Joint Pathology Center
Veterinary Pathology Services

WEDNESDAY SLIDE CONFERENCE 2011-2012

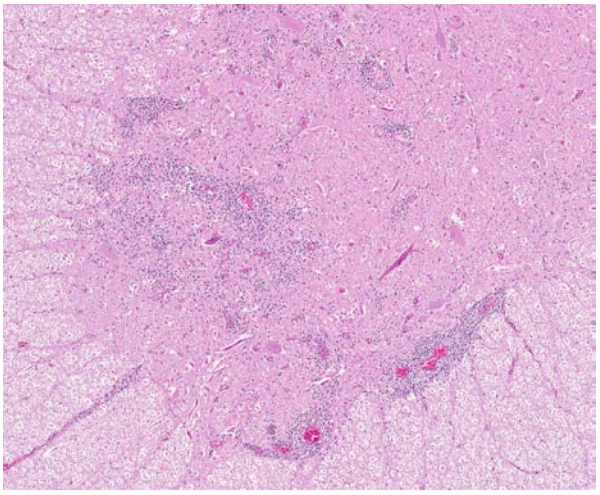
Conference 20

28 March 2012

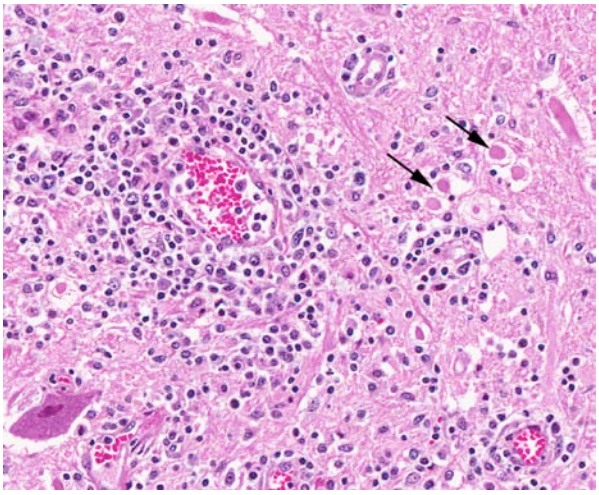
CASE I: W139-11 (JPC 4006397).

Signalment: 5-year-old Thoroughbred mare horse, *Equus caballus*.

History: The horse presented to the University of Melbourne referral equine clinic with acute, severe, uncontrolled abdominal pain. On examination, the mare was distressed and had no gut sounds, pale pink mucous membranes and marked tachycardia (heart rate 100). A displacement of the large colon was suspected based on rectal findings and at exploratory laparotomy, volvulus of the left dorsal and ventral colon was corrected. There was no visible compromise of the bowel and the volvulus did not appear to fully explain the severity of pain. Subsequently, the mare exhibited signs of severe pain despite intense multimodal analgesia including nonsteroidal anti-inflammatories, alpha-2 agonists, lignocaine and ketamine constant rate infusions and morphine. The horse was euthanized



1-1. Spinal cord, horse: Diffusely, vessels within the gray matter are outlined by an accumulation of lymphocytes and plasma cells within the Virchow-Robins space. (HE 4X)



1-2. Spinal cord, horse: The inflammatory infiltrate, primarily lymphocytes, plasma cells, and histiocytes, extends in some areas outward from the perivascular space and infiltrates the surrounding neutrophils. Neuronal changes, however, are limited to a few spheroids (arrows). (HE 240X)

approximately 24 hours after initial presentation. Euthanasia was based on the severity and refractory nature of the pain, of unknown origin.

Gross Pathology: The animal was in lean, fit body condition, with moderate amounts of internal body fat. There was a surgical incision site on the ventral mid-line of caudal abdomen with associated subcutaneous edema. A small amount of fibrin was noted on and over the serosa of the ventral cecum. The brain and spinal cord were grossly within normal limits. The CSF collected was watery and colorless (within normal limits).

Laboratory Results:

Lactate:	13.8mmol/L	(<2)
Fibrinogen:	5.6 g/L	(2.0 – 4.0)
Total bilirubin:	68 µmol/L	(0 – 40)
AST:	457 U/L (150 – 400)	
CK:	3439 U/L	(50 – 400)
Total protein:	58 g/L	(58 – 76)

CSF fluid collected at post mortem was within normal limits, with low cellularity and only a few lymphocytes identified in cytospin preparations.

Formalin fixed sections of brain and spinal cord were positive for Murray Valley Encephalitis (MVE) using PCR, and were negative for EHV-1 using PCR.

Contributor's Histopathologic Description: Sections of brain and spinal cord showed widespread changes affecting mainly the grey matter, with lesions sparing the cerebral cortex, but involving midbrain, brain stem, and spinal grey matter especially in thoracic and lumbar regions, but without any significant change in the nerve roots, ganglia or peripheral nerves. The cerebellar cortex was also spared.

Lesions consisted of thick perivascular cuffs comprised predominantly of small lymphocytes, with lesser numbers of large lymphocytes, plasma cells, and macrophages. In some areas, inflammatory foci extended into the parenchyma, and were associated with neuronal necrosis, especially in the spinal cord. Lesions were intense in the lumbar grey matter. A careful search for protozoa or inclusion bodies failed to reveal any. Apart from a few small ring hemorrhages perivascularly in the brain stem, the lesions were devoid of hemorrhage.

Contributor's Morphologic Diagnosis: Brain and spinal cord: Severe chronic non-suppurative polioencephalomyelitis consistent with Murray Valley Encephalitis.

