CANADA WEST
VETERINARY SPECIALISTS

SMALL ANIMAL CASE STUDIES IN CLINICAL NEUROLOGY

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ANATOMIC DIAGNOSIS

Brain: Prosencephalon, Pons-Medulla, Cerebellum
Cranial nerves

Spinal Cord: C1-C5: UMN/GP all four limbs
C6-T2: LMN thoracic limbs, UMN/GP pelvic limbs
T3-L3: UMN/GP pelvic limbs
L4-S1: LMN pelvic limbs
S1-Cd: LMN tail, anus, perineum, excretions

Nerves: Radial, Femoral, Sciatic

DIFFUSE LOWER MOTOR NEURON DISEASE (LMN)

Polyradiculoneuritis

Tick Paralysis

Botulism

POLYRADICULONEURITIS: MOLECULAR MIMICRY

Molecular mimicry is a presumed basis for the immune-mediated inflammation in polyradiculoneuritis. The patient is exposed to an antigen that is similar to a component of either the myelin or axon within its nerves. This would include such components as galactocerebrosides or glycolipids. Antibodies made against the exogenous antigen attack and destroy the patient's antigen (axon and/or myelin). In humans, this has occurred in patients exposed to Campylobacter jejuni, Mycoplasma pneumoniae, Cytomegalovirus and Epstein Barr virus.In dogs, especially coonhounds, the raccoon saliva is the presumptive source of the common antigen. The disease can be reproduced only in recovered dogs with the intradermal injection of raccoon saliva. This suggests that for this disease to develop, in addition to exposure to the appropriate antigen

there needs to be some alteration of the patent's immune system as well. Be aware that this polyradiculoneuritis can occur in dogs without exposure to a raccoon where the nature of the common antigen is unknown.

CANINE C1-C5 ANATOMIC DIAGNOSIS- PROGRESSIVE COURSE DIFFERENTIAL DIAGNOSIS

Compressive myelopathy:
Vertebral Stenosis:
Malformation/Malarticulation: congenital, acquired.
OCD may be involved in the development of the vertebral stenosis and malformation of the articular processes.
Malarticulation leads to degenerative joint disease that involves both the intervertebral disks as well as the articular processes.

C2-C3 meningeal fibrosis often accompanied by syringohydromyelia.
Diskospondylitis
Intervertebral disc extrusion
Neoplasia-extraparenchymal
Myelitis
Parenchymal neoplasm

ROTTWEILER: INHERITED DEGENERATIVE NERVOUS SYSTEM DISORDERS:

1. Neuroaxonal dystrophy: 1 to 2 years, cerebellar signs.
2. Leukoencephalomyelopathy- a primary demyelination: 1.5 to 3.5 years, C1 to C5 signs.
3. Motor neuron disease: 1 month, all lower motor neuron (LMN) signs, no dyspnea.
4. Myopathy-Duchenne type muscular dystrophy, a dystrophinopathy: 2 months, muscle disorder, no dyspnea but sialosis and difficult prehension.
5. Polyneuropathy-axonopathy: 2 months, LMN tetraparesis, inspiratory dyspnea, cataracts.
6. Distal neuropathy-axonopathy: adults 1-4 years, LMN signs, no dyspnea.
7. Encephalomyelopathy-polyneuropathy:
[Neuronal vacuolation, spinocerebellar degeneration: Kortz 1997
1 to 2 months, initially either inspiratory dyspnea or tetraparesis and ataxia (UMN/GP) or both at once; dysphagia, megaesophagus, cerebellar-vestibular signs, cataracts, microphthalmia also reported.

NEPHROBLASTOMA

Nephroblastoma is an embryonic renal neoplasm that in children most commonly occurs in the kidney but in dogs most commonly occurs in the subarachnoid space between the T10 and L2 spinal cord segments. The age range is from a few months to about 3.5 years. In children this is referred to as the Wilm tumor. It is associated with a gene mutation on chromosome 11. Immunocytochemical studies using antibodies prepared against the protein product of this mutated gene, reveal that the canine tumor exhibits a positive stain. Reports in the 70s and 80s mistakenly identified this canine neoplasm as an ependymoma. Recovery follows surgical removal but the tumor readily grows back indicating the need for postsurgical radiation therapy.

CANINE DEGENERATIVE MYELOPATHY (DM)
MULTISYSTEM CENTRAL AND PERIPHERAL AXONOPATHY.

(J. Coates, D. O'Brien-U.MO)

Affected dogs have a missense mutation in the SOD 1 gene. SOD is superoxide dismutase, a cellular antioxidant that converts the toxic oxygen radicle to H2O2 and oxygen.

