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CLINICAL SIGNS
Degenerative Myelopathy, which was initially also called chronic degenerative radiculomyelopathy, has first been described in the aging German Shepherd dog in 1973. Since then, it was observed in several other canine large breeds such as Bernese Mountain dog, Boxer, Chesapeak Bay Retriever, Collie, English Mastiff, German Shepherd Mix, Irish Setter, Irish Terrier, Kerry Blue Terrier, Kuvasz, Labrador Retriever, Old English Sheepdog, Siberian Husky, and Rhodesian Ridgeback. In our own experience it can be seen in the Hovawart and other retriever breeds too. The estimated prevalence of the disease in the breeds most commonly affected is 2.01% in German Shepherd dogs and 1.51% in Chesapeak Bay Retrievers. The Pembroke Welsh Corgi seems to be the only small breed affected more frequently by this condition, whereas as it is rare in other small breed dogs (Miniature Poodle) or cats. The name Degenerative Myelopathy is a fairly broad term from the neuropathological point of view and may actually include other degenerative spinal cord diseases. However, we will continue to use this term here, since it is a clinically well established name for the degeneration of certain spinal cord tracts in the aging dog of predominately large breeds.

The condition is best described in the German Shepherd dog, where it usually affects dogs older than 5 years (mean 9.6 years). The initial clinical signs are very unspecific and they can be erroneously misinterpreted as being caused by chronic orthopedic disease such as hip dysplasia. Dogs seem to be unstable in the rear limbs progressing to obvious rear limb ataxia with reduced conscious proprioception later on. Signs can be waxing and waning but usually progress over a few months. Clinical signs usually reflect a bilateral upper motor neuron lesion. However, some lateralization can be seen. Segmental spinal reflexes are usually normal or exaggerated, but in about 15% of case reduced patellar tendon reflexes (unilateral or bilateral) have been observed. Femoral nerve pathology was identified in several dogs, even though it is not clear if those changes reflect extension of the disease to the femoral nerve interfering with the sensory part of the reflex arc or if it represents a coincidental nerve pathology as it can be seen in older dogs. The later explanation could be supported by the known fact that about on third of dogs older than 9 years have uni- or bilaterally reduced flexor reflexes even without any other obvious neurological deficits. Once clinical signs progress, paraparesis becomes obvious, but it is still combined with ataxia, being often more severe than in dogs with compressive spinal cord lesions. Impairment of urinary and fecal control seems to be less common than in other spinal cord diseases. Progression usually leads to euthanasia within one year of establishing diagnosis.

Degenerative Myelopathy has also been described in two young German Shepherd dogs of 6 and 7 months of age with a 3 and 5 week history of progressive neurological deficits in both rear limbs of the upper motor neuron type. Both dogs had a normal conscious proprioception in the rear limbs tested by paw positioning, whereas the hopping reaction was reduced. It is not known yet if this disease in young German Shepherd dogs truly reflects a variation of the Degenerative Myelopathy in older dogs or if it is a rather completely different entity.
Degenerative Myelopathy has been described in 2 Boxer dogs of (9 and 10 years of age). Both showed a typical slowly progressive upper motor neuron paraparesis. In contrast to German Shepherd dogs, both Boxer dogs had absent patellar tendon reflexes in both rear limbs.

Another report describes a similar condition in 3 related Siberian Husky dogs at an age of 12 to 14 years. Clinical signs were similar as described for German Shepherd dogs. Imaging diagnostics did not reveal any lesion, but CSF analysis showed slight pleocytosis and a mildly elevated protein concentration in one dog. Histopathological changes consisted of disseminated vacuolation of the white matter at all levels of the spinal cord, with the thoracic segments being most severely affected. The fact that three related Huskies were affected suggests a hereditary etiology.

The Pembroke Welsh Corgi is the only small breed where Degenerative Myelopathy is seen more frequently. Those dogs tend to develop clinical signs between 9 and 15 years of age (median: 11 years). Total duration of clinical signs before euthanasia ranges from 10 to 37 months. With a few exceptions, clinical signs are similar as seen in German Shepherd dogs. Progression of the disease to paraplegia, which is rare in German Shepherd dogs, seems to be more common. In addition, some dogs may show mild front limb involvement, even though not resulting in obvious gait abnormality. Results of histopathological examination are similar as in German Shepherd dogs. Segregation analysis revealed a familial tendency. More recently, a genome-wide association analysis revealed a mutation in the superoxide dismutase 1 protein in affected Welsh Corgis, similar as in humans with multiple sclerosis.

