NOTE *Internal Medicine*

Hepatic Lymphangiomatosis in a Young Dog

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ABSTRACT. A 9-month-old intact male American cocker spaniel was referred because of hepatomegaly and ascites. Ultrasonographic evaluation of the liver revealed congestion and increased parenchymal echogenicity with focal and more hyperechoic nodules. Histopathology of the hepatic lesion revealed diffuse, ill-defined vascular proliferation. A single layer of endothelial cells, which showed signs of minimal cellular atypia, lined the irregular vessels. On immunohistochemistry, the proliferative endothelial cells lining the i rregular vessels were positive for an antiserum to factor VIII related antigen. Based on these findings, the dog was diagnosed with hepatic lymphangiomatosis.

KEY WORDS: canine, liver, lymphangiomatosis.

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Lymphangioma of infancy is regarded as a rare benign lesion that is believed to be a lymphatic malformation derived from congenital or developmental anomalies of the lymphatic system [2–4, 7, 8]. The lesion is usually a solitary, well-defined mass, although occasionally multiple sites or organs may be involved [4, 5]. In contrast, lymphangiomatosis is a diffuse, ill-defined lesion composed of variously dilated proliferative lymph vessels [3, 5, 8]. Lymphangiomatosis is a term used to describe lymphangioma affecting soft tissue or parenchymal organs in a diffuse or multifocal fashion [4]. The authors describe the clinicopathological findings in a young American cocker spaniel with hepatic lymphangiomatosis.

A 9-month-old, intact male American cocker spaniel, weighing 11.8 kg was presented to the Veterinary Medical Teaching Hospital at Nippon Veterinary and Animal Science University for further evaluation of a cardiac murmur. Physical examination revealed pale mucous membrane, abdominal distention due to hepatomegaly and ascites, and a systolic ejection murmur over the pulmonary valve area. On routine blood work, a regenerative anemia (RBC $3.55 \times 10^6/\mu l$, PCV 25%) with many schistocytes (fragmented red blood cells) and a mild increase in serum alkaline phosphatase activity (117 IU/*l*) were detected. Other hepatic indicators including alanine aminotransferase activity (57 IU/*l*), ammonia (39 μg/d*l*), total protein (5.8 g/d*l*) and albumin concentrations (3.5 g/d*l*) were within the reference ranges. Analysis of fluid obtained by abdominocentesis was consistent with a modified transudate (specific gravity:1.026, protein 2.8 g/d*l*). Moderate pulmonary stenosis was confirmed by echocardiography (calculated pressure gradient=64 mmHg). Abdominal radiographs showed a severely enlarged liver. Ultrasound of the liver revealed congestion and increased parenchymal echogenicity with focal and more hyperechoic nodules (Fig. 1). The former finding would be consistent with cardiac failure [6], whereas the latter finding may be seen with primary pathological changes such as a neoplastic lesion. In general, causes of schistocytes include disseminated intravascular coagulation, hemangiosarcoma, portsystemic shunting, chronic hepatic disease, lymphoma and glomerulonephritis [9]. Accordingly, the schistocytes found in this patient were consistent with the concurrent hepatic lesion.

An exploratory laparotomy was performed to obtain a wedge biopsy of the liver. Grossly, the liver was severely swollen with irregular protuberances over the surface. The intestinal tract was edematous, alimentary lymph vessels were congested, and a slight amount of ascites was also noted. The spleen and mesenteric lymph nodes were not enlarged.

The sample obtained was fixed in 10% buffered formalin, routinely processed for histopathological examination, and paraffin embedded sections were stained with hematoxylin and eosin (HE). Immunohistochemical staining was also performed by the avidin-biotin-peroxidase complex method with an antiserum to factor VIII related antigen (DAKO, Carpinteria, CA). Histopathological examination of the liver revealed irregularly arranged and proliferative vascular channels diffused in the parenchyma (Fig. 2). Some vessels had morphological evidence of connections to mildly dilated normal lymph vessels around the central veins and portal areas. Vascular spaces were empty or filled with a pale proteinaceous fluid containing a few lymphocytes or RBCs. The irregularly arranged channels were composed of endothelial cells with mild cellular atypia (Fig. 3). The endothelial cells of these channels had ovoid to spindle-shaped nuclei. The nucleoli were inconspicuous, with few mitotic figures observed. Immunohistochemical staining with an antiserum to factor VIII related antigen showed positive reaction in the cytoplasm of the irregularly arranged cells lining the vascular endothelium (Fig. 4) and in the cytoplasm of the normal endothelial cells of sinus, veins and

