Hindawi Publishing Corporation
Case Reports in Veterinary Medicine
Volume 2014, Article ID 915808, 5 pages
http://dx.doi.org/10.1155/2014/915808

Case Report

Bilateral Telencephalic Gliomatosis Cerebri in a Dog

Mario Ricciardi,[1] Antonio De Simone,[1] Pasquale Giannuzzi,[1] Maria Teresa Mandara,[2] Alice Reginato,[2] and Floriana Gernone[1]

[1] *"Pingry" Veterinary Hospital, Via Medaglie d'Oro 5, 70126 Bari, Italy*
[2] *Department of Biopathological Science and Hygiene of Food and Animal Productions, Faculty of Veterinary Medicine, University of Perugia, 06126 Perugia, Italy*

Correspondence should be addressed to Mario Ricciardi; ricciardi.mario@alice.it

Received 16 August 2014; Accepted 26 September 2014; Published 19 October 2014

Academic Editor: Paola Roccabianca

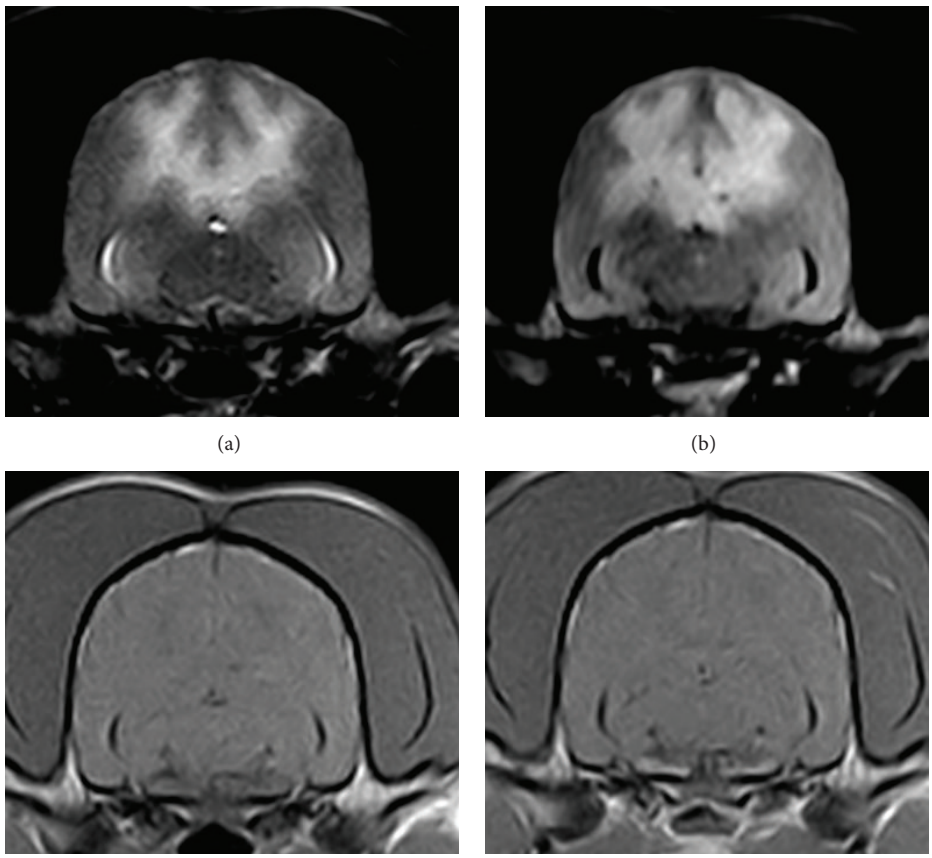
An 8-year-old intact male Lagotto Romagnolo was presented with forebrain signs. Neuroanatomic localization was diffuse prosencephalon. MRI revealed diffuse, bilateral, and symmetric T2 and FLAIR hyperintensities in the parieto-occipital white matter and corpus callosum. No mass effect or contrast enhancement was noted. Analysis of cerebrospinal fluid revealed normal protein content and mild mononuclear pleocytosis. Atypical cells were not identified. 15 days later because of the worsening of clinical condition the patient was euthanized upon owner's request. Neuropathological investigations were consistent with gliomatosis cerebri (GC). Such an unusual imaging pattern appeared similar to some cases of human GC and to a previous reported case in a dog, suggesting a possible repeatable imaging findings for this rare brain neoplasm. GC should be included in the MRI differentials for diffuse bilateral white matter signal changes and specific MRI findings described in this report may help in reaching a presumptive diagnosis of this tumor.