Onset of DM is 5 years or older and is slowly progressive over years. Four stages have been recognized by the University of Missouri investigators.

1. Pelvic limb upper motor neuron (UMN) paresis and general proprioceptive (GP) ataxia.

2. Non-ambulatory pelvic limbs to paraplegia with reflex loss in pelvic limbs, mild muscle atrophy and some incontinence.

3. LMN paraplegia, thoracic limb paresis and ataxia.

4. LMN tetraplegia with severe atrophy, mild dysphagia and paretic tongue.

In all of my experience, I never saw a dog with this disorder that was diagnosed at autopsy that had exhibited thoracic limb signs or lower motor neuron signs in the pelvic limbs. In this list, my patients only exhibited stage one clinical signs. This may be due to a shorter period of clinical signs in my patients prior to euthanasia and autopsy.

DNA test for SOD-1 mutation is available through the Orthopedic Foundation of America (OFA).
Results: 1. Clear: 2 normal copies of the gene
2. Carrier: 1 mutated copy of the gene
3. At risk: 2 mutated copies of the gene; NOT ALL are affected.

Breeds affected: German Shepherd Dog, Pembroke Welsh Corgi, Chesapeake Bay Retriever, Rhodesian Ridgeback.

DM is being studied as a possible animal model for Amyotrophic Lateral Sclerosis (ALS-Lou Gehrig disease) in humans. The amyotrophy refers to the lower motor neuron degeneration and resultant denervation muscle atrophy. The sclerosis is the spinal cord white matter degeneration of the lateral corticospinal tract secondary to motor cortex neuronal degeneration. A small percentage of humans with ALS have a mutation in their SOD-1 gene. In other patients, the cause is unknown. In these dogs with DM, primary motor neuron cell body degeneration has not been found although degeneration is present in many nerves in these old dogs. The "sclerosis" that is present is widespread in many spinal cord tracts including both upper motor neuron and sensory pathways. The horse is a model for ALS based on the lower motor neuron degeneration which is caused by deficiency of the antioxidant, Vitamin E.

EQUINE MOTOR NEURON DISEASE

The chief complaint is often loss of weight despite a good appetite because the weight loss is due to the extensive denervation muscle atrophy. In addition, poor performance, excessive recumbency, excessive sweating, shifting weight when standing, preference to walk rather than stand and muscle fasciculations are observed. Clinical signs slowly progress. These patients are often housed in a stall or dry paddock with no green feed or grain which leads to a deficiency in Vitamin E.

This is a primary degeneration of neurons that innervate Type 1 postural muscles with their high oxidative metabolism. Oxidative stress is from deficiency of antioxidants: vitamin E and superoxide dismutase (SOD 1). No SOD 1 gene mutation has been found in the affected horse. EMND can be produced by a diet deficient in vitamin E for 14 months or more. Clinical signs occur when 30% or more of the motor neurons are depleted.

RADIAL NERVE - FEMORAL NERVE

Loss of function of these two nerves results in loss of weight support in the thoracic limb (radial nerve) or pelvic limb (femoral nerve). Protraction of these limbs is normal but when the limb is placed on the bearing surface and expected to support weight, it collapses due to inability to extend the elbow or stifle, respectively. This results in a short stride in the affected limb as the patient depends on the opposite limb for its weight support. Nociception is compromised on the cranial surface of the antebrachium or dorsal surface of the forepaw for the radial nerve and the medial surface of the crus and hind paw for the femoral nerve where the skin is innervated by its saphenous nerve branch .

SCIATIC NERVE

Sciatic nerve dysfunction is characterized by the preservation of weight support and a protraction of the limb which is uninhibited due to the loss of hip extensor muscle function. Thus, hip flexion is brisk and the patient may exhibit a skipping form of gait. Stifle flexion is reduced and both extension and flexion of the tarsus and digits is compromised. This is evident when the patient bears weight and a passive overflexion of the tarsus ("a dropped hock") is exhibited (tibial nerve) and occasionally the patient will bear weight on the dorsal surface of the paw due to the loss of tarsal flexion and digital extensor function (fibular –peroneal nerve). Nociception will be compromised on the cranial, lateral and caudal surfaces of the crus and dorsal, lateral and plantar surfaces of the pelvic limb paw. These surface areas are innervated by the tibial and fibular branches of the sciatic nerve.

Be aware that rupture of any component of the common calcanean tendon can result in a " dropped hock" posture identical to that caused by a sciatic/tibial nerve dysfunction. This includes the gastrocnemius tendon, the tendon of the superficial digital flexor and an extension of the tendon of the biceps femoris laterally and the semitendinosus and gracilis medially. The specific tendon rupture can be defined with MR imaging.