Contributor's Comment: The horse described had both histological evidence of encephalitis and a positive PCR result for Murray Valley Encephalitis virus. Although the PCR has not been validated for fixed tissue, the histological lesions along with the PCR result are highly suggestive for Murray Valley Encephalitis (MVE). Experience with previously confirmed cases of EHV-1 at this institution has often showed extensive hemorrhagic lesions of brain stem and spinal cord of horses, with minimal inflammation. Based on the clinical presentation, CNS pathology and the negative PCR reaction, this case is not consistent with EHV-1.

There have been two neurological syndromes seen in horses in south-eastern Australia in 2011, peaking in March and April (autumn/fall) associated with arboviral infections: central neurological and musculoskeletal clinical diseases, with some overlap in the lesser affected horses. Neurological signs have most commonly included: ataxia, depression, behavioral changes, tremor, hyperesthesia, muscle fasciculations, hypermetria and colic.[1] Musculoskeletal signs reported in horses that have shown no CNS signs include: listlessness, reluctance to walk, stiff gait, pyrexia and anorexia.[1]

Three viruses- Murray Valley Encephalitis (MVE) virus, Kunjin virus and Ross River Virus (RRV), have been associated with these two syndromes. MVE and Kunjin have been most commonly associated with the neurological syndrome and RRV with the musculoskeletal syndrome. Horse deaths have occurred associated with Murray Valley Encephalitis and Kunjin, but most (≥ 85%) of the horses affected have recovered with supportive treatment.[2] The included table shows serological / viral data from thirteen horses with post mortem evidence of encephalitis / encephalomyelitis (spinal cord often not submitted) seen by the Department of Primary Industries, Victoria:

Number of horses with histological evidence of encephalitis	MVE	Kunjin	Hendra
5*	+	-	-^
6**	-	+	-
1*	+	+	NA
1	-	-	NA

*, The diagnosis is based on demonstration of viral agent(s).
**, In 2 of the 6 horses the diagnosis was based on serology results; the presence of antibodies against Kunjin virus and absence of antibodies against MVE. Kunjin virus was detected by PCR and/or virus isolation in the other 4 horses.
^, One of the 5 horses was not tested.

NA, Not assessed.

Tests used:
- MVE: Antibody assays (Virus neutralization test (VNT) and ELISA) and Agent detection tests (direct PCR and/or virus isolation followed by PCR and sequencing)
- Kunjin: VNT, direct PCR with or without sequencing and/or virus isolation followed by PCR and sequencing
- Hendra: Eleven of the 14 horses were tested for Hendra by PCR. All 11 tested negative (see table).
- Ross River virus testing is pending on these cases.

The prevalence of all three arboviruses this year is related to very high rainfall experienced over the preceding spring, summer and autumn and the resultant increase in mosquito vectors. The increase in water may also have affected the distribution of water birds (the main reservoir hosts for MVE and Kunjin). In many parts of Victoria the 2010-2011 rainfall measurements have been more than double the long term mean for each area.[3] This is particularly significant as most of the state has been in drought for up to 14 years (depending on area), with rainfall in these years often being much lower than the mean.

MVEV and Kunjin are *Flaviviruses* present in northern Australia, Papua New Guinea and Indonesia,[4] with more widespread Australian distribution when the seasonal conditions are conducive. Kunjin is closely related to West Nile Virus.[8] The main vector in Australia is *Culex annulirostris* and the main hosts appear to be water birds, although antibodies have been found in many bird and mammalian species.[4] Usually humans are subclinically infected, but MVE can produce mild disease featuring fever, headache, nausea and vomiting and with Kunjin, a rash, swollen joints, muscle weakness and fatigue. Rarely, both viruses can cause severe disease of meningitis or encephalitis sometimes resulting in death.

RRV is an arbovirus (Alphavirus) which commonly causes human disease in Australia, with approximately 5000 notifications yearly.[4,6] Symptoms of infection in humans include joint pain, joint effusion, rash and pyrexia.[4,6] In horses, the virus is known to cause in the musculoskeletal system the symptoms described above. Macropods and other marsupials are suspected to be the main reservoir species.

Hendra virus has been included in testing to rule out the possibility of this rare, zoonotic disease, which is not an arbovirus. All tested horses have been negative. Horses with Hendra virus infection can have very similar signs to those discussed previosuly including depression, fever, neurological signs and colic.[5] Another common (but not always present) clinical presentation is respiratory disease.[5]

JPC Diagnosis: Spinal cord: Poliomyelitis, lymphohistiocytic, diffuse, severe, with marked neuronal degeneration.

Conference Comment: The differential diagnosis for lymphohistiocytic poliomyelitis in a horse should include Murray valley encephalitis virus (MVEV), West Nile virus (WNV), Kunjin virus, the alphaviruses (Eastern, Western, and Venezuelan encephalitis viruses), other Flaviviruses such as Japanese encephalitits virus and Dengue virus, Borna virus, and Rabies virus. The lack of Negri bodies usually seen with rabies, lack of Joest-Degen bodies usually seen with Borna virus, and lack of neutrophilic involvement usually seen with the alphaviruses and other flaviviruses makes these conditions less likely. Of these remaining candidate conditions, MVEV is the only one to produce disease with the severity seen in the present case. WNV produces mild to moderate lesions of nonsuppurative polioencephalomyelitis with multifocal gliosis and occasional neuronal necrosis, and primarily affects the gray matter of lower brainstem and thoracolumbar spinal cord. Kunjin virus is typically even less pathogenic than WNV.[7,9]

