MUCINOUS CHOLANGIOCARCINOMA WITH METASTASES IN A TURKISH VAN CAT - A CASE REPORT

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Abstract

The pathomorphological and immunohistochemical features of cholangiocarcinoma in an 11-year-old female Van cat were described. At necropsy, the primary tumour was determined in the liver. The tumour was greyish-white, firm, and multinodular. The size of these nodules ranged between 1 cm and 3 cm. There were metastases in the mesentery, portal lymph nodes, peritoneum, and lung. Immunohistochemically, the tumour cells showed positive immunoreactivity for S100 and cytokeratin, and negative for α-fetoprotein. According to morphological and immunohistochemical findings, this tumour was defined as a cholangiocarcinoma.

Key words: Van cat, cholangiocarcinoma, histopathology, immunohistochemistry.

Cholangiocarcinoma (bile duct carcinoma) is a malignant tumour arising from bile duct epithelial cells (2, 5). In cats, lymphomas are comprised mostly of liver tumours, and primary tumours of the liver are rare (12). Cholangiocarcinoma comprises less than 1% of all neoplasm found in cats. It is seen in cats over 9-10 years of age and there is no known breed predilection (2).

Cholangiocarcinomas are readily distinguished from hepatocellular carcinomas histologically. Immunohistochemistry can assist in the identification of poorly differentiated cholangiocarcinomas within the hepatic parenchyma of cats (2). In humans, immunohistochemical techniques are widely used in the diagnosis of hepatic tumours. In the differential diagnosis of hepatocellular carcinomas from cholangiocarcinoma, α-fetoprotein (AFP), carcinoembryonic antigen (CEA), and cytokeratin (CK) are mostly used tumour markers (2, 3, 8, 15). The expression of S100A6 gene, which has particularly been used recently, has been seen preferentially in cholangiocarcinoma rather than hepatocellular carcinoma, suggesting S100A6 as a useful marker for the differential diagnosis of cholangiocarcinoma from hepatocellular carcinoma (8). Many studies on cholangiocarcinoma in human (3, 8, 15) and various animals, particularly dogs, have been reported (6, 7, 11, 14), while studies on morphological, histopathological (9, 13), and immunohistochemical evaluation (12) of cholangiocarcinomas in cats have been extremely rare. Here, we describe pathomorphological and immunohistological findings of metastatic cholangiocarcinoma with pleural effusion in a Turkish Van cat.

Description of the case and Discussion

A corpse of 11-year-old Van cat with a diagnosis of pleural effusion was sent to necropsy. At the necropsy, primary tumour masses were detected in all the hepatic lobes, 1-3 cm in diameter, multinodular, greyish-white, firm, and expansive. The sections of the masses were lobulated, moist, and lubricious. Metastatic tumours were found in the portal lymph nodes, peritoneum, mesentery, and in all lobes of the lungs.

The liver and metastatic tissue specimens were fixed in formalin, embedded in paraffin, and 4 µm sections were prepared. The sections for histological examination were stained with haematoxylin and eosin (HE), periodic acid-Schiff (PAS), and alcian blue. Immunohistochemical staining was performed using the standard avidin-biotin peroxidase complex (ABC, Dako, Carpinteria, USA) method. The specific antibody used was S100 (S100A6; Dako, USA), CK (AE1/AE3; Dako, USA), AFP (Ab-2; NeoMarkers, USA), and CEA (Ab-2; NeoMarkers, USA). For the determination of S100, CK, and CEA, the sections were heated in a microwave oven, in 0.01 M citric acid for 5 min at 700 watts and then cooled for 20 min. For AFP immunohistochemistry, no pre-treatment was required and the slides were directly washed with phosphate-buffered solution. Endogenous peroxidase was blocked by immersing the sections in 0.3 % hydrogen peroxide in absolute methanol for 30 min.
Fig. 1. Proliferating bile ductules and periductal fibrosis in the liver. HE. 160x