INHERITED POLYNEUROPATHY IN LEONBERGERS – D. SHELTON

The Leonberger dog is a product of breeding Newfoundland, Great Pyrennes and Saint Bernard dogs.

The polyneuropathy onset of clinical signs is 1 to 3 years with inspiratory dyspnea, overflexed tarsus ("dropped hocks") and walking with overflexion of the hips. Be aware that the inspiratory dyspnea may precede the evidence of a gait disorder which may influence your therapy. The gait disorder progresses over months to years to tetraparesis. This is inherited as an autosomal recessive gene but the specific genetic mutation is still being studied. This disorder is more common in males.

AORTIC VASCULAR COMPROMISE IN CATS

Caudal aortic thromboembolism only affects the blood supply to muscles and nerves of the pelvic limbs distal to the mid-thigh level. The blood supply to the lumbosacrocaudal spinal cord, tail, perineum and excretory orifices is unaffected due to the blood supply from the segmental lumbar arteries that branch from the abdominal aorta and this blood flow can bypass the aortic compromise. The spinal cord is unaffected. Muscle tone is normal in the muscles that control hip joint position and movement as well as the tail and excretory orifices. These cats can move rapidly along the ground by flexing their hips. This unique gait is characteristic of this disorder.

When cats have their abdomen compressed by the tire of a vehicle, the prolonged spasm of the lumbar arteries or possibly their thrombosis causes a poliomyelomalacia of the lumbar, sacral and caudal spinal cord segments. These cats have no muscle function or tone in their abdomen, pelvic limbs, tail, perineum or excretory orifices due to the necrosis of the spinal cord ventral grey columns. These same regions are also usually analgesic due to the necrosis of the dorsal grey columns. This same spinal cord lesion and clinical signs will result when the aorta is ligated in the region of the renal arteries.

DIFFUSE MYELOMALACIA

This spinal cord lesion most commonly is associated with a very small percentage of dogs that have an acute severe intervertebral disk extrusion between T10 and L3 that causes a severe focal transverse spinal cord necrosis and hemorrhage. This results in rapid paraplegia and pelvic limb analgesia. At the onset, the paraplegia reflects the loss of upper motor neuron function with hypertonia and hyperreflexia. In a small percentage of these dogs, 1 to 3 days later (occasionally longer), there is a rapid complete loss of muscle tone, spinal reflexes and nociception in the pelvic limbs followed by the tail and perineum and then the abdomen and thorax. In a few days these dogs are totally recumbent and have lost tone and reflexes in the thoracic limbs. This diffuse loss of lower motor neuron activity is associated with a loss of nociception evidenced by analgesia of the entire body caudal to the thoracic limbs and neck. If the myelomalacia extends into the cervical spinal cord, the dog will die from respiratory paralysis. These dogs often exhibit discomfort when handled in the area of the thoracic limbs and neck. These dogs are readily recognized by their clinical signs and are NOT candidates for any ancillary procedures. Surgical decompression at the time of the initial injury will not prevent the development of this diffuse myelomalacia.

The cause of this unique lesion is unknown but may involve an individual variation in the major arterial blood supply to the thoracolumbar spinal cord from the intercostal or lumbar arteries. This progressive myelomalacia may result when a major spinal cord arterial supply is compromised by the intervertebral disc extrusion.

MUSCLE DISORDERS
LABRADOR RETRIEVER INHERITED POLYMYOPATHY

There are at least four inherited myopathies in LabradorRetrievers:

1. Centronuclear polymyopathy:

This has been referred to as centronuclear myopathy, Type II fiber deficiency, or autosomal recessive muscular dystrophy. This is NOT a muscular dystrophy which indicates muscle cell degeneration (necrosis) and regeneration. In this inherited polymyopathy, a gene mutation has been identified that is associated with abnormal muscle cell tubules. Onset of tetraparesis is at 2 to 3 months old and the clinical signs slowly progress to 9 to 10 months of age; most dogs remain ambulatory but paretic and have a normal life span. There is no dyspnea or dysphagia,. Muscle serum enzymes are normal to slightly elevated. This is inherited as an autosomal recessive gene.

2. X-linked myotubular myopathy:

This occurs in male Labrador Retrievers with an onset of signs at 7 to 14 weeks of age. Clinical signs include a progressive short choppy stride and muscle atrophy, A flexed vertebral posture with a low head carriage is present. Patellar reflexes are absent. Recumbency may occur after 3 or 4 weeks of progressive paresis. In severely affected puppies there may be difficulty in mastication along with abnormal laryngeal and esophageal function. Serum creatine kinase levels are normal or slightly elevated. EMG exhibits non-specific positive sharp waves and fibrillations. The mutated gene normally codes for a myotubular protein.

