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# Partial Pancreatectomy Using Ultrasonic Scalpel for Exocrine Pancreatic Ductal Papillary Carcinoma in a Cat

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**Abstract :** This report presents a rare case of feline exocrine pancreatic ductal carcinoma including treatment and prognosis. A 4.6-year-old castrated male American Shorthair cat, weighing 5 kg was presented with intermittent vomiting, diarrhea and loss of appetite. Through physical examination and radiography, a cranial abdominal mass was identified. Exploratory laparotomy was carried out. The largest mass was connected to the left lobe of the pancreas, and there were several small, nodular masses scattered along the abdominal lining. The pancreatic mass was removed using an ultrasonic scalpel, and the patient recovered favorably. Histopathologically, the resected lesion was diagnosed as an exocrine pancreatic ductal papillary carcinoma. The patient was maintained with conservative therapy and euthanized on post-operative day 262. Partial pancreatectomy using an ultrasonic scalpel was accomplished safely without evidence of pancreatic leakage.

***Key words*** **:** exocrine pancreatic carcinoma, partial pancreatectomy, ultrasonic scalpel, cat.

## Introduction

Pancreatic neoplasia is the fifth most common cause of cancer-related mortality in humans. These tumors aggressively invade local tissues and metastasize readily, with a 90% mortality rate within 1 year of diagnosis (4). An exocrine pancreatic carcinoma (EPC) is a relatively rare tumor in cats, with an incidence of less than 0.5% (8). One previous study estimated that 12.6/100,000 cat patients each year are at risk of EPC; another study reported 5 pancreatic tumors out of 800 feline necropsies (10). It is considered a disease of old cats, typically 10.4-12 years old, and there is no predisposition with regard to sex or breed (2,3,6,8). The epithelial tumors of the pancreas originate either in the acinar cells or from the ductal epithelium (3), and carcinomas are more common than adenomas (5). There are few reports regarding feline EPC (fEPC), and information on the response to therapy is scarce.

The diagnosis of EPC is challenging, because clinical signs and laboratory data at presentation are often non-specific. EPC is sometimes difficult to distinguish from acute pancreatitis, even with diagnostic imaging. Vomiting is the most common finding, with anorexia, weight loss despite a normal appetite, and icterus (2,3). There may be a palpable abdominal mass with or without abdominal pain (5). Changes in liver enzymes can be more prominent than the activity of amylase and lipase, with evidence of extrahepatic biliary obstruction by the mass or metastatic condition (2). One canine study reported that serum lipase concentration 25 times the normal upper limit was highly suggestive of pancreatic carcinoma (3).

Radiographic findings include a mass effect, decreased serosal detail due to abdominal effusion, and irregular mottled opacity throughout the peritoneal cavity in case of carcinomatosis. On ultrasonography, ascites, pancreatic enlargement, and nodules or masses associated with or in the vicinity of the pancreas, as well as signs of extrahepatic biliary obstruction, can be detected. However, these findings are also shared with pancreatitis or nodular hyperplasia. Pancreatic tumors may appear as one discrete nodule or as scattered, multiple nodules. Ultrasonography of one feline pancreatic adenocarcinoma showed only a dilated pancreatic duct with no specific finding in the pancreas itself (6).

The differential diagnoses for mass lesions of the pancreas include pancreatitis, asymptomatic nodular hyperplasia, benign pseudocysts, adenomas, exocrine pancreatic tumors, metastatic tumors, rare endocrine tumors such as beta cell tumors, gastrinomas or multiple endocrine neoplasias (8). Histopathology is essential for the definitive diagnosis, but ultrasound-guided fine needle aspiration and needle biopsy can be diagnostic (2).

This tumor metastasizes early, most commonly to the liver, lymph nodes, abdominal organs, lungs, and peritoneum and is resistant to most forms of oncological therapy (9). Peritoneal effusion is commonly caused by peritoneal metastasis or compression of the primary mass on caudal vena cava or portal vein (3,9).

