

Cerebral Vascular Hamartoma in a Campeiro Bulldog

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ABSTRACT

Background: Vascular hamartomas (VH) are rare or simply underdiagnosed injuries in veterinary medicine and represent a non-neoplastic developmental anomaly disorganization and proliferation of endothelial tissue. VH occur in any region of the body, however in the brain present clinical relevance related with the potential for spontaneous bleeding, adjacent tissue compression and convulsive activity. The aim of these report is to describe clinical, pathological and immunohistochemical features of a case of cerebrovascular hamartoma and highlight the diagnosis of these rare brain disorder in dogs.

Case: A 10-year-old male dog, a Campeiro Bulldog breed presented convulsions episodes and died before an elective surgical procedure for eyelid nodule removal. Three red nodules were observed in the brain, one between the parietal lobe and the left occipital lobe (in the medium suprasylvian sulcus), the other in the caudal region of the corpus callosum and the third one in the cerebellar cortex. Central nervous system, eyelids and most organs and tissues samples were collected, fixed in 10% formaldehyde and processed for histopathological analysis. Histologically, in the eyelid was detected a sebaceous adenoma. The nervous system samples revealed well-differentiated sizes vascular structures with thin-walled and blood-filled, promoting compression of the brain. Normal neuropile was detected between the vascular structures substantiating cerebral vascular hamartoma diagnosis in the dog. Immunohistochemical assay was conducted with CD31 (monoclonal mouse antibody anti-CD31, Clone JC70A, Dako Corp.) and Von Willebrand factor (monoclonal mouse antibody anti-Von Willebrand factor, Clone F8/86, Dako Corp.) using the biotin–peroxidase–streptavidin method (PolyDetector Plus DAB–HRP, Bio SB) on CNS sections to confirm the vascular origin of the lining cells in the mass.

Discussion: Hamartomas are rarely reported in domestic animals and mostly are of vascular origin. VH in nervous tissues can trigger clinical signs related to hemorrhage, brain space occupation, compression and obstructive secondary hydrocephalus. In general, cerebral VH have a slow progression and usually affected animals are asymptomatic. On the other hand, cerebral vascular hamartomas may also cause clinical signs in very young animals about 15 to 16 months old. In humans, clinical presentation of VH may be related with acquired lesions such as trauma, ionizing radiation, and other central nervous system injuries. In the present case, the dog presented convulsion episode only at 10 years old during pre-chirurgical procedures. The morphological features of the vascular hamartoma we observed in the Campeiro bulldog is classified as capillary teleangiectasia composed by well differentiated capillaries lined with well differentiated endothelial cells interspaced by normal neuronal tissue. Histopathological and immunohistochemical assay are extremely important to differentiate hamartoma from other tumors, since they may be macroscopically similar. The immunolabeling of endothelial cells by anti-CD31 and anti-Von Willebrand factor antibodies in the cerebral VH, highlight the vascular origin of the masses detected. However, it is also important to perform systematic gross examination of the brain in detail to detect even the smallest injuries in asymptomatic animals avoiding underdiagnoses of cerebral VH.

Keywords: brain, tumor, malformation, hemorrhage, canine.

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INTRODUCTION

Vascular hamartomas (VH) are considered developmental anomalies, that represent an endothelial tissue disorganization and non-neoplastic proliferation in any region of the body [1,5,8,9,20,22,23,25]. VH may usually present low aggression to surrounding tissues depending on the location and also do not produce clinical signs, which lead to underdiagnoses [1]. The clinical importance of cerebrovascular hamartomas is related to the potential for spontaneous hemorrhage, compression of adjacent tissues and convulsive activity [20]. VH are rare in humans and animals and can occur isolated or in association with other injuries [1].

VH may be differentiated of hemangioma in nervous system due to the presence of normal neuronal tissue between the vessels, which is the main feature to the diagnosis of VH [4] and is absent or rare in cases of hemangiomas [17]. Immunohistochemical assay allow the identification of lining cells of vascular structures and also normal neural and glial components between the vessels in VH [20].

Generally, clinical diagnosis of cerebral VH is not considered in the diagnosis of brain disorders in dogs. Our report highlights the main pathological features relevant for identify cerebral VH and their differential diagnosis.

CASE

A 10-year-old male Campeiro Bulldog breed, weighing 35.5 kg received medical care for two years due to bilateral dry keratoconjunctivitis and develop a small nodule on the left eyelid. A surgical biopsy of the eyelid nodule had been scheduled, however, before the beginning of the preoperative examination, the patient presented convulsions episodes and died, and was taken for necropsy.