1. Case Presentation

An 8-year-old intact male Lagotto Romagnolo was evaluated for a 1-month history of abnormal mental status. Clinical and neurological examination findings included depression, decreased postural reactions in all four limbs, especially on the right side, and decreased menace response in both eyes. During clinical examination the dog had seizures. The medical case was considered to be consistent with a diffuse forebrain lesion. Because of the age of the patient and the absence of hyperthermia neoplasm was considered the most probable cause of neurological signs while inflammation was considered to be less likely. Complete blood count, serum chemistry, and urinalysis results were within normal limits.

MRI of the brain was performed under general anesthesia using a 0.25 Tesla permanent magnet (ESAOTE VET-MR GRANDE, Esaote, Genoa, Italy). MRI sequences protocol included Fast Spin Echo T2-weighted images acquired in sagittal and transverse plane, a FLAIR acquired in the transverse plane, and Spin Echo T1-weighted images acquired in the transverse plane before and after intravenous administration of paramagnetic contrast medium (Magnegita—gadopentatedimeglumine 500 mmol/mL—insight agents; 0.15 mmol/kg BW). MRI showed extensive, bilateral, and symmetric T2 and FLAIR hyperintensity of the parieto-occipital periventricular and subcortical white matter. The occipital lobes appeared severely involved. The lesions were isointense on T1-weighted images and did not enhance after contrast medium administration (Figures 1 and 2). On sagittal T2-weighted images the aboral part of the corpus callosum lacked homogeneous signal intensity and had ill-defined margins (Figure 3). Mass effect or loss of anatomical architecture was not present. Based on the imaging findings toxic-metabolic or degenerative disorders involving white matter (leukoencephalopathy) were considered the main differential diagnoses, while an inflammatory process, either immunomediated or infectious, and a diffuse infiltrative neoplasm were believed less likely.

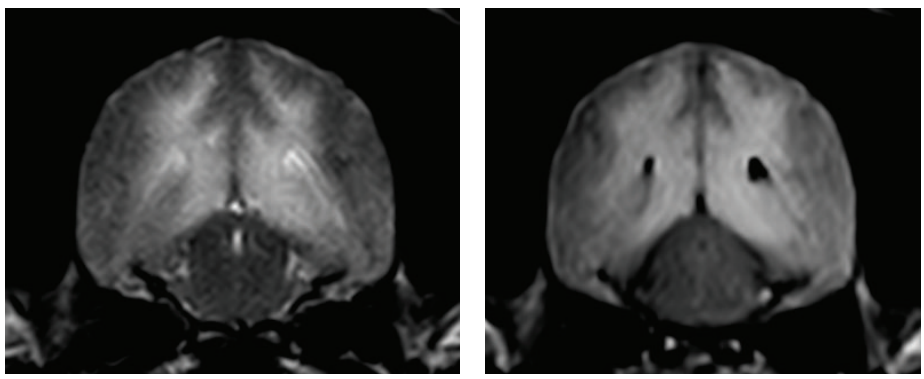
Analysis of CSF collected from cerebellomedullary cistern revealed normal protein content (20 mg/dL; range, <25 mg/dL) and mild mononuclear pleocytosis (30 cells/μL; range, <5 cells/μL). Atypical cells were not identified. The dog



(a) (b)

(c) (d)

Figure 1: (a) T2-weighted (TR = 3720 ms, TE = 90 ms, slice thickness = 3,5 mm), (b) FLAIR (TR = 4000 ms, TE = 100 ms, TI = 1000 slice thickness = 3,5 mm), and (c) T1-weighted (TR = 600 ms, TE = 18 ms, slice thickness = 3,5 mm) pre- and (d) postcontrast transverse images at the level of the caudal mesencephalic aqueduct. There is bilateral and symmetric T2 and FLAIR hyperintensity within the parieto-occipital periventricular and subcortical white matter. The lesions are isointense on T1-weighted images and did not enhance after contrast medium administration. No mass effect is present.



