Joint Pathology Center
Veterinary Pathology Services

WEDNESDAY SLIDE CONFERENCE 2025-2026

Conference #23 22 April 2026

CASE I:

Signalment:

2-year-old, neutered male, German shepherd dog, *Canis lupus familiaris*, canine

History:

This dog presented to the referring veterinarian for a three-month history of lethargy and neurologic signs, including a hypermetric gait and ataxia. Spinal radiographs and bloodwork were within normal limits. Given prior medical history of testing positive for Lyme borreliosis and anaplasmosis, doxycycline was prescribed, and the dog was referred to a neurologist. Neurological examination revealed hypermetria of the right forelimb, combined vestibular and sensory ataxia, and a broad-based stance. There were "slightly increased cells" in the cerebrospinal fluid and an MRI of the brain was within normal limits. The dog was treated with clindamycin and prednisone for suspected encephalitis. Three weeks later, a urine sample was negative for *Blastomyces dermatitidis* antigen, and a cervical MRI was within normal limits; treatment with doxycycline, clindamycin, and prednisone was continued. One month following the initial presentation, the dog's energy level and appetite had improved, but the dog continued to exhibit mild hypermetria in all four limbs. A recheck cerebrospinal fluid tap was within normal limits. Antemortem diagnostics for infectious diseases including *Toxoplasma gondii*, *Neospora caninum*, *Cryptococcus neoformans*, and *Blastomyces dermatitidis* all yielded negative results. Nerve and muscle biopsies were performed, and the nerve biopsies indicated possible increased fat droplets with a "possible suggestion of carnitine deficiency." The dog was started on gabapentin and enrofloxacin and was continued on prednisone and clindamycin. The dog continued to decline despite treatment, and was euthanized approximately three months after the initial presentation and submitted for necropsy.

Gross Pathology: After fixation and trimming, the cross sections of the entire length of the spinal cord exhibited well-demarcated, wedge or V-shaped, off-white pallor of the dorsal funiculi.

Laboratory Results: None.

Immunohistochemistry (IHC):

The following IHC preparations were performed:

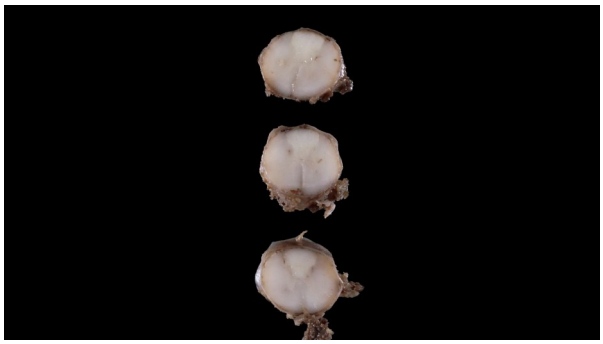

Figure 1-1. Spinal cord, dog: The dorsal funiculi are bilaterally pale along the length of the spinal cord. (*Photo courtesy of*: University of Minnesota Veterinary Diagnostic Laboratory, https://www.vdl.umn.edu/)

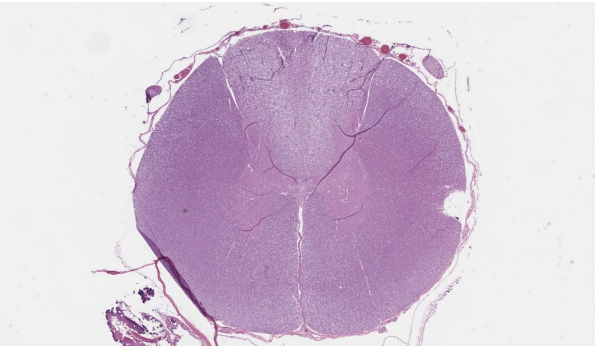

Figure 1-2. Spinal cord, dog: At subgross magnification, there is rarefication of the white matter of the dorsal funiculi. (HE, 23X).

Canine distemper virus antigen: There was no immunoreactivity (negative).

Borrelia burgdorferi antigen: The results were equivocal with mild nonspecific immunoreactivity.

Brain:

Canine distemper virus antigen: There was no immunoreactivity (negative).

Canine herpesvirus antigen: There was no immunoreactivity (negative).

Canine adenovirus (CAV-1 and CAV-2) antigen: There was very little immunoreactivity (equivocal result).

Microscopic Description:

Spinal cord (thoracic segments): In all of the examined cross sections, the white matter of the dorsal funiculi is diffusely and moderately to markedly vacuolated with myelin disruption and loss and axonal degeneration (Wallerian degeneration). Multifocally throughout the white matter of the dorsal funiculi, there are moderately to markedly dilated myelin sheaths, some of which contain gitter cells or eosinophilic cellular debris (ellipsoids); degenerate axons (spheroids); mild to moderate gliosis; and small to moderate numbers of lymphocytes and macrophages. Additionally, there are perivascular cuffs consisting of small numbers of lymphocytes surrounding small- and medium-caliber blood vessels within the dorsal funiculi. These lesions are in marked contrast to the lateral and ventral funiculi, which are within normal limits. There are small numbers of basophilic bacilli scattered throughout all sections (interpreted as postmortem overgrowth/cadaveric bacilli).

Special Stains:

The following special stains were applied to sections of the spinal cord (thoracic segments):

Hematoxylin & eosin/Luxol fast blue: Throughout the dorsal funiculi, there is extensive and marked myelin loss and disruption. These regions contain numerous astrocytes that exhibit haphazard arrangement of the eosinophilic fibrillary acidic proteins of their processes, as well as multifocal accumulations of eosinophilic cellular debris. Extensively scattered throughout the dorsal funiculi, there is rarefaction with vacuolation of the neuropil. Within one of the examined cross sections, there is a dorsal spinal nerve root which exhibits diffuse loss of myelin.

Bielschowsky silver: In all of the examined sections, there is a regionally extensive, marked decrease in axonal density throughout the dorsal funiculi. The axons that remain in this region are frequently shrunken or fragmented.

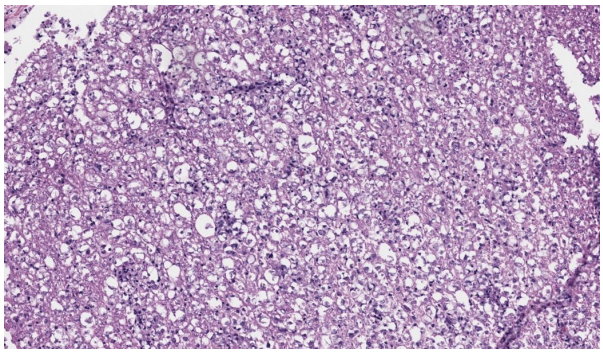

Figure 1-3. Spinal cord, dog: Within affected funiculi, myelin sheaths are diffusely dilated, and contain variably swollen axons, cellular debris, or Gitter cells. Vessels are cuffed by one or more layers of Gitter cells. (HE, 241X).

