.v. Anepol 1%; Hana Pharmaceutical Co., Seoul, Republic of Korea) was slowly injected via intravenous administration for induction and isoflurane (Ifiran 1.5–2%; Hana Pharmaceutical Co., Seoul, Republic of Korea) was used to maintain the anaesthesia. A 2 ml/kg dose of a non-ionic iodinated

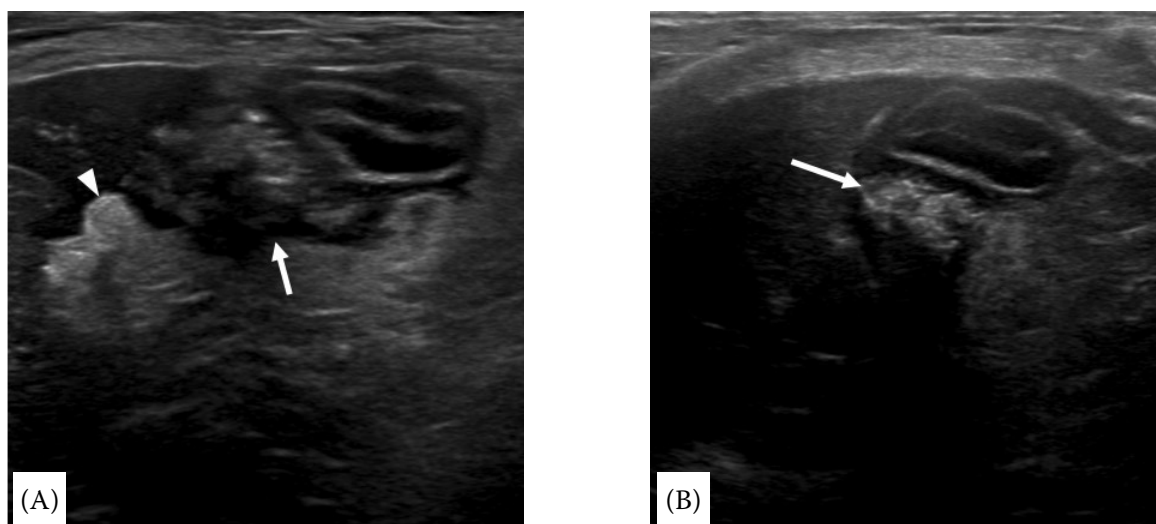


Figure 1. Abdominal ultrasonography of the pancreas

(A) The parenchyma of the pancreas had a hypoechoic peripheral rim (arrow) and a hyperechoic central region. In addition, the pancreas had irregular contours (arrow), and the echogenicity of the adjacent mesentery (arrowhead) was mildly increased. (B) Multiple calcification (arrow) with acoustic shadowing was observed in the pancreatic parenchyma

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contrast medium (Omnipaque 350; GE Healthcare, Cork, Ireland) was manually injected into the cephalic vein. Early phase scanning began after the injection of the contrast medium. Late phase scanning began 30 s after the end of the early phase.

The CT scan confirmed that the CBD was markedly distended (diameter 6 mm). In the pre-contrast images, the pancreas had multiple calcifications and an irregular contour. In the early phase, the pancreas showed a hypoenhancing parenchyma (about 75 HU) compared to the liver (about 150 HU) and the adrenal gland (right 233 HU, left 215 HU). In addition, the pancreas had an atrophic distal parenchyma with enlarged pancreaticoduodenal lymph nodes (Figure 2). Based on these results, an extrahe-

patic biliary obstruction secondary to the tentatively diagnosed chronic pancreatitis was diagnosed.

A laparotomy was performed to confirm the patency of the CBD. On the gross examination, the pancreas had a rough surface which appeared abnormal. A pancreatic biopsy was conducted. The histopathological features were as follows (Figure 2D): malignant tumour cells were observed replacing the normal parenchyma of the pancreas, this was accompanied by desmoplasia and proliferation of an invasive appearance. Tumour cells were growing while forming a solid island, trabeculae, and acini of various sizes. The tumour cells generally had clear intercellular boundaries, a cuboidal to low columnar epithelium, and varied

