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Case Report

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Multicentric Intrahepatic Biliary Cystadenoma in a Dog

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Abstract: This report describes a case of multicentric intrahepatic biliary cystadenoma observed in a 13-year-old, male, Irish setter dog. The dog had a history of chronic inappetence, weight loss, intermittent icterus, and diarrhoea. In the ultrasonographic examination of the abdominal organs, 5 spherical masses were found in various liver lobes. The largest mass was 12 cm in diameter and was located on the quadrate lobe. It had spongy consistency and had several cystic structures, 3 mm-2.5 cm in diameter, on the cut surface. While this mass bulged through the normal outline of the liver, smaller masses were engraved within the liver parenchyma. Histopathologically, cystic glandular structures lined by cubical to columnar epithelial cells were observed. Immunohistochemically, tumoural cells stained positively with anti-cytokeratin 7 and anti-cytokeratin 19 antibodies. We report herein a rare case of multicentric biliary cystadenoma in an Irish setter dog with histopathological and immunohistochemical findings.

Key Words: Dog, biliary cystadenoma, multicentric, cytokeratin, immunohistochemistry

Bir Köpekte Multisentrik Safra Yolu Kistadenomu

Özet: Bu çalışmada 13 yaşında, İrlanda Seteri bir köpekte teşhis edilen safra yolu kistadenomu rapor edilmiştir. İştahsızlık, aralıklarla devam eden ishal ve ikterus şikayeti ile gözlem altına alınarak karın ultrasonografisi uygulanan hayvanda farklı karaciğer lobları üzerinde 5 adet tümöral kitleye rastlandı. Köpek, kitlelerin sayı ve yerleşimi nedeniyle, metastaz yapan bir karaciğer tümörü olduğu düşünülerek, hayvan sahibinin izni alındıktan sonra ötenazi edilerek nekropsiye sevk edildi. Nekropside, en büyüğü lobus quadratusta olmak üzere farklı karaciğer loblarında yerleşim gösteren kistik ve kesit yüzü süngerimsi görüntü arz eden tümöral kitlelere rastlandı. Histopatolojik incelemede kistik glandüler yapıların, eozinofilik sitoplazma ve basofilik boyanma özelliği gösteren çekirdeklere sahip kübik-kolumnar hücreler tarafından döşendiği görüldü. Bu hücrelerin sitokeratin 7 ve sitokeratin 19 ile immunohistokimyasal olarak pozitif olarak boyandıkları tespit edildi. Histopatolojik ve immunohistokimyasal bulgular ışığında tümör multisentrik safra yolu kistadenomu olarak teşhis edildi.

Anahtar Sözcükler: Köpek, safra yolu kistadenomu, multisentrik, sitokeratin, immunohistokimya

Introduction

Primary and metastatic tumours are seen in the liver but metastatic involvement is more common. Hepatic tumours account for 0.8% of all canine neoplasms and can be categorized as hepatocellular, cholangiocellular (bile duct), mesenchymal, and neuroendocrine tumours (1-3). Bile duct tumours (BDTs) arise from the biliary epithelium, mostly within the liver parenchyma and rarely from the extrahepatic biliary system. Basically, there are 2 types of BDTs in cats and dogs: bile duct adenoma (BDA), also termed as biliary cystadenoma due to the macroscopic and microscopic appearance, and bile duct carcinoma (BDC) (3,4). BDTs occur rarely in domestic animals and have been reported in dogs, cats, sheep, and pigs (3). BDAs grow slowly and can reach large sizes before causing clinical signs and, in many cases, they are

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discovered accidentally during other examinations. Approximately 50% of benign and 25% of malignant hepatobiliary tumours are asymptomatic (1,3,4). Bile duct carcinoma is the most common member of the family (1,3,5) and predilections for females (1) and Labrador retriever dogs (6) have been proposed. There are no exact figures about the incidence, sex, breed predisposition, or anatomical locations of the biliary tumours in dogs due to the limited number of reports.