The only effective treatment in human medicine is surgical resection, because this tumor is resistant to chemotherapy and radiation therapy; however, chemotherapy with gemcitabine, a purine analogue, has been performed (2,8). Surgery can be attempted not only for treatment but also for diagnosis. Complete excision of the lesion is paramount for a radi-

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cal cure, but just biopsy may be performed to obtain samples for histopathologic examination. Gastrojejunostomy also can be considered for palliative purposes in case of a bile duct obstruction (3). The prognosis is extremely poor, and survival less than 3 months should be expected. Most patients have widespread disease at the time of diagnosis, and many are euthanized during surgery (4).

## Case

A 4.6-year-old, male, castrated American short-hair cat was presented with a 2 week history of weight loss, anorexia, episodic vomiting and diarrhea. The patient had lost 0.5 kg recently and was 5 kg at the time of presentation. He was mildly depressed, but in favorable body condition and had no history of disease previously diagnosed. A round mass was palpable in the upper abdomen during physical examination. Bloodwork (CBC, serum chemistry, and electrolytes panel) showed only elevated levels of liver enzymes and lipase; ALKP: 153 U/L (16-71), AST: 75 U/L (12-65), lipase 3348 IU (0-450).

With diagnostic imaging techniques, radiography showed an abdominal mass that caused deviation of the transverse colon and stomach, with unclear splenic opacity and serosal detail loss (Fig 1). The abdominal mass caudal to the stomach showed a homogenous parenchymal pattern with irregular contour on ultrasonography (Fig 2). The mass was more hypoechoic than surrounding tissues and had ambiguous continuity to the splenic body. Normal pancreatic echogenicity could not be clearly identified. The lesion was suspected to be a malignant neoplasm associated with the spleen or pancreas. Blood tinged abdominal effusion with echogenic sediment was analyzed and determined to be an exudate but had no diagnostic cells for the mass.

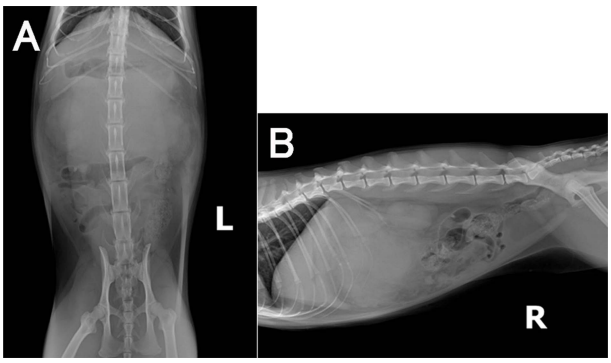


**Fig 1.** Plain abdominal radiographic images of ventrodorsal (A) and lateral (B) position. The cranial to middle abdominal mass was identified with serosal detail loss; thereby, the stomach and transverse colon were deviated cranially and caudally, respectively. There was also no clear opacity of the spleen.

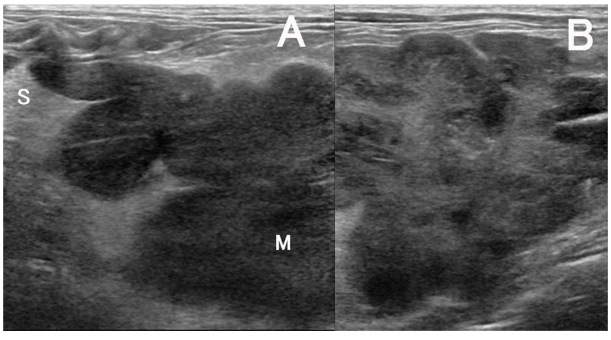


**Fig 2.** Ultrasonographic images of abdominal mass. The mass had an ambiguous border with the spleen, and a normal pancreatic structure was not clearly identifiable (A). The hypoechoic mass lesion showed a homogenous parenchymal pattern with irregular contour (B). S; spleen, M; mass.

The owner declined a CT scan. Exploratory laparotomy was then performed under general anesthesia (Fig 3). A left-sided, mid-abdominal mass with bloody effusion was apparent. The irregularly surfaced mass was highly vascularized, entwined with omentum, and contiguous with the visceral surface of the intact spleen and greater curvature of the stomach. Numerous metastatic nodules were identified on the peritoneum, mesentery, visceral surface of gastrointestinal tract, and capsule of the left kidney. Adhesion was carefully separated using an ultrasonic scalpel (Lotus® ultrasonic scalpel, SRA Developments, UK). The lesion contained most of the left pancreatic limb, and the intact pancreatic area proximal to the lesion was isolated and transected with the ultrasonic scalpel. Then, the mass was excised by double ligation of the splenic vasculature and transaction of pancreatic parenchyma using the ultrasonic scalpel. Removable metastatic masses on the peritoneum and kidney were also excised. The uneven, firm mass, $10.5 \times 9 \times 8$ cm, revealed a white to pale pink cut surface with a fragile necrotized core (Fig 4). It was well circumscribed and lobulated into several nodules. The patient recovered uneventfully, and ALKP and lipase were restored to their normal ranges at post-operative day (POD) 1.