(a) (b)

Figure 2: (a) T2-weighted (TR = 3720 ms, TE = 90 ms, slice thickness = 3,5 mm), (b) FLAIR (TR = 4000 ms, TE = 100 ms, TI = 1000 slice thickness = 3,5 mm) at the level of the rostral mesencephalon. There is bilateral and symmetric T2 and FLAIR hyperintensity of the parietal periventricular white matter and corona radiata. No mass effect is present.

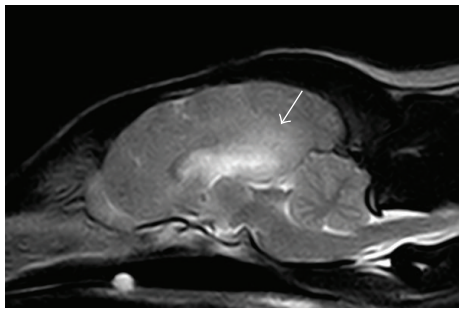


Figure 3: Sagittal T2-weighted image (TR = 3720 ms, TE = 90 ms, slice thickness = 3,5 mm). There is ill-defined T2 hyperintensity of the splenium of corpus callosum. No mass effect is evident.

was treated with phenobarbital (5 mg/kg *q* 12 hr). Pending on the PCR tests on the CSF sample for canine distemper virus, *Toxoplasma gondii*, *Neospora caninum*, *Ehrlichia canis*, and *Rickettsia* spp., clindamycin (15 mg/kg *q* 12 hr) was added on. All the required PCR investigations turned out to be negative. After 15 days the dog was reevaluated. Because of the worsening of clinical condition the dog was euthanized upon owner's request.

Soon after death the dog was submitted to necropsy that did not reveal significant gross visceral lesions. At neuropathological examination performed on formalin-fixed coronal brain sections, cortical white matter of centrum semiovale was markedly expanded to the detriment of cortical gray matter. No more gross brain lesions were observed.

At histologic examination a severe diffuse infiltration of neoplastic cells was observed affecting centrum semiovale, periventricular white matter, corpus callosum, septum pellucidum, fimbria fornix, and parahippocampal gyrus. The neoplastic cells had round to elongated nuclei with coarsely stippled chromatin and indistinct cytoplasm borders. They were haphazardly arranged in a finely fibrillary neuropile (Figure 4(a)). Focally the neoplastic invasion was associated with a diffuse vacuolization of white matter and a coexisting foam cell infiltration. A mild neoplastic infiltration of the fourth ventricle floor was also observed associated with necrosis of the medial vestibular nucleus. Immunolabeling on selected paraffin-embedded brain sections was performed with avidin-biotin peroxidase complex staining for GFAP (GFAP, rabbit polyclonal antibody, 1 : 500, Dako, Carpenteria, CA, USA). It showed a diffuse marked GFAP-immunoreaction of the neoplastic cells (Figure 4(b)). The histological findings were consistent with GC of astrocytic type.