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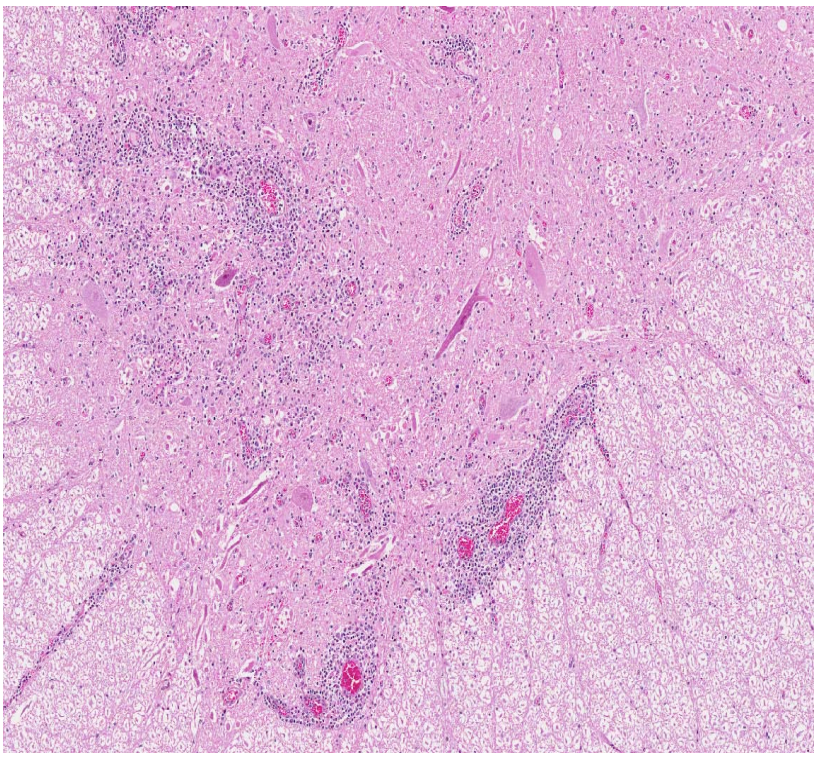
CASE II: A08276724 (JPC 3103238).

Signalment: 1-year-old male Rocky Mountain Horse, *Equus caballus*.

History: This colt from northern Indiana was euthanized along with a 2-year-old filly, and presented for necropsy in September 2007, after two days of weakness, depression, and neurologic signs including head pressing. Both horses had been reared on the premises and had received no vaccinations.

Gross Pathology: Ascarids were in the small intestine. Verminous arteritis with serpiginous intimal tracts was noted in the cranial mesenteric artery.



2-1. Cerebrum, horse: Multifocally, Virchow's Robins are expanded by a combination of neutrophils and histiocytes, with fewer macrophages. (HE 220X)

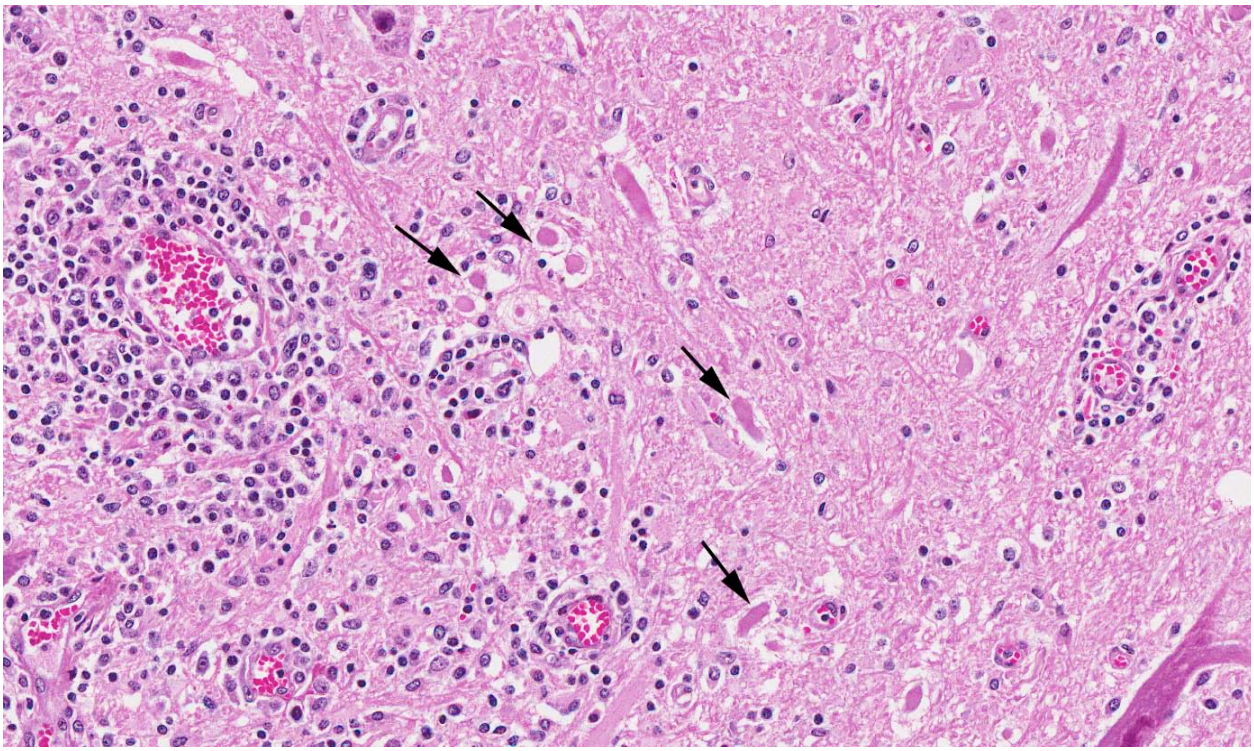
Cerebral leptomeninges were congested and wet. The lateral ventricles of the brain were slightly dilated.

