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Metastatic Pancreatic Acinar Cell Carcinoma In a Dalmatian: Clinical Pathologic and Immnohistochemical Aspects

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Abstract

The pancreas is a target organ for several diseases that can be inflammatory, degenerative, or neoplastic. Exocrine pancreatic neoplasms correspond to 0.5% of neoplasms that affect dogs and 1% of pancreatic neoplasms in humans. It may present as single or multiple nodules. Metastases are mainly seen in the liver, intestine, and abdominal lymph nodes. Due to the scarcity of studies of this neoplasm in domestic animals, a case of pancreatic acinar carcinoma in a seven-year-old Dalmatian female dog is reported. The animal was brought to the Veterinary Hospital of Veterinary Medicine and Animal Science School-UNESP, Botucatu, São Paulo, Brazil. The animal was admitted presenting hyporexia, apathy, olygodipsia, progressive weight loss, tachycardia, jaundice, and abdominal distention due to hepatomegaly and ascites. At necropsy, multiple yellowish-white hepatic neoformations were observed, also seen in the epiploon, regional lymph nodes, and body of the pancreas, from 0.5 to 17 cm. Microscopic analysis revealed the proliferation of epithelial cells arranged in acinar formations, whose morphology resembles exocrine pancreatic tissue. The diagnosis of pancreatic carcinoma was established based on the lesions seen at necropsy and confirmed by histopathological analysis of the neoformations and immunohistochemistry.

Keywords: Pancreatic carcinoma; Pancreas; Acini; Adenocarcinoma; Dog disease

Introduction

Exocrine pancreatic carcinoma is uncommon in domestic species, accounting for 0.5% of neoplasms in dogs and 1% of pancreatic neoplasms in humans [1-3]. It is an infrequent neoplasm in dogs less than four years of age, and there are no reports of sex, breed, or location predisposition [4]. Furthermore, its etiology is unknown [5].

Neoplasms of exocrine origin in the pancreas can arise from the ductal or acinar epithelium and are classified according to their histopathological features [5]. Carcinomas of acinar origin have a morphology and arrangement similar to pancreatic acini, composed of polarized cells with intracytoplasmic granules [4]. These tumors present a worse prognosis for patients, given their highly aggressive and metastatic potential, especially in humans, dogs and cats [6].

Usually, there are metastases to the liver, regional lymph nodes, small intestine, and lung [3,4]. In addition, its growth and infiltration can lead to the progressive destruction of normal pancreatic tissue and cause the development of diabetes mellitus or exocrine pancreatic insufficiency [2].

The aim of this paper is to report a case of metastatic pancreatic acinar adenocarcinoma in a dog treated at the Veterinary Hospital of the Veterinary Medicine and Animal Science School, UNESP, Botucatu, São Paulo, Brazil.

Case Presentation

The study was submitted and approved by the Ethics Committee on Animal Use (CEUA) of the FMVZ, UNESP Botucatu, according to Protocol 210/19.

A seven-year-old female Dalmatian canine weighing 14.6 kg was seen at the veterinary hospital. The animal was admitted with a history of hyporexia, apathy, and olygodipsia for three days, along with four months of progressive weight loss. Physical, hematological, biochemical, peritoneal fluid analysis, and radiographic examinations were performed. Due to the poor prognosis of the animal, euthanasia was performed, and a necropsy was performed.

Organ fragments obtained during necropsy were fixed in 10% buffered formalin solution and histologically processed for paraffin embedding. The stains used were Hematoxylin and Eosin (H&E) and Periodic Acid-Schiff (PAS).

The immunohistochemistry technique was used on dewaxed sections that were hydrated in decreasing concentrations of ethyl alcohol and then subjected to endogenous peroxidase blockade with 0.03% hydrogen peroxide in methanol, followed by antigen retrieval with a citrate buffer solution at pH 6.0 and incubation for 18 hours at 39˚F. ENVISION/HRP nonbiotinylated polymer amplification (Dako®, Carpinteria, CA, USA) was used as the detection system according to the manufacturer's protocol. The primary antibody panels used for tumor immunophenotyping were vimentin (mesenchymal cell intermediate filaments), clone V9 at 1:200 dilutions, and CK Pan (epithelial cell intermediate filaments), clone AE1/AE3 at 1:200 dilution (Table 1). The reaction revelation was performed using Di Amino Benzidine chromogen (DAB) (Dako®, Carpinteria, CA, USA) according to the manufacturer's protocol and counterstaining with Harris hematoxylin (QEEL- Quimica Especializada Erich Ltda., Sao Paulo, Brazil). Positive and negative controls were performed for immunolabeling fidelity.

Results

In the general clinical examination of the animal, tachycardia (152 bpm), apparent icteric mucous membranes, and a capillary refill time of two seconds were noted. In addition, abdominal distension due to hepatomegaly and ascites is noticeable on the fluid wave test.

