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NEOPLASTIC DISEASE

Acinar Cell Cystadenoma of the Pancreas in a Cat

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Summary

Cystic tumours of the pancreas are heterogeneous lesions with a spectrum of morphology and biological behaviour in people. These are poorly characterized in animals. A multicystic tumour of the pancreas was identified in an 11-year-old, female, mixed breed cat. The tumour was 5.5 cm in diameter and the largest cysts were 1.5 cm in diameter. Microscopically, the cysts were lined by single layered or pseudostratified, flat, cuboidal or columnar epithelial cells that occasionally formed papillary structures with a thin fibrous core. The tumour cells had eosinophilic granules in the apical cytoplasm, similar to zymogen granules, and the nuclei were uniform in size and shape. Mitotic figures were not observed. Immunohistochemically, the tumour cells expressed trypsin, but not cytokeratin 7. A diagnosis of acinar cell cystadenoma of the pancreas was made and this is the first report of this tumour in a cat.

Keywords: acinar cell cystadenoma; cat; pancreas

Tumours of the exocrine pancreas are rare in cats (Head *et al*., 2002). According to a multicentre survey, the estimated incidence of exocrine carcinoma is 12.6 per 100,000 cat-years-at-risk (Priester, 1974). Pancreatic exocrine adenomas are found infrequently in live animals because they rarely exceed 0.5 cm in diameter and usually cause no clinical signs (Head *et al*., 2002). Adenomas are encountered as an incidental finding at necropsy examination, but their frequency is lower than that of non-neoplastic nodular hyperplasia of acinar cells. Two distinct morphological types of adenoma, ductal and acinar, are listed in the World Health Organization (WHO) classification of pancreatic tumours in domestic animals (Head *et al*., 2003). Ductal adenomas are composed of duct-like structures lined by cuboidal to columnar cells, while acinar adenomas consist of well-differentiated small acini with eosinophilic granular cytoplasm and basal nuclei. Cystic neoplasms of the pancreas are less common in domestic animals. There is one description of cysts lined by benign neoplastic epithelium suspected to originate from pancreatic ducts (Head *et al*., 2002).

In contrast, the WHO classification of human pancreatic tumours describes four types of benign cystic neoplasm: serous cystadenoma, mucinous cystic neoplasm (MCN, mucinous cystadenoma), intraductal papillary mucinous neoplasm (IPMN) and acinar cell cystadenoma. Serous cystadenoma of the human pancreas is a relatively uncommon tumour composed of cysts filled with serous fluid (Terris *et al*., 2010). MCN is a relatively rare tumour, accounting for approximately 8% of cystic lesions excised from the human pancreas, and it is more prevalent in women (>95%) than men (Gourgiotis *et al*., 2007; Zamboni *et al*., 2010). This tumour is characterized by mucin-producing epithelium and a distinct stroma. IPMN is the most common cystic tumour, accounting for 20% of all cystic tumours of the human pancreas (Campbell and Azadeh, 2008; Adsay *et al*., 2010). IPMN arises from the main pancreatic duct or its branches and is subclassified into gastric, intestinal, pancreatobiliary and oncocytic types, based on the morphology of the mucin-producing epithelium (Adsay *et al*., 2010). Acinar cell cystadenoma is an

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extremely rare, cystic lesion of the pancreas (Albores-Saavedra, 2002; Zamboni *et al.*, 2002; Klimstra *et al.*, 2010).

An 11-year-old, female, mixed breed cat developed a multicystic mass in the tail of the pancreas adjacent to the visceral surface of the spleen. The mass and spleen were surgically excised and submitted to the Department of Veterinary Pathology, Nippon Veterinary and Life Science University. The mass was 5.5 cm in diameter and contained several cysts (0.1–1.5 cm). Follow-up clinical data on the cat could not be obtained. The tissues were fixed in 10% neutral buffered formalin and embedded in paraffin wax. Sections (4 μm) were stained with haematoxylin and eosin (HE), alcian blue and periodic acid–Schiff (PAS). Serial sections were subjected to immunohistochemistry (IHC) using Histofine Simple Stain MAX-PO (Nichirei, Tokyo, Japan) with mouse monoclonal antibodies against trypsin (MAB1482; 1 in 10,000 dilution; Millipore, Temecula, California, USA), cytokeratin (CK) 7 (clone OV-TL 12/30; 1 in 50 dilution; DAKO, Glostrup, Denmark), pan-CK (clone AE1/AE3; 1 in 50 dilution, DAKO), vimentin (clone V9; 1 in 100 dilution, DAKO), oestrogen receptor α (clone 1D5; 1 in 50 dilution; DAKO) and Ki-67 (clone MIB-1; 1 in 200 dilution; DAKO), and rabbit polyclonal antibodies against chromogranin A (1 in 400 dilution; DAKO) and synaptophysin (1 in 50 dilution; DAKO). The tissue sections were pretreated in citrate buffer (pH 6.0) for pan-CK, vimentin, synaptophysin, oestrogen receptor α and Ki-67, or in antigen retrieval solution (pH 9.0, Nichirei) at 121°C for 15 min for CK7. Pretreatment was not performed for trypsin and chromogranin A.