2. Discussion

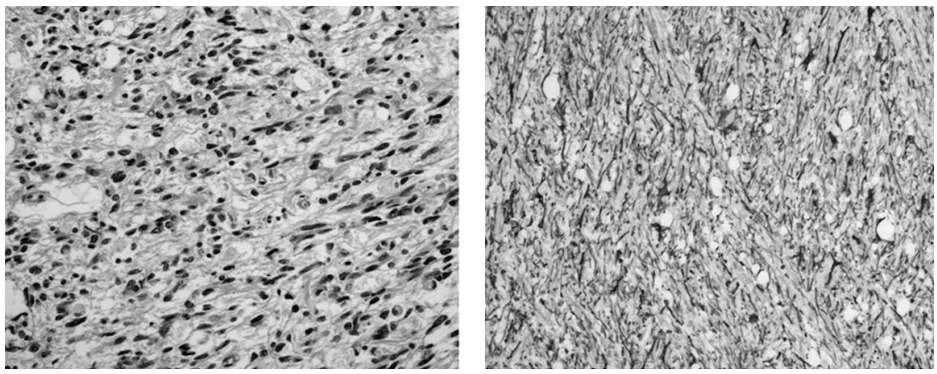
GC is a primary wide and diffuse infiltration of the CNS by neoplastic glial cells [1]. It has been reported in humans, with approximately 300 described cases [2–6], and very rarely in dogs, cats, and goats [7–15]. In humans two general forms of GC are recognized. Type I GC is characterized by neoplastic infiltration with good architecture preservation and without a grossly visible mass. Type II GC consists in a neoplastic infiltration accompanied by a mass lesion with ill-defined margins [1, 2, 4, 5, 7, 16]. Affected patients show clinical signs reflecting tumor localization. In humans GC is primarily localized in the telencephalon with mono- or bilateral involvement of different brain lobes. However, more areas may also be affected such as basal nuclei, thalamus, hypothalamus, corpus callosum, cranial nerves, cerebellum, brainstem, and spinal cord [17, 18]. Infiltration of the brain parenchyma typically occurs along the myelinated fibres producing extensive demyelination of the affected areas [19]. This condition gives a histological pattern, which strictly correlates with the hemispheric white matter signal changes seen on MRI [18–20]. In human medicine, MRI features of histologically confirmed GC include extensive, symmetrical, or asymmetrical and often poorly delineated T2-hyperintense lesions, which tend to be T1-iso to T1-hypointense with variable contrast enhancement [2, 16, 21, 22]. However, these findings are considered nonspecific for GC so that the differential diagnosis includes immunomediated or virus induced white matter diseases, leukodystrophy, and other brain tumors such as primary brain lymphoma or glioblastoma multiforme [18]. In people, the involvement of commissural structures such as the corpus callosum has been unequivocally related to GC allowing differentiating this neoplasm by a demyelinating disease [20, 21].

To date 12 cases of GC have been reported in dogs with multiple distributions of the lesions throughout the brain and spinal cord, while MRI patterns have been described in five cases [7, 9, 11, 12, 22–24]. Three dogs had telencephalic involvement [9, 11, 13] but only one of them showed bilateral and symmetric white matter T2 and FLAIR hyperintensities without any apparent mass effect or anatomical distortion [11]. Based on the MRI features in that case the lesions were misdiagnosed as a leukoencephalopathy of unknown origin. However information about the involvement of the corpus callosum was not available in the referred study [11].

In this report we describe a similar imaging pattern with bilateral and symmetric involvement of dorsal parieto-occipital white matter and corpus callosum, that showed inhomogeneous T2-hyperintensity at level of the splenium. Interestingly in people the involvement of corpus callosum has been reported in 8 out of 9 cases of cerebrum GC [17]. This is why this finding is nowadays considered very suggestive for GC [20, 21, 25].

Generally, bilateral and symmetric involvement of specific anatomic areas of CNS, without relevant mass effect and with anatomic preservation, is typical of metabolic-toxic and degenerative diseases [26–28]. On the contrary, primary CNS tumors usually appear as space-occupying lesions with mass effect and peritumoral edema of variable grade [26–28]. This peculiar distribution pattern of GC clearly subverts these rules and makes the MRI-based ante mortem diagnosis difficult.

Similar and sometimes overlapping imaging findings have been described in dogs with different brain diseases [13, 28–30]. In NLE, MRI findings are characterized by bilateral but not symmetric T2 and FLAIR hyperintensities in the telencephalic white matter [13, 29]. Moreover anatomical distortion may be present. Also in necrotizing leukoencephalitis



(a) (b)

Figure 4: (a) Brain tissue. Diffuse infiltration of the white matter by neoplastic cells having elongate nuclei and fibrillary cytoplasm. The neuropile shows a finely fibrillary pattern (H&E, ×20). (b) Brain tissue. The neoplastic cells show a diffuse marked immunoreaction for glial fibrillary acidic protein. They are characterized by long branched cytoplasmic processes (antiglial fibrillary acidic protein-immunolabeling, ×10).

