Short Communication

Hepatocellular adenoma in 10 years old Siberian husky dog

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Received: September 2023 Accepted: December 2023

Abstract

A 10-year-old neutered male Siberian husky was referred with a chief complaint of weakness,severe abdominal distension, inappetence, lethargy, vomiting, and diarrhoea that occured five days before the referral time. Hematological and biochemical evaluation revealed significant hepatopathy. Right-side heart enlargement with a large volume of peritoneal fluids was noted on radiology which were defined as transudative ascites after abdominocentesis and laboratory examination. Ultrasonography revealed hepatomegaly with multiple nodular lesions of varying sizes less than 2cm on the liver's surface. Ventrodorsal and lateral chest radiograph results showed no evidence of pulmonary metastases. Conservative therapy started with fluid therapy, broad-spectrum antibiotic, hepatoprotectant agents along with pimobendane and Enalapril tablet during 2 weeks. Unfortunately, medical interventions were not effective and icterus and hepatoencephalopathy was ocurred so the case was admitted for an abdominal exploration surgery.At laparotomy, about fifty well-oriented, reddish-brown, non-pedunculated, and non-invasive nodules were seen on the liver surface which distributed on different lobs and even cholangiohepatic ducts. Due to the extent of hepatic lesions, and with the owner's consent, the decision was made to euthanisia. Basded on the results of histopathological examinations, hepatocellular adenomas was confirmed. Despite the benign nature of the tumor, the severity of the liver damage addressed to hepatic failure and the patient grave prognosis. Large tumors or those affecting more than two lobes, can significantly reduced the life expectancy and unfortunatly in this case, the lesions were largly distributed on all liver lobes and even colangiohepatic ducts.This report sheds light on the complexities of hepatocellular adenomas, stressing the importance of accurate diagnosis and effective treatment to advance our understanding of this condition.

Keywords: Benign Hepatocellular adenoma, Liver, Dog

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Introduction

Primary hepatic neoplasms are less common than metastatic neoplasms of the liver and can be categorized as either carcinoma, carcinoid, sarcoma, or hemolymphoid in origin. Metastatic liver tumors, on the other hand, can originate from various internal organs and may be associated with lymphosarcoma. Liver tumors can be classified as benign or malignant, with hepatocellular carcinomas being the most common primary liver tumors in aged animals (>9 years), although they can occur in both dogs and cats (Withrow, 2012). Benign liver tumors encompass hepatocellular adenoma, bile duct adenoma, hemangioma, and leiomyoma, while malignant tumors include hepatocellular carcinoma (HCC), cholangiocarcinoma, neuroendocrine tumors, and sarcomas such as angiosarcoma, fibrosarcoma, and leiomyosarcoma. Malignant liver tumors tend to metastasize, while most liver tumors in cats are benign (Morrison and Dobson, 2002; Selmic, 2017).

Material and methods

A 10-year-old neutered male Siberian husky was presented to the veterinary hospital of Shahid Bahonar University, complaining of progressive abdominal distension, increased respiratory effort with a background of vomiting and diarrhea, weakness, lethargy and inappetence for more than 5 days. On clinical examination, the dog exhibited icteric pallor mucous membrane, hind limb edema, systolic (3/6) right-side murmur and severe abdominal distention.

The abnormalities noted on hematological and serum biochemical profiles were mild leukocytosis with a slight shift to left neutrophilia, hyperglobinemia, significant increase in alkaline phosphatase (ALP=620 U/L), alanine aminotransferase (AST= 180 U/L) and gamma-glutamyl transpeptidase (GGT=12 IU/L), elevated total bilirubin (10 mg/dl), and a notable decrease in total protein (4.1 mg/dl), serum albumin levels (1.5 mg/dl) and blood urine nitrogen (BUN=12 mg/dl). On the chest radiography, right-side heart enlargement with remarkable abdominal effusion was noted. Abdominocentesis was performed, and 1.5-2 liters of peritoneal fluid were drained in each daily checkup. Abdominal fluid analysis showed a transudative effusion with low protein (1.4 g/dl), low cellular (260/µL) fluid with specific gravity about 1.005resembleing hepatic and cardiac failure. Ultrasonographyr revealed hepatomegaly with multiple nodular lesions of varying sizes less than 2cm on the liver's surface. Ventrodorsal and lateral chest radiographs showed no evidence of pulmonary metastases.

Conservative treatment was started with crystalloid hypotonic fluid therapy (dextrose/saline solution), furosemide (4mg/kg), Marbofloxacin(5mg/kg) and metronidazole(15mg/kg), Vitamin E and Vitamin C as an antioxidant, Vitamin K and Omega3 as hepatoprotective agent and pimobendane (0.25mg/kg, q12h) combined with Enalapril (0.5mg/kg,

q24h). Unfortunately, despite the therapeutic plan, the patient's condition deteriorated significantly, and despite all efforts, no improvement was observed during 2 weeks. The severity of the liver damage caused hepatoencephalopathy, and icterus, consequently the case was admitted for an abdominal exploration surgery.

