Diagnostic Exercise

From The Davis-Thompson Foundation*

Case #: 99 Month: June Year: 2018

Answer Sheet

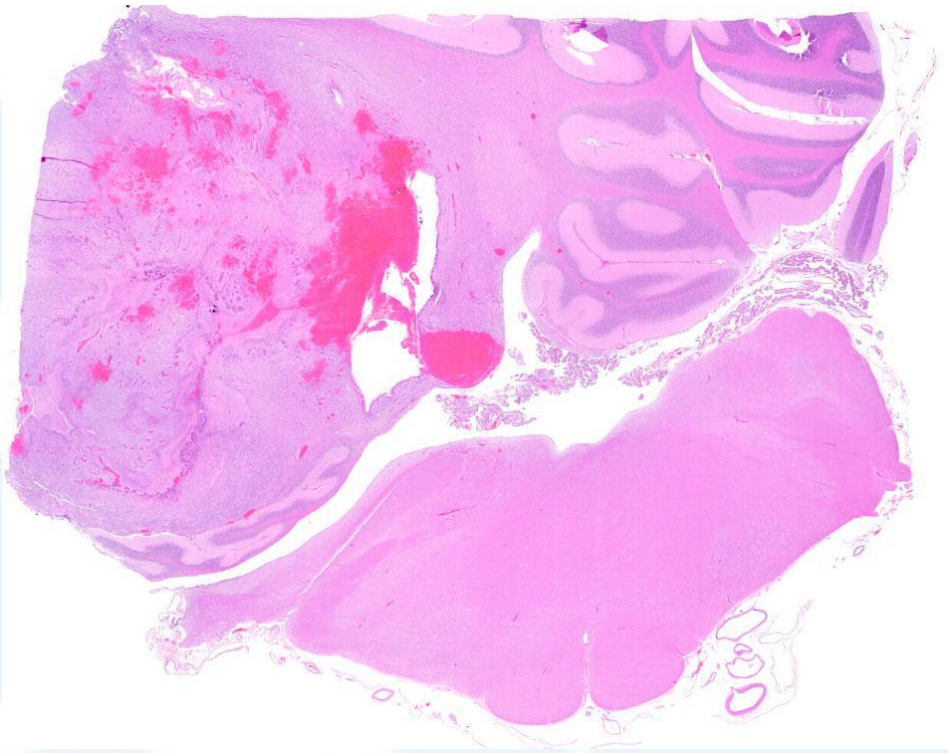
Title: Canine, Brain, Grade IV Glioblastoma.

Contributors: Sarah E. Stevens, DVM, MS and Kevin Woolard, DVM, PhD, DACVP, School of Veterinary Medicine, University of California, Davis, CA 95616.

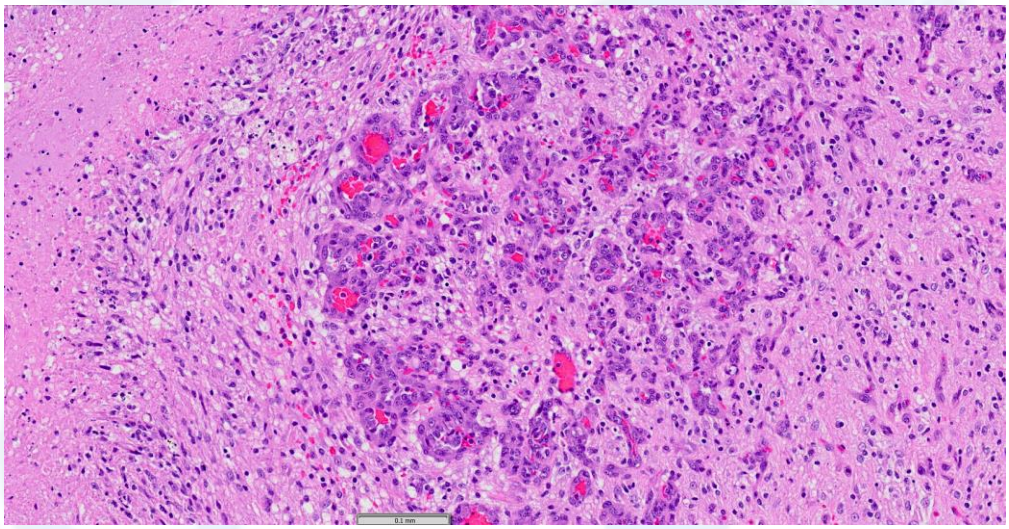
Differential Diagnoses: Meningioma, astrocytoma, oligodendroglioma, metastatic hemangiosarcoma, and round cell neoplasia.

Diagnoses: Brain, right cerebellopontine angle (cerebellum and brainstem): glioblastoma, grade IV, oligodendrocyte-rich. Brainstem, mesencephalon and fourth ventricle: moderate leptomeningeal edema, multifocal to periventricular gliosis and hydrocephalus. The well-defined astrocytic processes noted on the cytology specimen suggested a glial tumor with mild anisocytosis and anisokaryosis, which is consistent with a higher grade glial neoplasm. Lower grade tumors have very little anisocytosis (both cytologically and histologically).