Histopathologic examination (IDEXX laboratories, USA) confirmed high grade exocrine pancreatic ductal papillary carcinoma (Fig 5). Epithelial cells were polyhedral to occasionally cuboidal and formed branching papillary structures. Cells varied from a simple to a stratified layer. The nuclei were intensely hyperchromatic, round to ovoid, with abundant amounts of stippled chromatin and a single nucleolus. On average, there were 4 or more mitotic figures per high power field. The cells had minimal amounts of eosinophilic cytoplasm.

The owner did not consent to postoperative chemotherapy. There was no evidence of pancreatic leakage, and the patient had been doing well. On POD 262, however, he developed acute abdominal distension and depression and was euthanized at the local hospital. Necropsy was not performed.

## Discussion

This case report describes partial pancreatectomy using an ultrasonic scalpel for treatment of a large exocrine pancreatic ductal papillary carcinoma in a cat with abdominal carcinomatosis, involving dissemination of neoplasia to the parietal/visceral/connecting peritoneum (9). There were no findings of involvement in lymph nodes and parenchyma other than the pancreas by ultrasonography and exploratory laparot-

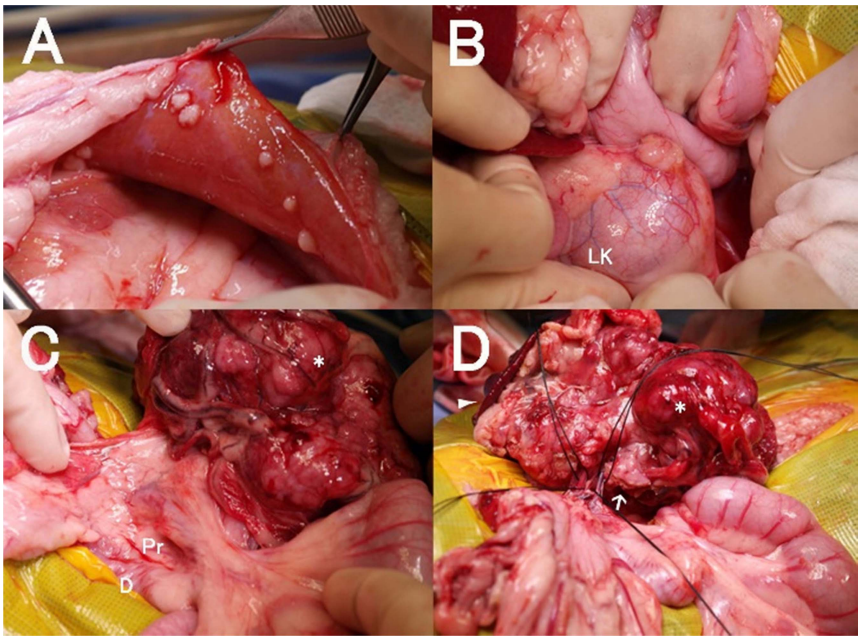


**Fig 3.** Exploratory laparotomy and partial pancreatectomy. White, small nodules were scattered on the parietal and visceral peritoneum (A) and capsule of the left kidney (B). The lesion appeared to be a continuous mass (*) with the left pancreatic limb after tremendous omental adhesion was separated (C). The pancreatic limb was cut using an ultrasonic scalpel and splenic vessels were double ligated and transected with an ultrasonic scalpel (D). White arrow; cut section of pancreas, Arrow head; spleen, LK; left kidney, Pr; right pancreatic limb, D; duodenum, *; pancreatic mass lesion.

