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Case Report

Poorly Differentiated Pancreatic Carcinoma Associated with Partial Alopecia in a Cat

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Abstract: The clinical, laboratory, ultrasonographic and pathological characteristics of a poorly differentiated pancreatic carcinoma in a 6-year-old cat are described in this study. Clinical abnormalities included severe dehydration, icterus, and partial alopecia on the medial surface of the limbs and ventral abdomen. A nodular mass was detected on abdominal palpation. Ultrasonography of the abdomen revealed a hypoechoic mass including hyperechoic and anechoic areas in the pancreatic region, and several hypoechoic areas and dilatation of the biliary duct and gallbladder in the liver. During necropsy, numerous tumorous foci were found, principally in the liver and various lymph nodes. There were several foci in the diaphragm, intercostal surfaces and lungs. Histopathological examination revealed a poorly differentiated exocrine carcinoma of the pancreas and numerous visceral metastases.

Key Words: Pancreatic carcinoma, alopecia, cat

Bir Kedide Parsiyal Alopesiye Eşlik Eden İyi Diferensiye Olmamış Pankreas Karsinomu

Özet: Altı yaşında bir kedide saptanan iyi diferensiye olmamış pankreas karsinomunun klinik, laboratuvar, ultrasonografik ve patolojik bulguları tanımlanmıştır. Hayvanda klinik olarak şiddetli dehidrasyon, ikterus ve bacakların iç yüzüyle ventral karın duvarında alopesi şekillenmişti. Abdominal palpasyonda nodüler bir kitle saptandı. Karın bölgesinin ultrasonunda, pankreas bölgesinde hiperekoik ve anekoik bölgeler içeren hipoekoik bir kitle ve karaciğerde çeşitli hipoekoik bölgeler ile safra kesesi ve kanallarının belirgin dilatasyonu belirlendi. Nekropside, başlıca çeşitli lenf yumruları ve karaciğerde olmak üzere çok sayıda tümörlü odak saptandı. Diyafram, interkostal yüzeyler ve akciğerlerde çeşitli odaklar mevcuttu. Histopatolojik inceleme, iyi diferensiye olmamış pankreas karsinomu ve çok sayıda iç organ metastazlarını gösterdi.

Anahtar Sözcükler: Pankreas karsinomu, alopesi, kedi

Introduction

Although pancreatic tumours are found with some frequency in humans, they are uncommon neoplasms in domestic animals (1-6). Most cases have been described in dogs. There is a sharply increased risk with age, with an average age of occurrence of 10 years in dogs and 12 years in cats (2,4). There is no sex or breed predilection, although there is a slight disproportion of females among dogs (2). Estimates of the frequency of pancreatic carcinoma among all confirmed tumours in dogs have accounted for about 1% of all tumours (1-3). They are also recognized in cats, cattle, horses, sheep, swine, snakes, rats, mice, and other laboratory and zoo animals (1,2,7-9).

The clinical signs are usually non-specific and are rarely diagnosed clinically. The most common signs are abdominal pain, vomiting, anorexia, weight loss, lethargy or depression and abdominal mass or masses at palpation (4-6). Despite the use of various diagnostic procedures, a definitive diagnosis prior to explatory laparatomy or necropsy is not made in many reported cases (4,6).

Pancreatic carcinomas are relatively aggressive neoplasms that invade locally and metastasize to instant sites. Direct invasion of the duodenal wall is frequent. Metastases most frequently occur in the liver, lungs, peritoneal surfaces and local lymph nodes, but they have also been found in the spleen, diaphragm and kidneys. As a result of extensive peritoneal implantation and liver involvement, ascites, icterus, and biliary cirrhosis may occur immediately (5-7).

Most cases are found in the duodenal (longitudinal) limb of the pancreas, which corresponds to the head of the human pancreas (3-4). The tumour forms a single discrete mass in the pancreas or else occurs as multiple masses throughout the entire pancreas. These are grey-white or pale yellow and usually have a firm consistency (3-4).

Pancreatic exocrine tumours may arise from either acinar or ductular epithelium. The histological pattern and the degree of differentiation of pancreatic carcinoma are extremely variable between neoplasms as well as within a single neoplasm. The neoplastic cells may be in the form of tubular structures, acini, or solid sheets of undifferentiated cells (3-8).