Result

At laparotomy, about fifty well-oriented, reddish-brown, non-pedunculated, and non-invasive nodules were seen on the liver surface which were well-oriented and surrounded by a thin capsule of connective tissue, sizes ranging from 0.5 to 2 cm. The nodules distributed on different lobs and even cholangiohepatic ducts. Benign and malignant primary hepatic neoplasm, or secondary hepatic neoplasm included our differential diagnosis list (Fig. 1).

According to results of exploratory laparotomy, unknown prognosis of the case and owner’s financial issues euthanasia has been required by the owner.

Figure 1: Reddish-brown encapsulated nodular lesions on liver's lobs.

Three biopsies of the different size hepatic lesion were obtained. Histopathological evaluation of the nodular lesions revealed regular hepatocytes with moderate to severe cytoplasmic steatosis. No evidence of increased mitotic index, atypia or nuclear polymorphism was detected. The lesions were diagnosed as hepatocellular adenomas, which are classified as benign tumor (Figs. 2 and 3).

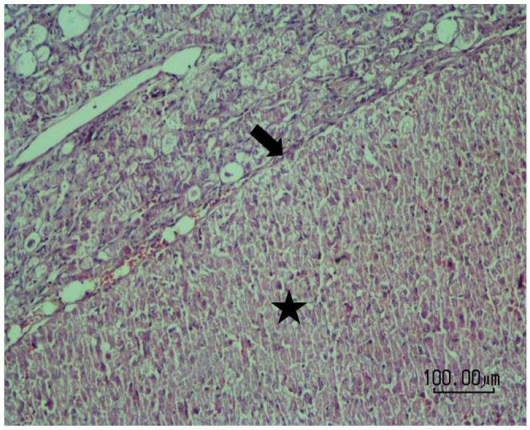

Figure 2: Hepatocellular adenoma (asterisk) is well demarcated from the adjacent parenchyma by a thin capsule of connective tissue (arrow) (HE, Scale= 100 µm).

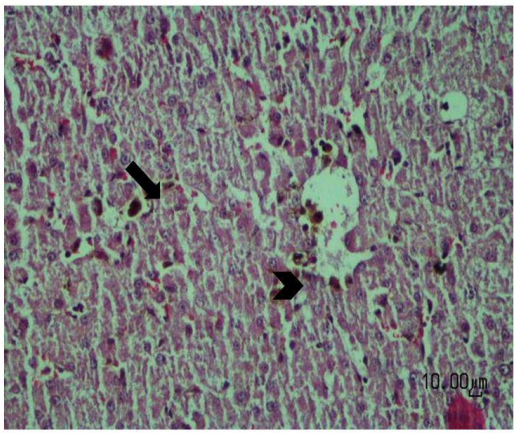

Figure 3: Hepatocellular adenoma. Well differentiated hepatocytes have round nuclei (arrowhead) with single prominent nucleoli. Brown bile pigments (arrow) are visible in the tumor parenchyma (HE, Scale= 10 µm).

Discussion

Primary hepatic neoplasms represent 0.6% to 1.3% of all canine neoplasms, making them extremely uncommon in dogs (Selmic, 2017). Animals beyond the age of ten to twelve years old are more likely to develop liver neoplasms. There are contradicting reports about sex predisposition and no breed predispositions have been identified. Hepatic neoplasia in dogs and cats lacks a clear etiopathogenesis, yet tumors have been experimentally produced in dogs subjected to several chemicals and radiation types (Morrison, 2002). Owing to the liver's crucial function in detoxifying, mutagenic substances may have an especially strong effect on the hepatobiliary system. Dogs have not been discovered to have any viral causes of hepatic neoplasia; nevertheless, liver flukes have been reported as a cause (Morris and Dobson, 2008).

Distinguishing between hepatocellular carcinoma and adenoma can be challenging and requires a comprehensive evaluation of dysplasia and histologic characteristics. Hepatocellular adenomas are large, pedunculated, benign tumors of epithelial origin that are demarcated and well differentiated from adjacent normal liver. Primary hepatic neoplasia in dogs frequently manifests as nonspecific symptoms, some of which were observed in the current case. These symptoms include anorexia, lethargy, vomiting, diarrhea, abdominal pain, and abdominal distension (Morrison, 2002). Hepatomegaly is the most prevalent physical finding as sonography demonstrated it in our case. Biochemical and hematological parameter changes are present, but they are non-specific since they cannot distinguish between inflammatory, degenerative, and neoplastic processes. Dogs with atypical adrenal hyperplasia linked to elevated levels of androgen or progesterone tend to have a higher prevalence of hepatocellular adenomas.