3. DYSTROPHINOPATHY:

Duchenne type muscular dystrophy. This is a sex-linked recessive, spontaneous mutation. Therefore male dogs of many breeds are affected. The onset of tetraparesis occurs at 1 to 2 months of age along with dysphagia with excessive drooling and limited range of mouth opening. Both muscle atrophy and hypertrophy are observed in different muscle groups. In addition, a myotonia occurs and contributes to the stiffness observed in the gait. A marked elevation of serum muscle enzymes is present.

4. EXERCISE INDUCED COLLAPSE
DR. SUSAN MERIC TAYLOR, UNIVERSITY OF SASKATCHEWAN.

The onset of this disorder occurs at 7 months to 2 years in muscular, excitable, aggressive field trial Labrador Retrievers engaged in strenuous activity with a high level of excitement. After a brief period of vigorous exercise of 5 to 15 minutes, the affected dog starts to collapse in the pelvic limbs but does not become short-strided. The dog struggles to continue moving but loses its ability to stand and collapses usually in sternal recumbency. As they struggle to stand, they often show a loss of balance and fall to one side. When collapsed, the pelvic limbs are hypotonic and patellar reflexes

are absent. For 3 to 5 minutes after the end of the exercise they often get worse. In severe cases, all four limbs are affected. After 15 to 20 minutes of rest, complete recovery occurs.

The anatomic diagnosis is not clear. It is unlikely to be solely neuromuscular as these dogs are not short-strided and some evidence of balance loss is present. It seems likely that the collapse reflects some loss of caudal brainstem UMN facilitation of the central pattern generators and includes some deficiency of vestibular nuclear function. Significant hyperthermia (107-108F) and panting are present in these collapsed dogs which is similar to normal Labrador Retrievers that do not collapse. All ancillary metabolic studies are normal. No lesions of the nervous or musculoskeletal systems are observed at autopsy.

Genetic studies have determined that this syndrome is inherited as an autosomal recessive disorder. A mutation in the dynamin 1 (DMN1) gene has been identified in affected dogs. DMN1 is a protein involved in repackaging neurotransmitters into synaptic vesicles for release in the brain and spinal cord and is required when there is an increase demand for neurotransmitters as occurs during intense exercise. DNA testing for this gene can be obtained at the College of Veterinary Medicine at the University of Minnesota.

Be aware that if dogs with this disorder are excessively exercised, they may collapse and die.

INFRASPINATUS CONTRACTURE

This occurs primarily in hunting dogs that are in the the field and step in a depression or hole that causes them to overextend one thoracic limb. The

distal end of the spine of the scapula is adjacent to where the tendon arises from the infraspinatus muscle. Overextension of this joint forces the distal end of the scapula into the infraspinatus muscle-tendon junction causing injury to that muscle. The affected dog walks lame for a few days, followed by a period of normal gait. After a few weeks to months, this dog will develop an unusual posture and action in that thoracic limb but without any evidence of discomfort. When the dog bears weight on standing, the humerus at the shoulder is partially rotated laterally which positions the elbow more medially under the thorax. When the dog protracts the limb to walk and the affected limb is not weight bearing, the humerus suddenly further rotates laterally causing the elbow to assume a more medial position. The paw will appear to be positioned more laterally during the stride. All of this is the result of the healing of the torn infraspinatus muscle which resulted in fibrosis and a shortening of the muscle. This shortened muscle causes a passive but persistent excessive lateral rotation of the humerus at the shoulder joint and the characteristic gait that represents this disorder. If you stand over this affected dog when it is bearing weight on both thoracic limbs, grasp both brachia and rotate them medially and laterally, you will feel resistance to medial rotation of the humerus at the shoulder of the affected limb. Surgical removal of the fibrotic portion of this affected infraspinatus muscle should correct the abnormality.

FIBROTIC MYOPATHY OF THE CAUDO-MEDIAL THIGH MUSCLES

This is the name of a disorder that is poorly understood. It is most common in large breed working dogs, especially the German Shepherd Dog. The pelvic limb gait disorder is usually a subtle change unassociated with any recognized traumatic experience or any discomfort in the use of

the affected pelvic limb. When these affected dogs walk, at the end of the protraction (swing) phase of the affected pelvic limb, the paw is abruptly slightly elevated as the stride is prematurely stopped and it is turned slightly medially. This medial rotation of the leg and paw can be seen at the stifle. This is considered to be due to a fibrosis of a caudomedial thigh muscle that inserts on the proximomedial surface of the tibia. The fibrosis is thought to be due to an injury of the affected muscle followed by healing with fibrosis that resulted in a shortened muscle. Most commonly the gracilis and semitendinosus muscles have been implicated. This might occur following intramuscular injections of large volumes of drugs into these muscles but most of these dogs do not have this history and the onset of clinical signs is usually insidious. Surgical removal of a portion of the affected muscle has had variable success as the clinical signs have often recurred a few weeks to months postoperatively.

