Perspectives on Cerebellar Abiotrophy

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The Clinical Diagnosis of CA

The clinical diagnosis of cerebellar abiotrophy requires a specific diagnostic protocol that confirms the expected symptoms of the disorder, and rules out the other disorders that can have similar clinical signs. The basis of the clinical diagnosis is the neuroanatomical localization of the pathological defect based on the neurological examination. For the videotape diagnostic protocol that Dr. de Lahunta and I developed for the clinical diagnosis of cerebellar abiotrophy, it is only useful if it contains the clinical symptoms that we would utilize in a neurological examination that would both rule in cerebellar abiotrophy and rule out other causes.

Cerebellar abiotrophy causes the loss of Purkinje cells in the cortex of the cerebellum; the part of the brain that controls muscular coordination. If the brain is considered an electrical junction box, The Purkinje cells act to connect and transmit signals to several layers of cells to modulate muscular movement and assist with proprioception. (Proprioception is the brain activity that tells you where your limbs are in space. This is what allows you to close your eyes and touch your nose, and know where your arms and legs are.) The result of this cellular loss is a pure cerebellar incoordination or ataxia, called hypermetria, without any other neurological symptom of pain, weakness, hypertonicity, or spasticity. Hypermetria is evidenced by a high stepping gait. An affected dog can also have an intention tremor of the head or body. This is due to over and undermodulation of muscular movement. As the Purkinje cell loss is symmetrical from the left and right sides of the body, the incoordination is also bilaterally symmetrical. However, either the forelimbs or the hindlimbs may be more significantly affected.

The videotape diagnostic protocol requires that the dog must demonstrate hypermetria of all 4 legs, and the clinical symptoms must be bilaterally symmetrical between the left and right sides of the body. These symptoms will be most evident with complicated motor activity, such as stairwalking, or running and chasing a ball. Many CA dogs compensate visually for their deficits when walking or gaiting, so we need complex movements to overcome the compensation. When going up and down stairs, they can float their front legs out, because they don't know where their leg is in relationship to the stair. This is a very specific movement for CA. It has caused some owners to question whether their dog may have a problem with vision, which is normal. Affected dogs also often stumble or miss a step with their hind paws.

When running, affected dogs can show truncal incoordination. They can often have a bouncy hind end, because they cannot modulate the muscular force needed to push off with their hind legs. Some owners joke that their front end and hind end can sometimes be in a race to get there first. Affected Scottish Terriers can stumble and roll, but then just get up and keep on going. The clinical signs are always present when doing the specific activities; whether just getting up from a nap, or after prolonged activity.

There are several symptoms that should not be present in the clinical evaluation for cerebellar abiotrophy. There cannot be evidence of a pathological weakness or sinking of the body. There cannot be hypertonicity as is seen with Scotty Cramp. With clinical symptoms of cramp, the limbs are held in flexion during movement, and there can be asymmetry where the left or right side of the body can be more severely affected. There cannot be spasticity present, which would localize the neurological lesion outside of the cerebellar cortex (in the spinal cord or other areas of the central nervous system). Cerebellar abiotrophy does not cause pain or discomfort.

For a confirmed clinical diagnosis, the clinical history of symptoms must show progression of the purely cerebellar cortical signs. In many cases the progression may take years to be evident. MRI can show a reduced relative size of the cerebellum in advanced cases, but data for when this reduction in size occurs, and guidelines or diagnostic cutoffs have not been established. Because of this, the absence of an MRI reduction in cerebellar size in mild cases cannot rule out the disorder. It must be based on the clinical symptoms.

Birth defects or conditions such as lack of oxygen would not cause progressive disease. Any brain injury or infection would expect to affect more brain tissue than just the Purkinje cells in the cerebellar cortex, and this would be evident in the clinical evaluation. The same is true of inflammatory diseases and toxins.

There are some specific disorders that people are claiming will cause the same signs of cerebellar abiotrophy. Legg-Perthes disease can cause an abnormal gait due to hip arthritis and instability. It would not cause hypermetria of all four legs, and cannot be confused with the clinical symptoms of CA. A disorder labeled "Antibiotic Responsive Ataxia" has also been offered. Do not try googling this term or looking for it in the Merck manual – it doesn't exist. They are referring to Neospora infection, which is a rare cause of encephalomyelitis in dogs. The disease process begins as muscle disease with hind end weakness, and rapidly progresses to severe ascending paralysis with rigid hind limb hyperextension. The most common neuroanatomical lesions are the lumbosacral spinal cord and muscles, but can also include peripheral nerves, several abdominal organs, and the skin. A few cases of dogs with Neosporosis have been reported with cerebellar signs. However, all of these cases had multiple other signs of lesions outside the cerebellum, which included depression, muscle inflammation, weakness, and severe balance loss. These cases would be differentiated from CA through the clinical diagnostic process.