Laboratory Results: Brain tissue from both horses was positive by PCR for Eastern equine encephalitis (EEE) virus, negative by fluorescent antibody test for rabies virus, and negative by RT-PCR for West Nile virus; EEE virus was also isolated in cell culture.

Contributor's Histopathologic Description: In this section of cerebrum, cortical gray matter is more severely affected than white matter by inflammatory changes and necrosis. Thin cuffs (1 or 2 cell layers) of lymphocytes, plasma cells, macrophages and neutrophils surround venules in the cerebral cortex. These perivascular cuffs are thicker (4 or 5 layers) in the cerebral white matter. The leptomeninges, especially in sulci, also have perivascular to diffuse infiltration by the same types of leukocytes. Some venules, especially in the cerebral cortex, have fibrinoid material in their walls or in surrounding tissue; a few have microscopic perivascular hemorrhage. There is widespread, predominantly neutrophilic infiltration of the cortical gray matter. Increased numbers of macroglia and microglia accompany the leukocytes. Focally, heavy neutrophil infiltration is noted in foci of parenchymal necrosis. Many neuronal soma are shrunken with intense cytoplasmic eosinophilia and pyknosis or karyolysis. Some of these dead neurons are surrounded by numerous neutrophils; others are not. A few are undergoing neuronophagia. Similar, but less severe neutrophilic inflammation is evident in the cerebral white matter.

Contributor's Morphologic Diagnosis: Cerebrum**,** neutrophilic poliomeningoencephalitis.

Contributor's Comment: Eastern equine encephalitis (EEE) was suspected because of the clinical signs in two young unvaccinated horses in late summer, so tissues were shipped to the National Veterinary Services Laboratories (NVSL) for diagnostic testing. Histologic changes of severe neutrophilic polioencephalitis supported the tentative diagnosis, which was confirmed by PCR and subsequent virus isolation in both horses. This colt proved to be the sentinel case in an EEE outbreak in northern Indiana. By late October 2007, 17 horses in 24 Indiana counties had tested positive for EEE. This outbreak was considered the widest dispersion of EEE in Indiana in the past 10-15 years. The fact that the first cases were not detected until September was attributed to dry weather in early and mid-summer followed by rainy weather in late summer to support the mosquito population. Horses are considered accidental hosts for EEE virus, which is maintained in birds and transmitted to horses, people and other animals by mosquito vectors.[1] After the development of viremia, the virus invades the brain hematogenously and replicates in neurons, glial cells and vessels. Histologic lesions target the cerebral cortex, sparing



2-2. Cerebrum, horse: Foci of neutrophils admixed with cellular debris are scattered throughout the cerebrum. (HE 160X)

white matter and ganglia, resulting in neuronal degeneration and death, typically with prominent neutrophil infiltration, especially in acute fatal cases.

JPC Diagnosis: Spinal cord: Meningoencephalitis, neutrophilic and lymphocytic, diffuse, moderate, with neuronal necrosis and neuronophagia.

Conference Comment: In some sections, there is rare vasculitis and thrombosis, with large areas of hemorrhage and necrosis. In horses with Eastern equine encephalitis (EEE), gross lesions are asymmetrical in the gray matter and include congestion, hemorrhage, malacia, cerebral hyperemia, edema, petechiation and focal necrosis.[2] Gray matter lesions are more severe in the frontal, rhinencephalic, and occipital areas of the cerebral cortex, as well as the thalamus and hypothalamus, and the intensity of inflammation diminishes as lesions progress caudally. Eastern equine encephalitis virus may cause small intestinal lesions that include multifocal myonecrosis, lymphomonocytic myositis and focal mild perivascular lymphocytic infiltration in the submucosa. Pigs typically develop myocarditis from EEE virus, and Guinea pigs and white mice are highly susceptible.[1]

Other new-world alphaviruses in the Togaviridae family include Western equine encephalitis (WEE) virus and Venezuelan equine encephalitis (VEE) virus. The three basic phases of alphavirus encephalitis, common to EEE, WEE, and VEE, are virus replication in peripheral tissue and subsequent spread, neuroinvasion, and viral spread within the CNS with primary infection of neurons and fatal neurodegeneration.[2] Western equine encephalitis is typically the least virulent of the three viruses, although lesions and pathogenesis are similar to EEE and VEE. In horses, VEE often presents as a purely nonsuppurative encephalomyelitis, sometimes accompanied by myeloid depletion of the bone marrow and lymphocytolysis in the spleen and lymph nodes. Necrotizing vasculitis, thrombosis and cerebrocortical necrosis are particularly prominent in VEE, but are also reported in EEE, as demonstrated in this case.[3] VEE has been shown to enter the CNS directly via olfactory neuroepithelium to the olfactory bulbs.[2]

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CASE III: D-09-8307 (JPC 3164937).

Signalment: Nine-year-old gelding Thoroughbred, *Equus caballus*, equine.

History: The owner complained that the horse seemed to be lame when riding in sand. Over the next 24 hours there was rapidly ascending paralysis. The horse was dog sitting and then became recumbent with complete loss of deep sensation to the rear limbs. Cerebral spinal fluid (CSF) was collected from the lumbar region and appeared to be blood. CSF collected from the thoracic region was cloudy. The owner opted for humane euthanasia and a post mortem examination was performed.