The purpose of this report is to describe the clinical, laboratory, ultrasonographic and pathological features of a poorly differentiated exocrine pancreatic carcinoma in a cat with numerous visceral metastases associated with partial alopecia.

Case report

A 6-year-old domestic short-haired cat with a six-month history of inappetence, progressive weight loss, apathy, and lethargy was presented. Its condition deteriorated over the last 3 weeks. Supportive therapy was not beneficial. Symptomatic therapy composed of intravenous and subcutaneous fluid (5% dextrose + isotonic NaCl®, Eczacıbaşı), balanced electrolite solutions (Electrovet®, Vilsan), Vitamin B complex (Berovit B-12®, Roche) and Vitamin C (Redoxone amp®, Roche) was implemented.

Clinical abnormalities included severe dehydration, icterus, and partial alopecia in the skin of the medial surface of the limbs and the ventral abdomen. Body temperature was 37.5 ºC. A nodular abdominal mass on the right of the median line was detected on abdominal palpation. Abdominal radiographic evaluation, however, did not reveal any finding or mass.

The complete blood count results were red blood cell 9.56 x $10^6/mm^3$, mean red blood cell volume 51 μ^3, haematocrite 48.4%, haemoglobin 12.3 g/dl and total white blood cell counts 9.4 x $10^3/mm^3$.

Serum values were urea 73.8 mg/dl, creatinine 2.1 mg/dl, glucose 278 mg/dl, total bilirubin 7.5 mg/dl, aspartate aminotransferase (AST) 185 IU/l, alanine amino-transferase (ALT) 210 IU/l, alkaline phosphatase (ALP) 217 IU/l, gammaglutamyl transferase (GGT) 7 IU/l, lactate dehydrogenase (LDH) 717 IU/l, creatinine kinase (CK) 6990 IU/l, amylase 1670 U/l, lipase 16 U/l, total protein 7 g/dl, albumin 2.4 g/dl, globulin 4.6 g/dl, albumin/globulin 0.52, sodium 140 mmol/l, potassium 4.56 mmol/l, chloride 110 mmol/l, calcium 2.45 mmol/l and phosphate 1.74 mmol/l.

Indirect abdominal radiography showed constriction of the duodenum and a delay of flow of contrast material from the stomach to the duodenum, but without any foreign material in the lumen. There was evidence of fluid accumulation proximal to intestinal thickening/mass associated with localized ileus. Ultrasonography of the liver revealed remarkable dilatation of the cystic and hepatic biliary ducts and gallbladder, hypoechoic areas and free abdominal fluid between the lobes. One of the masses was compressed immediately adjoining the biliary ducts (Fig. 1). The outline of the mass was poorly-delineated. A hypoechoic mass in the pancreatic region contained hyperechoic and anechoic areas. This mass typically appeared in close proximity to the duodenal and colonic wall (Fig. 2).

The initial clinical impression was that of advanced primary liver disease according to the clinical, laboratory and ultrasonographic findings. The animal died during examination despite continued supportive treatment, and was necropsied at the owner's request.

At necropsy, the mucous membranes, subcutaneous fat and visceral organs were markedly icteric. There was approximately 0.5 l of yellowish ascitic fluid in the abdominal cavity. The liver was the most extensively involved (Fig. 1). On the parietal surface of the liver there were a few foci similar to scar tissue approximately 0.5-1 cm in diameter (Fig. 1). The visceral surface of the liver contained several small and large nodular masses which varied from 1-5 cm in diameter. Numerous foci compressed the surrounding liver parenchyma and biliary ducts. The masses were usually deep and did not protrude