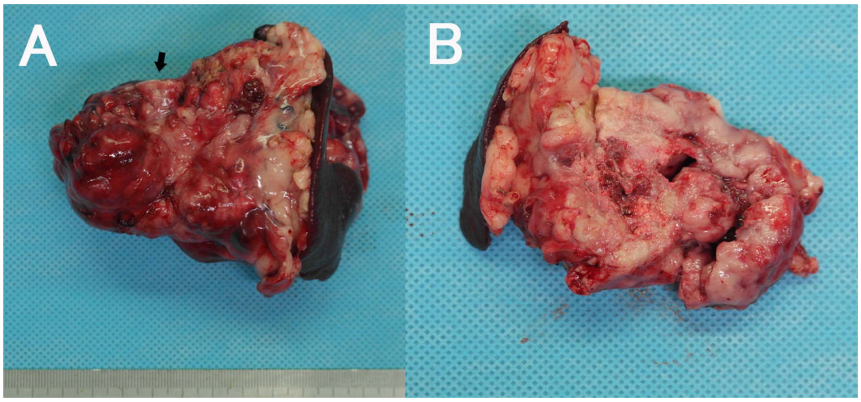


**Fig 4.** Gross appearance (A) and cut surface (B) of the pancreatic mass. The irregular mass was approximately 10.5 × 9 × 8 cm. The firm mass was well circumscribed, and revealed a white to pale pink and partially yellow cut surface, and lobulated nodules with necrotized centers. Black arrow; transected site of intact left pancreatic limb.

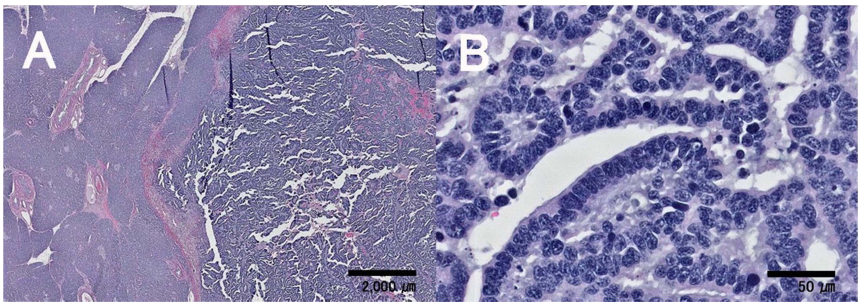


**Fig 5.** Histopathologic images of the exocrine pancreatic ductal papillary carcinoma in a cat (H&E stain). (A) × 10, pancreas with adjacent tumor, (B) × 400, papillary structures formed by epithelial neoplastic cells with hyperchromatic nuclei, stippled chromatin, and more than 4 mitotic figures per HPF (high power field).

omy; the clinical stage was $T_1N_0M_1$ according to the World Health Organization system. In this case, it was a discrete nodular type of the distal end of the left limb, but the multiple scattered nodular type throughout the pancreas is also possible (10). In general, the pancreatic body is considered to be more involved than the tail, but this cancer is more diffuse in cats (5). One feline study reported 75% of pancreatic exocrine tumors as the diffuse type (10).

The patient in this report was 4.6 years old, much younger than others in previous reports. Three other young cats (4-, 5-, 7-years-old) have been reported to be diagnosed with pancreatic adenocarcinomas (10). There was also a similar reported case of fEPC with ductal origin in a 6-year-old cat, in which the carcinoma arose at the distal end of the right limb (1). The patient in that report died during examination, so definitive diagnosis was made by necropsy. There was another case of pancreatic carcinoma accompanying bilaterally symmetrical non-pruritic alopecia of the ventrum, limbs, and perineal area as a characteristic paraneoplastic syndrome that resolved after surgery (12). This cat was euthanized 18 weeks after surgery because of recurrence of signs and metastasis. Other cats with pancreatic adenocarcinomas and concurrent diabetes mellitus, hyperadrenocorticism, or a thyroid carcinoma were reported (10). Long-standing diabetes mellitus is a risk factor for pancreatic cancer in humans, but the correlation is unclear in cats. In a previous report of 8 exocrine pancreatic neoplasias in 37 diabetic cats, there was no correlation between the presence of neoplasia and glycemic control or survival time. Chronic pancreatitis, on the other hand, has been considered as an independent risk factor of development of pancreatic adenocarcinoma (7).