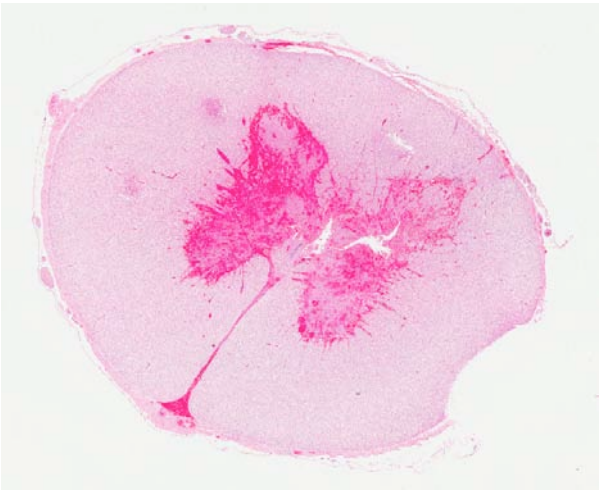
Gross Pathology: Hemorrhage at the lumbosacral region. No fracture was detected. No other significant findings. Sections of the spinal column were submitted to the Tai Lung Veterinary Laboratory for histological interpretation. These sections of the spinal cord were fixed in 10% neutral buffered formalin, processed, sectioned and stained with haematoxylin and eosin (H&E).

Pathologist's findings: On trimming of the spinal cord sections submitted for histological examination, the segment from lumbar vertebra 1 to lumbar vertebra 4 was visibly compressed with a 15 mm x 4 mm dorsal protrusion.

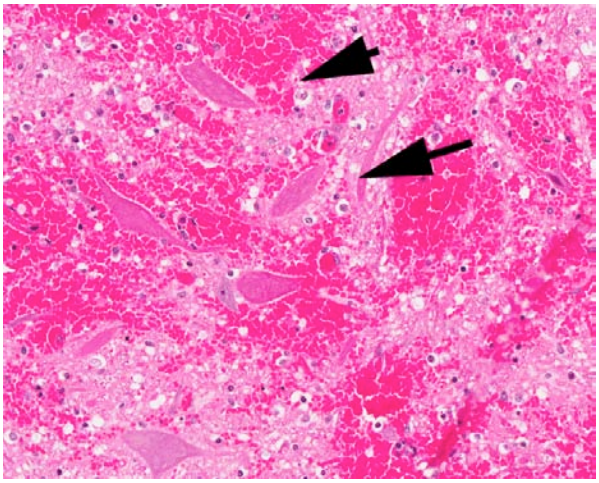
Laboratory Results: Cytology Examination results:
Cerebrospinal fluid (lumbosacral – per submitting veterinarian): Field was entirely composed of red blood cells and marked numbers of neutrophils and macrophages.
CSF for culture – No significant findings
PCR for Japanese Encephalitis – Negative
PCR for West Nile Virus – Negative
Virology – Rabies:
Negri Bodies – Negative
Immunofluorescent Test - Negative

Contributor's Histopathologic Description: Spinal cord: One cross section and one longitudinal section from the area of lumbar vertebra four (L4) are examined. L4-L6 represents the most devastatingly affected segment with large areas of gray matter loss (cavitation). In both the dorsal and the ventral gray column there is severe hemorrhage, neuronal necrosis, spheroids, high protein perivascular edema and an inflammatory cell infiltrate consisting of neutrophils, macrophages and fewer lymphocytes. Blood vessels radiating from the gray matter into the surrounding white matter are surrounded by perivascular edema and hemorrhage. Multifocally, in the white matter there are swollen, eosinophilic axons (spheroids) and Wallerian degeneration characterized by the presence of gitter cells in dilated myelin sheaths. White matter changes also include vascular diapedesis and perivascular cuffs composed of neutrophils, macrophages and lymphocytes. There are multifocal areas of hemorrhage seen in the white matter and the meninges. Multifocally, vascular fibrinoid necrosis is also evident.

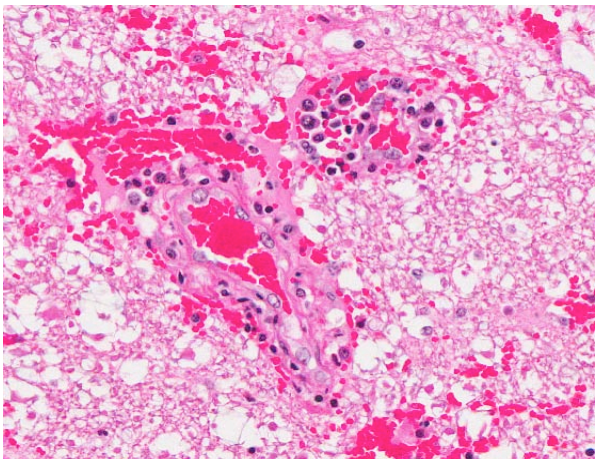
Contributor's Morphologic Diagnosis: Spinal cord, lumbar: Myelopathy, necrotizing, ischemic, extensive, severe, acute, neutrophilic and histiocytic with massive hemorrhage and Wallerian degeneration, Thoroughbred, equine.