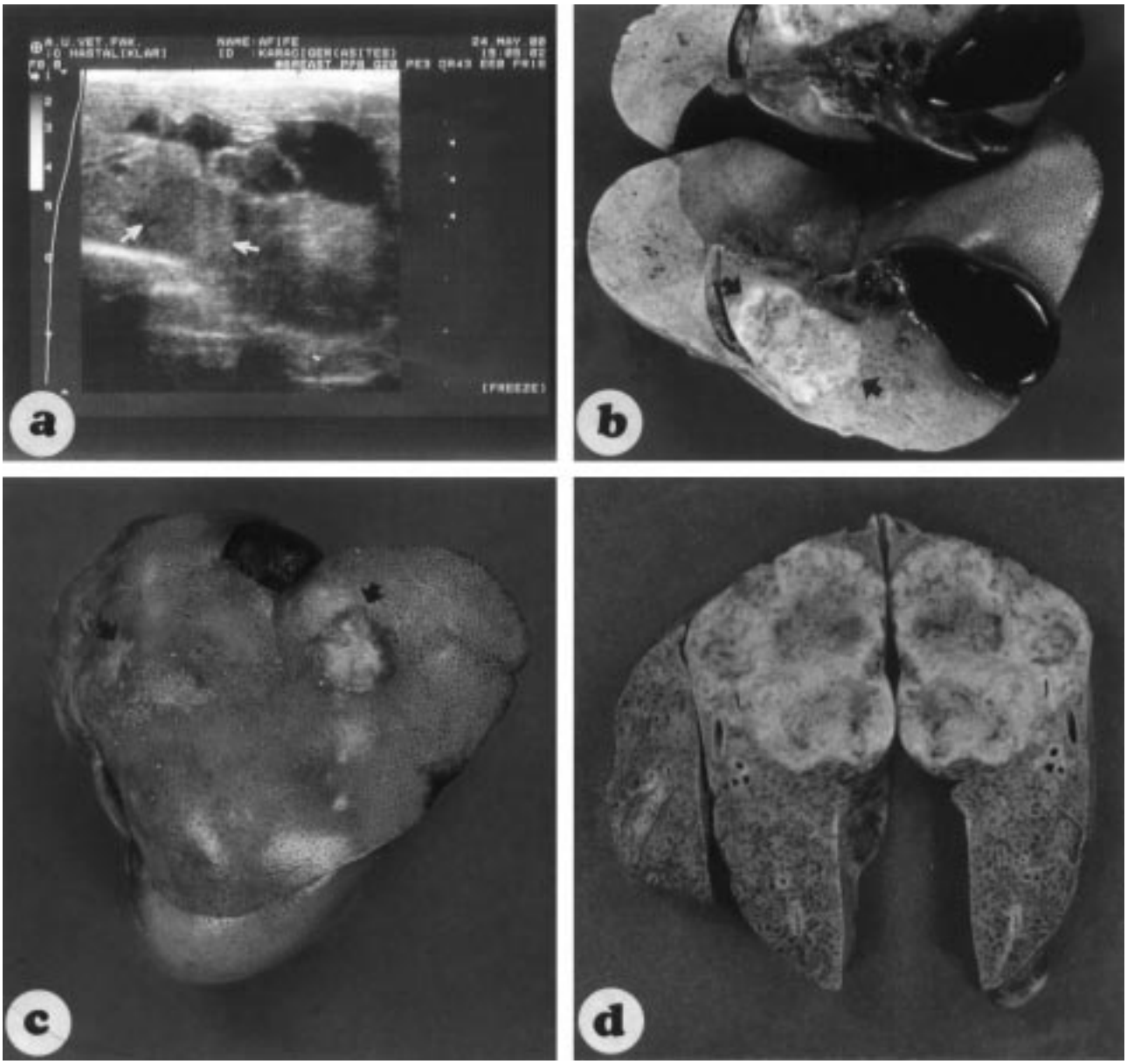

Figure 1. The ultrasonographic and gross appearances of the liver concerned. (a) ultrasonogram of the liver shows remarkable dilatation of the cystic and hepatic biliary ducts and gall bladder and a hypoechoic mass (arrows). Note the mass compressed immediately adjoining the biliary duct. (b) The cut surface of the liver as a sectioned approximately adjoining plane with the ultrasonogram of Figure 1a. Note ill-defined tumorous mass (arrows) and dilatation of the cystic and hepatic biliary ducts and gall bladder by this tumorous mass. (c) The surface of the liver including foci similar to scar tissue (arrows). (d) The cut surface involved by extensive tumorous foci.

above the surface of the liver except for the visceral surface (Fig. 1). A section of the liver on the ultrasonogram shown in Figure 1a revealed an ill-defined mass 1.2 x 2 cm in dimension causing the biliary obstruction as seen in Figure 1b. The gallbladder, cystic duct and common duct were enlarged and, in cross section, resembled a balloon full of dense, green, viscous bile.