mononuclear pleocytosis is generally found at cerebrospinal fluid analysis [13, 29]. In our case mild mononuclear pleocytosis detected at CSF analysis was consistent with previous cases of GC in dogs in which normal or mild increased CSF cell count has been found [7, 12, 22]. Canine distemper meningoencephalitis has been reported in an adult dog showing diffuse bilaterally and symmetric T2 hyperintensity of the subcortical parietal and frontal white matter [30]. In that case the predominately white matter distribution of signal intensity changes was consistent with the extensive white matter involvement occurring in the chronic forms [30]. As in this previous report, in our case the negativity of the PCR analyses made chronic distemper encephalitis less likely; any way it did not allow us to rule out distemper definitely. Cerebral edema is generally T1-hypointense, T2-hyperintense and it does not enhance after contrast medium administration [28]. Moreover, edema tends to diffuse along white matter and may outline the corona radiata providing a typical spiked pattern and uniform signal changes [28]. However, extensive cerebral edema is generally associated with a primary brain lesion either vascular, inflammatory, or neoplastic [28]. None of these lesions were evident in our case. To the authors' knowledge none of the toxic-metabolic and degenerative diseases described in dogs show an imaging pattern of diffuse bilateral and symmetric T2 and FLAIR hyperintensities in the white matter. On the contrary, bilateral but selective focal involvement of different brain areas has been observed in thiamine deficiency [31, 32], hepatic encephalopathy [28, 33], osmotic myelinolysis [28], and L2-hydroxyglutaric aciduria (L2-HGA) [34]. A degenerative disease showing MRI patter comparable to that observed in this case is the adult cheetah leukoencephalopathy [35]. This is a diffuse and bilateral white matter disease of unknown etiology described in 1999 in a group of cheetahs, characterized by axonal and myelin degeneration and reactive astrocytosis [35]. However, there are no reports on a similar disease in dogs.

In this study the areas affected by neoplastic infiltration did not express contrast enhancement suggesting blood-brain integrity [36] as described for low-grade gliomas [26–28] and GC in humans [16, 37] as in dogs [9, 11, 22, 24].

In conclusion we describe a distinct MRI pattern of GC in a dog in which bilateral and symmetric T2 and FLAIR white matter hyperintensities were found in the parieto-occipital lobes and corpus callosum. The lesions were isointense on T1W images without contrast enhancement and mass effect. Our imaging findings, unusual for brain tumor, were confirmed as repeatable imaging pattern in canine GC. The most likely differential diagnoses based on MRI signal changes and anatomical preservation seem to be chronic canine distemper meningoencephalitis and NLE. To the authors' opinion GC should be considered in the list of differential diagnosis in a dog having a so peculiar MRI pattern.

Abbreviations

GC: Gliomatosis cerebri
MRI: Magnetic resonance imaging
FLAIR: Fluid attenuated inversion recovery
CSF: Cerebrospinal fluid
PCR: Polymerase chain reaction
GFAP: Glial fibrillary acidic protein
CNS: Central nervous system
NLE: Necrotizing leukoencephalitis.

Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

References

[1] P. L. Lantos and J. M. Bruner, "Gliomatosis cerebri in tumors of the nervous system," in *World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of the Nervous System*, P. Kleihues and W. K. Cavenee, Eds., pp. 92–93, IARC Press, Lyon, France, 2000.

[2] G. N. Fuller and J. M. Kros, "Gliomatosis cerebri," in *WHO Classification of Tumours of the Central Nervous System*, D. N. Louis, H. Ohgaki, O. D. Wiestler, and W. K. Cavenee, Eds., pp. 50–52, IARC Press, Lyon, France, 4th edition, 2007.

[3] S. Nevin, "Gliomatosis cerebri," *Brain*, vol. 61, no. 2, pp. 170–191, 1938.

[4] S. Taillibert, C. Chodkiewicz, F. Laigle-Donadey, M. Napolitano, S. Cartalat-Carel, and M. Sanson, "Gliomatosis cerebri: a review of 296 cases from the ANOCEF database and the literature," *Journal of Neuro-Oncology*, vol. 76, no. 2, pp. 201–205, 2006.