3-1. Spinal cord, horse: Extensive hemorrhage outlines the gray matter. (HE 5X)

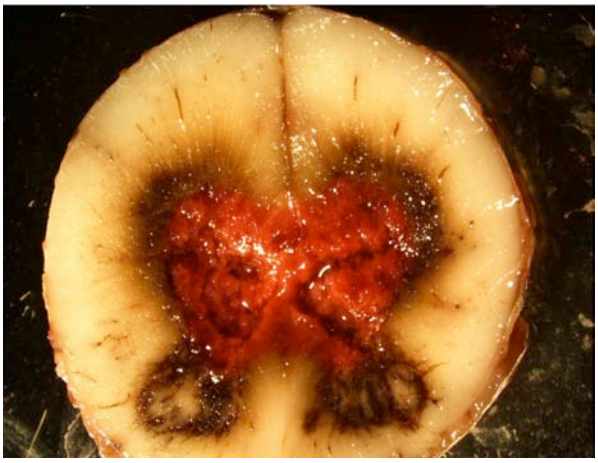


3-2. Spinal cord, horse: In areas of hemorrhage, neurons exhibit degenerative signs such as swelling, hypereosinophilia, and loss of Nissl substance (arrows). (HE 150X)



3-3. Spinal cord, horse: Scattered throughout the hemorrhagic gray matter, vessel walls are often expended by fibrin, infiltrating neutrophils and histiocytes, and cellular debris (fibrinoid vasculitis). (HE 188X)

3-4. Spinal cord, lumbar. Severe hemorrhage and cavitation.



3-5. Spinal cord, lumbar. Liquefactive necrosis of the gray matter.

Contributor's Comment: The most likely cause of the devastating changes seen in the spinal column and considering the rapid onset of clinical signs, aggressive progression of paralysis and the protrusion of the spinal column seen grossly is trauma. There was neither history of degenerative disk disease nor evidence of fibrocartilaginous emboli but these scenarios were considered due to the sudden onset of clinical signs and the ischemia evident histologically.[1] However, in the literature it is thought that the cervical spinal cord is the area primarily affected by fibrocartilaginous emboli in the horse.[4]

Despite there being no evidence of vertebral fracture during post mortem examination, acute compression of the spinal column and resultant ischemia would account for the changes seen histologically. It has been reported that direct injuries to the spinal cord can occur without obvious injury to the vertebrae with devastating effects.[2]

Grey matter with its high metabolic rate and dependence on oxygen is much more sensitive than white matter to ischemic changes.[5] This would explain why the gray matter in this case is so much more severely affected than the white matter.

Acute, traumatic spinal cord injury generally occurs by primary and secondary mechanisms. The primary event is the mechanical injury to the tissue, which may include compression. The secondary mechanism consists of the interruption in vascular supply and perfusion.[5]

The gray matter is composed primarily of cell bodies and dendrites of nerve cells. Neurons are the most sensitive to injury out of all the cells in the central nervous system as they have limited energy stores. They are dependent on an intact blood flow to supply oxygen and nutrients, particularly glucose. Neurons are dependent on a continuous supply of oxygen to remain viable and if the supply is interrupted, vulnerable neurons will degenerate. It is reported that the more rapid the onset of ischemia, the more severe the lesion tends to be. The severe hemorrhage seen primarily in the gray matter is consistent with damage to the capillary framework which tends to be more concentrated in the gray matter than in the white matter. There are also fewer anastomoses in the vessels that supply the white matter.[6]

It is thought that the tendency for spinal cord tissue to become soft and suffer liquefactive necrosis is due to the abundance of lipids and enzymes and a lack of fibrous connective tissue in the CNS.[6]

JPC Diagnosis: Lumbar spinal cord, gray matter: Hemorrhage and necrosis, diffuse, severe.

Conference Comment: Although not reported in the history, conference participants considered post-anesthesia hemorrhagic myelopathy as a possible ruleout in this case. When horses are anesthetized and laid in dorsal recumbency, compression of the azygous vein can result in venous infarction and ischemic necrosis, and poliomyelomalacia of the caudal spinal cord is the most common histopathological finding.[3] Another possible cause is fumonisin B1 toxicity from the consumption of corn contaminated with the saprophytic fungus *Fusarium verticillioides*, which typically causes edema and necrosis of the cerebral white matter, but chiefly cause gray matter necrosis in the brain stem and spinal cord.[2] Also considered was purpura hemorrhagica, which causes vasculitis, vascular necrosis and hemorrhage secondary to antigen-antibody complexes; or endotoxemia, although accompanying inflammation would be expected.[6]

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CASE IV: AFIP 2 (JPC 4003090).

Signalment: Third trimester fetus, male Arabian horse.

History: The dam aborted the fetus approximately 2 months before the expected foaling date.

Gross Pathology: The liver is markedly friable, and the subcapsular surface is stippled yellow and red. Within the thymus is a moderate amount of white to yellow opaque material.

Laboratory Results: Fluorescent antibody testing for equine herpesvirus-1on liver tissue was positive. Additional ancillary test results were as follows: bacterial culture of the stomach contents did not isolate organisms; bacterial culture of the thymus isolated few *Staphylococcus xylosus* and *Acinetobacter lwoffii*, interpreted as contaminants; serology for *Leptospira* spp. and equine viral arteritis virus was negative.

Contributor's Histopathologic Description: Scattered randomly throughout the liver are numerous small foci of coagulative necrosis infiltrated by numerous macrophages, lymphocytes, and plasma cells. Within hepatocytes adjacent to the areas of necrosis are variable numbers of large, eosinophilic, intranuclear inclusion bodies that marginate the chromatin to the periphery. Within the portal triads are numerous mononuclear cells consistent with hematopoietic precursor cells. Immunostaining for equine herpesvirus demonstrates marked positive immunoreactivity within inflammatory cells and necrotic cellular debris in the areas of hepatocellular necrosis.