Contributor's Morphologic Diagnosis: Spinal cord (dorsal funiculi) – myelin loss and disruption with axonal degeneration (Wallerian degeneration), diffuse, moderate to marked, subacute to chronic, with mild lymphocytic and histiocytic infiltration, lymphocytic perivascular cuffs, and gliosis

Contributor's Comment:

The gross and microscopic lesions observed in this case, particularly the diffuse Wallerian degeneration of the dorsal funiculi throughout the entire length of the spinal cord, are suggestive of canine ganglioradiculitis, also known as sensory neuropathy or sensory neuronopathy. Canine ganglioradiculitis is described as a rare, idiopathic disease of adult dogs characterized by various degrees of inflammation within the peripheral ganglia, dorsal root ganglia, dorsal spinal nerve roots, and dorsal funiculi of the spinal cord.[1,3,5-9] On histopathology, the characteristic features of the disease include nonsuppurative inflammation of the dorsal root spinal ganglia and cranial sensory ganglia with secondary, extensive Wallerian degeneration in the dorsal funiculi throughout the entire length of the spinal cord.[5] In the case presented here (but not included in the submitted sections), there were variable degrees of mononuclear inflammation, gliosis, myelin loss, and neuronal degeneration within select dorsal nerve roots and dorsal root ganglia; however, the most striking gross and histopathologic lesions involved the dorsal funiculi throughout the entire length of the spinal cord (as exhibited on the submitted slide). These lesions included marked Wallerian degeneration characterized by myelin disruption and loss, with axonal degeneration. Mononuclear infiltration, both in the form of perivascular cuffing as well as throughout the dorsal funiculi, was also an important feature in this case.

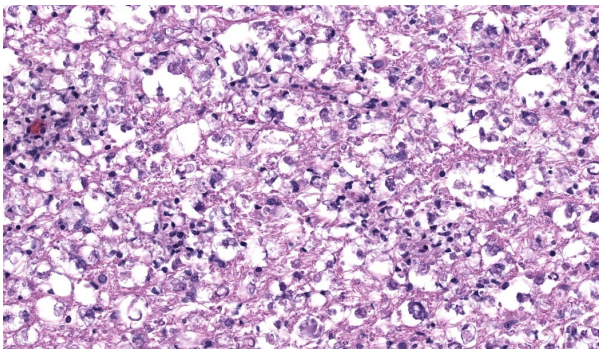

Figure 1-4. Spinal cord, dog: Higher magnification of axonal degeneration within the dorsal funiculi. (HE, 241X).

Canine ganglioradiculitis has been reported to be a sporadic disease usually affecting adult dogs with no breed or sex predilections.[5] This condition is considered a general proprioceptive disorder without involvement of the motor system.[3] The clinical signs associated with this condition are usually abrupt in onset and slowly progressive (over several months) and can be asymmetrical. In this case, the dog initially presented with hypermetria of the right forelimb and the signs progressed toward sensory ataxia and a hypermetric gait in all four limbs. The clinical signs of canine ganglioradiculitis are variable, but often include generalized sensory ataxia, hypermetria, base-wide stance, depression or loss of spinal reflexes, reduced postural reactions, facial hypalgesia, dysphagia, masticatory muscle wasting, and megaesophagus.[5] Additionally, cerebrospinal fluid findings can be normal or exhibit increases in both cells and proteins, as was reported in this case.[8]

Hereditary sensory neuropathies have been reported in Long-haired Dachshund dogs and in Pointer dogs.[2,4] In the case of Long-haired Dachshunds, the clinical signs include loss or reduction of proprioception, reduced

or absent pain sensation, and urinary and fecal incontinence. Histologically, there is a decrease in the number of myelinated nerve fibers in numerous peripheral nerves (including the radial and saphenous nerves) as well as axonal degeneration, particularly of unmyelinated C fibers.[4] With Pointer dogs, the condition is clinically characterized by acral mutilation and insensitivity and is histologically characterized by reduction in the number of neurons within ganglia; however, neuronal degeneration and degenerating myelinated axons within the ganglia are considered rare in these cases.[2] A decrease in the density of myelinated fibers within the dorsolateral fasciculus of the spinal cord has been associated with the hereditary condition in Pointer dogs.[2] An additional clinical differential to be considered is Coonhound paralysis or idiopathic polyradiculitis; however, the pathologic changes of this neuropathy are usually concentrated at the ventral roots and associated clinically with motor deficits such as tetraplegia.[5]

The cause of canine ganglioradiculitis remains unknown. Hypotheses concerning the cause of this condition include an immune-mediated pathogenesis (with cell-mediated and/or humoral components), a viral infection, or a toxic etiology. Autoantibody detection using indirect immunofluorescence assay on the sera from two dogs did not detect autoantibodies against canine ganglion tissues.[5]

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JPC Morphologic Diagnosis:

Thoracic spinal cord, dorsal funiculi: Axonal degeneration and loss, chronic, diffuse, marked, with mild lymphocytic perivascular leukomyelitis.

JPC Comment:

Dr. Jey Koehler, from Auburn University's School of Veterinary Medicine (and our Department consultant on all things neuropathological), moderated this year's 23rd conference with a lineup of neuro cases that integrated anatomy, histology, and clinical neurology. Before diving into this first case, there was a review of the three true forms of ataxia: cerebellar, vestibular, and proprioceptive. Understanding the differences can help clinicians and pathologists localize neurologic disease, and it is common to have more than one type play a role. Cerebellar ataxia is characterized by ataxia and dysmetria or hypermetria of all four limbs, a "goose-stepping" gait, wide-based stance, truncal sway, and intention tremors, but with normal strength and proprioception. Vestibular ataxia can also have a wide based stance, but affected animals have more of a "crab-walking" or "wall-walking" gait, have lateralized lesions (i.e., head tilt, leaning or circling to one side, etc.), falling/stumbling, and a loss of balance when the head is lifted

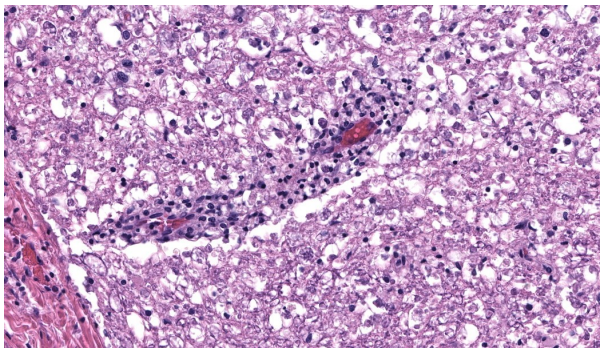

Figure 1-5. Spinal cord, dog: Vessels are cuffed by moderate numbers of Gitter cells and lymphocytes. (HE, 574X).

or the eyes are covered. Lastly, animals with a proprioceptive ataxia show scuffing of the toes when walking, knuckling, crossing over of the limbs, truncal sway, "abnormal stance", and exaggerated circumduction, abduction, and adduction. This dog's history suggested combined vestibular and proprioceptive ataxias. In vestibular ataxia, there is a dysfunction of the vestibular reflex pathways that maintain eye, head, and body position, while proprioceptive ataxia is secondary to loss of neural input from proprioceptors (i.e., muscle spindles, ligaments, joint receptors, etc.). This ataxia review emphasized why a good history is crucial for interpretation of neurologic lesions.