[5] T. Inoue, T. Kumabe, M. Kanamori, Y. Sonoda, M. Watanabe, and T. Tominaga, "Prognostic factors for patients with gliomatosis cerebri: retrospective analysis of 17 consecutive cases," *Neurosurgical Review*, vol. 34, no. 2, pp. 197–208, 2011.

[6] G. E. Vates, S. Chang, K. R. Lamborn et al., "Gliomatosis cerebri: a review of 22 cases," *Neurosurgery*, vol. 53, no. 2, pp. 261–271, 2003.

[7] B. Porter, A. De Lahunta, and B. Summers, "Gliomatosis cerebri in six dogs," *Veterinary Pathology*, vol. 40, no. 1, pp. 97–102, 2003.

[8] F. J. F. de Sant'Ana and C. S. L. Barros, "Gliomatosis cerebri in a dog," *Brazilian Journal of Veterinary Pathology*, vol. 4, no. 1, pp. 58–61, 2011.

[9] A. Gruber, M. Leschnik, S. Kneissl, and P. Schmidt, "Gliomatosis cerebri in a dog," *Journal of Veterinary Medicine Series A: Physiology Pathology Clinical Medicine*, vol. 53, no. 8, pp. 435–438, 2006.

[10] T. Ide, K. Uchida, F. Kikuta, K. Suzuki, and H. Nakayama, "Immunohistochemical characterization of canine neuroepithelial tumors," *Veterinary Pathology*, vol. 47, no. 4, pp. 741–750, 2010.

[11] S. Ródenas, M. Pumarola, L. Gaitero, À. Zamora, and S. Añor, "Magnetic resonance imaging findings in 40 dogs with histologically confirmed intracranial tumours," *Veterinary Journal*, vol. 187, no. 1, pp. 85–91, 2011.

[12] A. Galán, S. Guil-Luna, Y. Millán, E. M. Martín-Suárez, M. Pumarola, and J. M. de las Mulas, "Oligodendroglial gliomatosis cerebri in a Poodle," *Veterinary and Comparative Oncology*, vol. 8, no. 4, pp. 254–262, 2010.

[13] A. de Lahunta and E. Glass, *Veterinary Neuroanatomy and Clinical Neurology*, Elsevier, St. Louis, Miss, USA, 3rd edition, 2009.

[14] B. Stierstorfer, B. Janowetz, and W. Schmahl, "Gliomatosis cerebri in a cat. A case report," *Tierarztl Prax Ausg K Kleintiere Heimtiere*, vol. 30, pp. 282–285, 2002.

[15] U. Braun, M. Hilbe, and F. Ehrensperger, "Clinical and pathological findings in a goat with cerebral gliomatosis," *The Veterinary Journal*, vol. 170, no. 3, pp. 381–383, 2005.

[16] M. Yip, C. Fisch, and J. B. Lamarche, "Gliomatosis cerebri affecting the entire neuraxis," *Radiographics*, vol. 23, no. 1, pp. 247–253, 2003.

[17] P. Peretti-Viton, H. Brunel, O. Chinot et al., "Histological and MR correlations in Gliomatosis cerebri," *Journal of Neuro-Oncology*, vol. 59, no. 3, pp. 249–259, 2002.

[18] M. E. Novillo López, A. Gómez-Ibáñez, M. Rosenfeld, and J. Dalmau, "Gliomatosis cerebri: review of 22 patients," *Neurologia*, vol. 25, no. 3, pp. 168–173, 2010.

[19] J. Schoenen, L. De Leval, and M. Reznik, "Gliomatosis cerebri: clinical, radiological and pathological report of a case with a stroke-like onset," *Acta Neurologica Belgica*, vol. 96, no. 4, pp. 294–300, 1996.

[20] G. J. Felsberg, S. A. Silver, M. T. Brown, and R. D. Tien, "Radiologic-pathologic correlation: gliomatosis cerebri," *The American Journal of Neuroradiology*, vol. 15, no. 9, pp. 1745–1753, 1994.

[21] J. G. Chi, "Gliomatosis cerebri: Comparison of MR and CT features," *The American Journal of Roentgenology*, vol. 161, no. 4, pp. 859–862, 1993.

