Mac. Vet. Rew. Vol 33, No. 1, 33 - 37, 2010

Original article

УДК: 637.7.09:616.8-003.8

DEGENERATIVE MYELOPATHY IN DOGS

Nikolovski Goran.[1], Atanaskova Elena.[1]

[1]*Department of internal diseases in companion animals and horses,*
Faculty of Veterinary Medicine in Skopje
e-mail: gnikolovski@fvm.ukim.edu.mk

ABSTRACT

One of the chronic progressive disorders of the spinal cord in dogs is the degenerative myelopathy (DM). The most predisposed age in dog is 5 to 14 years, while rarely noted in younger, there is no gender predisposition. This disorder most commonly appears in dogs of the German shepherd breed, but it can appear in other breeds too. The main changes about this disease are degeneration of the myelin, especially in the thoracic-lumbar segments of the spinal cord and the dorsal nerve roots. The progression of the disease is slow and can last months to years. Undoubtedly, diagnosis is made by examinations of the CSF and establishing elevated level of protein segments.

Key words: *dog, degenerative myelopathy, CSF.*

INTRODUCTION

Spinal disruptions can be caused by anomalies, degenerative conditions, tumors, inflammations, external trauma, internal trauma as result of disc dislocation and infarction. One of the most common chronic progressive disruptions if the spinal cord in dogs is Degenerative myelopathy (DM). This disorder is characterized with myelin and axon loss, generally present in adult animals.

Degenerative myelopathy in dogs has been known for more that 35 years, mostly apparent in patients between 5 and 14 years, not often in younger dogs (1). At the beginning this disease was mend to be specific for German shepherds and was called German shepherd myelopathy (2). Later it had been named chronic degenerative reticulomyelopathy, because changes in nerve's roots were noticed, that was used as explanation of the present hyporeflexy (7). Latest examinations showed that DM can be present in other breeds too. The disease have been described in this breeds *Pembroke Welsh Corgi, Boxer, Rhodesian Ridgeback , English foxhound, Retriever, Jack Resell terrier, Afghanistan hound* and *Pyrenean Mountain dog* (3). In dog's DM there is no sexual predisposition; first clinical signs of the disease are related with covert progressive ataxia and paresis of the lower limbs, which in a period of 6-12 mounts leads to loss of ability to stand. (1, 2, 4). In this stage of the disease, examination of spinal reflexes indicates paresis of the upper motor neurons. It's typically the function of the higher limbs, the urinary and fecal incontinence are not present until the last stages (5).

Conventional diagnostic test for affected dogs are: radiography, myelography and cerebrospinal liquid analyses. Most sensitive diagnostic method for describing spinal morphology is computer tomography. (23)

The clinical parameters are generally in physiological ranges, except increased protein level in the

cerebrospinal fluid in the lumbar cistern. The proteins that are measured in the cerebrospinal liquor are: myelin basic protein *MBP* (17, 18), S-100 and C-reactive protein, which in the later phases is used for differencing the bacterial from viral meningoencephalitis (19, 20). Myelin basic protein had been examined by some authors, who revealed increased *MBP* concentration in cerebrospinal fluid taken from lumbar cistern from dogs with DM, but not in the cerebrospinal liquor from cistern magna (18). These findings showed that there are active demyelination changes in the spinal cord. In these studies is also confirmed the relation between *MBP* and the demyelination degree in the affected animals (18). These tests have limited availability and are still in phase of academic interest in the veterinary medicine.

Electromyography examinations revealed absence of lower motor affection encourages the localization of the process in the white matter of the spine. Spinal cord radiography, including myelography is normal in cases of uncomplicated DM. Unfortunately myelography can be associate with declining of the clinical signs and has certain risks for some patients.(9) Genetic, metabolic, nutritional, vascular and immune etiologic causes are suspected, but without evidence of specific pathogen mechanisms.

From many aspects DM has similarity with Multiplex sclerosis (MC) in the human population. Based on the latest information that refers to the MC, the conclusion is that DM is actually MC in dogs. (9)

CHARACTERISTICS OF THE CHANGES

On affected dog's necropsy, there are no macroscopic changes in the brain, spinal cord and peripheral nerves. Primary microscopic lesions are axons degenerations and axon loss. The degeneration is characterized with outspreading axons and myelin layers along the white matter. The degenerative changes that have been described in different dog breeds, refer to the white matter in the funiculus, dilatation of the myelin layer, inflating axons and proper fragmentation and phagocytosis of the axons and myelin fragments (5,7,8). Reducer blue coloring by Luxol confirms the myelin degeneration; changed astrocytes follow the degenerative changes. In the most of the studies in large breed dogs with DM, scattered single degenerations and fiber loss are described without group incorporation inside the follicular parts of the axon. (7,8,9). All white matter folliculus are affected, with predomination in the lateral and dorsal folliculus, mostly around T12 (10). The lesions of the spinal cord are not symmetric and are not limited. The pathological changes are more emphatic in the thoracic segments, and there is moderate degeneration in cervical and lumbar segments (11). The disease is thought to be sporadic and probably acquired.