Microscopically, the mass consisted of numerous cysts separated by fibrous connective tissue (Fig. 1). The cysts contained eosinophilic material and were lined by single layered or pseudostratified, attenuated, cuboidal or columnar epithelial cells that occasionally formed low papillary structures with delicate fibrous connective tissue cores (Fig. 2). Small clusters of pancreatic acini were found in the stroma of the cyst wall (Fig. 2). The tumour cells had apical granular eosinophilic cytoplasm and uniform round to oval nuclei with prominent nucleoli (Fig. 3a). Mitotic figures were not observed. The granules of the apical cytoplasm stained faintly positive with PAS, but the neoplastic cells did not stain with alcian blue. Normal pancreatic parenchyma was displaced to the periphery of the tumour (Fig. 1). The spleen was histologically normal.

Immunohistochemistry results are summarized in Table 1. The apical cytoplasm of the tumour cells labelled positively for trypsin (Fig. 3b), similar to normal acinar cells. Normal ductal cells expressed CK7, but tumour cells and normal acinar cells were negative for this marker (Fig. 3c). Ductal cells labelled intensely for pan-CK, but the tumour cells and normal acinar cells were labelled weakly. Both tumour cells and the underlying stromal cells were negative for oestrogen receptor α. Tumour cells did not express vimentin or the neuroendocrine markers including chromogranin A and synaptophysin. The Ki-67 labelling index of the tumour was low (0.24%).

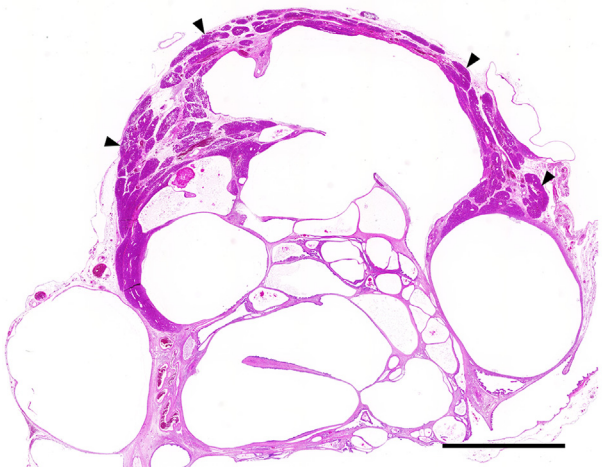

Fig. 1. Low-power view of the pancreatic tumour. Multiple cystic structures are present in the pancreas. Normal pancreatic parenchyma (arrowheads) is displaced to the periphery of the tumour. HE. Bar, 0.5 cm.

Cystic tumours of the pancreas are reported rarely in domestic animals and have not been subclassified (Head *et al.*, 2002, 2003). The features of the present case were compared with those of cystic tumours of

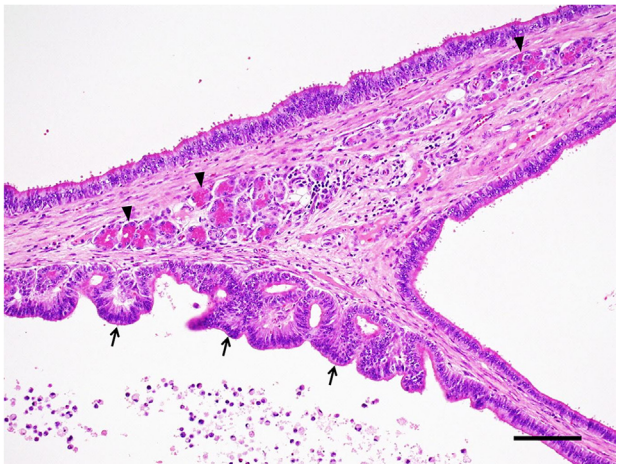

Fig. 2. Cystic pancreatic tumour. Cysts are lined by single layered or pseudostratified columnar epithelial cells. Papillae with fibrous cores project into the cystic lumen (arrows). Normal acini are observed in the stroma (arrowheads). HE. Bar, 100 μm.