Participants were encouraged to always pay attention to neuroanatomic location when evaluating the nervous system and to be as specific as possible. This was a theme that ran through all four cases in this conference, and Dr. Koehler shared tips on how to determine precisely at which level of the spinal cord a particular histology section may have been taken from, based on the shape of the cord, gray-to-white matter ratio, and the presence of specific tracts. The cervical spinal cord characteristically is either top-heavy (especially pronounced at the level of C1) or is symmetrically oval with a high proportion of white matter. She emphasized how caudal cervical and proximal lumbar segments can look deceptively similar on histology, and how careful attention to the dorsal columns, particularly the medially located fasciculus gracilis (pelvic limb input) and more lateral fasciculus cuneatus (thoracic limb input), can help orient the pathologist. She shared a clever mnemonic to make the distinction between their functions memorable: "If you want to be a graceful dancer, you need legs; if you want to write in cuneiform, you need arms."

The thoracic spinal cord, by comparison, is more spherical and has very little grey matter compared to the other segments. Here, there may be lateral horns (intermediate column) that are composed of visceral motor neurons. In the lumbar segment, the spinal cord becomes bottom-heavy with large ventral horns and a dorsal "caterpillar" shape. The lumbar cord also has a higher proportion of grey matter compared to the cervical segment. Lastly, the sacral cord, is comparatively small with a high proportion of grey matter and usually can be relied upon to have several "nerve friends" nearby. As cited by Dr. Koehler during conference, the University of Minnesota's online "Spinal Cord Anatomy Lab" is an excellent resource for learning the distinguishing histologic features of each cord segment.

Then on to this particular case - many of the major features of sensory neuropathy/ ganglioradiculitis discussed during conference are covered in the contributor's excellent write-up. One of the central discussions during this case was whether it should be given a morphologic diagnosis of leukomyelitis, axonal degeneration, or as demyelination. The inflammation in this particular section was minimal, leading some participants to balk at the idea of using the "-itis" terminology. Dr. Koehler emphasized that, while she views this condition as fundamentally inflammatory since current literature points to the pathogenesis likely being immune-mediated with predominant T-lymphocyte infiltrates, this case lacked the histologic features necessary to truly label it as leukomyelitis.[7] Additionally, inflammation in cases of sensory neuropathy is often

minimal in the cord itself, but may be prominent in the dorsal ganglia.[7] As such, the primary lesion is thought to occur in the ganglia with secondary degeneration of the central projections in the dorsal columns.[7] Without the dorsal root ganglia in section, the group was left to interpret the pattern of a disease restricted to the ascending sensory tracts (white matter), with Wallerian-like degeneration.[6,7] This was reflected in the JPC's morphologic diagnosis, which prioritized the axonal degeneration and loss as the primary process in this slide, with a secondary leukomyelitis.

References:

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CASE II:

Signalment:

Male, European Badger *(Males males),* Mustelidae

History:

Two badgers were found by walkers at the edge of the forest and were brought to the Zagreb Zoo. The animals very quickly developed neurological signs similar to epileptiform seizures. They were treated with fenbendazole, but within a few days they stopped responding to the therapy and were euthanized.

Gross Pathology:

Animals were in good nutritional condition. No significant pathological changes were observed macroscopically. Blood vessels of meninges and brain cortex were moderately congested.

Laboratory Results:

lmmunofluorescence test for Rabies Virus Antigen: Negative.

PCR testing for Herpesvirus was positive

and sequencing showed the virus to be of badger *Gammaherpesvirus.* PCR testing for Flaviviridae was negative.

Microscopic Description:

Cerebrum; multifocally affecting the meninges, the gray matter, and to a lesser extent the white matter, there is perivascular cuffing with low to moderate numbers of lymphocytes, plasma cells and fewer macrophages, that expand Virchow-Robin space up to four times normal. Within gray matter, neurons are occasionaly swollen with eosinophilic cytoplasm (degeneration), or are shrunken and angular with hypereosinophilic cytoplasm and nuclear pyknosis (necrosis). Affected neurons are occasionally surrounded by glial cells (satellitosis). Multifocally, there are small areas of hemorrhage.

Contributor Morphologic Diagnosis:

Cerebrum; Meningoencephalitis, perivascular, lymphoplasmacytic, multifocal, mild to moderate, with neuronal degeneration and necrosis, and mild hemorrhage.

Contributor Comment:

The European badger *(Meles meles*), also known as the Eurasian badger, is a badger species in the family Mustelidae native to almost all of Europe and some parts of Western Asia. Literature data about diseases in this species are generally limited and mostly related to selected infections, such as bovine tuberculosis, canine distemper and rabies.[1,5,9] It is also afflicted with a wide range of parasites that are mostly just a random finding and have no major impact on the badger population health.[10]

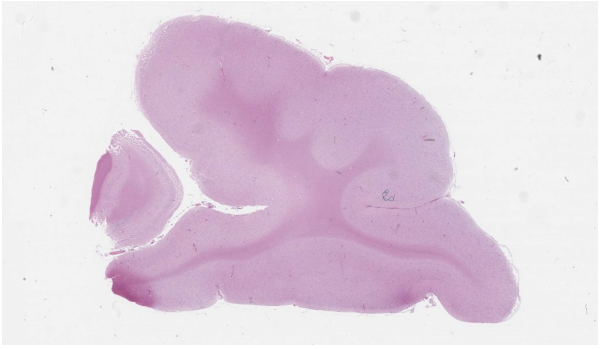

Figure 2-1. Cerebrum, badger: One section of cerebrum is submitted for examination. Other than a slight flattening of the gyri, there are no discernable lesions at subgross magnification. (HE, 7X)

In recent years, it has been found that *Mustelid gammaherpesvirus 1* (MusGHV-1) is circulating in the badger population in Europe.[2,11,12,15] Phylogenetic analysis of sequence data demonstrates that MusHV-1 is a member of the *Rhadinovirus* genus within *Gammaherpesvirinae* closely related to equine herpesvirus 2 and 5.[2,12] For the first time, it was isolated from pulmonary fibroblasts cultures established from a European badger that additionally had eosinophilic, probably verminous pneumonia, but no other obvious association to disease.[2] Few later studies found high prevalence of MsGHV-1 in the genital tracts of European badgers.[11,12,15] It is highly prevalent amongst wild badgers in the UK and Ireland, where MusGHV-1 DNA isolation from blood shows near 100% infection rate at some localities.[14] Badgers have a highly promiscuous, polygynandrous mating system, characterized by repeated mating behavior, likely putting them at a particular risk of contracting sexually transmitted infections that possibly includes also MusGHV-1.[7,13.15]

Regarding meningoencephalitis, except the previously mentioned distemper and rabies, we found no data on herpesviruses as a possible cause of meningoencephalitis in badgers. In domestic animals, encephalitic her-

