DEGENERATIVE MYELOPATHY

BY: Kathleen Carter
PO Box 72 5454, Berkley, MI. 48072-1192
wyntr@voyager.net
Phone: 313-372-7638
http://my.voyager.net/~farrago/WYNTRHM.html

Degenerative Myelopathy (DM) is a disorder that has long been associated with old age in our pets. For many it can be a difficult diagnosis to face after so many years of loving companionship.

There are many articles and published papers available which describe in detail the causes, diagnostic methods and typical disease progression. This article will provide some of this information with links at the end to find published sources for later reading in more detail (1).

IDENTIFYING DM

DM is typically described in clinical terms as a process of noninflammatory axonal and myelin degeneration of the spinal cord. Typical age of onset appears to be between the ages of nine to thirteen in cardigans, but has occassionally occurred at younger and older ages and in some cases may not occur until age fifteen or even later. In GSDs an early onset variety has been noted, sometimes affecting dogs as young as six months (2), but so far has not been noted in cardigans.

The usual first signs of DM are often very slight and may be simply identified as a normal part of aging. To some degree this is probably true, but should not be ignored. The most common early symptoms are reduced coordination and weakness in the rear (ataxia). More difficulty when climbing stairs or jumping has also been noted.

These symptoms have been associated with osteoarthritis, hip dysplasia and other structural problems such as luxating patella or subluxating hocks, so it is important to get a correct diagnosis. A veterinary exam should be done and the vet can at that time also conduct some simple tests to evaluate reflex and coordination as a part of the initial diagnosis. Referral to a specialist may involve additional testing for better confirmation and potential prognosis.

As the disorder progresses, the dog may show an increased tendency to drag or scuff their feet and scrape their toenails or toes as they walk. This will most often occur with the rear feet, but the front feet may be involved as well. The dog may be more prone to losing their balance and tripping or falling. Loss of weight and muscle mass may be noted, particularly in the rear limbs. Eventually paralysis of the rear limbs will occur as nerve function fails. In time this can lead to complete paralysis and death when critical organ functions become affected.

TREATMENT OPTIONS

Treatment options so far have been limited and if no other late onset health issue takes precedence, the disorder will gradually take it's toll to an inevitable, incurable conclusion.

Some alternative and holistic methods have been used as a means to help slow the onset of DM, though none have been well enough studied to be proven reliable as treatments, preventions or cures.

Diet has been thought to play some role in the onset or progression of DM and that years of low intake of important vitamins and nutrients may be detrimental to support of healthy nerve function. There is some proof that vitamin deficiency, particularly vitamins A and B complex, may play a significant role in damage to nerve function, but for this to occur, a very severe level of malnutrition or pancreatic failure would need to be present, as in the cases reported in a black-maned lion (3) and in a domestic cat (4).

Dr. R.M. Clemmons, DVM, PhD has done some very good work in identifying a diet and therapy plan which may help some dogs suffering from DM (5), but at this time clinical therapeutic studies including the use of aminocaproic acid, N-Acetylcysteine and oral vitamin supplementation as a means to delay the progression of DM have been ruled inconclusive or ineffective (6).

The most effective treatment identified so far has been regular exercise (7). Low impact activites such as daily walks have been at least minimally beneficial. Hydrotherapy and exercises which manipulate and flex the limbs have been shown to be useful because this stimulates nerve function and encourages use of muscles to help maintain muscle mass without putting stress on weakened limbs (8).

HISTORY AND THE DNA TEST

In 1973 DM was first identified and described in GSDs. By 1989 the GSD Club of America was regularly funding research for the study of this disorder. The disease, by then, had been further identified in many other dog breeds and was thought to be an autoimmne disease. DM was often described as being similar to multiple sclerosis (MS), though differences in disease process and later studies eventually ruled this out.

In 1984 DM was defined as a potentially inherited disorder in a study of related Siberian Husky dogs which had been positively diagnosed (9).

In 2002 and 2003 as the Dog Genome Project (10) was making great progress, mapping many canine genetic markers, studies determined DM to have a definite genetic component. Possible markers for this gene were being studied, with Phene ID 1939, Group 001162 identified as an early possible candidate.

By 2005 concerned owners and breeders of Boxers, Chesapeake Bay Retrievers, German Shepherd Dogs, Pembroke Welsh Corgis, and Rhodesian Ridgebacks and their breed clubs were working together to participate in research studies and contribute DNA and pedigree information in order to help positively identify a marker gene.