Ultrasonography is useful for detection of pancreatic masses, not just for localization but also for identification of metastasis, especially in the liver (1). Sensitivity and specificity of ultrasonography for the detection of pancreatic tumors were reported to be as high as 90% and 98.8%, respectively, in human medicine (6). The sensitivity for the detection of pancreatic tumors in dogs was 19% for radiography and 75% for ultrasonography. Even with this technique, it may not be easy to distinguish malignancy from pancreatitis or nodular hyperplasia, although one study reported a tendency of malignant neoplasms to appear as a single pancreatic nodule or larger lesion exceeding 2 cm, while hyperplastic nodules appeared as smaller nodules. Further attempts have been made to visualize the feline pancreas using CT or MRI; however, cytopathology and histopathology through exploratory laparotomy or necropsy are currently the best methods to confirm pancreatic neoplasia and differentiate it from pancreatitis (1,10).

As for the gross appearance of EPC, individual nodules are white or beige, and it has variable consistency. Calcification and necrosis sometimes accompany the nodules. In the case of the diffuse type, it can resemble chronic pancreatitis or nodular hyperplasia. The corrosive effects of leakage of proteolytic enzymes from carcinomas of the pancreas may result in cystic changes in the primary tumor and necrotizing steatitis in the omental and peritoneal fat. The combination of rapid local growth, early metastasis, and the proteolytic side effects makes EPC an aggressive and painful neoplasm (5).

Complete resection of carcinomas has resulted in the best long-term survival in human patients (8). Complete pancreatectomy or pancreaticoduodenectomy has been described but is not reasonable in veterinary medicine, due to the highly metastatic behavior of the disease (3). Partial pancreatectomy can be performed by suture fracture, blunt dissection and ligation, a stapling device, bipolar-vessel sealing device, or ultrasonically activated scalpel (3,11,13). Up to 75-90% of the pancreas can be removed without impairment of the exo/endocrine function, if the duct to the remaining portion is left intact (3). The ultrasonic scalpel used in the present case is a simultaneous cutting and hemostasis device via protein denaturation with high frequency ultrasonic vibration. It provides easy, excellent hemostasis with a clear parenchymal stump and induces less thermal damage to adjacent tissue (11). The device is useful in biliary-pancreatic surgery due to tight sealing of the branches of the pancreatic duct, which may prevent leakage of pancreatic fluids onto the cut surface and therefore prevent fistula formation after reconstruction.

Although there have been advances in therapeutic modality combining surgery, radiation, and chemotherapy, 5 year survival rates are still ≤ 18% in human patients (10). One retrospective study of 34 cats with fEPC reported a median survival time (MST) of 97 days (8). In that study, MSTs with or without treatment were 165 days and 6 days, respectively. Treatments included surgery and chemotherapy with gemcitabine, carboplatin, mitoxantrone, or administration of non-steroidal anti-inflammatory drugs (NSAIDs). MST in cats that received surgery or not was 165 days and 30 days, respectively, and post-operative chemotherapy did not extend the MST. A combination of surgery and chemotherapy can be performed to relieve clinical signs and therefore improve the quality of life. MST of fEPC with peritoneal effusion was 30 days. The longer-than-1-year survival rate was 8.8% in that study, and one cat survived 510 days.

Histological patterns or degrees of differentiation of pancreatic EPCs are extremely variable, even within a single neoplastic lesion. Great variation can also occur within metastases from the same tumor in other organs (1). Ductular cells are known to be pluripotent, and the degree and direction of differentiation are unpredictable. Histopathological differentiation or mitotic figure, or the size or number of nodules was not statistically related to survival or disease progression. Metastatic disease is usually regarded as a poor prognostic indicator, but it also had no statistical significance in that study (8). Development to metastasis was also not related to the duration of clinical signs (10).

The young patient in the present study had peritoneal effusion and peritoneal metastasis (carcinomatosis) at the time of diagnosis and survived 262 days after surgery. A large pancreatic mass occupying most of the upper abdominal space was not recognized until after it induced a gastrointestinal disorder through mechanical irritation, and at that point metastasis had already occurred. In general, therapeutic failure for EPC is attributed to the advanced stage of disease at the time of diagnosis. Consequently, early detection of disease might be a key to improving the prognosis (2,10), and a longer survival time would be anticipated with earlier detection in this case.

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