The mode of inheritance of cerebellar abiotrophy in the Scottish Terrier (and all of the four breeds being studied by Dr. Olby) is simple autosomal recessive. This has been scientifically established. Trinucleotide repeat disorders have been found to cause some forms of cerebellar ataxia in humans, and many of these genes have been identified. All of these identified trinucleotide repeat disorders are caused by autosomal dominant inheritance, and cause clinical anticipation. This means that all affected individuals have an affected parent. It also means that the severity of the clinical signs increases from generation to generation. Only one of the CA affected Scottish Terriers had an affected

parent, and we do not see clinical anticipation with canine CA. All of the cerebellar ataxia genes identified in man have been evaluated in canine CA, and have not been found to be involved. This is why Dr. Olby's research has moved on to the more complicated genome screening, instead of the much easier candidate gene approach.

I have now gone on for over a thousand words to repeat and provide more depth to aspects of CA in Scottish Terriers that have already been presented to you in the past. This is required because some breeders and STCA members continue to pursue a campaign of misinformation to try to prevent the fruition of a realistic and reliable genetic disease management program for CA. They would lead you to believe that the scientific clinical evaluation of CA is unscientific, haphazardly applied, and diagnoses CA in Scottish Terriers simply because they walk funny. All of the scientific advisors to the STCA have agreed on the scientific basis of the clinical diagnostic process for cerebellar abiotrophy. For those of you who have not reviewed the previous releases, you should look at the STCA website and review the letters from Dr. Olby and me from November, 2005, and the article "Cerebellar Abiotrophy: It's Cause and Diagnosis" published in the October, 2004 Bagpiper (present in Scottiephile under cerebellar abiotrophy, and in the new CA Central section of the website).

Moving Forward

What is most important for the Scottish Terrier breed is what we do from here with the available information. In March, 2006, the voluntary open database list of Scottish Terriers affected with cerebellar abiotrophy will be published. How you use this list will have long term effects on the health and viability of the Scottish Terrier breed and gene pool. I have seen breeds devastate their gene pool by witch hunting and blindly eliminating all dogs and their close relatives that have produced a recessive genetic disorder. It is a natural emotional response to feel, "I cannot breed this dog due to CA risk." You all have to remember that the primary goal of dog breeding is to produce a quality Scottish Terrier. The decision to breed a dog should be based on its quality. Its CA risk may only alter HOW you breed the dog.

Reviewing the list of CA affected dogs reveals that some of the best quality Scottish Terriers were carriers of CA, or are closely related to carriers of CA. Eliminating their influence from future matings will devastate the breed. The important goal for current breeders is to reduce the chance of producing more affected dogs. If breeders of dogs with high carrier risk select mates with low carrier risk, then the chance of producing affected dogs is greatly diminished. Replacing high carrier risk dogs with their lower carrier risk offspring for breeding moves each breeder and the breed away from the defective gene, without losing the quality breeding lines that have been carefully bred over the generations. DNA and semen should also be stored for use in the future, when a genetic test is available. Many breeds have used this process to effectively control genetic disorders; including some who still do not have genetic tests for carriers. While we hope for quick progress, in all likelihood it will take many years (i.e., several generations of breeding Scottish Terriers) to identify the recessive defective gene and have a genetic test for carriers of CA.

The future of the Scottish Terrier breed is in your hands. We can have far less influence on the Scottish Terrier gene pool by continuing to breed blindly regarding genetic disorders and commiserating with owners over their affected dogs. Genetic tests, open registries, and relative risk analysis are power tools, and can cause damage if used without reading the instructions. All breeders should review the following articles in Scottiephile on the STCA website: "Breeding Strategies to Manage Genetic Disorders", "Removing the Stigma of Genetic Disease", and "Using Relative Risk Analysis and Open Health Registries to Plan Matings". The Scottish Terrier breed can have a healthier future if breeders work together by objectively and realistically putting CA in perspective within the overall effort of breeding quality Scottish Terriers.