A single discrete mass was found in the caudal end of the right lobe of the pancreas. This mass was similar to scar tissue in external appearance, had a firm consistency and extended from the wall of the overlying duodenum outward into the peripancreatic fat. A transverse cut through the mass revealed a lobulated, nodular, approximately 3.5 cm in diameter focus including yellow-greenish and greyish-white areas (Fig. 2). The duodenal

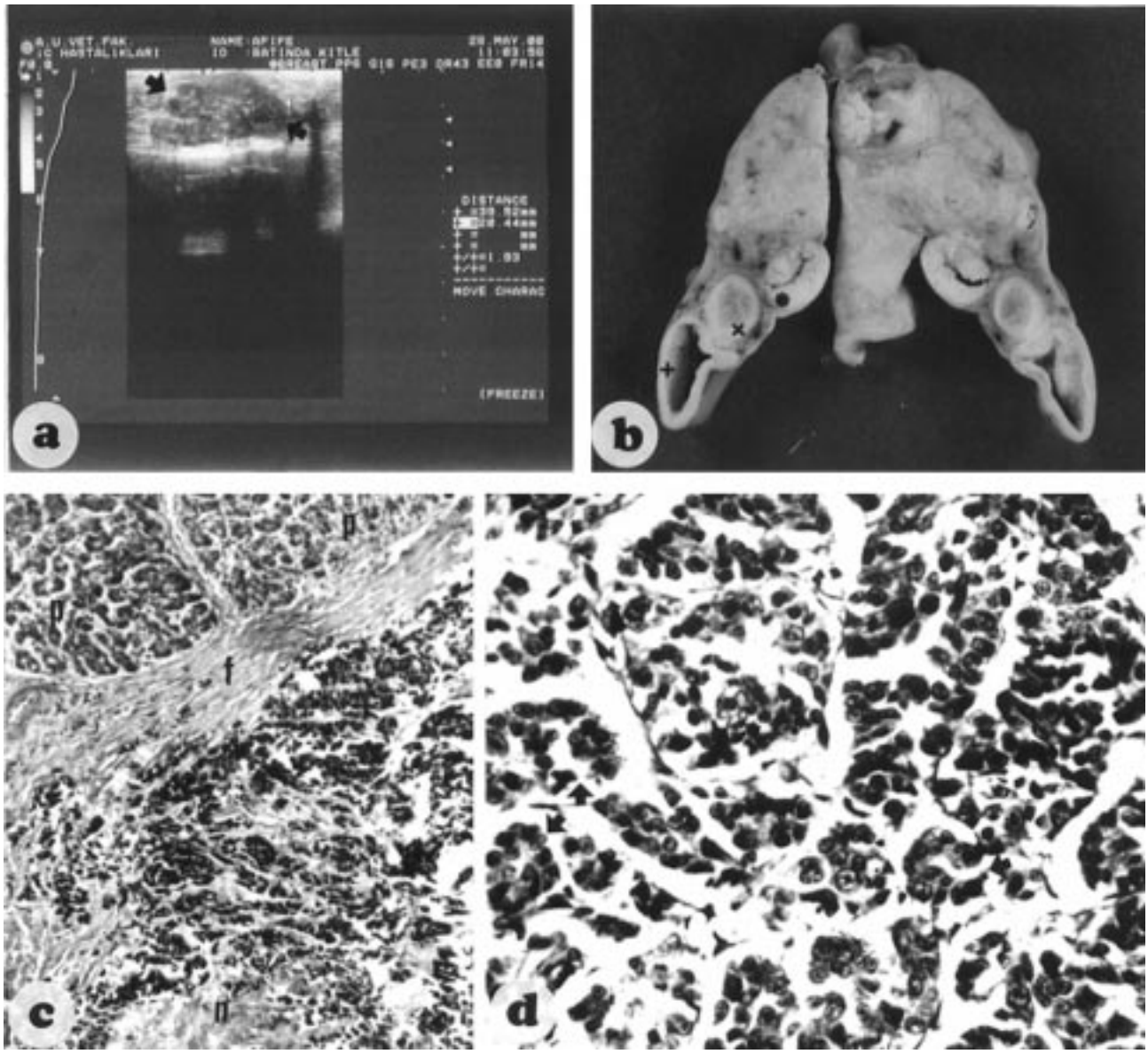

Figure 2. The ultrasonographic, gross and histopathological appearances of the mass in the pancreatic region. (a) The ultrasonogram shows a hypoechoic mass (arrows) containing hyperechoic (due to tumorous tissue) and anechoic (duodenal and colonic lumina) areas. This mass was noted adjacent to the descending duodenum and the colon, and it was first considered to be metastasis of the liver tumour. (b) A transverse cut through the pancreatic mass which is lobulated, nodular and includes yellow-greenish areas. Note duodenal wall invasion. *: duodenum, x: colon, +: ceacum. (c) Solid sheets of undifferentiated cells surrounding by a dense fibrous connective tissue. p: pancreas, f: fibrous connective tissue, n: central necrosis. Haematoxylin and eosin x100. (d) Poorly differentiated area with gland-like arranged cells (arrows) separated by thin fibrous stroma. Haematoxylin and eosin x400. Definitive diagnosis is poorly differentiated pancreatic carcinoma.

wall was surrounded and constricted by this mass. It was a clear invasion of the duodenal wall. The pancreas was grossly normal except for this mass.

Most of the visceral lymph nodes, such as the mesenteric, omental, costal and diaphramatic, were enlarged and replaced by a firm nodular, yellow-greenish mass. The diaphragm included numerous nodules with a range of a few millimetres in size. Nodules ranging from a few millimetres to 1 cm in diameter were found in the lungs and intercostal surfaces.

Histopathological examination revealed a poorly differentiated exocrine carcinoma of the pancreas and its numerous visceral metastases. A striking feature of both primary and metastatic tumorous foci was central necrosis of large masses of tumour cells which were surrounded by a dense matrix of fibrous tissue.

The primary tumour was principally composed of solid sheets of undifferentiated cells surrounded by more or less fibrous connective tissue septa (Fig. 2). Tumour cells were characterized by densely basophilic nuclei, sparse, streaming cytoplasm and indistinct cell margins, and had a high nuclear to cytoplasmic ratio. Mitotic figures were commonly seen. In some areas, the tumour cells were arranged in lobules, nests, or cords often surrounded by a fine fibrous stroma. Poorly differentiated areas with gland-like arranged cells separated by thin fibrous stroma were also observed occasionally (Fig. 2). In some areas, the tumour had a characteristic structure consisting of sheets of spindle-shaped cells. The clumps of the neoplastic cells were located as irregular masses in the parenchyma, in the perineural and periductal lymphatics and also in the tunica muscularis of the duodenum.