In 2007, a study involving 110 pembrokes was published, determining a definite common genotype for DM (11).

A closer study of 38 affected pembrokes along with 17 clinically normal individuals having pedigree in common, allowed researchers to positively identify the SOD1 gene as a definite marker sequence associated with DM (12). This gene sequence was also kown to be the identified marker associated with amyotrophic lateral sclerosis (ALS) in humans. Comparative study of collected tissue samples confirmed DM is the canine form of ALS. This genetic marker was then positively identified in the four other participating dog breeds (Boxer, Chesapeake Bay Retriever, German Shepherd Dog, and Rhodesian Ridgeback). As DNA samples of additional breeds were submitted and screened, this same marker was further identified in many dog breeds, including the cardigan. This DNA marker has been identified as an autosomal recessive and is described with A/A meaning the individual is 'at risk', A/N is a 'carrier' and N/N, 'normal'.

In May of 2008, a DNA test for this genetic marker became available to all breeds through the OFA, with recommendation that the cardigan could be a breed at higher risk (13).

INCIDENCE AND POSSIBLE SECONDARY TRIGGERS

Early test results have so far identified a high carrier rate for DM in cardigans. Fortunately a very low number of individuals have tested as 'at risk' in these results and there are very few reports of clinically affected individuals. These numbers could change as more cardigans are submitted to the registry and more information from pet owners and breeders becomes available. Fortunately the carrier versus clear numbers have been improving and a more complete picture will hopefully emerge over time.

Because so few pembrokes and cardigans have been diagnosed with clinical signs of DM in spite of their 'at risk' genetic status, there have been doubts voiced by some breeders about the accuracy of the test. As with early doubts about the PRA test, these may be cleared with more information. Understanding the use of terms preferred by researchers might help.

When researchers use terms such as 'likely' or 'higly unlikely', it may sound uncertain to the average reader. The preferred use of these terms is because disorders like DM have additional variables such as age of onset and exposure to environmental factors which may influence disease process. This makes it harder for researchers to remark on it in definite terms than they might in more controlled work in a laboratory environment. Even in highly controlled environments, researchers are reluctant to use definite terms. This does not mean that the underlying facts in any published article are innacurate or uncertain. It just means that researchers are always ready to update and revise these facts as more information becomes available. There is a very large body of previous work and critical peer review involved in a project like the DM genetic marker test, well before any information from a paper or abstract goes to open publication.

The example of the fluff test has also been used to voice uncertainty of genetic testing. In the case of cardigans, yes the original test may not have accounted for other genomic alleles, but this did not change the underlying factors and specific genetic link to long coat, particularly in other breeds. Human perception and opinion of what constitutes a 'fluff' coat in both cardigans and Pembrokes has also played a role in the original accuracy of this test. Later submissions of DNA from related individuals along with pedigree data has helped to improve reliability.

In the case of DM, there is an identifiable disease process which can be studied and in post mortem samples it has been correctly identified in connection to the genetic marker. Other associated or coexisting genetic markers such as those which may influence age of onset have not yet been identified, but in time this may also be possible. This does not change the accuracy of the known genetic marker and its link to the human marker for ALS. Fortunately for breeds like the cardigan, there may also be a high incidence of genes which influence the onset of DM so that it will frequently occur much later in life than seen in many other dog breeds. For this reason, many cardigans may develop other fatal diseases long before they develop symptoms of DM. By understanding the late or delayed onset factor of DM through the contribution of DNA and other information by cardigan owners and breeders, it may even be possible to help human patients diagnosed with ALS to live symptom free for a much longer time.

Other factors which may affect the onset of clinical signs of DM are environmental stress, anesthesia and the presence or absence of other disease processes. Nutrition and dietary supplementation has been previously listed above and currently there is little conclusive evidence or consistent proof that these have any affect in confirmed cases of DM.

Environmental stress may increase clinical symptoms. Separation anxiety, boarding, travel, moving to a new location or rehoming, the introduction of a new family member and any other large changes to lifestyle or environment could increase onset of clinical symptoms of DM. Corgis do tend to be very adaptable, so these concerns may not be as serious as it might be for other breeds, but still worth taking precautions.

Anesthesia may also induce earlier onset of clinical DM or may complicate surgical procedures due to weakened respiratory and heart condition in individuals affected by DM. This problem has been reported by some pet owners and is a known concern for humans with ALS (14). At this time it is not certain if anesthesia somehow increases problems involving blood flow which can affect nerve function or if there might be an unintended immune response to anesthesia affecting the nervous system in the case of individuals who are at risk for DM.