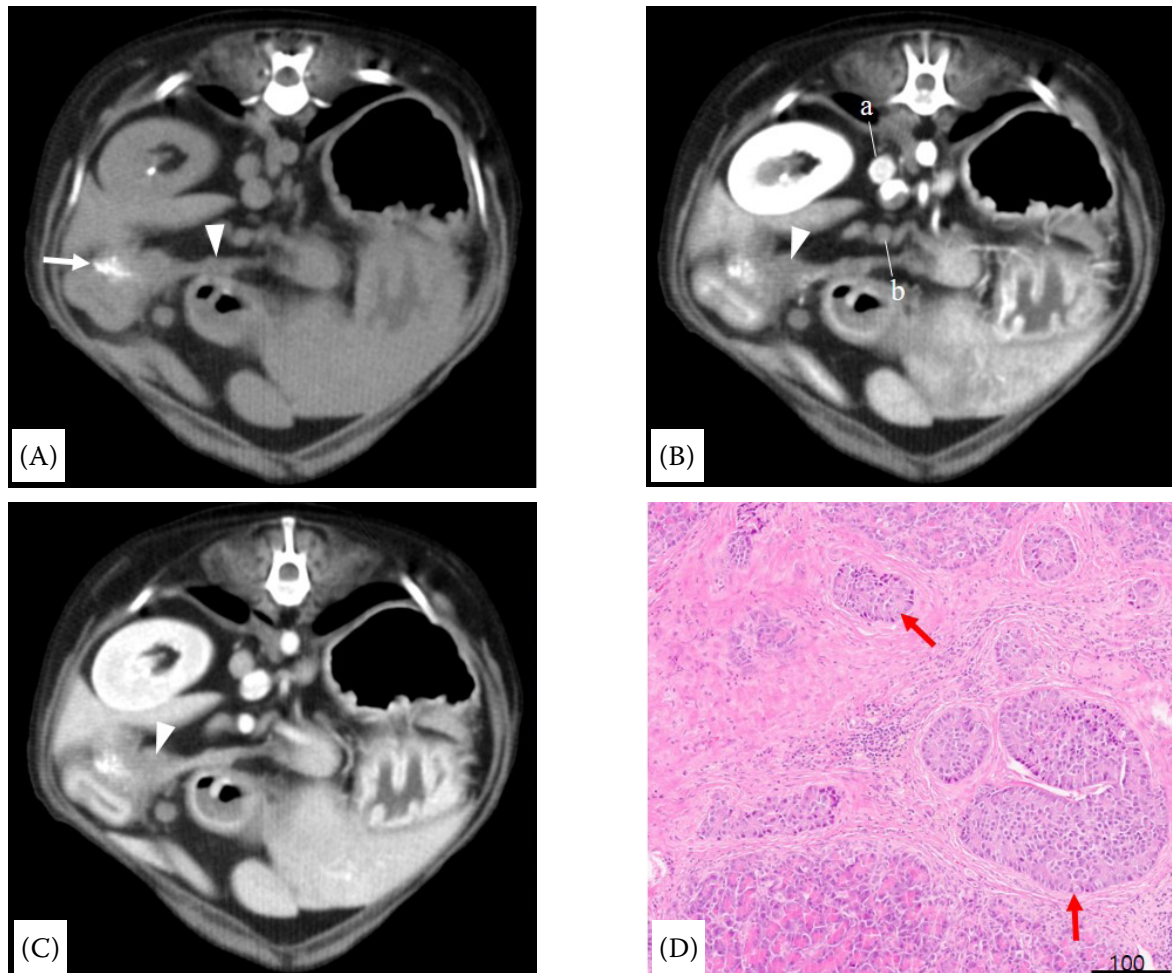


Figure 2. Computed tomography in a soft tissue window, transverse view (A–C) and histopathological examination of the pancreas (D)

(A) The pancreas had areas of calcification (arrow) and an atrophic distal parenchyma (arrowhead) in the pre-contrast image. (B and C) The pancreas showed a hypoenhancing parenchyma (arrowheads) compared to the liver in the early (B) and late phases (C). (D) The histopathological examination showed malignant tumour cells (arrows) replacing the normal parenchyma of the pancreas. The final diagnosis was exocrine pancreatic adenocarcinoma

a = right adrenal gland; b = portal vein

in size. Round or oval nuclei were located at the base or centre of the cells. One or two distinct nucleoli were observed in the nuclei and 1–3 mitotic figures were observed at 400 × magnification. Tumour emboli were observed in some lymphatic vessels as well as infiltration of inflammatory cells, including macrophages. The final diagnosis was exocrine pancreatic adenocarcinoma.

After a week, the symptoms improved and the patient was discharged. However, after 2 weeks, a recurrence of the jaundice was confirmed via telephone. Three months later, the patient was still alive, but there has been no follow-up since then.

