大韓獸醫學會誌(2009) 第49卷 第3號
Korean J Vet Res(2009) 49(3) : 249~252

Primary hepatic hemangiosarcoma (HSA) in a Schnauzer dog

Min-Hee Kang, Ra-Young Heo, Hee-Myung Park*

BK21 Basic & Diagnostic Veterinary Specialist Program for Animal Diseases and Department of Veterinary Internal Medicine, College of Veterinary Medicine, Konkuk University, Seoul 143-701, Korea
(Accepted: September 8, 2009)

Abstract : A 6-year-old, neutered male, Schnauzer was presented with a one year history of weight loss and exercise intolerance. Physical examination revealed abdominal distention and ecchymosis on the abdominal skin. CBC and serum chemistry profiles revealed anemia and increased serum liver enzymes. Ultrasonography revealed a large liver mass which was characterized by multiple hypoechoic lesions. Postmortem examination revealed primary hepatic hemangiosarcoma. The tumor had extended to the mesentery and diaphragm, but distant metastasis was not found. This case report describes primary hepatic hemangiosarcoma which is very rare in a dog.

Keywords : dog, liver, primary hemangiosarcoma

Hemangiosarcoma (HSA) is a highly malignant tumor of vascular endothelial origin which represents approximately 5% of all non-cutaneous primary malignant neoplasms in the dog [7, 10]. It can occur in any site; however the spleen, skin, right atrium, and liver are the most common primary sites. In general, primary neoplasms of the liver and biliary tracts are rare in dogs, varying from 0.6% to 1.3% of all neoplasms [8]. The most common canine hepatic tumors are hepatocellular carcinoma and bile duct carcinoma. Carcinoids are less common, and sarcomas are rare [8]. Among the sarcomas, HSAs are the most commonly described [5]. This case report describes the clinical and pathological features of HSA originating in the liver of a dog.

A 6-year-old, castrated male, Schnauzer was presented with one-year history of weight loss and exercise intolerance. Four days before examination, the dog showed abrupt hematuria, which was resolved within 48 hours with broad-spectrum antibiotics. Physical examination revealed pale mucous membrane (> 2 sec capillary refill times), ecchymosis on the ventral skin, and swelling of the right hind limb. The hemogram revealed a moderate leukocytosis ($34.42 \times 10^3/\mu L$; reference range, $6\text{-}17 \times 10^3/\mu L$), regenerative anemia (hematocrit 12.8%, reference range, 37-55%) and severe thrombocytopenia ($60 \times 10^3/\mu L$; reference range, $200\text{-}500 \times 10^3/\mu L$). Serum chemistry profiles showed hypoproteinemia (4.1 g/dL; reference range, 5.0-7.2 g/dL), hypoalbuminemia (1.5 g/dL, reference range, 2.3-3.9 g/dL) and hypoglycemia (62 mg/dL; reference range, 67-147 mg/dL). Alanine aminotransferase (680 U/L, reference range; 3-50 U/L), aspartate transferase (239 U/L, reference range, 10-37 U/L) and alkaline phosphatase (319 U/L, reference range, 20-155 U/L) were all elevated. Prothrombin time was delayed (10.8 sec; reference range, 5.8-7.9 sec), while activated partial thromboplastin time was within reference range (13.5 sec; reference range 13.1-15.4 sec).

Radiographic findings included distended abdomen with generalized loss of serosal details. Homogeneous fluid opacity is uniformly distributed throughout a distended abdomen (Fig. 1). Abdominal ultrasonography revealed peritoneal fluid and multifocal hypoechoic masses in the liver (Fig. 2). Cytological examination of ultrasound-guided fine-needle aspiration of the hepatic mass was not performed because of the likelihood of blood loss and possible shedding of cancer cells. Abdominocentesis was performed to evaluate peritoneal fluid, which revealed modified transudate with hemorrhagic effusion (protein concentration 2.4 g/dL, total nucleated cell count 19.6×10^3 cells/μL). In

*Corresponding author: Hee-Myung Park
College of Veterinary Medicine, Konkuk University, Seoul 143-701, Korea
[Tel: +82-2-450-4140, Fax: +82-2-444-4396, E-mail: parkhee@konkuk.ac.kr]

addition, abundant erythrocytes, non-regenerative neutrophils, a few reactive mesothelial cells, and malignant neoplastic cells were also noted. Based on the clinical signs, laboratory examination and diagnostic imaging, the dog was diagnosed with a malignant hepatic tumor.