Possible disease processes which could affect the onset of DM might be other autoimmune problems which have been known to influence vitamin absorption and nerve function, such as pancreatic disorders (EPI/PAA), Addison's, Cushing's and hypothyroidism. Currently no studies have been conducted to correlate these factors and work is still in progress to identify genetic markers for these disorders, so more will have to be done to determine if these play any role in the clinical onset of DM.

OTHER CONCERNS

There has been some concern voiced that this new test may cause breeders to eliminate too many individuals identified as carriers or 'at risk' from their breeding programs which may also result in the loss of quality animals and an unnecessary narrowing of the gene pool.

When following this line of thinking, it might also be necessary to consider that similar breeding methods are routinely used by breeders to eliminate other undesirable traits such as mismarks, drop ears, non-merle blue eyes, 'off' bites and incorrect coat type or color.

Similar concerns were also raised when the PRA test was first made available and yet, over ten years later the quality of the breed has not been affected by a current lack of PRA carriers. Breeders are now able to test for PRA carrier status and safely breed accordingly without the worry of producing PRA affected puppies. The same can be possible for DM.

CONCLUSION

At this time the higher identified carrier rate in cardigans could mean that breeders might have to use carriers or even at risk individuals for the next few generations in their breeding programs. They will have to set priorities for the problems they want to solve most, but instead of breeding 'blind' they will now have tools like DNA testing available to prevent combining the most serious problems and avoid producing affected individuals. This may take a while, but that doesn't mean it can't be done.

Genetic tests like the current one available for DM will offer a better future for breeders because it will eventually allow them to concentrate more on producing quality rather than worrying over the possibility of disasters.

Kathleen Carter
Wyntr Cardigans

REFERENCES

1. Degenerative Myelopathy of Dogs (Merck Veterinary Manual)
http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/100702.htm

Degenerative Myelopathy (University of Sydney)
http://www.vetsci.usyd.edu.au/lida/index.php?Pg=7&DName=Degenerative+Myelopathy&DID=483&Op=2

Good description of DM and treatment options.
http://www.michvet.com/library/neurology_degenerative_myelopathy.asp

2. A Degenerative Myelopathy in Young German Shepherd Dogs
S. L. Longhof 1, I. D. Duncan 1 A. Messing
University of Wisconsin-Madison, School of Veterinary Medicine, Madison WI 53706, USA
http://www3.interscience.wiley.com/journal/119370244/abstract
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3. Degenerative myelopathy and vitamin A deficiency in a young black-maned lion (Panthera Leo)
Kimberly A. Maratea1, Stephen B. Hooser and José A. Ramos-Vara
Corresponding Author: Kimberly A Maratea, Animal Disease Diagnostic Laboratory, Purdue University, 406 South University St, West Lafayette, IN 47907
http://jvdi.org/cgi/content/abstract/18/6/608

4. Degenerative myelopathy associated with cobalamin deficiency in a cat.
Salvadori C, Cantile C, De Ambrogi G, Arispici M.
Dipartimento di Patologia Animale, Facoltà di Medicina Veterinaria, Viale delle Piagge, 2 - I-56124 Pisa, Italy.
http://www.ncbi.nlm.nih.gov/pubmed/12887621

5. R.M. Clemmons, DVM, PhD
Associate Professor of Neurology & Neurosurgery, Small Animal Clinical Sciences
http://neuro.vetmed.ufl.edu/neuro/DM_Web/DMofGS.htm

6. Evaluation of a proposed therapeutic protocol in 12 dogs with tentative degenerative myelopathy.
Polizopoulou ZS, Koutinas AF, Patsikas MN, Soubasis N.
Diagnostic Laboratory, Faculty of Veterinary Medicine, Aristotle University of Thessaloniki, 546 27 Thessaloniki, Stavrou Voutyra st. 11, Greece. poliz@vet.auth.gr
http://www.ncbi.nlm.nih.gov/pubmed/18828481

7. Daily Controlled Physiotherapy Increases Survival Time in Dogs with Suspected Degenerative Myelopathy
I. Kathmann, S. Cizinauskas, M.G. Doherr, F. Steffen A. Jaggy
Department of Clinical Veterinary Medicine, Section of Neurology, Vetsuisse Faculty, University of Bern, Switzerland
Referral Neurology Clinic Aist, Helsinki, Finland
Department of Clinical Veterinary Medicine, Division of Clinical Research, Vetsuisse Faculty, University of Berne, Switzerland
Department for Small Animals, Vetsuisse Faculty, University of Zurich, Switzerland