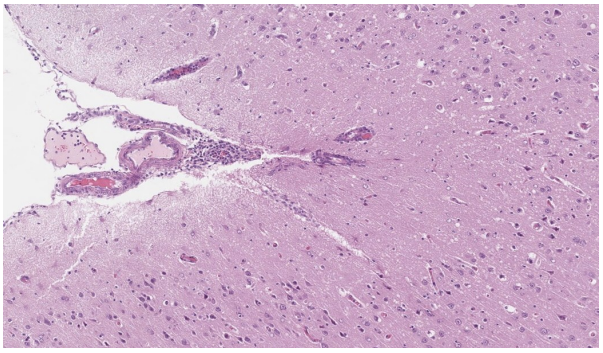

Figure 2-2. Cerebrum, badger: There is mild multifocal lymphoplasmacytic inflammation within the meninges. (HE, 217X)

pesviruses are mostly members of the subfamily Alphaherpesvirinae, and cause cell injury through necrosis of infected neurons and glial cells, necrosis of infected endothelial cells and secondary effects of inflammation, cytokines and chemokines. However, some gammaherpesviruses can also cause lesions in the nervous system such as e.g. murid gammaherpesvirus 4, rhesus macaque rhadinovirus, ovine herpesvirus 2 in cows, and several gammaherpesviruses exist in ursine species and cause neurological lesions.[3] Herpesviruses enter the CNS principally by retrograde axonal transport; however, entry by hematogenous spread via viremia and leukocytic trafficking may occur. These viruses also have a unique survival mechanism that allow them to hide in a latent form in nervous tissue, such as the trigeminal ganglion. Stress or other factors can activate latent virus, resulting in encephalitis.

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JPC Morphologic Diagnosis:

Cerebrum: Meningoencephalitis, lymphoplasmacytic, subacute, diffuse, mild, with neuronal necrosis, gliosis, and rare intranuclear viral inclusion bodies.

JPC Comment:

This case challenged participants with both neuroanatomic orientation and its identification as a viral meningoencephalitis, as the submitted slides varied in their anatomic level. Dr. Koehler began by anchoring everyone to two reliable landmarks on the slide that she received: the olfactory stria and the olfactory tubercle, the latter memorably described as "the wiggly bits." Conference participants, however, received a slide that included cerebrum with hippocampus and thalamus rather than the olfactory stria and tubercle. Despite variation in tissue cuts among slides, the lesions were consistent and included a multifocal lymphoplasmacytic meningoencephalitis with neuronal necrosis, edema, and perivascular cuffing, although intranuclear viral inclusions were more readily identified on the section containing thalamus.

The inflammatory pattern prompted discussion of reactive astrocytes, with Dr. Koehler

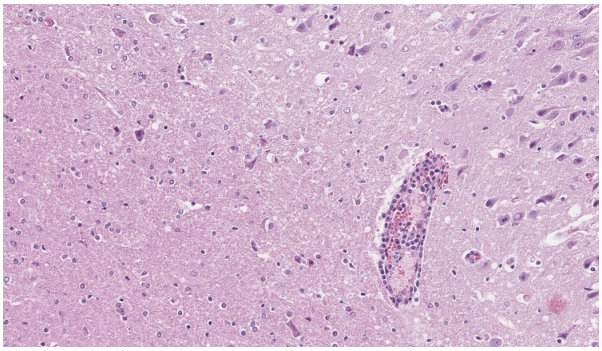

Figure 2-3. Cerebrum, badger: Lymphoplasmacytic inflammation extends down along Virchow-Robin's spaces within the grey matter. (HE, 381X)

emphasizing that the umbrella term "reactive astrocytes" is now preferred over attempting to subtype astrocytic morphologies.[8] The constellation of dead neurons, edema, and perivascular lymphoplasmacytic cuffs strongly supported an inflammatory etiology, and herpesvirus rose quickly to the top of the differential list, along with canine distemper virus (canine morbillivirus), as this has also been reported in American badgers.[4,10]

Participants reviewed the biology of Mustelid gammaherpesvirus-1 (MusGHV-1), also known as Badger herpesvirus, a gammaherpesvirus in the genus Percavirus that is highly prevalent in European badgers.[6] Several studies have demonstrated near-universal infection rates in some populations, with high viral loads in the genital tract.[15] Combined with the badger's polygynandrous mating system, this supports sexual transmission as a major route of spread.[7,15]

While MusGHV-1 is widespread in European badger populations, its role in neurologic disease is less well-defined. PCR alone cannot distinguish latent from active infection, which is a key point when interpreting herpesvirus-associated lesions. Dr. Koehler noted that more definitive attribution of the lesions to MusGHV-1 would require in-situ hybridization (ISH) or virus-specific immunohistochemistry. She and other participants felt, however, that the striking eosinophilic intranuclear viral inclusions in neurons and glial cells in this case support active infection.

Participants also discussed mustelid herpesvirus-2, an alphaherpesvirus identified in sea otters that is primarily associated with ulcerative oral lesions and skin plaques, particularly in Alaskan populations.[6,16] This virus is

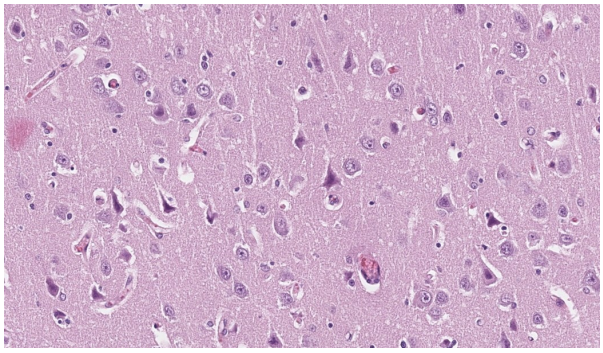

Figure 2-4. Cerebrum, badger: Scattered gray matter neurons are contracted and necrotic. (HE, 496X)

closely related to badger herpesvirus and serves as a reminder that mustelids host multiple herpesviruses with differing tissue tropisms and pathogenic potential.

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CASE III:

Signalment:

1-year-old, intact male (stud colt), American Quarter Horse, *Equus caballus,* horse.

History:

The animal was presented to the large animal teaching hospital for progressive lameness of the hind limbs and a possible pelvic injury after a collision with another horse in pasture six months prior resulted in a fall. Lameness examination revealed a marked grade three lameness of the left hind limb and limited flexion of the stifles with both hind toes worn down from dragging. On neurologic examination, he circumducted his outside hind limb when turning in tight circles. When his head was lifted and he was walked forward, his forelimbs hovered for a prolonged period before he placed them back on the ground. He had mild difficulty backing up and stumbled when walking down the grass hill. Radiographs of the cervical spinal cord revealed severe dorsal deviation of C3 relative to the caudal endplate of C2 and severe stenos is of the spinal canal at C2-C3. The owners elected for euthanasia and an autopsy was performed the same day.

Gross Pathology:

The 2nd and 3rd cervical vertebral joints were stiff and fixed in a flexed position with minimal manual flexion available. The flexed position resulted in a narrow cervical spinal canal at the level of the 2nd and 3rd cervical vertebrae with dorsal compression and flattening of the underlying spinal cord.