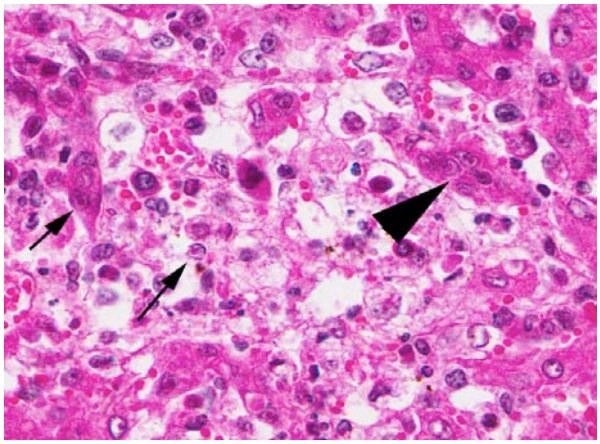
Within the spleen, white pulp is markedly expanded by karyorrhectic cellular debris, and few intact lymphocytes remain.

The thymic medulla contains a moderate amount of necrotic debris and is infiltrated by numerous eosinophils. Rarely, thymic reticular cells contain a single, large, eosinophilic intranuclear inclusion body. Within the lung, alveolar septa contain variable amounts of necrotic cellular debris. (Thymus and lung were not submitted)

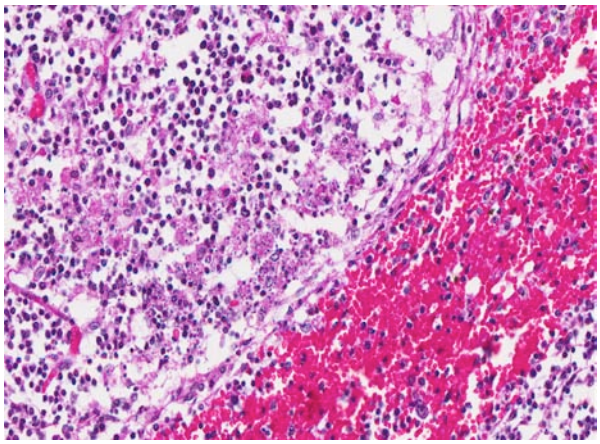
Contributor's Morphologic Diagnosis: Liver: Severe, acute, random, necrotizing hepatitis with hepatocellular intranuclear inclusion bodies.
Spleen: Marked lymphoid necrosis.
Thymus (not submitted): Moderate to marked lymphoid necrosis.
Lung (not submitted): Mild, multifocal, necrotizing interstitial pneumonia.

Contributor's Comment: Herpesviral abortion occurs in horses, cattle, goats, pigs, dogs, and cats.[9] In horses, herpesviral abortion is most commonly attributed to equine herpesvirus-1, an alphaherpesvirus that causes abortion, neonatal disease, respiratory disease, or neurologic disease in horses.[7,9] Most horses are infected with equine herpesvirus as young animals, as the virus is widespread.[7] Equine herpesvirus 1 can cause abortion as a result of initial infection with the virus or as a result of recrudescence of latent virus within the dam.[7] Most equine herpesvirus abortions occur in the third trimester of pregnancy, as was the case in the submitted fetus.[5,7]

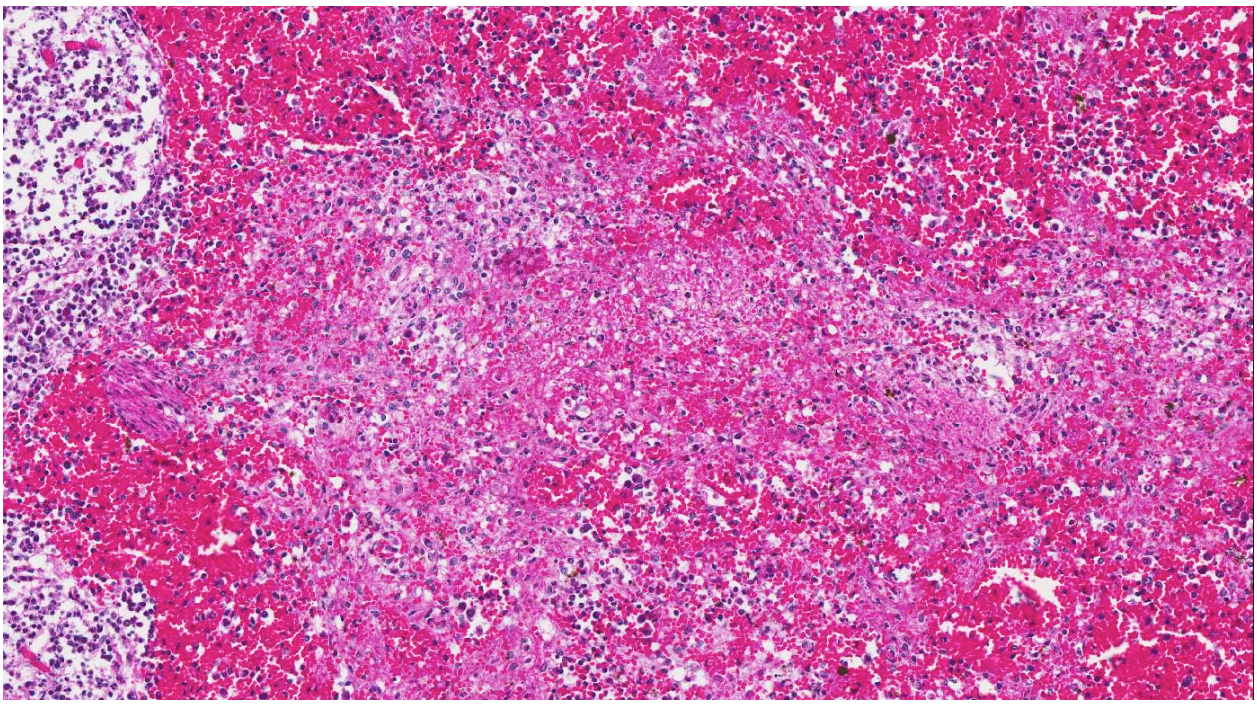
This fetus demonstrated the classic histologic lesions of equine herpesvirus abortion including multifocal necrotizing hepatitis, splenic and thymic necrosis, and