**HISTOPATHOLOGY**

Histopathological changes mostly restricted to the white matter are consistent between dogs and affect ascending and descending tracts of the cervical, thoracic and lumbar spinal cord to a varying degree. Lesions involving all funiculi, except the fasciculus proprius, are most severe in the middle to lower middle thoracic region. Generally lesions are not symmetric with respect to distribution and intensity. Lesions are characterized by demyelination, axonal loss and associated astrogliosis. Both, motor and sensory tracts are involved. In addition, mild neuronal loss can be seen in the dorsal spinocerebellar tract. Pathology may extend into the dorsal rootlets were individual axons and myelin sheaths are lost. The theory that Degenerative Myelopathy may be a dying-back phenomenon was rejected based on spinal cord morphometric studies. Others have reported associated changes, including chromatolysis, gliosis and neuronal loss in the red nucleus, the lateral vestibular nucleus and, sometimes in the dentate nucleus. It was suggested that those intracranial changes are caused by Wallerian degeneration of ascending tracts. Following loss of their spinal connections, brain motor neurons may undergo retrograd axonal reaction.

Histopathological changes in the two young German Shepherd dogs varied slightly from the description above. Degeneration was limited to the white matter of the ventral and lateral funiculi with relative sparing of the fasciculus proprius and no lesions in the dorsal funiculus. Histological changes were characterized by degeneration of axons and myelin, with some mild gliosis. In one case, there was mild evidence of additional axonal degeneration in the cerebellar white matter. Therefore, Degenerative Myelopathy in young German Shepherd dogs varies from the classical form in so far as all funiculi including the dorsal funiculus are affected in older dogs.
This difference explains why conscious proprioception was normal in the two young dogs, whereas it is usually reduced in older dogs.

ETIOLOGY

Several investigations have been undertaken to identify the underlying pathology, specifically in German Shepherd dogs. Autoimmune etiology has been suspected based on the observation of an impaired response to thymus-dependent mitogens. Immunohistochemical evidence for immunoglobuline and complement deposition was found in the spinal cord of German Shepherd dogs with Degenerative Myelopathy. However, there are no histopathological signs of any inflammation in those dogs. Others suspected a relative or absolute vitamin E deficiency. Attempts however, to identify a similar mutation as seen in humans diseased by Ataxia with Isolated Vitamin E Deficiency failed in German Shepherd dogs with Degenerative Myelopathy. Similar, vitamin B12 deficiency was investigated. One study found reduced vitamin B12 levels in 50% of German Shepherd dogs with Degenerative Myelopathy, but those dogs did not respond to vitamin B12 supplementation. Another study failed to identify a vitamin B12 deficiency in dogs with Degenerative Myelopathy.

DIAGNOSTICS

Definite diagnosis of Degenerative Myelopathy is established postmortem by histopathology. Therefore, diagnosis in living patients is challenging because of the lack of diagnostic test available at present. Clinical diagnosis in a living patient aims for excluding other conditions interfering with spinal cord function and collecting bits of information which are consistent with Degenerative Myelopathy.

In 1980, a possible association between Degenerative Myelopathy and an immune system dysfunction, a suppressor t-cell deficit, was investigated in order to develop an intra vitam test for Degenerative Myelopathy. Affected dogs had a reduced response of peripheral white blood cells to the cell mitogens concanavalin A and phytohemagglutinin. Based on those findings the Flash-test was developed testing for the existence of the 11021 allele of a gene being responsible for the MHC II function. The significance of those findings and their diagnostic value has not been established.

Imaging diagnostics including CT and MRI have traditionally been considered being helpful in excluding other likely differential diagnoses such as chronic type II intervertebral disc disease and neoplasias, but they are not able to diagnose Degenerative Myelopathy itself. More recently, CT myelography changes were described in 8 German Shepherd dogs with suspected Degenerative Myelopathy. Following parameters were smaller in dogs with Degenerative Myelopathy than in control dogs: spinal cord/dural sac ratio, spinal cord/vertebral canal ratio, vertebral canal/vertebral body ratio. In addition, those dogs showed signs of spinal canal stenosis and chronic disc disease more frequently than control dogs. The lack of histological confirmation warrants critical interpretation of those results, as done by the authors themselves. It is questionable if those results really describe CT characteristics in German Shepherd dogs with Degenerative Myelopathy only or if they are rather findings in dogs with suspected Degenerative Myelopathy and concurrent chronic spinal cord compression.
Dogs with Degenerative Myelopathy may have elevated protein on CSF analysis. The myelin basic protein in the CSF of dogs with Degenerative Myelopathy indicating demyelination is higher than in normal control dogs.

The mutation in the superoxide dismutase 1 protein (SOD1 protein), very recently identified in Pembroke Welsh Corgis, has been established as marker test for being at risk for developing Degenerative Myelopathy. The test is offered for all breeds by commercial laboratories. However, the SOD1-Protein-Test does not determine if the patient is currently suffering from Degenerative Myelopathy, but if he is at risk of developing clinical signs.

THERAPY

It has been widely accepted that there is no effective medical therapy for Degenerative Myelopathy even though occasionally aminocaproic acid has been recommended because of its antiprotease activity. Several other medications, including lipid statins, cyanocobalamin, alpha-tocopherol, and methionin have been tried without any proven benefit so far. Intensive physiotherapy seem to be effective in prolonging time of being ambulatory in dogs with Degenerative Myelopathy.

REFERENCES