Laboratory Results: N/A

Microscopic Description:

Cervical spinal cord: Most severely affecting the white matter of the ventral and lateral funiculi, and to a lesser extent the dorsal funiculus, is extensive axonal degeneration in which 60% of myelin sheaths are markedly dilated and occasionally coalesce to form up to 80-um diameter clear spaces. The dilated myelin sheaths frequently contain swollen, eosinophilic axons (spheroids) or fragments of cellular debris with occasional axonophages (digestion chambers).

Contributor's Morphologic Diagnosis:

Cervical spinal cord: Axonal degeneration, locally extensive, marked, chronic with spheroids and digestion chambers (Wallerian degeneration).

Contributor's Comment:

The clinical course of the disease paired with the gross and histopathologic findings are consistent with cervical vertebral stenotic myelopathy (CVSM) with static stenosis. CVSM (also called cervical vertebral malformation-malarticulation or colloquially referred to and cited in older text as wobbler syndrome) is a common cause of spinal cord compression in horses and dogs.[1,4,5] The

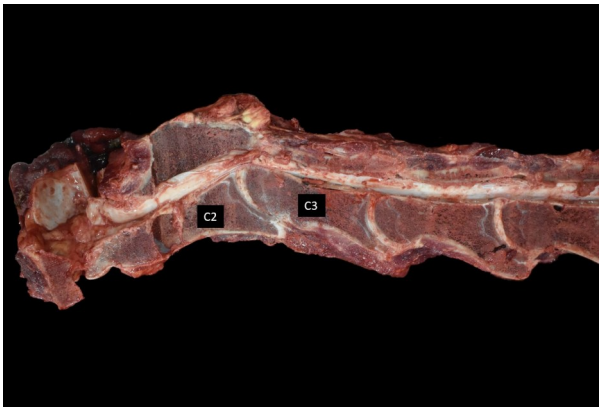

Figure 3-1. Cervical spine, horse: The 2nd and 3rd cervical vertebral joints were fixed in a flexed position resulting in narrowing of the cervical spinal canal and compression of the cord. (*Photo courtesy of*: Auburn University, https://www.vetmed.auburn.edu/academic-departments/dept-of-pathobiology/)

condition is characterized by a stenotic cervical vertebral canal and secondary extramedullary compression of the cervical spinal cord.[1,2,4] Microscopically, lesions within the affected spinal cord are typical of compressive injury to the spinal cord with extensive axonal degeneration leading to demyelination at the compression site.[1,4] White matter degeneration rostral to the compression is typically limited to the ascending tracts of the dorsal funiculi, while caudal is limited to the descending tracts of the ventral funiculi.[1]

In horses, two manifestations of the condition include cervical vertebral instability (dynamic stenosis) and cervical vertebral malformation (static stenosis). Dynamic compression occurs intermittently when the neck is flexed and typically occurs at C3-C5 vertebrae in horses 8 to 18 months of age.[1,4,5] In contrast, static stenosis is a constant compression regardless of neck position and typically occurs in horses 1-4 years of age and older, with dorsal or dorsolateral narrowing of the canal most commonly at C5-C7 vertebrae.[1,4] Lesions thought to contribute to stat-

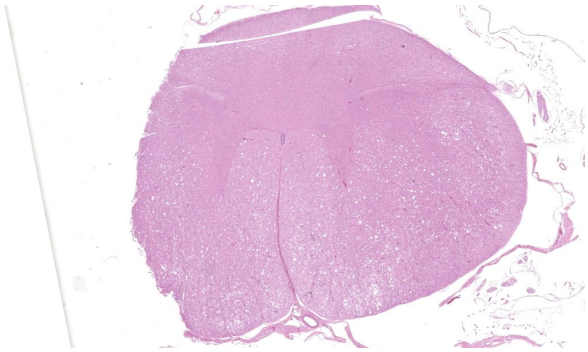

Figure 3-2. Cervical spinal cord, horse: At subgross magnification, there are numerous dilated-myelin sheaths within the ventral and lateral funiculi. (HE, 16X)

ic stenosis include thickening of the ligamentum flavum, thickening of the dorsal lamina, or osteophytosis or osteochondrosis of the articular processes.[4,5] Bone cysts of the articular processes have also been reported, but further investigation is needed to determine their significance and correlation/causation.[2] The time required for development of lesions may account for the older age of onset seen with static stenosis. For this case, changes to the articular facets were not appreciated and a section of the ligamentum flavum was histologically unremarkable.

The pathogenesis of CVSM remains incompletely understood and is thought to be multifactorial with proposed pathways including disordered bone and cartilage maturation or abnormal biomechanical forces and altered vertebral structure.[2,5] Predisposing factors are thought to include rapid growth rates, nutritional over supplementation, and genetic predisposition.[1,2,4] Males and large breeds (thoroughbreds, Tennessee Walking Horses, and Warmbloods) have been shown to be at greatest risk for development.[1,3,4]

An interesting component of this case history is the worsening of lameness immediately following a traumatic incident (collision with another horse and fall). As the severity of CVSM is considered dependent on the speed and extent of spinal cord compression, one can speculate that the incident likely induced rapid compression of the damaged axons and secondary damage that the tissue was unable to accommodate for, in contrast to the slowly progressive compression induced by the static stenosis alone.[1]

Contributing Institution:

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College of Veterinary Medicine
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JPC Morphologic Diagnosis:

Cervical spinal cord, ventral and ventrolateral funiculi: Axonal degeneration and loss, subacute, regionally extensive, severe.

JPC Comment:

This case provided an excellent opportunity to revisit the neuroanatomic significance behind cervical vertebral stenotic myelopathy (CVSM) and the characteristic ventral white

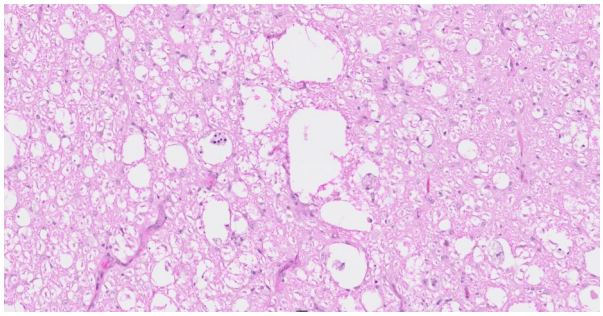

Figure 3-3: Cervical spinal cord, horse: In the ventral funiculi, 60% of myelin sheaths are markedly dilated and occasionally coalesce to form up to 80-um diameter clear spaces (HE, 100X) (*Photo courtesy of*: Auburn University, https://www.vetmed.auburn.edu/academic-departments/dept-of-pathobiology/)