Case History

A 13-year-old, male, Irish setter dog with long term inappetence, weight loss, intermittent icterus, and intermittent diarrhoea was referred to a veterinary clinic. After the routine clinical and ultrasonographic examination, tumoural masses, different in size, were noticed in various liver lobes. The number and the location of the masses were taken into consideration and euthanasia was performed with the consent of the owner. At necropsy, a total of 5 spherical, pale white to pale grey, well-circumscribed masses were observed on the liver. The largest mass was located on the quadrate lobe and had a diameter of 12 cm (Figure 1). The mass had spongy consistency and exhibited several cystic structures, 3 mm-2.5 cm in diameter, on the cut surface (Figure 2), which were filled with sero-mucinous fluid. Other masses were on the right (2 masses) and left lateral lobes (2 masses), were 2-5 cm in diameter, and had spongy to solid cut surfaces. The large mass bulged through the normal outline of the liver, whereas the smaller masses were engraved within the liver parenchyma. No abnormalities were observed in the hepatic lymph node, gall bladder, or other organs in both abdominal and thoracic cavity. The signs related with icterus were not noticed in the dog.

Tissue samples taken from the masses, liver lobes, hepatic lymph node, gall bladder, and other organs were fixed in neutral formalin and processed routinely. All slides were stained with haematoxylin-eosin and some selected slides were stained immunohistochemically with the streptavidin biotin peroxidase method using monoclonal mouse-anti-human cytokeratin 7 (MNF116, Dako, Glostrup, Denmark) and anti-cytokeratin 19 (RCK108, Dako) antibodies as described previously (7). Briefly, sections were dewaxed in xylene for 15 min, rehydrated, and treated with 3% H_2O_2 for 10 min to block endogenous peroxidase activity. Incubation with 1:100 diluted primary antibodies was performed for 1 h at room temperature, and the slides were then incubated with the linking antibody and with the peroxidase-conjugated streptavidin for 20 min at room temperature. Peroxidase activity was developed in diaminobenzidine (DAB) chromogen for 15 min. Slides were counterstained with haematoxylin, dehydrated, and mounted. Negative control sections were incubated with PBS instead of the primary antibodies.

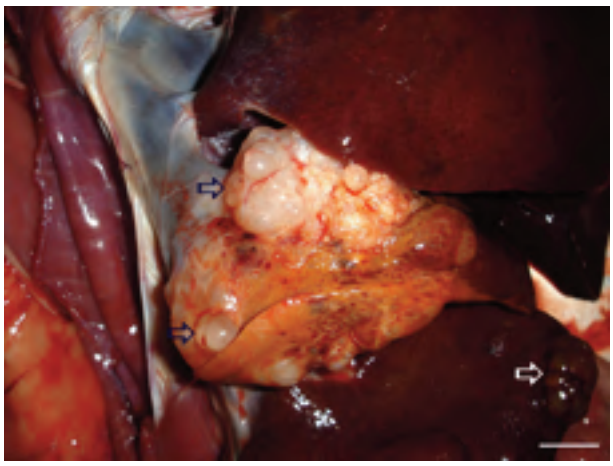

Figure 1. Liver, cystic tumoural mass in quadrate lobe, cysts in various sizes (black arrows), cysts in right lateral lobe (white arrow), Bar = 2 cm.

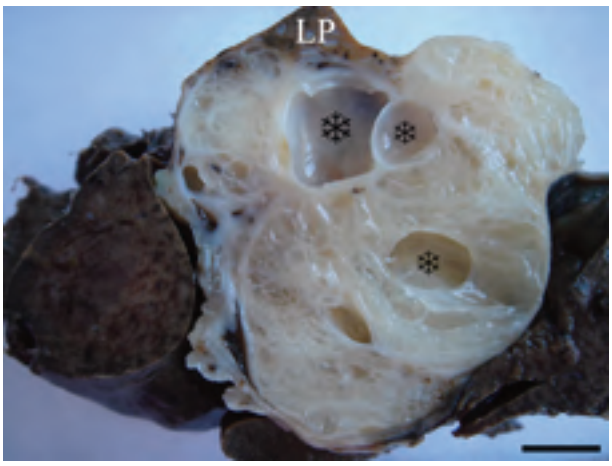

Figure 2. Cross section of the quadrate liver lobe and tumoural mass, liver parenchyma (LP), cysts in various sizes (snow flakes), Bar = 2 cm.

Results and Discussion

The masses were diagnosed as multicentric biliary cystadenoma. Histopathologically, the tumours were composed of cystic glandular structures lined by cubical to columnar epithelial cells (Figure 3). Cysts had various sizes and were supported by moderate amounts of collagenous stroma. The biliary epithelial cells had moderate amounts of pale eosinophilic cytoplasm and round to oval, vesicular, basally oriented nuclei. Nucleoli were small or inapparent. In some cystic structures, the epithelial cells formed papillary projections into the lumen. Mitotic figures were uncommon and no signs of blood vessel or lymphatic invasion were noticed. In both macroscopically and microscopically, no local or distant organ metastases were found in any organs studied. Immunohistochemically, tumoural cells, as well as the biliary epithelium in the unaffected liver parenchyma, were positively stained with anti-cytokeratin 7 (Figure 4) and anti-cytokeratin 19 antibodies. No distant or peritoneal metastases and invasion of hepatic lymph node were observed.