Increased liver enzyme activity, particularly alkaline phosphatase (ALP), along with modest changes in transaminase levels, had been frequently observed despite that, in our case, liver transaminase activity raised up moderately, and in abdominal sonography and exploratory laparotomy, no adrenal hyperplasia was detected (Olgivie *et al*., 1995; Munday *et al*., 2016). In other words, increased liver enzyme activity and adrenal hyperplasia was not connected in this case (Morrison, 2002).

Ultrasonography offers a more precise method of detecting the site of origin of an abdominal mass and could be used to address to achieve fine needle aspirates, as in our case ultrasonography results identified increased hepatic echogenicity and gall bladder wall thicknesses. Meanwhile biochemical profile results, showed a decline in total protein, albumin and urea levels that indicating non-adequate liver function, on the other hand, clotting factors had not been analyzed, thus liver biopsy with sono guide has not been to avoiding the risk of biopsy-associated hemorrhage.

In order to determine a definitive diagnosis and prognosis,

histopathological evaluation of liver tissue was mandatory. Both cytological and histological methods of evaluation have advantages and disadvantages, and each is dependent on the interpretive skills of the pathologist and the quality of the history and tissue submitted (Roth, 2001). The primary advantages of cytological examination of fine-needle aspirates include reduced cost, obtaining the specimen, sedation required and a lesser degree of invasiveness. The major disadvantages are small sample size and the difficulty in sampling focal hepatic lesions. Probability cells disruptions during the smear preparation of cytologic examination, causing loss of the relationship between detached cells, and tissue fragments, which may be an important source of information (Selmic, 2017). Nevertheless, in our case, the cytopathological diagnosis was not made by ultrasound-guided fine-needle aspiration and diagnosis steam by post-mortem histopathologic evaluations.

In this case report, we present a notable clinical study of hepatocellular adenoma in a dog, highlighting the diagnostic challenges encountered and discussing the surgical consideration.

The size of tumors and the number of affected lobes had a significant effect on the post-operative life span. With a tumor size of <5 cm and a lesion covering less than two lobes of the liver, life expectancy was significantly longer and the prognosis was more favorable. In cases of large tumors or those affecting more than two lobes, life expectancy was significantly reduced and the prognosis was cautious to unfavorable (Vilkovyskiy *et al*., 2020). Unfortunatly in this case, the lesions were largly distributed on all liver lobes and even colangiohepatic ducts.

By elucidating the complexities associated with hepatocellular adenomas and emphasizing the need for accurate diagnosis, this report aims to contribute to the existing knowledge surrounding this condition and facilitate improved clinical management strategies for affected dogs. The dog has been considered as a model for novel treatment options in human cancer and this clincal peresentation will provide benefit to both canine and human populations during the management of hepatic cancers (Gibson *et al*., 2022).

References

Gibson, E.A., Goldman, R.E. and Culp, WTN. 2022. Comparative Oncology: Management of Hepatic Neoplasia in Humans and Dogs. *Vet Sci*, 9(**9**):489. DOI: 10.3390/vetsci9090489.

Morris, J. and Dobson, J., 2008. Small animal oncology. John Wiley & Sons. Wiley-Blackwell ,130-137.

Morrison, W.B., 2002. Cancer in dogs and cats: medical and surgical management. Teton NewMedia. 782P.

Munday, J.S., Löhr, C.V. and Kiupel, M., 2016. Tumors of the alimentary tract. *Tumors in Domestic Animals*, 27, 499-601. DOI:10.1016/s0195-5616(85)50059-5.

Olgivie, G.K. and Moore, A.S., 1995. Managing the veterinary cancer

patient: a practice manual. *Veterinary Learning Systems*, DOI:10.4236/ojvm.2014.49024.

Roth, L., 2001. Comparison of liver cytology and biopsy diagnoses in dogs and cats: 56 cases. *Veterinary Clinical Pathology*, 30(**1**), 35-8. DOI:10.1111/j.1939-165x.2001.tb00254.x.

Selmic, L.E., 2017. Hepatobiliary neoplasia. *Veterinary Clinics: Small Animal Practice*, 1, 47(**3**), 725- DOI:10.1016/j.cvsm.2016.11.016.

Vilkovyskiy, I.F., Vatnikov, Y.A., Kulikov, E.V., Sotnikova, E.D., Yagnikov, S.A., Seleznev, S.B., Krotova,E.A.,Byakhova,V.M.,Grishi,V.N and Avdotin, V.P. 2020. Influence of hepatic neoplasia on life expectancy in dogs. *Vet World.* 13(**3)**:413-418. DOI: 10.14202/vetworld.2020.413-418.

Withrow, S.J., 2012. Withrow & MacEwen's Small Animal Clinical Oncology. Original. Medical Ltd. 455-482.