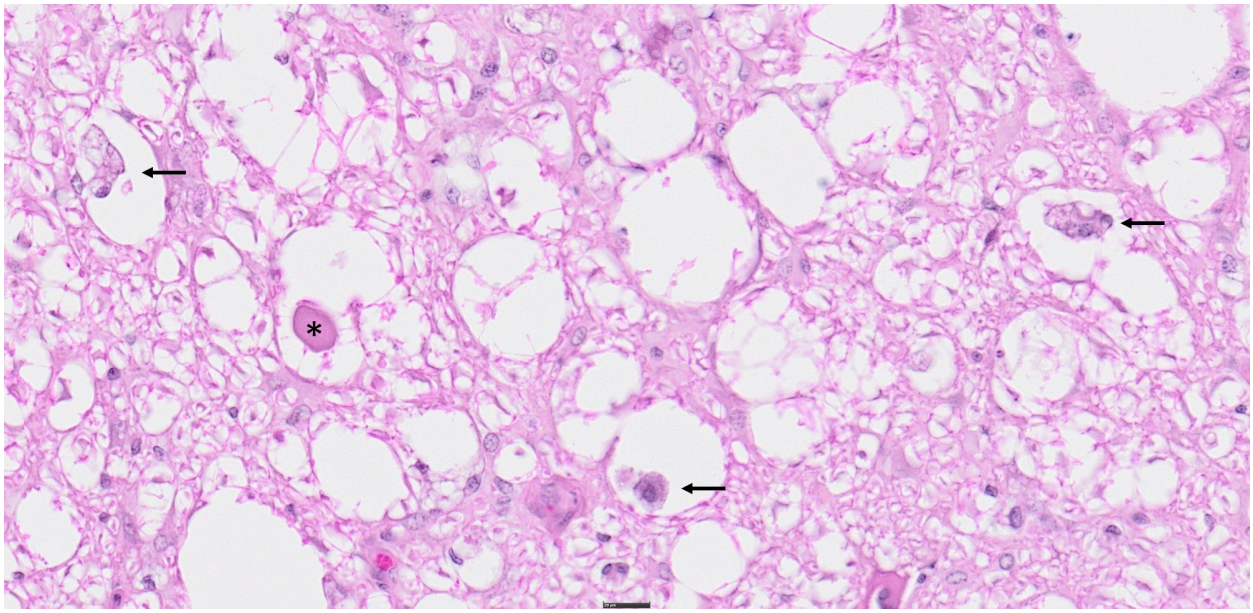

Figure 3-4. Cervical spinal cord, horse: Dilated myelin sheaths frequently contain swollen, eosinophilic axons (spheroids) (asterisk) or fragments of cellular debris with occasional axonophages (digestion chambers) (arrows). (HE, 200X) (*Photo courtesy of*: Auburn University, https://www.vetmed.auburn.edu/academic-departments/dept-of-pathobiology/)

matter degeneration that results from chronic spinal cord compression. This case was classic for this disease in almost all aspects. The clinical presentation and provided imaging correlated beautifully with the histologic pattern of ventral funiculus-predominant Wallerian-like degeneration, with spheroids, digestion chambers, and myelin loss. Many thanks to our contributor for providing fantastic supplemental images!

Participants reviewed the organization of spinal cord tracts, noting that descending motor pathways—including the lateral and ventral corticospinal tracts, reticulospinal tracts, and vestibulospinal tracts—are concentrated in the ventral and ventrolateral funiculi. In contrast, the dorsal and dorsolateral funiculi are dominated by ascending sensory tracts. This distinction is crucial because a lesion that selectively affects ventral white matter is almost always a descending motor tract problem. In horses, the spinal cord compression that occurs in this condition results in the proprioceptive ataxia that earns the condition the colloquial name of "Wobbler's disease."[6] The contributor provides a well-written overview of the two manifestations of this syndrome in horses.[1,4,6]

The age and breed in this case were somewhat atypical, prompting discussion about how trauma, growth rate, genetics, and vertebral conformation can result in differences in the expected presentation.[2] Regardless of the initiating factors, the histologic result is the same: chronic compression leading to Wallerian-like axonal degeneration.

Dr. Koehler highlighted the distinction between Wallerian degeneration and Wallerian-like degeneration, a nuance that often confuses trainees. True Wallerian degeneration was originally defined in the context of acute, severe, transecting injury to the spinal cord, where axons undergo rapid fragmentation distal to the site of injury.[2] In contrast,

Wallerian-like degeneration describes the same morphologic process, but arising from chronic, progressive insults such as compression, ischemia, or metabolic injury.[2] Histologically, the two are nearly indistinguishable; the difference lies in the tempo and mechanism of axonal injury. In this case, the chronicity of the lesion supports the use of the term "Wallerian-like". Similar to case 1, the JPC's morph reflects the participants' view that axonal degeneration and loss are the primary lesions in this case and encompass many of the other findings, including spheroids, digestion chambers, and demyelination since these are all considered manifestations of or sequalae to axonal degeneration/loss.

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CASE IV:

Signalment:

5-year-old female spayed Blue Heeler Mix, Canis lupus familiaris, Canine.

History:

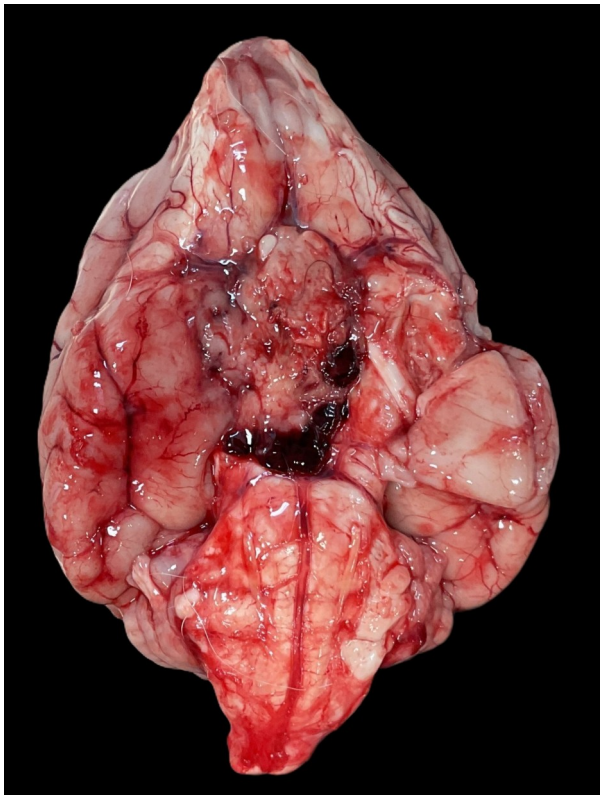

Figure 4-1: Hypothalamus, dog. A neoplasm obscures the pituitary gland and optic nerve. (*Photo courtesy of*: National Institutes of Health Comparative Biomedical Scientist Training Program (CBSTP) in collaboration with Colorado State University Veterinary Diagnostic Laboratory https.//nih-cbstp.nci.nih.gov/; https.// vetmedbiosci.colostate.edu/vdl/)