Hemogram revealed red blood cells (2,930,000 L, reference range (IR) 5,500,000-8,500,000); hemoglobin (5.7 g/DL, IR 12–18); hematocrit (17%, IR 37-55); platelets (301,000/L, IR 160,000-430,000), and leukocytosis (50,500/µL, IR: 6,000-17,000) by neutrophilia (48,500/µL, IR: 3,000-11,500). Biochemical tests revealed azotemia (urea (193 mg/dL, IR 21.40-59.92) and creatinine (2.05 mg/dL, IR: 0.50–1.50), Alanine AminoTransferase (ALT) (120 IU/L, IR: 21-73), Alkaline Phosphatase (ALP) (321 IU/L, IR 20–156), and Gamma GT (GGT) (62.01 IU/L, IR 1.2-6.4 Included, cytopathological diagnosis of a neutrophilic inflammatory process in the 600 mL sample of serosanguinous abdominal fluid.

Radiographic findings showed hepatomegaly, heterogeneous liver parenchyma associated with the presence of cavitary neoformations and abdominal lymph node reactivity. The next day, the animal returned to the veterinary hospital with clinical worsening in view of episodes of emesis after feeding, diarrhea, and adipsia.

Due to the serious condition, the dog was euthanized and necropsied. Cachexia and marked jaundice were observed. In evidence, hepatomegaly and multiple hepatic neoformations (0.5 to 17 cm in diameter), friable, nodular to multinodular, yellowish-white, soft, and sometimes cystic, filled with yellowish fluid. Similar lesions were also seen in the epiploon (0.5 cm), regional lymph nodes (5.0 cm), and in the region of the body of the pancreas (2.0 cm) (Figure 1). In addition, bilateral endophthalmitis and 200 mL of turbid Sero sanguinolent abdominal contents could be observed.

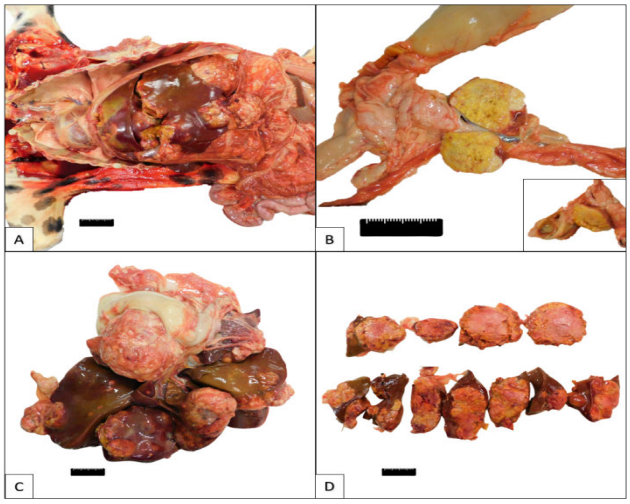

Figure 1: Macroscopy of acinar pancreatic carcinoma in a dog. (A) Severe hepatomegaly with cranial diaphragmatic distension due to metastasis of pancreatic carcinoma. (B) Metastasis of pancreatic carcinoma into a peripancreatic lymph node, exposing yellowish coloration on cutting. (Inset B) Pancreatic neoplasm cut surface with yellowish coloration and cystic center filled with yellowish-green mucous content. (C) Liver with friable nodules, with yellowish-pink coloration, characterized by metastasis. (D) Cut the surface of liver neoformations, exposing a yellowish-pink surface. Veterinary Pathology Service, FMVZ-UNESP, Botucatu/SP, 2019.

The formations were microscopically examined and revealed acinar pancreatic carcinoma with metastases to the liver, epiploon, mesentery, and peripancreatic lymph nodes. The neoplasm was characterized by a proliferation of epithelial cells arranged in acinar formations that sometimes showed eosinophilic and amorphous material at the center, interspersed with thick fibrocollagenous tissue, foci of necrosis, calcification, and cholesterol clefts. The acinar cells exhibited marked pleomorphism, anisocytosis, anisokaryosis, a columnar to rounded shape, and eosinophilic and slightly granular cytoplasm. The nucleus is rounded, basal, and occasionally paracentral in shape, with coarse chromatin and nucleoli (Figures 1 and 2). Fourteen mitotic figures were observed in 10 high-power fields (400X), in addition to the presence of binucleated, multinucleated cells, karyomegaly, and neoplastic invasion into lymphatic vessels.

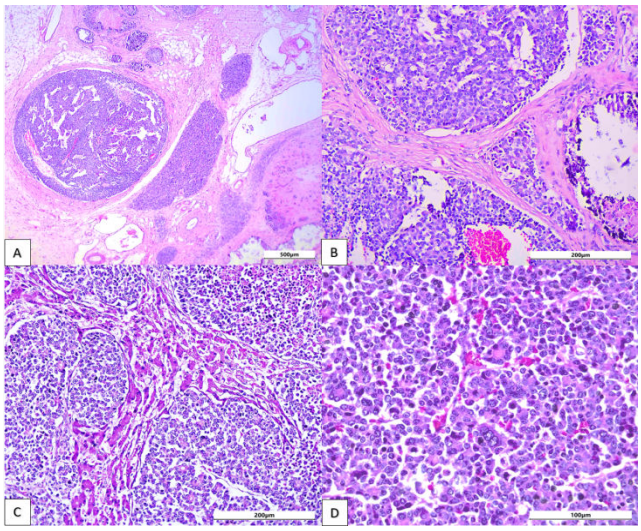

Figure 2: Photomicrographs of acinar pancreatic carcinoma in dog. (A) Pancreatic epithelial proliferation encapsulated by fibrous tissue and typical pancreas remnants. H&E, obj.5X. (B) Acinar arrangements of pancreatic neoplastic epithelial cells. H&E, obj.20X. (C) Metastasis of pancreatic carcinoma acinar liver tissue with interspersed remnant hepatocytes. H&E, obj.20X. (D) Pleomorphic neoplastic cells, with an acinar pattern in liver metastatic site. H&E, 40X obj. Veterinary Pathology Service, FMVZ-UNESP, Botucatu, 2019.