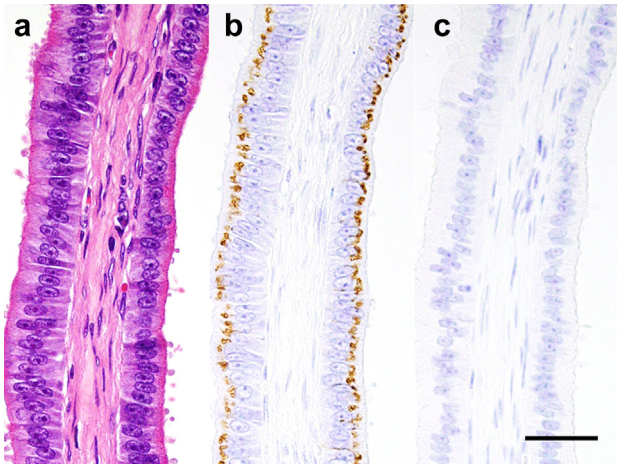

Fig. 3. (a) Tumour cells are characterized by eosinophilic granules in their apical cytoplasm. HE. (b) The apical cytoplasm expresses trypsin. IHC. (c) Tumour cells are negative for CK7. IHC. Bar, 50 μm.

the human pancreas. Serous cystadenoma of the human pancreas is composed of cysts lined by clear cuboidal epithelial cells containing abundant intracytoplasmic glycogen (Terris *et al.*, 2010), which are presumed to show intercalated duct/centroacinar cell differentiation (Adsay, 2007). The histology of the MCN and the IPMN is characterized by cysts lined by tall, columnar, mucin-producing cells (Adsay *et al.*, 2010; Zamboni *et al.*, 2010). In contrast, the tumour in the present case was composed of neither glycogen-rich clear cells nor mucinous columnar cells, but apical granular cells similar to acinar cells. Another characteristic of MCN is a pericystic stroma consisting of densely packed spindle cells that express oestrogen and/or progesterone receptors, referred to as 'ovarian-type stroma'. On this basis, MCN is hypothesised to arise from rests of embryological ovarian tissue (Adsay, 2007). The feline tumour lacked the hypercellular stroma expressing oestrogen receptor α. Acinar cell cystadenoma is defined in the human WHO classification (Klimstra *et al.*, 2010) as a benign cystic lesion lined by cells similar to normal acinar cells with evidence of pancreatic exocrine enzyme production. In the present case, trypsin immunolabelling conclusively demonstrated acinar cell differentiation of the tumour cells, suggesting a diagnosis of acinar cell cystadenoma.

Some differences in labelling for CK7 were seen between the current case and previous reports in people. In the present case, the tumour cells were negative for CK7, while human acinar cell cystadenomas express this marker (Zamboni *et al.*, 2002). Previous reports have shown that normal human acinar cells are negative for CK7, while CK7 is expressed in serous cystadenoma, MCN and IPMN, as well as the normal pancreatic ductal system, including centroacinar cells (Campbell and Azadeh, 2008). In the normal feline pancreas, acinar cells were also negative for CK7, but ductal cells were positive. These findings suggest different phenotypes of acinar cell cystadenoma between people and cats, with stronger acinar differentiation in cats.

The low Ki-67 labelling index of the tumour suggested that it was benign. To the best of our knowledge, this is the first report of acinar cell cystadenoma of the pancreas in a cat. If echocardiography confirms multicystic lesions in the abdomen, a pancreatic tumour should be considered as a differential diagnosis. As this is the only reported case of acinar cell cystadenoma in a cat, and no clinical follow-up was available, the behaviour of this type of tumour in the cat could not be determined. However, all cases reported in human patients have been clinically benign (Klimstra *et al.*, 2010).

Table 1
Summary of immunohistochemical findings

Antigen	*Tumour cells*	*Normal acinar cells*	*Normal ductal cells*	*Normal islet cells*
Trypsin	+	+	–	–
Cytokeratin 7	–	–	+	–
Pancytokeratin	+	+	+ +	–
Vimentin	–	–	–	–
Chromogranin A	–	–	–	+
Synaptophysin	–	–	–	+
Oestrogen receptor α	–*	–	–	–
Ki-67 (% labelled cells/ total cells)	0.24%	2.28%	0%	NE

*Both tumour cells and stromal cells were negative. Normal feline uterus was used as positive control tissue. NE, not examined.

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