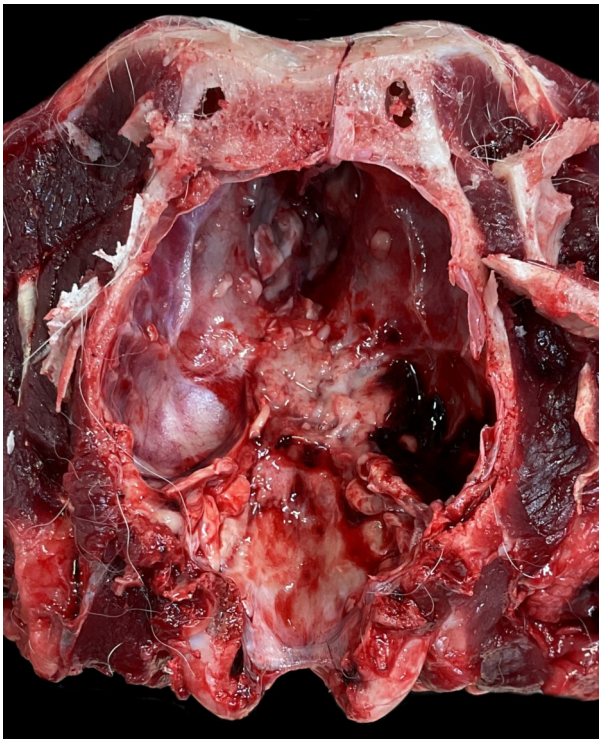

Figure 4-2. Skull base, dog. A neoplasm fills the sella turcica and extends along the right caudal cranial fossa and sellar region, accompanied by hemorrhage.. (*Photo courtesy of*: National Institutes of Health Comparative Biomedical Scientist Training Program (CBSTP) in collaboration with Colorado State University Veterinary Diagnostic Laboratory https.//nih-cbstp.nci.nih.gov/; https.//vetmedbiosci.colostate.edu/vdl/)

The patient had a two-week history of progressive clinical signs, initially presenting with bilateral elevation of the third eyelids, corneal ulcer in the right eye, coughing, leaving the tongue out of the mouth, and declining demeanor. Upon presentation to Colorado State University Urgent Care Service for evaluation of dysphagia and lethargy, dull mentation was noted. Neurological examination revealed absent palpebral and menace responses, as well as absent nasal sensation bilaterally. A negative direct and consensual pupillary light reflex was noted in the right eye. Due to quality-of-life concerns and an uncertain prognosis, humane euthanasia was elected.

Gross Pathology:

Along the ventral aspect of the brain, obscuring the optic nerve and pituitary gland, is a poorly demarcated region of soft white material surrounded by hemorrhage. Similar material is identified filling the sella turcica and extending along the right caudal cranial fossa and sellar region.

On the right eye there is a focal, centrally located, corneal ulcer measuring approximately 5mm X 3mm. Within the oral cavity, along the caudal right buccal mucosa there are multiple regions of ulceration, which sometimes align with adjacent dentition, ranging in size from 0.5cmX0.9cm to 0.7cmX1.2cm.

Laboratory Results:

Not performed.

Microscopic Description:

Captured in section is the optic chiasm, infundibulum, and pituitary. Effacing the pituitary and extending dorsally within hypothalamus, invading the surrounding leptomeninges, and infiltrating the piriform lobe is a poorly circumscribed, expansile and variably invasive, densely cellular neoplasm subdivided in lobules and packets by fibrovascular stroma. There are three neoplastic cell populations that haphazardly intermix, forming the mass effect. The predominate cell type (80%) consists of small, poorly differentiated polygonal cells with scant granular eosinophilic cytoplasm, indistinct cellular borders, and round nuclei with coarse chromatin arranged in nests and packets. Anisocytosis and anisokaryosis are mild with 17 mitotic figures per 10HPF (2.37mm^2). The second cellular population is comprised of round to polygonal cells with indistinct cellular borders, scarce eosinophilic cytoplasm

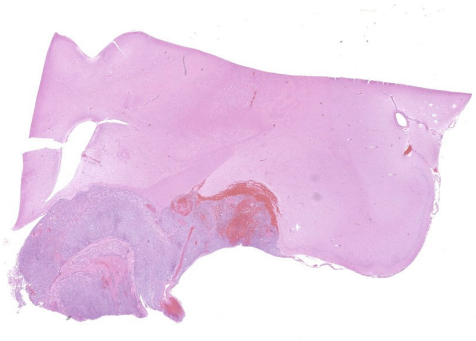

Figure 4-3. Hypothalamus, dog: A neoplasm infiltrates the hypothalamus. There are multifocal areas of thrombosis, necrosis and hemorrhage. (HE, 10X)

with prominent clear cytoplasmic vacuoles arranged in nests and packets. Nuclei are round to ovoid, eccentrically placed with finely stippled chromatin and prominent nucleolus. Anisocytosis and anisokaryosis are mild to moderate with rare mitotic figures identified. Finally, the third population are clusters of columnar cells with abundant amphophilic cytoplasm and indistinct cellular borders occasionally arranged in acini scattered throughout the mass**.** Nuclei are centrally placed, ovoid with finely stippled to vesicular chromatin. Anisocytosis and anisokaryosis are moderate with few scattered mitotic figures. Acini structures occasionally encircle granular basophilic to amphophilic material which sometimes has cellular debris. Throughout the neoplasm there are large regions of necrosis characterized by loss of tinctorial cellular staining, infiltrating viable and degenerate neutrophils, karyorrhectic debris, as well as hemorrhage and fibrin. Hemorrhage and neoplastic cells extend within the adjacent neuropil which exhibits spongy change. Multiple vessels are moderately to markedly ectatic and variably occluded by poorly organized fibrin and sometimes erythrocytes, platelets, and circulating leukocytes (thrombi). A few blood vessels are lined by hypertrophied endothelial cells and surrounded by cuffs of lymphocytes and plasma cells. There is rarefaction adjacent to the third ventricle as well as infiltration of Gitter cells.

Contributor's Morphologic Diagnosis:

Cerebrum: Malignant mixed germ cell tumor – suspect suprasellar germ cell tumor.

Contributor's Comment:

Masses in the pituitary and sellar region include primary pituitary neoplasia (e.g., adenoma or carcinoma), metastatic neoplasia (e.g., lymphoma, melanoma, mammary adenocarcinoma), meningioma, craniopharyngioma, and suprasellar germ cell tumor.[1,5,8,13,15] In this case, the absence of systemic disease lowered the likelihood of primary pituitary or metastatic neoplasms. Histopathologic examination further excluded these differentials, revealing neoplastic cells with varied morphology – predominantly poorly differentiated germ cells, along with hepatoid and epithelial components. Based on the location, mixed neoplastic morphology, as well as marked local invasion and destruction, a diagnosis of suprasellar germ cell tumor was made.