Antibodies	Clone	Dilution	Immunostaining
Pan cytokeratin	AE1/AE3	0.180556	Positive
Vimentin	V9	0.180556	Sparse positive

Table 1: Panel of primary antibodies used for tumor immunophenotyping of pancreatic acinar cell carcinoma.

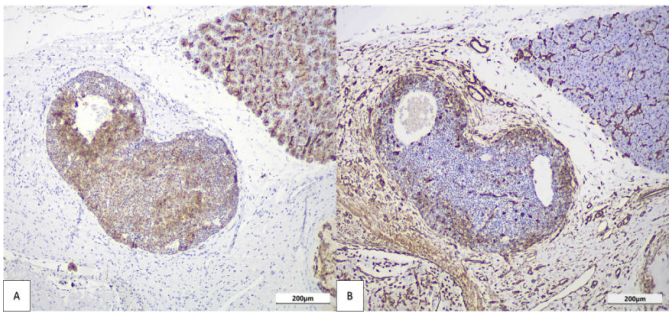

Figure 3: Photomicrographs of immunohistochemistry of primary pancreatic carcinoma, obj.10X. (A) Neoplastic cells of the primary site showing positive staining for cytokeratin (clone AE1/AE3). (B) Positive staining for vimentin of neoplastic cells (clone v9), obj.10X. Veterinary Molecular Pathology Diagnostics and Research-VETMOL, Botucatu, 2019.

Discussion

The clinical signs presented by the animal, such as hyporexia, anorexia, vomiting, diarrhea, and abdominal distension, were nonspecific and mimicked pancreatitis, which was also observed in other reports of pancreatic adenocarcinomas [7,8].

Jaundice, as in other dogs, is likely caused by biliary tract obstruction and liver involvement by metastases, as shown in biochemical examinations by increased liver enzymes (ALT, FA, and GGT), radiographic examinations, and anatomopathological findings [8,9].

Hematological changes such as anemia, decreased plasma protein, and neutrophilic leukocytosis have also been reported in some studies, although other authors associate this increase in neutrophils with areas of tissue necrosis [10-12]. The abdominal effusion (600 ml) in this case occurred secondary to hypoproteinemia and may be associated with portal vein compression and tumor implantation in the peritoneum [8,12]. Cytopathological analysis of these effusions should always be performed; however, most often it does not reveal the presence of neoplastic cells, as these do not exfoliate easily. Exploratory laparotomy and histopathological analysis are indicated to reach this diagnosis [8].

In this report, the tumor was located in the body of the pancreas. Authors report this region of the pancreas as the most affected by the neoplasm, and it can present in a focal nodular or multifocal manner [2,13].

There was metastasis to the liver, regional lymph nodes, and epiploon. In the literature consulted, it was observed that metastasis and infiltration of pancreatic carcinomas into neighboring tissues are frequent [5,14]. Other authors have reported the presence of intracranial metastases in the small intestine, mesentery, and stomach [7,10]. In addition, metastases were not detected in some cases [11,15].

The diagnosis of pancreatic adenocarcinoma was established from microscopic analysis of the neoformations using H&E staining. The tumor subtype should be defined according to the predominant cellular arrangement [4]. Through the dominant morphology, one can define acinar cell origin.

On immunohistochemical examination, there was immunoreactivity for cytokeratin, as expected and reported in exocrine pancreatic epithelial neoplasms [16]. In addition to sparse labeling for vimentin in tumor cells. The expression of vimentin in human pancreatic neoplasms has been studied, and some authors have revealed that positive labeling correlates with shorter survival times [17,18], epithelium-mesenchymal transition [18], and systemic metastasis [19], which corroborates the findings of the present case, given the metastatic foci in the liver, regional lymph nodes, and epiplon.

Among the differential diagnoses, we can mention several conditions, such as chronic hepatitis, cholangiocarcinoma, hepatocellular carcinoma, chronic pancreatitis, insulinomas, alimentary lymphomas, and intestinal carcinoma [20].

Conclusion

In conclusion, diagnosis of pancreatic carcinoma was established based on the lesions seen at necropsy and confirmed by histopathological analysis of the neoformations and immunohistochemistry. The clinical pathological lesions of the above case show that pancreatic acinar carcinoma is a silent disease and that necropsy and histopathological exams. These were required for the definitive diagnosis; early diagnosis of this disease remains a challenge in both veterinary and human medicine.

Acknowledgement

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