Invasion tended to occur by clusters of neoplastic cells. Metastatic sites in the lungs and the diaphram were numerous, and the majority included only small cell clumps without central necrosis, while a few foci included large cell clumps with central necrosis.

Metastatic foci in various lymph nodes such as the mesenteric, omental, costal and diaphragmatic, diaphram, lungs, intercostal surfaces and ribs usually contained cells with a morphology and histological pattern similar to the primary tumour. In metastatic sites, as well as the primary tumour site, non-encapsulated neoplastic cells invaded and replaced the normal tissue structure (Fig. 3). In the liver, neoplastic cells were numerous in the lymphatics of the portal triads, and hepatic parenchyma were also displaced by them. When the cellular morphology and the arrangement of cells of the primary pancreatic focus were compared, the gland-like formation was more evident in liver metastases.

Discussion

Pancreatic tumours are thought to be uncommon in domestic animals because the veterinary literature contains few articles on primary tumours of the pancreas in domestic animals; in contrast, pancreatic carcinoma is one of the most prevalent neoplasms in humans, and it has been reported that the rate is increasing (2,4,10). The present case is the second case with primary pancreatic neoplasia reported from a cat in Turkey. The first case was reported approximately 40 years ago. It was found in a 12-year-old domestic cat (7) and our case bears a close similarity to it except for its age.

Paraneoplastic alopecia has been reported previously in pancreatic (11) and hepatic (12) neoplasia cases, and a causal link between ventral alopecia and pancreatic neoplasia has been suggested in cats (11). In the present case, partial alopecia was also found in the skin of the medial surface of the limbs and the ventral abdomen, but examination of the sections obtained from the involved skin revealed no marked histopathological changes. However, it may be considered, clinically at least, that the partial alopecia in our cat was due to the pancreatic tumour and its visceral metastases.

In pancreatic disorders in dogs, most laboratory test results are not specific and usually include abnormalities in test results of hepatic and renal function, and variable levels of amylase and lipase activity (6,13-15). Similarly, there was evidence of inadequate liver and renal function according to the clinical signs and laboratory findings in the present case. The cat had high alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase and creatinine kinase activities and total bilirubin concentration. Serum creatinine, urea and glucose values were high. Sodium, calcium, and chloride concentrations were low, while potassium and phosphorous concentrations were normal. In contrast, amylase and lipase values were low.