The main gross findings observed were multifocal reddish nodules ranging from 0.3-1.3 cm in diameter in the brain between the parietal lobe and left occipital lobe (suprasylvian sulcus medial region), cerebellar cortex and in the medial region of the telencephalon (specifically in the corpus callosum), promoting ventral compression of the lateral ventricle and parietal lobe (Figure 1). The lateral ventricles cavities were filled by red viscous fluid without apparent ventricular dilatation. In the left eyelid there was a small, circumscribed, whitish 0.4 cm nodule.

Central nervous system, eyelids and most organs and tissues samples were collected and fixed in 10% formalin, processed in paraffin, cleaved at 4 µm and stained with Hematoxylin and Eosin for histopathological analysis. In addition, immunostaining with CD31 (monoclonal mouse antibody anti-CD31, Clone JC70A)¹ and Von Willebrand factor (monoclonal mouse antibody anti-Von Willebrand factor, Clone F8/86)¹ was performed using the biotin-peroxidase-streptavidin method (PolyDetector Plus DAB-HRP)² on CNS sections.

Microscopically, the nervous system samples revealed several vascular structures of varying sizes, lined by well-differentiated endothelial cells and filled with blood in the white and gray matter of the telencephalon, cerebellum and corpus callosum interspaced by areas of normal brain parenchyma (Figure 2). Endothelial cells lining the anomalous vascular structures showed strong immunostaining for CD31 (Figure 3) and von Willebrand factor. In the eyelid was detected a sebaceous adenoma composed by a proliferation of uniform cells organized in small lobes with central nucleus and condensed chromatin, and abundant foamy cytoplasm. No other gross or microscopic changes were detected in other tissues or organs. Clinical-pathological and immunohistochemical characteristics of lesions in the central nervous system allowed to conclude the diagnosis of cerebral vascular hamartoma.

DISCUSSION

Vascular hamartomas (VH) are non-neoplastic proliferations of vascular tissue. They are congenital defects of vascular formation and development, giving rise to normal tissue that is organized in a disorderly manner [1,2,4,10,15,18,20] and are also considered benign tumors [6,8,14,26]. VH has been recently considered neoplastic because it exhibits chromosomal aberrations that are acquired through complete somatic mutations [11]. The link between abnormality and neoplasia is recognized due to disorganized overgrowth of vascular cells lining abnormal blood vessels and form a tumor-like mass [24]. In addition, the wide morphological variation of vascular hamartomas is considered a condition aiming to progress in a true neoplasia [17]

Hamartomas are rarely reported in domestic animals and mostly are of vascular origin [1,6,15,16,24], and frequently present no predisposition of age, breed or



Figure 1. Brain, longitudinal section, dog. Multifocal reddish nodules in the parietal lobe, cerebellar cortex and corpus callosum.

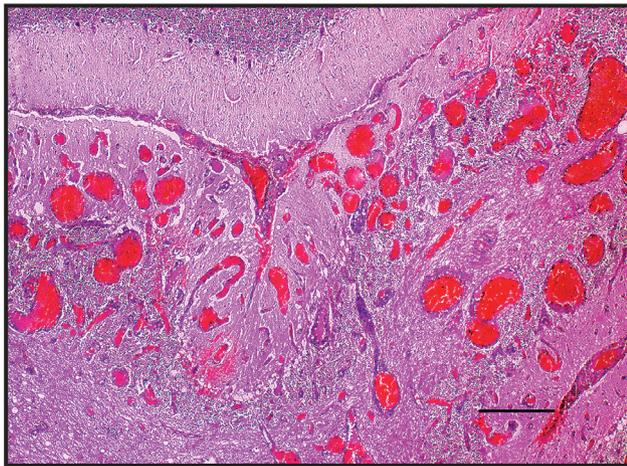


Figure 2. Cerebellum, dog. Vascular structures of varying sizes filled with blood in the white and gray matter interspersed by areas of normal brain parenchyma [H&E; Bar= 250 μ m].

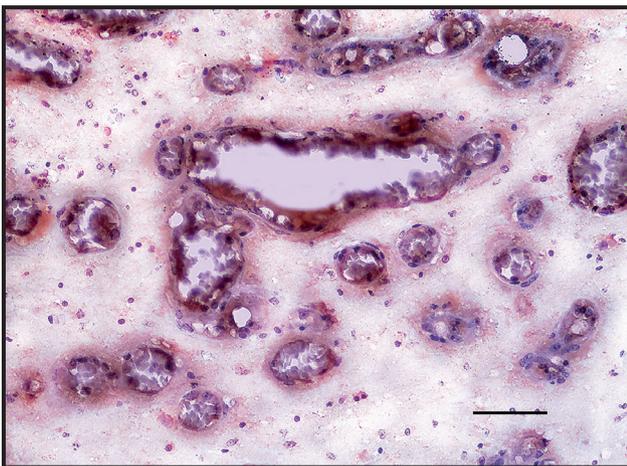


Figure 3. Telencephalon, dog. Endothelial cells lining the anomalous vascular structures presenting strong immunostaining for CD31 [Immunoperoxidase stain; Bar= 50 μ m].