Biliary cystadenomas are rare cystic tumours that arise in the liver or less frequently in the extrahepatic biliary system. The tumour does not cause any characteristic signs and is generally found during the examination of the animal for another reason (3). In the present case, the tumour was also found accidentally and no extrahepatic involvement was observed. It was reported that the left lateral lobe in dogs (1) and right hepatic lobe in humans (8) affected most and the tumoural masses were observed in various liver lobes. The quadrate lobe was severely affected in the present case. Although, multiple lesions might suggest an intrahepatic lymphogenous metastasis, the tumour did not show any signs of malignancy. Thus, a multicentric origin should not be ruled out. Generally, BDCs have multicentricity in the liver (9); clinicians who encounter such kind of liver lesions in various lobes during ultrasonographic examinations should be taken into consideration that the tumour can be benign as in the submitted case.

The authors used anti-cytokeratin 7 and 19 antibodies, which had previously been proven to be reactive with normal biliary epithelium and lining epithelial cells of BDTs in humans and dogs (2,10), to characterize the precise origin. The neoplastic cells from various liver lobes displayed strong positive reaction against both antibodies.

According to the referring veterinarian of the dog, no signs or blood chemistry findings related with liver functions were noticed in the dog. As BDCs have been proposed to originate from the benign counterpart in some cases in humans (9) and animals (1,4), biliary cystadenoma should also be considered in differential diagnosis. To the authors' knowledge, this is the first report of BDA in this breed and we believe that this case report has scientific merit as it reports the occurrence of the BDA in a multicentric fashion. The exact frequency, sex, breed, or age predisposition of BDTs needs to be clarified with further reports.

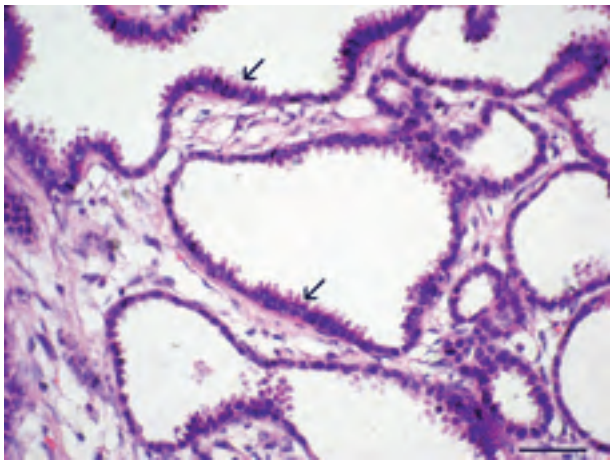

Figure 3. Tumoural mass, cysts lined by cubical biliary epithelial cells (arrows), haematoxylin-eosin, Bar = 26 mm.

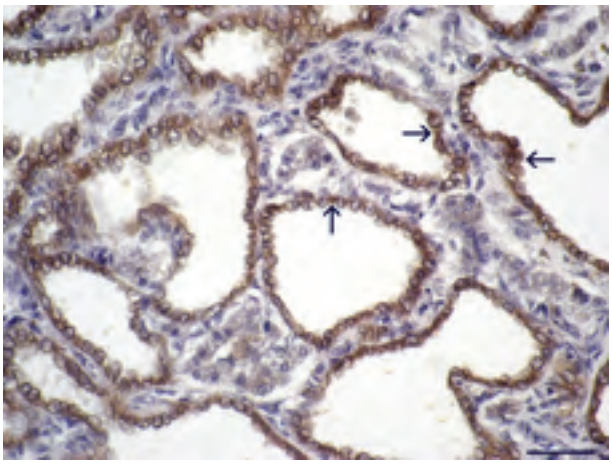

Figure 4. Tumoural mass, cysts lined by cubical biliary epithelial cells are stained with anti-cytokeratin 7 antibody (arrows), Streptavidin-biotin-peroxidase complex method. DAB chromogen, haematoxylin counterstained, Bar = 26 mm.

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