Correspondence: Dr. med. vet., DECVN, Department of Clinical Veterinary Medicine, Section of Neurology, Länggassstrasse 128, 3012 Bern, Switzerland; e-mail: iris.kathmann@bluewin.ch.
http://www.ncbi.nlm.nih.gov/pubmed/16955818

8. Webpage listing hydrotherapy centers for pets in the US:
http://www.mzjf.com/pools.html
Website with good information on exercises, stretches and links for dogs with DM:
http://home.woh.rr.com/exercisesfordm/

9. Degenerative Myelopathy in a family of Siberian Husky dogs.
P Bichsel, M Vandevelde, J Lang, S Kull-Hächler
Comparative Neurology, University of Berne, Switzerland.
J Am Vet Med Assoc. 1983
http://lib.bioinfo.pl/pmid:12002594

10. The Dog Genome Project
http://research.nhgri.nih.gov/dog_genome/

11. Clinical Characterization of a Familial Degenerative Myelopathy in Pembroke Welsh Corgi Dogs
Joan R. Coates, Philip A. March, Michael Oglesbee, Craig G. Ruaux, Natasha J. Olby, Roy D. Berghaus, Dennis P. O'Brien, John H. Keating, Gary S. Johnson, David A. Williams
Departments of Veterinary Medicine and Surgery, College of Veterinary Medicine, University of Missouri, Columbia, MO
Departments of Veterinary Pathobiology, College of Veterinary Medicine, University of Missouri, Columbia, MO
Departments of Veterinary Clinical Science, College of Veterinary Medicine The Ohio State University, Columbus, OH
Departments of Veterinary Biosciences, College of Veterinary Medicine The Ohio State University, Columbus, OH
Department of Clinical Sciences, College of Veterinary Medicine, North Carolina State University, Raleigh, NC
Department of Small Animal Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Texas A & M University, College Station, TX
Department of Population Health, College of Veterinary Medicine, University of Georgia, Athens, GA
Departments of Clinical Sciences, Cummings School of Veterinary Medicine, Tufts University, North Grafton, MA
Departments of Biomedical Sciences, Cummings School of Veterinary Medicine, Tufts University, North Grafton, MA
Correspondence to DVM, MS, Diplomate ACVIM (Neurology), Department of Veterinary Medicine and Surgery, 379 E. Campus Drive, College of Veterinary Medicine, University of Missouri, Columbia, MO 65211
e-mail: coatesj@missouri.edu.

http://www.ncbi.nlm.nih.gov/pubmed/18196743

12 A SOD1 missense mutation in dogs with degenerative myelopathy: a spontaneous amyotrophic lateral sclerosis model.
G. S. Johnson1, T. Awano, C. M. Wade, M. L. Katz1, G. C. Johnson, J. F. Taylor, M. Perloski, T. Biagi, S. Long, S. Khan, D. P. O'Brien, K. Lindblad-Toh, J. R. Coates
Dept. of Veterinary Pathobiology, Univ. Missouri, Columbia, MO;
Broad Institute of Harvard and MIT, Cambridge, MA
Center for Human Genetic Research, Massachusetts General Hospital, Boston MA;
Mason Eye Institute, Univ. Missouri, Columbia, MO;
Division of Animal Sciences, Univ. Missouri, Columbia, MO;
Section of Neurology and Neurosurgery, Univ. Pennsylvania, Philadelphia PA;
Dept. of Veterinary Medicine and Surgery, Univ. Missouri, Columbia, MO;
Dept. of Medical Biochemistry and Microbiology, Uppsala Univ., Sweden.
http://www.ashg.org/2008meeting/abstracts/fulltext/f20625.htm

13. Orthopedic Foundation for Animals
2300 E Nifong Boulevard Columbia, Missouri, 65201-3806
Email: ofa@offa.org
DNA Disease Testing page.
http://www.offa.org/dnatesting/

14. Epidural Anesthesia and Pulmonary Function in a Patient with Amyotrophic Lateral Sclerosis
Kaoru Hara, MD, Shinichi Sakura, MD, Yoji Saito, MD, Mayumi Maeda, MD, and Yosihiro Kosaka, MD
Department of Anesthesiology, Shimane Medical University, Izumo, Japan
http://www.anesthesia-analgesia.org/cgi/reprint/83/4/878.pdf

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Bonnie Money at blmoney@att.net