gender [20]. However, Scottish Terrier and Airedale Terrier dog breeds are highlighted to present a predisposition to develop VH [28]. Isolated cases of these vascular growths have been reported in the brain of dogs, cats, calves, goats and foals [18,20,21]. The telencephalon is considered the most frequent location of cerebral VH and

mainly affect the piriform lobe [20]. Cerebral VH have been also reported in hippocampus [20] and cerebellum [21] of dogs and cats. In the Campeiro Bulldog, foci of VH were detected in the telencephalon, cerebellum and in corpus callosum. The multiple locations of VH in the central nervous system (CNS) of the dog observed here is uncommonly reported.

The clinical signs development observed in the dog could be attributed to the surrounding neural parenchyma compression [4,16]. Lesions progress for several years, but usually show no clinical signs and do not undergo malignant transformation, remaining unrecognized unless other circumstances arise, such as a significant increase in their size or pressure on other organs [1]. The up to 10 years old dog we are reporting here had never presented neurological signs. Some asymptomatic patients [3,8,12,24] or with a delayed onset of clinical signs [13] were reported in animals and humans with cerebral VH. Despite the multifocal VH in the brain tissues of the dog, possibly the anomalous vascular growth did not cause significant injury in the surrounding tissues to produce neurological impairment. Vascular hamartomas have been diagnosed most frequently in symptomatic young patients [3,5,16,21,25,27], such as reported in cats with cerebellar and cervical cord vascular hamartomas [16,21]. The development of clinical signs is attributed to hemorrhage observed in and around the lesions, as well as its ability to act occupying space [7,13,16,20], which may lead to compression of the surrounding brain parenchyma and obstructive hydrocephalus secondary to the injury [13,20]. The Campeiro Bulldog presented convulsion episodes prior to death, probably in consequence of compression of neural tissues and hemorrhage to the ventricular cavity. Convulsions are the main clinical signs in patients with cerebral vascular hamartomas [18].

Cerebral VH in dogs are described as discrete softening multi-lobulated masses in the cerebral parenchyma with a red-brown color ranging from 0.4 to 2.0 cm in diameter [20]. This description is consistent with that identified in the dog of this report in different anatomical regions of the CNS. Hemorrhage and edema surrounding the mass [18], and vascular hamartomas in other organs [13,21] were not detected in our case. VH have been also reported in the liver [5], ovary [2] and in the mandible involving practically the entire right incisor region [27] of domestic animals.

The microscopic features observed in the CNS lesions of the dog support the diagnosis of cerebral VH [4,13,20,21]. Some reports of cerebral VH presented multiple thrombosis [5,18,20,21], varying degrees of hemorrhage and edema, neutrophil and macrophage infiltrate [18,20], mineralization and Purkinje cell chromolysis [21], however, these pathological changes were not detected in the dog.

Important differential diagnoses for vascular hamartomas include, angiomatosis secondary to lymphedema and capillary hemangiomas [14,25], hemangioblastomas and these can be differentiated on the basis of histopathological features [28]. However, angiomatosis secondary to lymphedema are accompanied by characteristic hypoplasia of the deep lymphatic vessels and markedly dilated lymphatics, which were not seen in the current case. Capillary hemangiomas do not show neuropile present between vascular structures [19,28]. One of the main features of VH is that its component vessels are separated from each other by normal neural parenchyma [9,14,19].

Vascular hamartomas are classified as arteriovenous, venous or cavernous malformations and capillary telangiectasia [13]. Arteriovenous malformations are considered the most common form in dogs [10]. The ce-

rebral VH hamartoma observed in the Campeiro Bulldog presented vascular structures composed by small dilated capillary vessels interspaced by normal brain parenchyma, a morphological hallmark of capillary telangiectasias [13,18]. Additionally, the immunolabeling of endothelial cells by anti-CD31 and anti-Von Willebrand factor antibodies in the cerebral VH, highlight the vascular origin of the masses detected [18].

Considering the similarities of the macroscopic aspect between VH and other vascular tumors, histopathological and immunohistochemical analysis are essential to the correct diagnosis of intra-cranial lesions. It is important to note, cerebral VH may be asymptomatic and usually an incidental finding at necropsy or slaughter. Therefore, clinical diagnosis of cerebral VH is generally not considered in the diagnosis of brain disorders in dogs. Our report highlights the main pathological features relevant for identify cerebral VH and their differential diagnosis.

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