Hamartoma in the Medulla Oblongata with Marked Mineral Deposits in a Dog

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ABSTRACT. A mass lesion in the medulla oblongata in a 9-year-old female Golden Retriever was examined pathologically. The medullary mass was 1 to 2 cm in diameter and poorly demarcated. The cut surface was discolored with numerous sand-like materials. Histologically, the mass lesion consisted of complex proliferation of irregularly arranged vessels as well as astrocytes with numerous mineral deposits. The astrocytic components exhibited no apparent anaplastic morphology. The proliferating vessels were either veins with muscle layer and capillaries. A few axons and myelinated fibers were also found in the lesion. The number of ki-67-positive cell nuclei progressed. The dog therefore was euthanized by deep general anesthesia under pentobarbital sodium treatment, and necropsied. The whole brain in 10% formalin solution, was then submitted to the Department of Veterinary Pathology, the University of Tokyo for pathological examinations. A focal mass lesion, 1 to 2 cm in diameter, was found in the dorsal medulla oblongata. The transverse cut surface of the mass was oval-shaped, poorly demarcated and tan-colored. The mass contained sand-like materials (Fig. 2).

Paraffin sections of 3–4 μm thick were stained with hematoxylin and eosin (HE). Masson’s trichrome, Periodic acid-Schiff (PAS), Kossa’s method and Watanabe’s silver impregnation. Immunohistochemistry was performed by the Envision polymer method (Dako Japan, Kyoto, Japan). Antibodies used were anti-glia fibrillary acidic protein (GFAP, 1:400; Dako), neurofilament (prediluted; Dako), myelin basic protein (MBP, 1:1,000; Dako), alpha-smooth muscle actin (SMA, 1:100; Dako), factor VIII-related antigen (1:500, Dako), Ki-67 (prediluted; Dako). Deparafinized sections were first treated for antigen retrieval in 10 mM citrate buffer, pH6.0, by autoclaving at 120°C for 10 min, for MBP and ki-67 immunostainings. After antigen retrieval, they were treated with 1% hydrogen peroxide/methanol for 30 min to inactivate endogenous peroxidase, and then incubated in 8% skim milk/Tris buffered saline (TBS, pH 7.4) at 37°C for 40 min to block non-specific binding of antibodies. The tissue sections were incubated at 4°C overnight with the primary antibodies diluted in 8% skim milk/TBS. Following washing in 3 times in TBS, the sections were incubated with Envision polymer reagent (Dako-Japan) for 40 min at 37°C. Finally, the reaction products were visualized with 0.05% 3–3’-diaminobenzidine (DAB) and 0.03% hydrogen peroxide in Tris/HCl buffer, followed by counterstain with Mayer’s hematoxylin or methylgreen.

Histologically, the mass lesion was loosely demarcated from the surrounding tissue, and was composed of complex
Fig. 1. Mid-sagittal view of a T1-weighted MRI showing a lesion at the dorsal part of the medulla oblongata (arrows).

Fig. 2. The transverse cut surface of the mass lesion (arrows). The lesion is oval-shaped, poorly demarcated and tan-colored, and contains sand-like materials.

Fig. 3. The lesion is composed of complex proliferation of blood vessels and well-differentiated astrocytes with numerous psammomatous mineral deposits (arrows). HE. Bar=50 μm.

Fig. 4. Irregular-shaped, tortuous veins varied in size in the area of coarse proliferation of astrocytes. HE. Bar=30 μm.

Fig. 5. The presence of abundant collagen and reticular fibers in the vessel wall and interstitium. Watanabe’s silver impregnation. Bar=50 μm.

Fig. 6. Endothelial cells are intensely immunopositive for factor-VIII. Bar=30 μm.
proliferation of blood vessels and well-differentiated astrocytes with numerous psammomatous mineral deposits (Fig. 3), positive for Kossa’s method and negative for PAS. The proliferating blood vessels were irregular-shaped, tortuous and varied in size with various amounts of collagen and smooth muscles (Fig. 4). Masson’s trichrome stain and Watanabe’s silver impregnation showed the presence of collagen and reticular fibers in the vessel wall (Fig. 5), and well demonstrated that capillary buds were bound together by thin layer of connective tissue. Moreover, glomeruloid endothelial proliferation was occasionally observed. Astrocytes were irregular-shaped, and had the eosinophilic cytoplasm with abundant cytoplasmic processes, and the oval to round nucleus with an indistinct nucleolus. There were no cellular atypia and mitotic figures in the astrocytes. The tissue surrounding the lesion in the medulla oblongata was atrophied without tissue damage.

Endothelial cells were intensely immunopositive for factor-VIII (Fig. 6), and astrocytes were immunopositive for GFAP (Fig. 7). SMA immunoreactivity was restricted to the venous walls in the lesion (Fig. 8). Within the mass lesion, a few neurofilament-positive axons and bundles of MBP-positive fibers were also present. The number of cells with Ki-67-positive nucleus was extremely small, approximately 1–2 cells under ×100 magnification, indicating low growth activity of the cells (Fig. 9). All the findings indicated that the present lesion in the medulla oblongata was not neoplastic, but was hamartomatous.

In the canine central nervous system, various types of hamartomas including vascular, hypothalamus [3] and spinal cord [9] have been described, which contained abnormal neurons admixed with glial cells, as in humans cases [9]. However, hamartomas with endothelial proliferation and marked mineral deposition are rare even in humans. There was a case report concerning human hamartomatous lesion with marked psammomatous calcification, composed of well differentiated astrocytes and collagen-producing fibroblasts [12]. In human brain tumors, interstitial calcification has been often reported in gangliogliomas [1, 7], oligodendrogliomas [4] and rarely in an astrocytoma [10] and a gliofibroma [5]. Even in dogs, numerous mineral deposits have been found in a ganglioglioma [11].

The irregularly arranged vessels, such as tortuous veins with amounts of collagen and smooth muscles, and astrocytes in the present lesion, are well-differentiated and had no anaplasia. The extremely low number of ki-67-positive cells and the atrophy of the tissue surrounding the lesion in the medulla oblongata also indicate that the lesion had grown very slowly or the growth had already been arrested. These findings strongly suggest that the present lesion was hamartomatous. And an astrocytic reaction is generally viewed as a reparative response in the CNS, akin to scarring in extraneural sites [9]. Consequently, the present lesion was diagnosed as vascular and glial hamartoma in the medulla oblongata.
REFERENCES