On two occasions, surgeons have submitted the muscle that they removed for study and in each dog, on one side of the muscle specimen, a prominent longitudinal band of collagen was present in the epimysium with no lesion in the muscle itself. Why and how this band of connective tissue develops remains an enigma. From a practical viewpoint, if you make this diagnosis, consider leaving the dog alone as this band does not cause obvious discomfort or interfere with their physical activity at all.

PERIPHERAL VS. CENTRAL VESTIBULAR SYSTEM CLINICAL SIGNS

A lesion limited to the vestibular nerve causes a head tilt, loss of balance and an abnormal nystagmus. There is no paresis and no general proprioceptive ataxia. The affected dog knows exactly where its limbs are located and can generate very fast normal limb movements to help compensate for its loss of balance. Postural reactions are normal. Lesions in the caudal brainstem (pons and medulla) that affect the vestibular nuclei also cause a head tilt, loss of balance and abnormal nystagmus. However, these lesions also usually affect the adjacent tracts and reticular formation nuclei which results in a variable degree of upper motor neuron paresis and general proprioceptive ataxia. Postural reactions are abnormal. Cranial nerve involvement other than VII and VIII also implicates a brainstem anatomic diagnosis

A unique form of central vestibular disease is referred to as paradoxical vestibular syndrome in which the head tilt and balance loss are directed toward the side opposite to the central lesion which usually involves one caudal cerebellar peduncle. An explanation for this paradox is based on the rule that the direction of the head tilt and balance loss is towards the side of least vestibular system activity. With peripheral vestibular system disorders such as otitis interna, the loss of facilitatory activity of vestibular nerve axons results in decreased activity of the ipsilateral vestibular nuclei. The head tilt and balance loss are directed towards this decreased vestibular nerve activity. In the cerebellum, the Purkinje neurons of the flocculus and nodulus are unique in that instead of projecting to a cerebellar nucleus, these inhibitory neurons project directly via the caudal cerebellar peduncle to the ipsilateral vestibular nuclei. When this pathway is interrupted, the overactive, disinhibited vestibular nuclei cause a head tilt and balance loss directed to the opposite side.

CEREBELLAR CORTICAL ABIOTROPHY

Cerebellar cortical abiotrophy is most common in dogs and in most breeds consists of a progressive premature degeneration of Purkinje neurons as the primary lesion. In most breeds the clinical signs are first observed at a few weeks of age and progress at a variable rate. Advanced lesions can be recognized on T2W median plane images where the sulci between dorsal vermal folia are enlarged secondary to the atrophy of the cerebellar cortex. In the Kerry Blue Terrier and Chinese Crested breeds, following the clinical signs of Purkinje neuronal abiotrophy, other systems in the brain degenerate which is the basis for this being called a multiple system degeneration in these two breeds. A late onset of many years before clinical signs of Purkinje neuronal degeneration is recognized has been reported in the Gordon Setter, Old English Sheepdog, Scottish Terrier, American Staffordshire Terrier, and Brittany Spaniel. At the onset the clinical signs are subtle and they progress slowly. In many of these breeds a genetic mutation has been identified and genetic testing for the identification of carrier animals is available. When the clinical signs of cerebellar ataxia are subtle in the early stages of the abiotrophy, we have found that having the patient climb or descend stairs will markedly exacerbate the ataxia.

SCOTTIE CRAMPS VS. CEREBELLAR CORTICAL ABIOTROPHY

Scottie cramps is an example of a movement disorder which is defined as an episodic, uncontrolled, involuntary contraction of various muscle groups in a conscious patient with a normal sensorium during rest or activity. In the Scottish Terrier this has been related to an abnormal metabolism of serotonin resulting in a decrease in its activity. In subtle cases, methysergide, which blocks serotonin receptors, will increase the incidence and severity of the clinical signs. This disorder is inherited as an autosomal recessive gene. This is an episodic disorder associated with activity.

In cerebellar cortical abiotrophy, the clinical signs may be subtle but are ALWAYS present whereas the clinical signs in Scottie cramps are EPISODIC and associated with activity. In addition, the cerebellar ataxia will be exacerbated when the dog goes up or down stairs.