Most of the DM studies in the large breed dogs described „scattered"individual fiber degenerations and loss without group axon loss in certain regions (9).

Clinical signs of DM include progressive ataxia, paresis and muscle atrophy of the lower limbs. Most dogs show little or no signs of spinal hyperpathia. There is still no effective treatment (3).

Routine hematologic and chemistry profiles (total protein, albumins, urea, ALT, AP) are in normal ranges. In certain examinations in affected dogs methionine deficiency and changes in methionine synthesis has been noticed, spatially in dogs fed with inner organs from ruminants (13).

The most of the necropsies revealed local hemorrhage and moderate enlargement in the 7 and 8 thoracic segment from the spine. Cross section of the enlarged parts reveals dark-red, friable tin bordered tissue; normal parenchyma repressed to Dura mater (12).

Dogs affected with DM have depressed lymphocyte blastogenesis. The depression of the immune cell response is in correlation with the clinical phase and severity of the disease. This suppression is present due to genesis of the circulating suppressor cells. The immunoglobulins are on the borders of the lesions in the spine in dogs with DM (9). Imunohistochemicals are proving of the immunoglobulins and deposition of the complement in the lesions of the spine reveals that these conditions are followed by disruption in the immune responses (15). Other investigations revealed that deficit of vitamin E can be the reason, although the latest information indicates that the genes of dog's α-tocopherol transfer proteins are involved in the DM pathogenesis in

German shepherd dog (16). Other study in Siberian hacky dogs indicates possible involvement of the hereditary factor (6).

Microscopic lesions of the nerve's tissue are content of wide spine demyelization, with higher lesions concentration in the thoracic-lumbar part of the spine. In the more affected regions, there is a reduced number of axons and higher number of astroglial cells and high density of teeny vascular elements. In some dogs there are similar lesions scattered in the white matter of the brain. In many patients plasma cell infiltrates are found in the kidneys through gastro-intestinal tract, provides evidence of immune failure -the reason for DM. (9)

THERAPY OPTIONS AND CONTROL OF THE DISEASE

There is no therapy for degenerative myelopathy in dogs, but there are some measures that can be undertaken in order to decrease and to detain the progression of the disease. Walking and swimming can help the animal to maintain the muscle tone and the brain function.

Medications that can help in detaining the process of the DM are aminocaproic acid (EACA) and n-acetilcistein (NAC). It is considered that the aminocaproic acid inhibits the deterioration of the myelin layer, while n-acetilcistein acts as antioxidant. Their application is not always successful (14). The application of prednisolon in the first 2 weeks of the disease can be useful, but also in the period of worsening of the clinical signs (22).

Beside the medications, it's very important the patient to be on special diet and vitamin and mineral supplement. Vitamins B complex are essential for the nerve function, vitamin C, E and selen have antioxidantive or protective function. Vitamins B6 and B12 help in maintenance and strength of the myelin layer, protecting the nerves from damages. Vitamin E and Se are known as antioxidants. The difference is that Se doesn't cross the blood-brain barrier, unlike the vitamin E. From other side Se helps the function of vitamin E (9,14). In many cases, acupuncture gives good results, placing the needles in the right place releases the pain (9).

In dogs affected by DM physical activity like walking and swimming has positive effect. Usual movement of the dogs on proper distance and known trace not only improves the muscle tone, but improves the brain function, which can be very useful in dogs suffering from senile dementia with DM (21).

CONCLUSIONS

Degeneration of the nerve tissue can appear as result of intoxication or metabolic disorder. Likely enough, many of the sporadic degenerative conditions are with unknown background or suspicious diseases with unproved familiar/congenital finding, are acquired toxic or metabolic diseases.

Generally, degenerative changes, including DM in dogs are relatively rear condition. After all these disorders have wide spectrum of changes, which basically are represents of important group of diseases. Degenerative myelopathy is very similar to MC in human and dogs are model for investigating of the pathogenesis of this disease. Sadly a little is known about this condition from clinical signs and clinical changes to pedigree relations (21). Newest diagnostic procedures are not available in practice; they can allow the veterinarians to research this disease on molecular level.

There is a number of evidence showing that in many nerve-degenerative conditions, including the DM, exist common courses of molecular changes that appears besides the clinical and morphological signs.

Characteristics of the disease on molecular level can help in the early diagnosis and opens odds for new therapeutic protocols.

REFERENCES:

1. Averill D.R. (1973.) Degenerative myelopathy in the aging German Shepherd dog: Clinical and pathological findings. *J Am Vet Med Assoc* 162: 1045-1051

2. Griffiths, I.R., Duncan, I.D., 1975. Chronic degenerative radiculomyelopathy in the dog. Journal of Small Animal Practice 16, 461–471.