Moreover, the number and extent of tumorous foci found at necropsy may be misleading. Extensive liver involvement was first considered to be a hepatocellular or bile duct carcinoma, and the mass in the region of the pancreas, namely pancreatic neoplasia, was considered as it may become a metastasis of the liver tumour. In addition, clinical, laboratory, and ultrasonographic findings were compatible with primary liver disease more than the signs of pancreatic involvement. In addition, from the point of view of involvement of most of the visceral lymph nodes, the case resembled the alimentary form of feline lymphoma. As a result, definitive diagnosis was made by the histological examination of tissues.

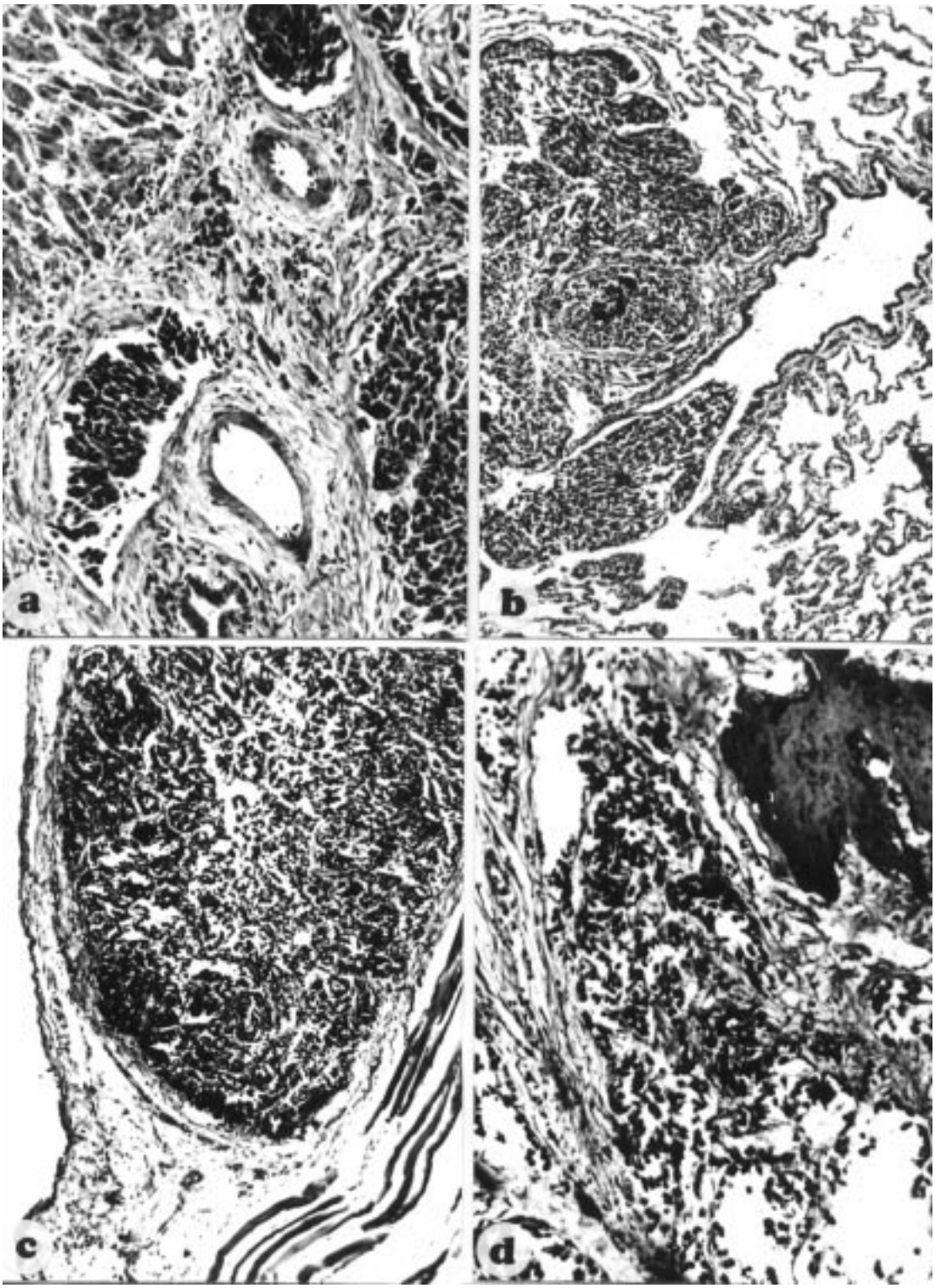

Figure 3. Histopathological appearances of the liver (a), the lung (b), the diaphragm (c), and the costal bone (d) metastases. Haematoxylin and eosin x 200 (a), x 100 (b), x 100 (c), x 100 (d). In the liver tumorous cells are in the lymphatics of the portal triad and hepatic parenchyma. In the lung tumorous cell clumps are within the alveoli. Note peribronchiolar surrounding and projecting into the bronchiolar lumen; all of them included solid sheets of undifferentiated cells.

There are several studies comparing ultrasound with other imaging methods, such as computed tomography and magnetic resonance imaging, in establishing pancreatic carcinoma in humans (10). It has also been reported that ultrasound is the most frequently used initial method to investigate patients with pancreatic carcinoma and that it is relatively inexpensive, readily available, can accurately distinguish obstructive from non-obstructive jaundice and is very sensitive in identifying liver metastases (10). There have only been a few reports describing the benefits of ultrasonography of pancreatic masses in dogs (14,15). In the present case, we used ultrasonography in the diagnosis of icterus and found the liver masses causing the biliary obstruction. Unfortunately, we first considered that the pancreatic mass might be a metastasis of a primary liver tumour instead of a primary pancreatic neoplasia and its liver metastases. We therefore recommended that a diagnosis of pancreatic neoplasia should now be suspected in animals with icterus and the liver masses causing the biliary obstruction, although such masses may also be due to hepatocellular or cholangiocellular tumours, or other carcinomas. In addition, the pancreatic region should be carefully examined in cases in which the clinical signs, laboratory and even ultrasonographic findings may be misleading, as in the present case. As a result, ultrasonography should be considered a useful method for the identification of pancreatic neoplasia in cats with various visceral metastasis, especially in the liver.