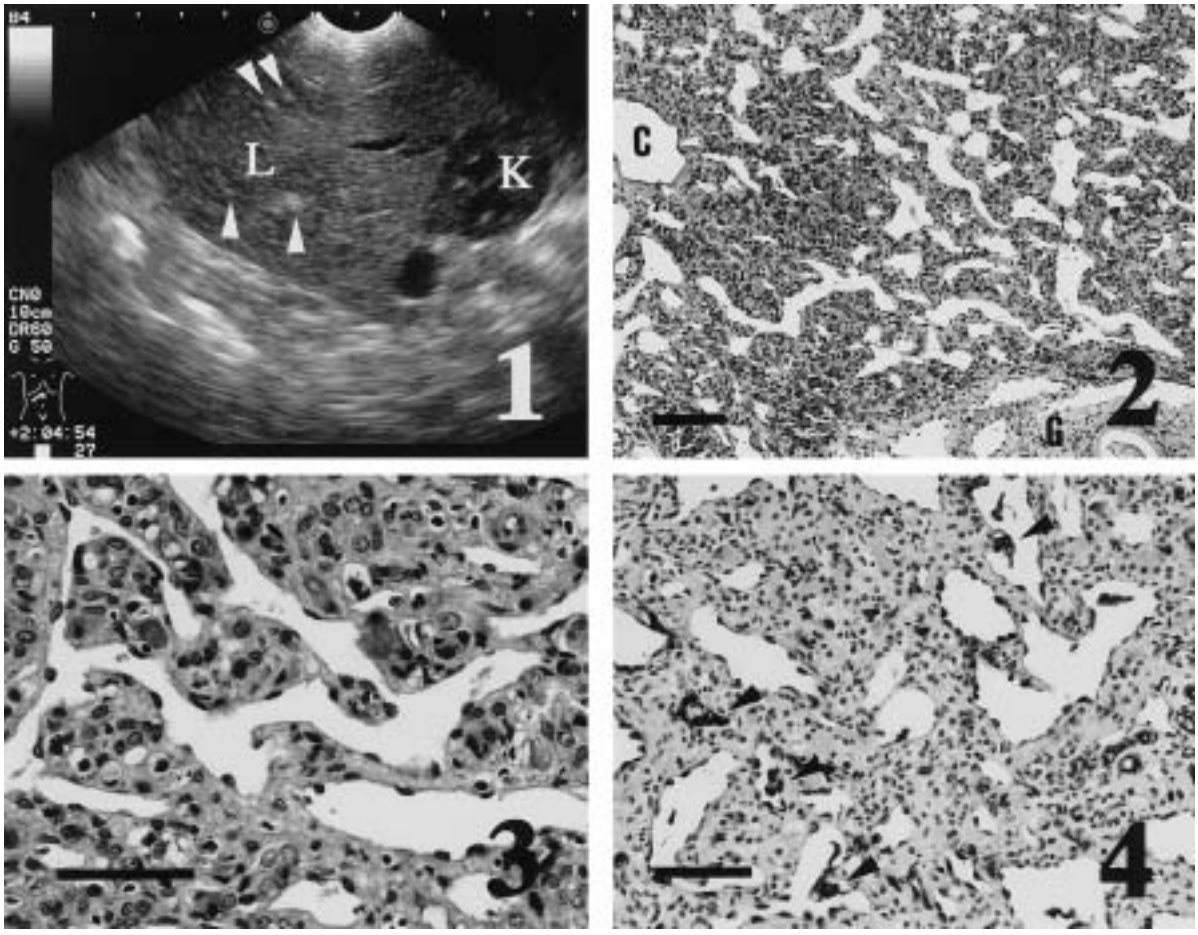

Fig. 1. Hepatic ultrasonography. Congestion and increased parenchymal echogenicity with focal and more hyperechoic nodules (arrowheads). L: Liver, K: Right Kidney.

Fig. 2. Photomicrograph of the liver. Irregularly arranged proliferated vessels in parenchyma, around Glisson's area (G) and the central vein (C) were observed. HE, Bar=30 μm.

Fig. 3. Higher magnification of proliferative vessels. Single layer of endothelium with round to ovoid nuclei showing minimal nuclear atypia lining proliferative vessels. Fine fibrosis was observed around proliferative vessels. HE, Bar=10 μm.

Fig. 4. The endothelial cells lining proliferative vessels were positive for an antiserum to factor VIII related antigen (arrowheads). Avidin-biotin-peroxidase complex method, hematoxylin counter stain. Bar=15 μm.

arteries.

Irregular and slight fibrosis was also observed around the central veins, portal areas and among the hepatocytes. There were none of the findings typically associated with heart failure, i.e. centrilobular congestion, centrilobular sinus dilatation and centrilobular fibrosis or severe vacuolization of hepatocytes, which are suggestive of chronic congestion due to cardiac failure. In addition, the lesion showed minimal inflammatory cell infiltration. These findings indicate that the cause of hepatomegaly was proliferation of lymph vessels and its ectasia of these abnormal vessels. A diagnosis of hepatic lymphangiomatosis was made [4].

In this case, hemangiomatosis should be included as a differential diagnosis. Hemangiomatosis is also characterized by an ill-defined proliferative vascular-rich lesion, but the proliferative vessels are commonly filled with RBCs [4, 7]. In the present case, the vascular spaces were empty or filled with a pale proteinaceous fluid containing a few lymphocytes or RBCs. This finding suggests that the lymphatic system was the origin of the proliferative vessels within the lesion [2–5, 8]. Another problem when evaluating these tissues was that the endothelial cells of blood vessels reacted positively to an antiserum to factor VIII related antigen. Nevertheless, it must be emphasized that it is not always possible to clearly differentiate angiomatosis from lymphangiomatosis because overlapping exists between these conditions [3, 4]. In the spectrum extending from morphologically normal lymph vessels to the lesion, this case would be considered hepatic lymphangiomatosis. The influence of heart failure on this condition was thought to be minimal, at least at the time of histopathological diagnosis.

The diagnosis of this condition at birth is uncommon, because it seems that a latent period is required for these lesions to reach sufficient size for symptoms to become apparent [5]. In this case, moderate pulmonary stenosis was also diagnosed; hepatomegaly due to congestive heart failure and lymphatic congestion due to lymphangiomatosis might progress and causes symptoms. In this patient, anti-inflammatory doses of prednisolone were administered to prevent hepatic fibrosis, but the efficacy of this remedy remains unclear. As there have been no reports on hepatic lymphangiomatosis in dogs, and some debate still remains as to whether this lesion is hamartomatous or a true neoplasm [3, 4], further observation and study is required to evaluate the prognosis of this rare condition.

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