4-1. Liver, foal: Small areas of necrosis are scattered throughout the liver and hepatocytes at the periphery contain small eosinophilic herpesviral inclusions which marginate the chromatin (arrows). A muntinucleated viral synctytium with inclusions within multiple nuclei is also present (arrowhead). (HE 400X)



4-2. Spleen, foal: Splenic white pulp is markedly depleted, and expanded with abundant cellular debris. (HE 400X)



4-3. Spleen, foal: There are rare foci of red pulp necrosis scattered throughout the parenchyma. (HE 400X)

interstitial pneumonia.[7] Adrenal gland necrosis is also reported to occur.[9] The florid hepatic necrosis with intranuclear inclusion bodies is somewhat atypical, as in most cases of equine herpesviral hepatitis, inclusion bodies are rare.[7] Inclusion bodies are most commonly identified in the bronchiolar and alveolar epithelium, reticular cells of the spleen and thymus, and, less often, in hepatocytes.

Gross examination of this fetus revealed a friable liver, and foci of hepatic necrosis were not seen grossly. In addition, white to yellow fluid seen grossly in the thymus likely corresponded to necrotic cellular debris identified microscopically. Additional gross lesions that may occur in equine herpesviral abortions include pulmonary edema, bronchiolar fibrin casts, splenic petechiation, and renal cortical hemorrhage.[7] These lesions were not identified in this fetus.

Upon infection with equine herpesvirus 1, primary viral infection occurs within the upper respiratory tract, resulting in viremia. Viremia enables spread of the virus to the gravid uterus with infection of uterine endothelial cells. In the uterus, the virus may induce vasculitis and infarction of microcotyledons with subsequent spread to the feto-placental unit.[5,9] Uterine endothelial cells are more susceptible to infection in late pregnancy, leading to the increased risk of abortion in the third trimester.[5]

Though this fetus was aborted, occasionally foals will be born infected with the virus. In these cases, foals typically die with an interstitial pneumonia, and they may develop focal necrosis of intestinal crypt epithelium with intranuclear inclusion bodies in crypt epithelium.[7]

In this case, histopathologic changes were highly suggestive of equine herpesvirus infection. Immunohistochemistry was performed for confirmation. In addition to histopathology and immunohistochemistry, other methods of equine herpesvirus 1 diagnosis include virus culture and isolation and polymerase chain reaction.[5,7]

JPC Diagnosis: 1. Liver: Hepatitis, necrotizing, multifocal and random, moderate, with lymphohistiocytic pericholangitis and hepatocellular, endothelial, and biliary viral syncytia and intranuclear inclusion bodies.
2. Spleen, white pulp: Lymphoid necrosis, diffuse, severe, with random red pulp necrosis, fibrin, and intrahistiocytic intranuclear viral inclusion bodies.

Conference Comment: Equine herpesvirus 1 (EHV1) proliferates rapidly in nasal, pharyngeal, and tonsillar mucosa, and infects primarily T-lymphocytes, resulting in viremia and subsequent endothelial infection in numerous sites including the lungs, uterus, and CNS. This results in vasculitis, thrombosis, and ischemic necrosis. With damage of maternal uterine endothelial cells following viral infection, there is thrombosis, inflammation, and perivascular edema which leads to infarction of the endometrium and separation of

maternal and fetal placental layers. Viral infection of fetal endothelium and other cells in many organs leads to abortion or birth of weak foals that die soon after pneumonia. Infection in older foals, usually greater than 1 year-old, is typically a self-limiting upper respiratory disease.[1,2,3,4,5,7]

Viral replication occurs in the nucleus, and the viral envelope is acquired by budding through the inner layer of nuclear membrane. Positively charged residues in EHV1, glycoprotein B and glycoprotein C, bind to heparan sulfate moieties of host cells, and equine major histocompatibility complex (MHC) I acts as a functional receptor for glycoprotein D (gD), facilitating entry and infection of the cell.[6]

This case was atypical because portal hepatitis and edema of the capsule and the space of Disse were the prominent features instead of necrosis. Another unusual feature was the abundance of syncytial cells within hepatocytes, biliary epithelium, and endothelial cells.

Other causes of equine abortion include equine herpesvirus 4, which occurs sporadically and is considered a milder pathogen then EHV1 and which generally causes lesions only in the endometrium and not the fetus; equine viral arteritis, an Arterivirus that causes fetal autolysis and myocardial arteritis; *Streptococcus zooepidemicus*, which causes fetal autolysis and fibrinonecrotic placentitis around the cervical star; *Leptospira* sp., which also causes fetal interstitial nephritis; nocardioform abortion due to *Crossiella equi* occurring in late gestation, which causes necrotizing placentitis involving the base of the uterine horns; and *Salmonella* sp., most commonly *S. typhimurium* and rarely *S. abortus-equi*; causing maternal septicemia and fibrinonecrotic placentitis. Other bacteria such as *E. coli*, *Streptococcus equi*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Actinobacillus equuli*, and *Klebsiella pneumoniae*, as well as late gestational fungal infection by *Aspergillus fumigates*, *Mucor* sp., *Candida* sp., and *Histoplasma capsulatum* can cause abortion due to necrotizing placentitis.[7] Mare reproductive loss syndrome, associated with the eastern tent caterpillar (ETC) and possibly the result of non-beta-hemolytic *Streptococcus* and *Actinobacillus* spp. infection or a toxin related to the ETC, is another potential cause of equine abortion.[8]

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