Cerebral Vascular Hamartoma with Thrombosis in a Dog

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ABSTRACT. A cerebral vascular hamartoma was identified in the frontal lobe, striatum and thalamus of the right side of the brain of a male, 7-year-old Shih Tzu. Histologically, the lesion consisted of thin-walled vessels, which showed various sizes and occasionally contained fibrin thrombi. These vascular walls were composed of a single layer of fibromuscular tissue lined by flat endothelium with various amount of collagen, but devoid of large coat of smooth muscles and elastic tissue. Immunohistochemically, the lining endothelial cells were positive for von Willebrand Factor antibody. Neuropil between the vessels was stained with Klüver-Barrera stain, and positive for synaptophysin and GFAP antibodies. Based on these findings, the lesion was diagnosed as vascular hamartoma, which might resemble venous malformation in humans.

KEY WORDS: canine, cerebrum, malformation, vascular hamartoma.

Vascular hamartomas, which are considered as developmental malformation rather than true neoplasm due to their limited growth, are defined as disorganized and excessive proliferations of vascular tissue [7]. In human brain, vascular hamartomas are classified as capillary telangiectasias, cavernous angiomas, and arteriovenous or venous malformations [8]. In veterinary literature, vascular hamartomas have been rarely described in canine [11], feline [12], equine [5] and bovine brain [1], whereas single cases of such malformations have been reported in the spinal cord of a dog [4], a Hereford calf [3], a goat [9] and a foal [6]. Classification of such lesions remains confusing, and terminology among the reports tends to vary. Terms such as angiomatous hamartoma, telangiectatic hamartoma, and cerebral angiomatosis have been used to describe morphologically similar lesions [5, 10]. The objective of this study was to characterize a histology of vascular lesion of the canine brain diagnosed as vascular hamartoma. Histochecmistry and immunohistochemistry were used as additional tools for further investigation about vessel structure and relationship between the vessels of hamartoma and the surrounding brain parenchyma.

The case of this report was a male Shih Tzu, aged 7 years and 6 months. The dog showed seizures accompanied with vomiting twice a week since November 2004, and then seizures increased since January 2005. In the neurological examination, the dog had central blindness with normal light reflexes and loss of conscious proprioception in fore and hind limbs of the left side. No abnormalities were detected in the general somatoscopy. Hematology and serum biochemical findings were normal. Computed tomography (CT) demonstrated well-demarcated mass in the frontal lobe, striatum and thalamus of the right cerebrum. The mass was demonstrated more clearly in computed tomography angiography (CTA). The seizure was controlled for about a month from the first practice. However, on 21 March 2005, the dog showed frequent seizures accompanied with vomiting and died.

A complete necropsy was performed. Tissues were routinely fixed for light microscopy in 10% neutral buffered formalin embedded in paraffin wax, then sectioned at 4 μm, and stained with hematoxylin and eosin (HE) stain. In addition, Klüver-Barrera (KB) stain, Elastica van Gieson stain and Azan stain were performed. Immunohistochemically, antibodies specific for synaptophysin (PROGEN Biotechnik GmbH, Heidelberg, Germany), glial fibrillary acidic protein (GFAP) (Dako, Glostrup, Denmark), α smooth muscle actin (α-SMA) (Dako) and von Willebrand Factor (vWF) (Dako) were used by labeled streptavidin-biotin (LSAB) (Dako) method.

At necropsy, a mass (2 cm in a diameter), which composed of many vessel-like structures, was observed in the frontal lobe, striatum and thalamus of the right side of the brain (Fig. 1). Marked hemorrhage and edema were observed around the mass. The swollen cerebrum compressed the cerebellum, and tonsillar and tentorial herniations were observed. No significant gross lesions were found in other organs. Histologically, the mass consisted of many thin-walled blood-filled vascular structures, involving both gray and white matter in the right cerebrum (Fig. 2). Most of vascular structures were separated by eosinophilic neuropil, but the vascular structures occasionally abutted each other. The vascular structures of various sizes were lined by flattened endothelial cells. Occasionally, multiple thrombosis, variable degrees of fresh hemorrhage and edema, and infiltration of neutrophils and macrophages were observed (Fig. 3). Immunohistochemically, endothelial cells of the vascular structures were positive for vWF.