[22] P. Martin-Vaquero, R. C. Da Costa, K. E. Wolk, C. Premanandan, and M. J. Oglesbee, "Mri features of gliomatosis cerebri in a dog," *Veterinary Radiology and Ultrasound*, vol. 53, no. 2, pp. 189–192, 2012.

[23] B. L. Plattner, M. Kent, B. Simon et al., "Gliomatosis cerebri in two dogs," *Journal of the American Animal Hospital Association*, vol. 48, no. 5, pp. 359–365, 2012.

[24] H. Fukuoka, J. Sasaki, H. Kamishina et al., "Gliomatosis cerebelli in a Saint Bernard dog," *The Journal of Comparative Pathology*, vol. 147, no. 1, pp. 37–41, 2012.

[25] J. Cambier, B. Lechevalier, F. Chapon, V. de La Sayette, F. Viader, and L. Devarrieux, "Diffuse cerebral gliomatosis: a clinicopathological case," *Revue Neurologique*, vol. 148, no. 2, pp. 129–132, 1992.

[26] M. T. Mandara, C. Cantile, M. Baroni, and M. Bernardini, *Neuropatologia e Neuroimaging—Testo Atlante*, Poletto, Vermezzo, Italy, 2011.

[27] M. Vandevelde, R. J. Higgins, and A. Oevermann, *Veterinary Neuropathology—Essential of Theory and Practice*, Wiley-Blackwell, Oxford, UK, 2012.

[28] P. R. Gavin and R. S. Bagley, *Practical Small Animal MRI*, Wiley-Blackwell, Ames, Iowa, USA, 2009.

[29] M. J. Higginbotham, M. Kent, and E. N. Glass, "Noninfectious inflammatory central nervous system diseases in dogs," *Compendium: Continuing Education For Veterinarians*, vol. 29, no. 8, pp. 488–497, 2007.

[30] J. F. Griffin IV, B. D. Young, and J. M. Levine, "Imaging diagnosis—chronic canine distemper meningoencephalitis," *Veterinary Radiology and Ultrasound*, vol. 50, no. 2, pp. 182–184, 2009.

[31] L. S. Garosi, R. Dennis, S. R. Platt, F. Corletto, A. de Lahunta, and C. Jakobs, "Thiamine deficiency in a dog: clinical, clinicopathologic, and magnetic resonance imaging findings," *Journal of Veterinary Internal Medicine*, vol. 17, no. 5, pp. 719–723, 2003.

[32] M. Singh, M. Thompson, N. Sullivan, and G. Child, "Thiamine deficiency in dogs due to the feeding of sulphite preserved meat," *Australian Veterinary Journal*, vol. 83, no. 7, pp. 412–417, 2005.

[33] S.-J. Moon, J.-W. Kim, B.-T. Kang, C.-Y. Lim, and H.-M. Park, "Magnetic resonance imaging findings of hepatic encephalopathy in a dog with a portosystemic shunt," *Journal of Veterinary Medical Science*, vol. 74, no. 3, pp. 361–366, 2012.

[34] L. S. Garosi, J. Penderis, J. F. McConnell, and C. Jakobs, "L-2-hydroxyglutaric aciduria in a West Highland white terrier," *Veterinary Record*, vol. 156, no. 5, pp. 145–147, 2005.

[35] L. Munson, "Leukoencephalopathy in cheetahs (*Acinonyx jubatus*)," in *Report of Workshop on Ataxia in Cheetah Cubs*, J. J. Callanan, L. Munson, and N. Stronach, Eds., University College, Dublin, Ireland, 1999.

[36] M. Law, S. Yang, H. Wang et al., "Glioma grading: sensitivity, specificity, and predictive values of perfusion MR imaging and proton MR spectroscopic imaging compared with conventional MR imaging," *The American Journal of Neuroradiology*, vol. 24, no. 10, pp. 1989–1998, 2003.

[37] P. Ponce, M. V. Alvarez-Santullano, E. Otermin, M. A. Santana, and M. G. Ludeña, "Gliomatosis cerebri: findings with computed tomography and magnetic resonance imaging," *European Journal of Radiology*, vol. 28, no. 3, pp. 226–229, 1998.