Neuropathology:
Brian Summers

CASE #1
History: at 3 months of age the dog had diarrhea, otitis, and dermatitis responded to treatment 2 weeks prior to admission he was noticed to have difficulty walking, the gait was clumsy. He occasionally fell and became unable to get up a few days prior to admission.

Exam revealed an alert and responsive dog with normal cranial nerves, he could stand up on his thoracic limbs but not his pelvic limbs. When held up there was no voluntary movement of the left pelvic limb and occasional movements of the right pelvic that were delayed in onset and ataxic. He had a mildly paretic/ataxic left thoracic limb and his right thoracic limb was normal.

Postural reactions were absent in LH / slow in RH / slow in LF / normal RF
All affected limbs had normal to increased tone and no atrophy
Patellar reflexes were +2 - +3 / flexor reflexes were normal / nociception was normal
Vertebral column palpated normal and no pain was elicited upon palpation.

Anatomic Diagnosis:
T3 – L3: because the hind limbs had normal to increased tone but slow/absent post reactions
C1 – C6 – medulla: because the left forelimb had slow post reactions and had normal to increased tone
Left > right because the left side was more affected than the right side

Differential diagnosis:

Inflammatory disease in the canine Central Nervous System (ENCEPHALOMYELITIS)

1. Canine distemper
   a. inclusion bodies in astrocytes
2. Protozoal disease
   a. encysted organisms / contracted limbs / necrosis with severe loss of recognizable neural tissue
3. Fungal disease (cryptococcosis)
   a. visible in the CSF, organism with thick capsule stains with PAS surface oriented
4. Granulomatous meningoencephalomyelitis (GME)
   a. vessel oriented
   b. whorling about vessels mostly in white matter
5. Pug dog encephalitis (Maltese)
   a. lesion goes from grey matter to extend into the white matter
   b. predominately in the prosencephalon
6. Necrotizing encephalitis of Yorkshire terriers
   a. cavitating lesions taking out deep white matter
   b. leaving grey matter alone
7. Immune mediated, steroid responsive meningitis, meningeal polyarteritis
   a. discolored CSF with neutrophils eating RBCs
   b. increased CSF IgA
8. Other mycotic infections in the CNS
   a. Pyogranulomatous
i. giant cells – look for organisms
ii. aspergillus/coccidiodes/blastomyces/cladosporium

9. Rickettsial meningoencephalitis
10. Neoplasia

Clinical Pathology:
CSF Tap: 4-12 w/cmm and 45-53 mg/dl
mononuclear cells

Protein without a lot of cells // humoral cytological dissociation should be no more than 20-25mg protein

I. Canine distemper:
   a. multisystem disease affecting lymphoid tissue and respiratory, alimentary, urogenital, and central nervous systems
   b. CNS is thought to be infected in up to 100% of cases but many do not show clinical CNS signs
   c. There are two forms of the CNS disease
      i. white matter
      ii. grey matter
   d. regardless of the form of canine distemper virus there is always a transient white matter portion of the disease
      e. Many will clear this but others will become persistently infected

II. Grey matter disease:
   a. neuronal degeneration
      i. pyknosis, chromatolysis, satellitosis, neuronophagia – middle laminae in the cerebral cortex
      ii. gliosis – microglia, astroglia
      iii. vascular hyperplasia – endothelial and adventitial (pericyte) cell hypertrophy
      iv. meningitis – nonsuppurative
      v. eosinophilic inclusions – INTRANUCLEAR (or intracytoplasmic) in astrocytes, neurons, ependyma
   b. The grey matter form produces lesions in the cerebral cortex (laminar), brain stem, and spinal cord
   c. Most common form in:
      i. Infection of puppies 6-12 weeks of age
      ii. Specific strain of virus that is grey matter tropic such as the SNYDER HILL strain (in any age of animal)
      iii. Post vaccinal disease (vaccine causes the disease) mainly pontine lesions with abundant inclusions

III. White matter disease:
   a. primary demyelination with axonal sparing
   b. some axonal injury occurs also.
   c. The demyelination is initially noninflammatory (occurring in the absence of lymphocytic / plasmocytic perivascular cuffing)
   d. the lesions contain hypertrophic reactive astroglia some of which are virus infected and may form syncytia.
   e. The mechanism for the demyelination is unclear – it is difficult to show infected oligodendrocytes (infection in oligodendrocytes does not produce inclusion bodies because it appears the the virus can not replicate in the oligodendrocyte – infection still injures them but the do not readily appear infected) dog that die suddenly
may die with noninflammatory demyelination, dogs that have a more chronic course will develop nonsuppurative inflammatory demyelination (perivascular cuffs that are lymphocytic/plasmocytic). Some of the dogs with white matter disease will develop necrotizing encephalomyelitis in which the nonsuppurative inflammation that follows the initial primary demyelination causes necrosis due to the inflammatory response

Most of the time do not see gross lesions if severe may see cavitations

Characteristics = patchy lesion // white matter & grey matter forms // most common is lesion of primary demyelination and inflammation → inflammation itself causes problems

Most inflammation in white matter

Perivascular cuffing typical of viral encephalomyelitis Don’t try to identify all of these cells. Cells on the edges are glitter cells cleaning up necrotic debris - non suppurative disease myelin loss may be from initial viral disease or may be due to the inflammation

Inclusion body of canine distemper → astrocyte nucleus
In white matter form of disease the disease attacks where the CSF is in contact with the white matter. A great spot is in the cerebellar peduncles (pure white matter) and optic tracts, and spinal cord (all white matter surface).

profound loss of myelination in the cerebellar peduncle, with a couple of perivascular cuffs.

Perivascular cuff with inflammatory cells and necrosis. Loss of myelin.
Optic tract lesions loss of myelin
Along with crus cerebri (below)

Inclusion bodies in astrocyte nucleus with cytoplasmic processes

White matter versus grey matter –
1. Age of animal
2. Immune status of animal
3. Strain of virus
Grey matter disease form of distemper
50% have acute polioencephalitis which is fatal
50% recover
White matter disease form of distemper
33% have subacute demyelinating encephalitis which is fatal
33% have chronic demyelinating encephalitis
33% recover
GFAP (GLIAL FIBRILLARY ACIDIC PROTEIN) stain showing reactive astrocytes

GFAP stain is good to check for fibrosis (chronic encephalitis) / reactive astrocytes / astrocyte neoplasms

Syncytial formation of astrocytes - product of the canine distemper virus disease (in the middle of the slide) GFAP stain
Immunocytochemistry to pick up viral particles - most astrocytes infected oligodendroglial infected cells function is screwed up but the virus does not replicate in them

Choroid plexus – viral particles (immunocytochemistry)

Fornix of hippocampus showing profound demyelination