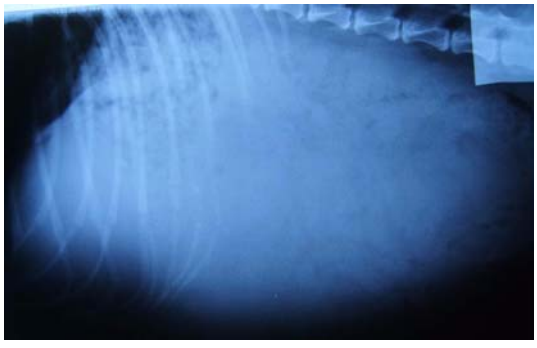

Fig. 1. A lateral abdominal radiograph. Homogeneous fluid opacity is uniformly distributed throughout a distended abdomen.

Treatment was initiated with blood transfusion, which increased the pack cell volume to 26.3%. Metronidazole (5 mg/kg, PO, q 12 h; Se Jin Pharm, Korea), enrofloxacin (5 mg/kg, SC, q 12 h; Bayer Korea, Korea), furosemide (1 mg/kg, SC, q 12 h; HanDok, Korea), vitamin K1 (1 mg/kg, PO, q 24 h; CJ Pharm, Korea) were also given for palliative purposes. However, because of the dog's poor prognosis, the owner declined further diagnostic procedures or therapy. All medication was discontinued and the dog died seven days later.

On post-mortem examination, hemorrhagic effusion was observed in the abdominal cavity. Discrete nodules of various sizes were found in the right hepatic lobes

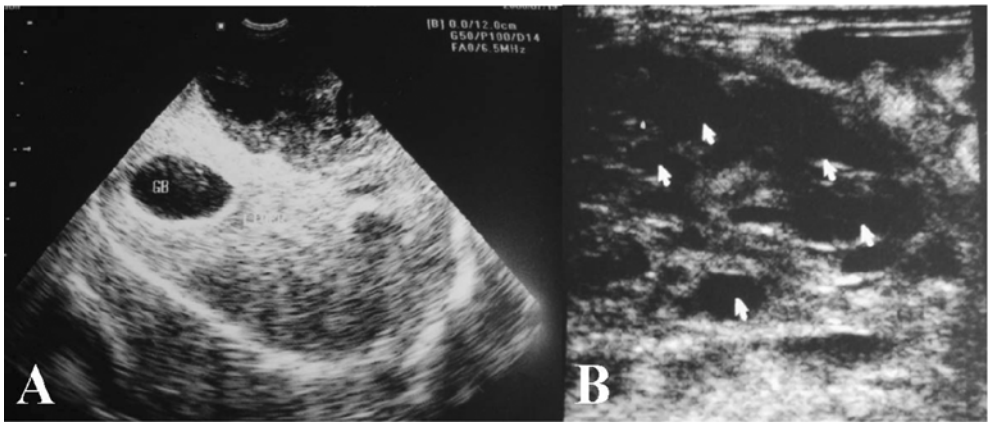

Fig. 2. An ultrasonographical image of the liver. (A) A large liver mass was identified, (B) characterized by a mixed echogenicity with multiple hypoechoic lesions (white arrows).

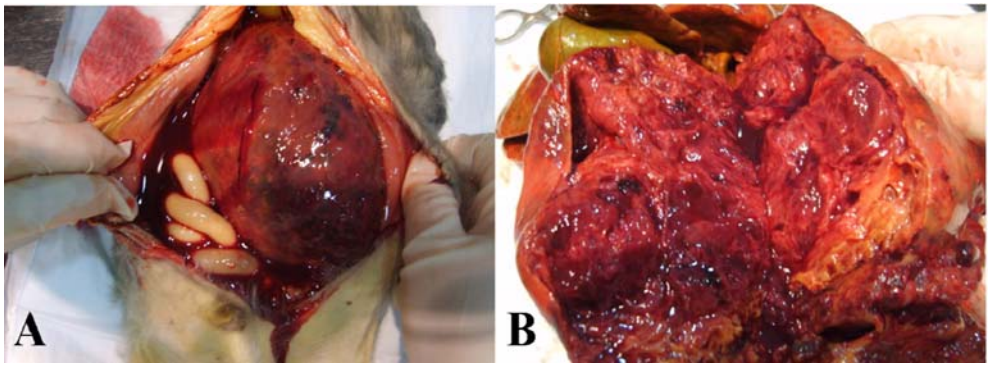

Fig. 3. The postmortem findings of primary hemangiosarcoma in this case. (A) Hemorrhagic effusion was observed. (B) Multilobulated masses involving liver parenchyma were apparent.