DISCUSSION

In this case, the pancreatic adenocarcinoma showed similar imaging features to chronic pancreatitis. Exocrine pancreatic carcinoma is rare compared to pancreatitis in dogs and cats. We initially diagnosed chronic pancreatitis. In veterinary medicine, classic features of chronic pancreatitis based on the US are the mild thickening and increased echogenicity of the pancreas (Mattoon et al. 2020). In humans, the classic ultrasonographic finding is pancreatic calcification. Other features are alterations of the size and echogenicity (normal or decreased), irregular contour and dilatation of the CBD (Remer and Baker 2002; Conwell et al. 2014). In human medicine, there are many reports on CT features of chronic pancreatitis which include pancreatic calcifications, dilatation of the pancreatic duct, and parenchymal atrophy (Remer and Baker 2002; Kim and Pickhardt 2007; Siddiqi and Miller 2007). In veterinary medicine, the pancreatic parenchyma of chronic pancreatitis displays fibrosis and fat replacement, which, on CT, may give the appearance of hypoattenuation and poor contrast enhancement (Wisner and Zwingenberger 2015; Bertolini 2017). In this case, we diagnosed chronic pancreatitis based on the ultrasonographic findings of the irregular contour of the pancreas, heterogenous parenchyma, and multiple hyperechoic foci, and the CT findings of multiple calcifications in the pancreas in the pre-contrast images and hypoattenuating and hypoenhancing parenchyma in the early phase.

This case showed a pancreatic adenocarcinoma with atypical imaging traits compared to the commonly seen features that have a mass-like

appearance in the pancreatic region. In humans, pancreatic adenocarcinoma usually manifests as a hypoechoic mass with ill-defined margins on the US, as poor vascularity on colour doppler images, and as poor enhancement on all phases of the contrast-enhanced US (Lee and Lee 2014). Most pancreatic adenocarcinomas appear as ill-defined and focal hypoattenuating and hypoenhancing masses on contrast-enhanced CT (Kalra et al. 2003; Francis 2007; Wolske et al. 2019). Although most focal pancreatic adenocarcinomas show typical results, some may have atypical CT appearances, such as isoattenuation, compared to the pancreatic parenchyma in humans. In this atypical pancreatic adenocarcinoma, indirect signs, such as the mass effect and atrophic distal parenchyma, are important signs for the presence of a tumour in humans (Prokesh et al. 2002). Additionally, diffuse pancreatic adenocarcinoma is usually homogeneously hypoattenuated compared to normal pancreatic parenchyma and is heterogeneously hypoattenuated (Choi et al. 2008). The early phase of CT in this case could be assumed to be an arterial phase as there was strong contrast enhancement of the parenchymal organs, such as the adrenal glands, and insufficient contrast enhancement of the portal vein (Figure 2B). Unlike a normal pancreas and a classic exocrine pancreatic adenocarcinoma of the arterial phase, the early phase in this case showed a diffuse hypoenhancing pancreas similar to that seen in chronic pancreatitis with a poorly contrast-enhancing parenchyma in the arterial phase (Wisner and Zwingenberger 2015; Bertolini 2017) and an atrophic distal parenchyma. These features are similar to the CT findings of atypical pancreatic adenocarcinomas in humans.

It is important to note that, in humans, chronic pancreatitis can also be a risk factor for adenocarcinoma (Kirkegard et al. 2017; Rawla et al. 2019). The imaging features of this case were closer to those of chronic pancreatitis than a classic pancreatic adenocarcinoma; thus, we assumed the former. However, in some tissues of the pancreas, pancreatic adenocarcinoma was histopathologically confirmed. In our report, we estimate that this patient had diffuse pancreatic adenocarcinoma, but there is a possibility that chronic pancreatitis was embedded in the pancreatic adenocarcinoma. This deduction is due to the fact that chronic pancreatitis is a risk factor for pancreatic adenocarcinoma in humans and also due to the imaging features in this case.

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Although there are several reports on classic CT features of pancreatic adenocarcinoma in dogs, pancreatic adenocarcinomas with atypical CT features are rarely reported. We suspect the following reasons: first, exocrine pancreatic carcinomas are rare in dogs and cats. Second, an abdominal ultrasound remains the most widely available modality for diagnosing pancreatic diseases in veterinary medicine. Third, a histopathological evaluation of the pancreas for accurate diagnosis of pancreatic tumours is not routinely performed in veterinary medicine.

In conclusion, canine exocrine pancreatic adenocarcinoma can mimic chronic pancreatitis in diagnostic imaging, such as US and CT. Therefore, when diagnostic imaging features are similar to the features of chronic pancreatitis, the possibility of exocrine pancreatic adenocarcinoma and the histopathology of the pancreas should be considered.

Conflict of interest

The authors declare no conflict of interest.

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