Exocrine carcinomas of the pancreas tend to arise more often in the body of the pancreas. They are more or less spherical and circumscribed, and may have some resemblance to masses of scar tissue (3,4). In the present case, the tumour was found in the caudal end of the right lobe of the pancreas, and its characteristics were similar to the above findings.

The great majority of primary pancreatic exocrine tumours are histologically defined as carcinoma or adenocarcinoma according to their ductal or acinar origin (3,4,6-8). In the present case, the tumour evidently originated from the duct epithelium, and transition from normal epithelial cells to neoplastic cells was observed. Thus, it is possible that the tumour was ductal in origin. Given the extreme variation in cellular structure and histologic pattern, several morphological types have been described such as adenocarcinoma, anaplastic or undifferentiated carcinoma, alveolar carcinoma and endocrine-like carcinoma (6). In addition, three fairly distinct morphological types of adenocarcinoma have also been classified: small tubular, large tubular and acinar cell (3). This variation has been apparent in a single tumour, among different tumours, or within the metastases of the same tumour in other organs. Similarly, this variation was clear in the present case. However, systematic differences in the immunocytochemical profiles of several exocrine carcinomas of the pancreas have not been observed (16), and it has been pointed out that this distinction is rather arbitrary because the degree and direction of differentiation are unpredictable and the ductular cells are known to have a pluripotent capacity (4). Thus, differentiated or undifferentiated carcinoma of the exocrine pancreas is the most favourable and simple expression. In conclusion, all of them are aggressive neoplasms that invade locally and metastasize to instant sites.

In the present case, it was not possible to estimate the early progress of the tumour. Ascites and icterus were due to extensive lymphatic obstruction with biliary obstruction and hepatocellular damage, and the resulting debilitation was due to the liver metastases, not to the primary pancreatic neoplasia. It was interesting that the gland formation was more evident in liver metastases than primary pancreatic tumour focus, and that some of the metastatic foci in the liver were larger than the primary pancreatic neoplasia. This condition runs contrary to the common rule that the primary neoplasm is larger than the metastasis and that the resulting debilitation of the affected animal is due to the primary neoplasm and not to the metastasis. This explains why the liver metastases occurred early in the course of neoplastic development and why the initial clinical impression was one of primary liver disease.

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