Mixed germ cell tumors are rare in domestic

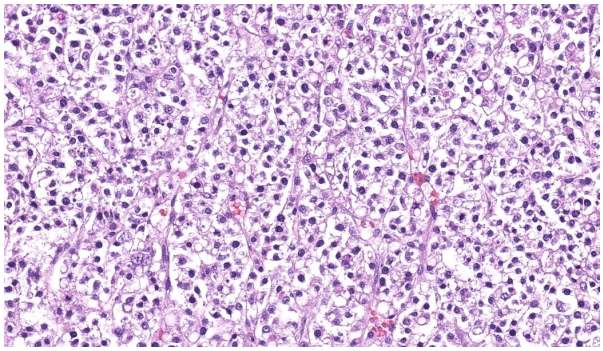

Figure 4-4. Hypothalamus, dog: The predominant morphology of the cells in the neoplasm are polygonal cells in nests and packets with moderate amounts of finely granular cytoplasm. (HE, 528X)

species, most frequently occurring in the gonads.[4,13,16] Extragonadal germ cell tumors are thought to arise from ectopic embryonic germ cells that become widely distributed.[1] In dogs, extragonadal tumors have been commonly reported in the suprasellar region with isolated cases also reported in the spinal cord and eye.[2,3,5,8,9,11,18] Key features of suprasellar germ cell tumors include: a midline mass effect above the sella turcica and dorsal to the pituitary gland; pleomorphic histomorphology with the tumor being composed of several distinct cell types including populations which resemble seminoma/ dysgerminoma as well as secretory glandular and/or squamous elements (teratomatous differentiation); and positive immunoreactivity for alpha-fetoprotein (AFP).[18] In this case, all three criteria for a suprasellar germ cell tumor could not be met as AFP immunohistochemistry was unavailable at the laboratory.

Given the overlapping location, another differential considered in this case was craniopharyngioma. These tumors are presumed to arise from remnants of Rathke's pouch and are histologically characterized by sheets of round to polygonal neoplastic cells and clumps of palisading epithelial cells support-

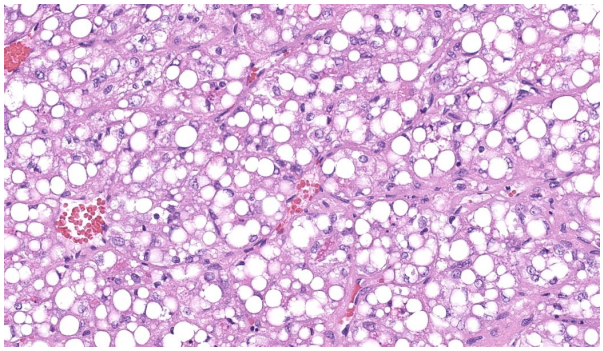

Figure 4-5. Hypothalamus, dog: The predominant cell type in the neoplasm are polygonal cells in nests and packets with moderate amounts of finely granular cytoplasm. (HE, 528X)

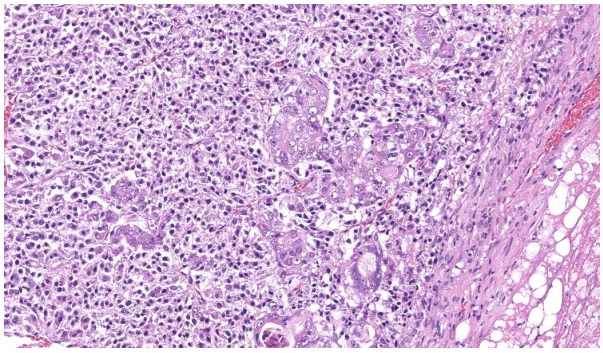

Figure 4-6. Hypothalamus, dog: A third, but far least common morphology of the neoplastic cells are cuboidal polygonal cells forming acini. (HE, 381X)

ed on a collagenous stroma[1,13] Distinguishing between craniopharyngioma and suprasellar germ cell tumors can be challenging, and differentiation often relies on the assessment of AFP immunoreactivity. AFP is produced by the yolk sac of a developing fetus and serves as a useful marker for germ cell tumors in both humans and dogs.[10,18] Neoplastic cells of suprasellar germ cell tumors exhibit AFP immunoreactivity, whereas craniopharyngiomas lack such reactivity. Further complicating differentiation between these neoplasms, the diagnosis of a suprasellar germ cell tumor is not precluded with weak or absent AFP immunoreactivity.[2]

Clinical signs associated with tumors in the pituitary region often include altered pituitary hormone secretion (e.g., hyperadrenocorticism) and can progress to deficits in cranial nerve function as well as central nervous system dysfunction caused due to tumor extension.[15] In the present case, clinicopathologic data were unavailable, and there was no history of underlying endocrinopathy. The intensifying cranial nerve deficits and declining mentation were attributed to the tumor's expansive growth and broad regions of necrosis.

Contributing Institution:

National Institutes of Health Comparative Biomedical Scientist Training Program (CBSTP) in collaboration with Colorado State University Veterinary Diagnostic Laboratory https.//nih-cbstp.nci.nih.gov/

https.//vetmedbiosci.colostate.edu/vdl/

JPC Morphologic Diagnosis:

Cerebrum, thalamus: Suprasellar germ cell tumor.

JPC Comment:

This final case provided an excellent opportunity for discussion of the complexities of midline embryologic tumors and for a brief review of cranial nerve anatomy. This helped participants understand how a midline suprasellar mass might disrupt multiple cranial nerve pathways either through direct compression, distortion of the diencephalon, or secondary effects on the brainstem.

Anatomic orientation was, as with all four of these cases, the next challenge. This cerebral section included thalamus with optic chiasm, third ventricle, and paleocortex, placing this tumor squarely in the suprasellar region. As mentioned by the contributor, the most common locations for extragonadal germ cell tumors in dogs include the suprasellar region, mediastinum, eye, and spinal cord.[10] They are often seen in young to middle-aged dogs, sometimes causing neurological or visual deficits.[10]

Immunohistochemistry plays a central role in the diagnosis. Participants were cautioned that pancytokeratin can cross react with GFAP, a pitfall that can mislead pathologists when evaluating tumors of the CNS.[7] In this case, the neoplasm exhibited weak to moderate immunoreactivity for alpha-fetoprotein (AFP), supporting germ cell differentiation.

The differential diagnoses discussed in this case included craniopharyngioma, teratoma, and pituitary carcinoma, all of which can arise in or near the sella turcica. However, the combination of midline location, mixed cellular morphology, and AFP immunoreactivity align best with a mixed germ cell tumor under the 2021 WHO classification guidelines. Among the listed suprasellar neoplasms, this was the diagnosis that participants agreed best fit the morphologic and immunophenotypic profile.

Dr. Koehler also emphasized the developmental significance of the midline. This region is a crossroads of embryologic migration, fusion, and differentiation, making it a hotspot for tumors derived from ectopic germ cells. The presence of multiple divergent cell populations within the tumor further supported this developmental origin.

Finally, the group discussed the contributor's use of the term "malignant." Some participants preferred not to use that term, noting that primary brain tumors can be fatal due to location alone, even when their biological behavior is histologically benign. While this neoplasm did show histologic invasion and necrosis, there is no established prognostic literature for canine suprasellar germ cell tumors and applying the term "malignant" risks implying a known clinical course. Dr. Koehler framed this as a bit of a philosophical issue for the intents and purposes of conference, however, because, in neuro-oncology, "malignancy" is often a function of where a tumor is, not just what it is.[12]

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