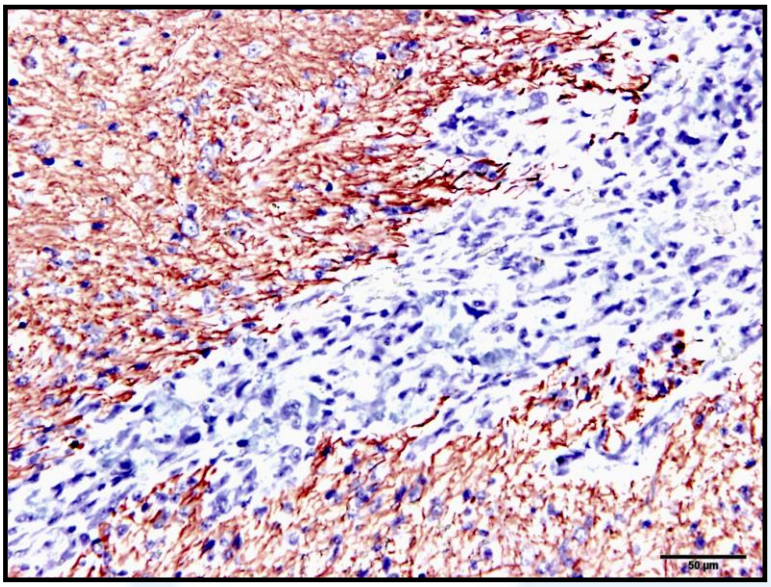
Histological description: The mass is unencapsulated, densely cellular and composed of neoplastic cells that form broad cellular streams mixed with serpiginous islands of microvascular proliferation and large swaths of necrosis. Neoplastic cells range from round or polygonal to elongate with variably defined margins and small amount of wispy, amphophilic cytoplasm. Nuclei are oval to angular with dense chromatin. Anisocytosis is mild, and anisokaryosis is moderate to marked. There are approximately 15 mitotic figures per 10 high power fields with frequent bizarre mitoses. Regions of necrosis are commonly rimmed by perpendicularly arranged neoplastic cells (pseudopalisading). Multifocal aggregates of microvascular proliferation are characterized by clusters of dense small blood vessels lined by 3-5 layers of hypertrophied endothelial cells (occasionally arrayed in a glomeruloid manner). Throughout the mass are clusters of cells that morphologically differ from the primary neoplastic population: they are round with scant amount of lightly eosinophilic cytoplasm, a round nucleus with vesicular chromatin and a clear halo rimming the cell (oligodendroglial differentiation). The fourth ventricle is lined by hypertrophied and vacuolated ependymal cells and the leptomeninges are expanded by moderate clear space (edema).



Above is a subgross image of a transverse section through part of the cerebellum and brainstem in which there is a large, destructive, expansile and compressive mass with regions of hemorrhage and necrosis. The mass elevates and compresses the overlying cerebellar parenchyma.



The neoplastic cells are arranged into interlacing streams of variable densities. The cells are pleomorphic with wispy fibrillar cytoplasm and oval to elongate nuclei. Glomeruloid microvascular hyperplasia or proliferation is present in the neoplasm in semicircular garlands that hug the regions of necrosis.



Glial fibrillary acidic protein (GFAP) is an intermediate filament protein expressed by astrocytes and some other CNS cells. GFAP immunohistochemistry highlights strongly reactive fibrillary processes.

Discussion: In dogs, there appears to be a predisposition for glioma brain tumor types in brachycephalic breeds, including Boxers and Boston terriers. Clinical signs associated with gliomas include altered mentation, seizures, vestibular signs and loss of vision. Glioblastoma is a high-grade glioma of predominantly astrocytic differentiation, although the cell of origin continues to be a matter of controversy. According to the 2016 update of the human WHO glioma classification scheme, both oligodendroglioma and astrocytoma (including glioblastoma) and the previously diagnosed oligoastrocytoma are grouped as "diffuse glioma" with distinct molecular signatures. Classification of canine gliomas within veterinary medicine has recently been under revision to more closely reflect the human classification scheme. Within this scheme, astrocytomas are classified as either localized (grade I) or diffuse (grades II-IV). Glioblastoma is considered a grade IV, diffuse glioma and histologically is an infiltrative astrocytic tumor with generally a high mitotic index, necrosis, microvascular proliferation and pseudopalisading of neoplastic astrocytes around regions of necrosis. A small study in dogs found that glioblastomas primarily occur within the proencephalon or the caudal brainstem, which differs from this case's location. Gliomas of the cerebellopontine angle are uncommon in both veterinary and human literature.

References:

1. Stoica G, Levine J, Wolff J and Murphy K. Canine astrocytic tumors: a comparative review. Veterinary Pathology. 2011; 48(1): 266-275.

2. Brat, Daniel J. Astrocytic tumours. In: Greenfield's Neuropathology, 9th Ed. London: CRC Press; 2015.

*The Diagnostic Exercises are an initiative of the **Latin Comparative Pathology Group (LCPG)**, the Latin American subdivision of The Davis-Thompson Foundation. These exercises are contributed by members and non-members from any country of residence. Consider submitting an exercise! A final document containing this material with answers and a brief discussion will be posted on the CL Davis website (http://www.cldavis.org/diagnostic_exercises.html).

Associate Editor for this Diagnostic Exercise: Patricia Pesavento

Editor-in-chief: Vinicius Carreira