Fig. 2. Metastatic cholangiocarcinoma in the lung. HE. 160x

Figs 3-4. Cytokeratin and S100 staining in cholangiocellular area. Avidin-biotin-peroxidase method, Mayer’s haematoxylin counterstain. 320x
Subsequently, the slides were incubated with the respective primary antibodies (S100, CK, AFP, CEA) and eventually diluted in PBS for 60 min at room temperature. After washing with PBS, the sections were incubated for 20 min with biotinylated goat anti-rabbit antibodies at room temperature. After washing again, the immune complexes were detected by the streptavidin-biotin horseradish peroxidase complex using aminoethyl carbazole (AEC) as chromogen (DAKO). Mayer’s haematoxylin was used for counterstaining. Negative control sections were treated as described above except that primary antibodies were omitted.

Microscopically, the tumours in the liver were composed of cells that resemble biliary epithelium. The cells were cuboidal or columnar, with a moderate amount of clear or slightly granular cytoplasm. Most of their nuclei were vesicular, different in size, and hyperchromatic. Nucleoli were frequently seen. In the tumour mass, various sized ductules, acinar structures, and sometimes, papillary formations were observed. The acinar structures were lined with multiple layers of epithelial cells. Large areas of necrotic tissues were noted. Tumour emboli were observed in the lumen of some vessels. Besides, the intensive development of stromal and periductal fibrosis took place (Fig. 1). The histological features in metastatic lesions were similar to those in the primary tumour areas (Fig. 2). In some acinar structures, PAS and alcian blue stained mucin was observed.

Immunohistochemically, tumour cells were positive for cytokeratin and S100 protein staining (Figs 3–4), and negative for AFP. Based on histopathological and immunohistochemical findings, the tumour was defined as a cholangiocarcinoma.

The breed predilection was reported to be unimportant in cholangiocarcinoma (2) and the literature review revealed no detailed information on this factor. The case presented is related to a Turkish Van cat, which is a rare breed. Cholangiocarcinoma is reported to metastasise into the peritoneum, lungs, regional lymph nodes, diaphragm, spleen, kidneys, eyes, pancreas, heart, adrenals, and the bone marrow (3, 10, 12). In the presented case, there were metastases into the lungs, mesentery, and the peritoneum.

S100, AFP, CEA, and CK are a useful marker for the differentiation of cholangiocarcinoma from hepatocellular carcinoma. AFP is present in hepatocellular carcinomas, but not in cholangiocarcinomas. CEA, S100A, and CK are positive in cholangiocarcinomas (3, 8, 11). AFP does not appear to be always helpful in the immunohistochemical diagnosis of hepatocellular carcinoma. Although CEA is considered to be one of the most important tumour markers in differentiating cholangiocarcinoma from hepatocellular carcinoma, it does not give positive results in all cases as in many tumour markers, and different polyclonal CEA antibodies may give different results. This condition is attributed to differences between the specificity and sensitivity of the techniques, antibodies, and reagents (4, 11). Concordant with the previous view, CEA was not detected in this investigation. On the other hand, CK positive cells were frequently observed. The presence of the S100 protein has been evaluated in many different malignant tumours (15). In humans, expression of S100A6 has been detected as a new marker for cholangiocarcinoma rather than primary hepatocellular carcinoma (8). Immunohistochemical examination of the tumour tissues using monoclonal antibody specific to S100A6 showed that 100% of cholangiocarcinoma tissue samples examined were positively stained, but only two of 20 (10%) specimens from patients with primary hepatocellular carcinoma were weakly stained (8). Consistent with the previous study; S100A6 was also stained strongly positively in the case.

Mucinous and gelatinous abdominal effusions are rarely found in animals (5). In human cholangiocarcinomas, pleural effusion may often develop following hepatectomy (1). In animals, pleural effusions related with cholangiocarcinomas (10) are as rare as abdominal effusions (5). The pleural effusion observed in this case may be probably secondary to lung metastasis of cholangiocarcinoma.

References

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