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Fig. 1. Vascular hamartoma. Coronal section of brain at level of cerebral striatum, demonstrating the gross appearance of the vascular hamartoma in the right cerebral hemisphere.

Fig. 2. Vascular hamartoma. Proliferations of thin-walled blood-filled vascular structures involve brain parenchyma. HE stain. Bar, 200 μm.

Fig. 3. Vascular hamartoma. Organized thrombus (arrow) and moderate hemorrhage (arrowhead) are observed. HE stain. Bar, 100 μm.

Fig. 4. Vascular hamartoma. Vascular structures are lined by vWF-positive cells. Immunohistochemistry. Bar, 50 μm.

Fig. 5. Vascular hamartoma. Vascular structures are lined by single layered α-SMA-positive cells. Immunohistochemistry. Bar, 50 μm.

Fig. 6. Vascular hamartoma. Various amount of collagen, which is stained with Azan stain, is observed around vascular structures (arrow). Azan stain. Bar, 100 μm.

Fig. 7. Vascular hamartoma. Vascular structures are separated by neuropil, which is positive for synaptophysin antibody (A) and stained with KB stain (B). Immunohistochemistry (A) and KB stain (B). Bar, 50 μm.

Fig. 8. Vascular hamartoma. GFAP-positive astrocyte (arrows) is observed in neuropil between vascular structure. Immunohistochemistry. Bar, 50 μm.
antibody (Fig. 4), and the single-layered cells, which were present in subendothelial areas, were positive for α-SMA antibody (Fig. 5). The vascular structures were surrounded by various amount of collagen, which was stained with Azan stain (Fig. 6). Elastic fiber, which is stained with Elastic a van Gieson stain, was not detected in the vascular walls. Neuripil, which were stained with KB stain and immunohistochemically positive for synaptophysin antibody, were observed between vascular structures (Fig. 7). Astrocytes, which were positive for GFAP antibody, were also found (Fig. 8).

The histological findings in this case can be summarized as follows; 1) there were many blood vessels which were structurally similar to veins, 2) neuripil was present between these vascular structures and 3) the vascular lesions occasionally exhibited fibrin thrombosis and hemorrhage. Based on these findings, a final diagnosis of cerebral vascular hamartoma with thrombosis was made. In human, the presence of neuripil between the hamartoma vessels is considered to be a main criterion for differentiating venous malformations and capillary telangiectasias from cavernous angiomas. Cavernous angiomas have very little or no intervening neural tissue [2]. In this case, neuripil was apparently identified between vascular structures. Histologically, it is difficult to differentiate venous malformations from capillary telangiectasias in human medicine [8]. Most of capillary telangiectasias which are frequently observed in the pontine basis near the raphe nuclei and cannot be identified by angiography. On the other hand, most of venous malformation are observed in the cerebral hemisphere and are characterized by confluent large medullary veins [8]. In this case, the vascular hamartomatous lesion was located in the right cerebral hemisphere, and the lesion was identified in CTA. The vascular lesions were structurally similar to veins. These findings strongly suggest that the lesion in this case may be classified as venous malformation. In this case, the cells positive for α-SMA antibody was detected in the subendothelial areas, whereas vascular endothelial cells positive for vWF antibody and collagen were demonstrated. Thus, the vascular structures in this case were well differentiated. Therefore, the dysregulation of vein formation may cause this hamartomatous lesion. In human, vascular malformations including venous malformation are frequently accompanied with thrombosis, which is considered to lead to hemorrhagic infarction in the brain. Hemorrhage is generally parenchymal or intraventricular but may leak into the subarachnoid spaces producing all the signs of subarachnoid hemorrhage [8]. In this case, multiple thrombosis and hemorrhage might cause some clinical signs such as seizure with vomiting, central blindness and loss of conscious proprioception. We need further clinicopathologic studies using greater case numbers and adequate histopathologic grading criteria for vascular hamartoma in the central nervous system in dogs.

REFERENCES