(Fig. 3). The nodules were metastasized to the mesentery and diaphragm, but lungs, spleen, heart or any other organs were not affected. To evaluate the hepatic mass, initially impression cytology was performed, which revealed malignant mesenchymal cells (Fig. 4). For histopathology, all tissues were fixed in 10% buffered formalin, embedded in paraffin and cut at 4 µm. The sections were then stained with hematoxylin and eosin. Histopathological examination revealed that the liver mass was composed of small blood filled channels lined by neoplastic endothelial cells with necrosis and hemorrhage prominent in the center of the mass (Fig. 5A). The neoplastic cells lining these vascular channels were quite plump with abundant cytoplasm and round to ovoid nuclei. These cells generally had high nuclear to cytoplasmic ratios and often had multiple and bizarre nucleoli (Fig. 5B). Result of the immunohistochemistry using CD31 also showed strong cytoplasmic immunoreactivity (Fig. 5C). Based on the clinical observations, and results of histopathology and immunohistochemistry, this case was diagnosed as a primary hepatic hemangiosarcoma.

According to previous reports [1, 3, 7, 9], primary hepatic HSA is very rare in dogs. But the liver is the most common site of metastatic HSA. In human

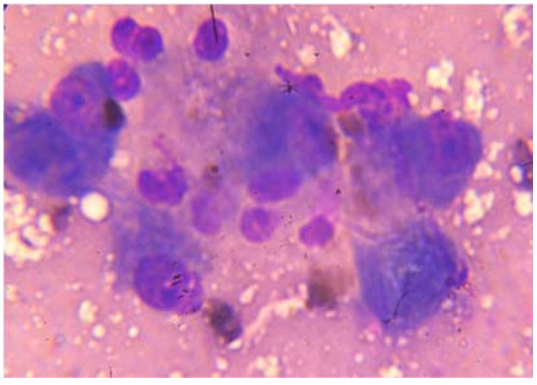

Fig. 4. A microphotograph of impression cytology. Note the pleomorphic malignant spindle cells which have prominent nucleoli and coarse chromatin. (Diff-Quik stain, ×1,000).

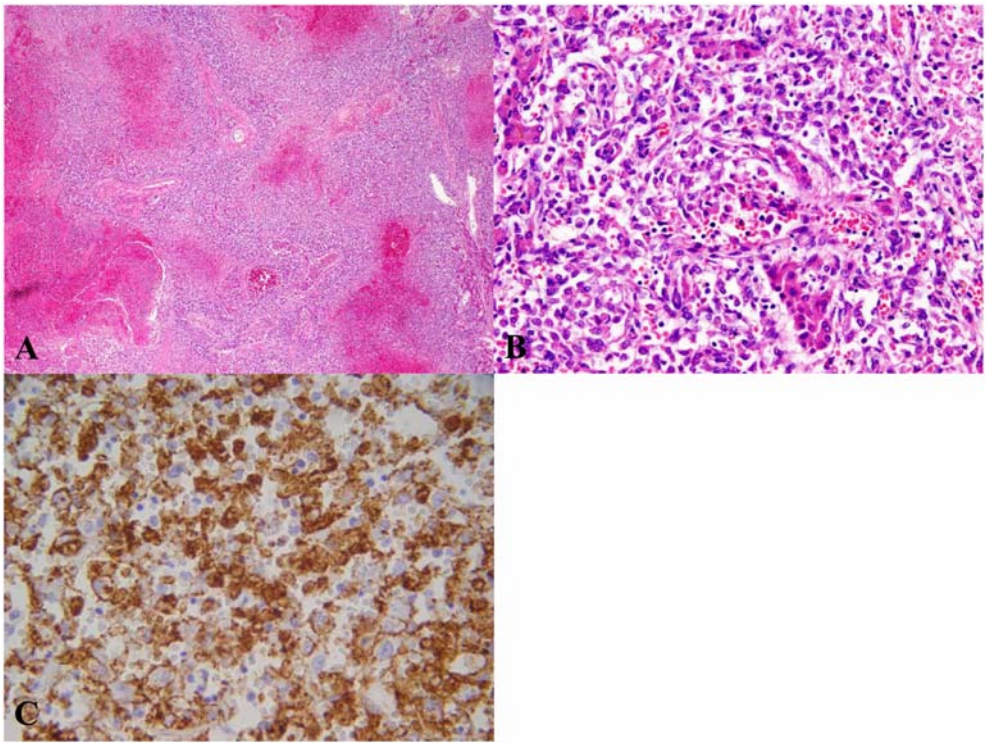

Fig. 5. Microphotographs of histopathology and immonohistochemistry. (A) Massive hemorrhage and necrotic center were observed (H&E, ×200). (B) Irregular blood-filled channels were lined by plump, neoplastic endothelial cells. (H&E, ×400). (C) Note the cytoplasmic staining of neoplastic cells with strong immunoreactivity for CD31 (×400).