3. Coates J.R et al. (2007) Clinical characterization of a familial degenerative myelopathy in Pembroke Welsh corgi dogs. *J Vet Intern Med* 21:1323-1331

4. Griffiths I.R., Duncan I.D. (1975) Chronic degenerative radiculomyelopathy in the dog. J Small Anim Pract 16(8):461-471

5. Clemmons R.M. (1989): Degenerative myelopathy. *In*: Current Veterinary Therapy X Small Animal Practice, ed. Kirk RW, pp 830-833, WB Saunders, Philadelphia, PA.

6. Bishcel P., Vandevelde M., Lang J., Kull-Hachler S (1983) Degenerative myelopathy in a family of Siberian husky dogs. J Am Vet Med Assoc 183(9): 998-1000

7. Braund K.G., Vandevelde M. (1978): German shepherd dog myelopathy a morphologic and morphometric study. Am J Vet Res 39 (8) 1309-1315

8. Johnston P.E.J., Knox K., Gettinby G., Griffiths I.R., (2001) Serum α-tochopherol concentrations in German shepherd dogs with chronic degenerative radiculonyelopathy. Vet Rec (148):403-407

9. R.M. Clemmons, DVM, PhD, Associate professor of Neurology & Neurosurgery Small Animal Clinical Science: Degenerative Myelopathy German Shepherd Dogs www.neuro.vetmed.ufl.edu

10. P. A. March, J. R. Coates, R. J. Abyad, D. A. Williams, D. P. O' Brien, N. J. Olby, J. H. Keating and M. Oglesbee: Degenerative myelopathy in 18 Pembroke Welsh Corgi dogs; Vet.Pathol 46:241-250 (2009)

11. E. MacKillop, N. J. Olby, K.E. Linder and T.T. Brown: Intramedullary Cavernous Malformation of the spinal cord in two dogs; Vet Pathol 44:528-532 (2007)

12. B.J. Sheahan, J.F. Cafferey, H.M. Gunn and J.N. Keating: Structural and Biochemical Changes in a Spinal Myelopathy in Twelve English Foxhounds and Two Harries; VetPathol 28:117-124 (1991).

13. Dawn M. Smith: Managing Degenerative Myelopathy in Dogs www.dog-care.suite101.com (2008).

14. Barclay, K.B., Haines, D.M., 1994. Immunohistochemical evidence for immunoglobulin and complement deposition in spinal cord lesions in degenerative myelopathy in German shepherd dogs. Canadian Journal of Veterinary Research 58, 20–24.

15. Fechner, H., Johnston, P.E., Sharp, N.J., Montague, P., Griffiths, I.R., Wang, X., Olby, N., Looman, A.C., Poller, W., Flegel, T., 2003. Molecular genetic and expression analysis of alpha-tocopherol transfer protein mRNA in German shepherd dogs with degenerative myelopathy. Berliner und MuËnchner TieraËrztliche Wochenschrift 116, 31–36

16. Summers, B.A., Whitaker, J.N., Appel, M.J., 1987. Demyelinating canine distemper encephalomyelitis: measurement of myelin basic protein in cerebrospinal fluid. Journal of Neuroimmunology 14, 227–233

17. Oji, T., Kamishina, K., Cheeseman, J.A., Clemmons, R.M., 2007. Measurement of myelin basic protein in the cerebrospinal fluid of dogs with degenerative myelopathy. Veterinary Clinical Pathology 36, 281–284

18. Fishman, R.A., Ransohoff, J., Osserman, E.F., 1958. Factors influencing the concentration gradient of protein in cerebrospinal fluid. Journal of Clinical Investigation 37, 1419–1424.

19. Stearman, M., Southgate, H.J., 1994. The use of cytokine and C-reactive protein measurements in cerebrospinal fluid during acute infective meningitis. Annals of Clinical Biochemistry 31 (Pt. 3), 255–261

20. S. Siso, D. Hanzlırcek, G. Fluehmann, I. Kathmann, A. Tomek, V. Papa, M. Vandevelde 2006. Neurodegenerative diseases in domestic animals: A comparative review The Veterinary Journal 171, p.p. 20–38

21. Smith, D.M. 2008, Managing degenerative myelopathy in dogs.

22. Polizopoulou Z.S., Koutinas A.F., Patsikas M.N., Soubasis N. 2008. Evaluation of proposed therapeutic protocol in 12 gods with tentative degenerative myelopathy. Acta Vet. Hungarica, Vol 56 No. 3 pp 293-301

23. Jeryl C. Jones, Karen D. Inzana, John H. Rossmeisi, Robert L. Bergman, Tana Wells, Katherine Butler : CT myelogrphy of the thoraco-lumbar spine in 8 dogs with degenerative myelopathy, J.Vet.Sci. (2005), 6(4), 341-348