literature, primary hepatic HSA is also rare mesenchymal tumor of the liver in elderly men [2]. For the definite diagnosis of hepatic neoplasia, histopathologic evaluation is required. However, due to the high vascularity of HSA, a liver biopsy could be harmful. Thus further diagnostic approaches were not used in this case because of multifocal hepatic nodules and dog owner's declination. Except for those reasons, in this case, we could not conduct antemortem liver biopsy because of the possible bleeding tendency. In this dog, hematologic findings included regenerative anemia with leukocytosis, which were consistent with previous reports that low hematocrit values, high reticulocytes count, and neutrophilic leukocytosis were observed in canine HSA [3]. Hemoperitoneum was also found in this dog, which was commonly observed in dogs with HSA [1].

Through a postmortem histopathologic examination, those lesions were consistent with hepatic HSA. Based on previous reports [4, 6], metastasis and local infiltration of tumor cells generally occur early in the disease process, with the liver and lungs being the most frequently occuring metastatic sites [3]. Therefore, distinguishing between the primary and metastatic sites in dogs with HSA is crucial for the treatment and prognosis. In this case, the lungs, spleen, heart or any other organs were not involved. However, metastasis to the mesentery and diaphragm were noted through histopathologic examination.

A previous report incorporating traditional chemotherapy (vinblastine, doxorubicin, and cyclophosphamide) showed partial remission and prolonged survival time. More recently, anti-angiogenic therapy, an important field of investigational anticancer therapy in humans, is also the subject of numerous ongoing clinical studies for canine HSA [4]. Furthermore, a pilot study using an intraperitoneally delivered allogenic vaccine derived from canine HSA also has been reported to improve survival in dogs with HSA [10].

In conclusion, this case demonstrates that even though primary hepatic HSA is very rare, it should be included or considered as a differential diagnosis for primary hepatic tumors.

Acknowledgments

This study was supported by the Brain Korea 21 (2 step).

References

1. **Aronsohn MG, Dubiel B, Roberts B, Powers BE.** Prognosis for acute nontraumatic hemoperitoneum in the dog: A retrospective analysis of 60 cases (2003-2006). J Am Anim Hosp Assoc 2009, **45**, 72-77.
2. **Brady J, Liberatore F, Harper P, Greenwald P, Burnett W, Davies JN, Bishop M, Polan A, Vianna N.** Angiosarcoma of the liver: an epidemiologic survey. J Natl Cancer Inst 1977, **59**, 1383-1385.
3. **Brown NO, Patnaik AK, MacEwen EG.** Canine hemangiosarcoma: Retrospective analysis of 104 cases. J Am Vet Med Assoc 1985, **186**, 56-58.
4. **Clifford CA, Mackin AJ, Henry CJ.** Treatment of Canine Hemangiosarcoma: 2000 and Beyond. J Vet Intern Med 2000, **14**, 479-485.
5. **Hammer AS, Sikkema DA.** Hepatic neoplasia in the dog and cat. Vet Clin North Am Small Anim Pract 1995, **25**, 419-435.
6. **Kim SE, Liptak JM, Gall TT, Monteith GJ, Woods JP.** Epirubicin in the adjuvant treatment of splenic Hemangiosarcoma in dogs: 59 cases (1997-2004). J Am Vet Med Assoc 2007, **231**, 1550-1557.
7. **MacEwan EG.** Hemangiosarcoma. In: Withrow SJ, MacEwan EG (eds.). Small Animal Clinical Oncology. 3rd ed. pp. 639-645, Saunders, Philadelphia, 2001.
8. **Patnaik AK, Hurvitz AI, Lieberman PH.** Canine hepatic neoplasms: a clinicopathologic study. Vet Pathol 1980, **17**, 553-564.
9. **Smith AN.** Hemangiosarcoma in dogs and cats. Vet Clin North Am Small Anim Pract 2003, **33**, 533-552.
10. **U'ren LW, Biller BJ, Elmslie RE, Thamm DH, Dow SW.** Evaluation of a novel tumor vaccine in dogs with Hemangiosarcoma. J Vet Intern Med 2007, **21**, 113-120.