Cardiac Laminopathy (CLAM) Update – September 2023

Dilated cardiomyopathy (DCM) is characterized by decreased systolic function and dilation of one or both ventricles of the heart, often leading to heart failure or sudden death. Two 10-month-old sibling Nova Scotia Duck Tolling Retrievers (NSDTR) died acutely with evidence of dilated cardiomyopathy (evaluated by echocardiograms in living dogs) with myocardial fibrosis (based on necropsy findings). Pedigree analysis showed a recent inbreeding loop, and a second related litter with similar inbreeding had three young dogs that died suddenly. A third litter unrelated to the first two litters also had a young dog with sudden death and evidence of myocardial fibrosis.

Using genetic techniques of genome-wide association and whole genome sequencing a mutation was identified in a gene that causes DCM with sudden death in people. This mutation appears to only be in NSDTR. Two additional affected puppies were identified that had necropsies showing the same myocardial fibrosis and they also had two copies of CLAM. All genotyped affected individuals (N=5) had two copies of CLAM. Four dogs with one copy of CLAM were evaluated by echocardiography and did not show evidence of cardiac disease. One 8-year-old with one copy of CLAM also had a 24-hour portable electrocardiogram monitor that showed no evidence of arrhythmias. Five dogs in the pedigree that were tested and had one copy or were obligate carriers lived from 11-17 years.

Recently, a 5-year-old with one copy of CLAM who was the sibling to the sire of the first litter had sudden death and a necropsy which showed myocardial fibrosis. Evaluation of the age of death of dogs with one copy of CLAM (N=20) compared to dogs without CLAM (N=44) did not reveal a statistically significant age difference (1 copy average age 12.12 years, 0 copies average age 13.12 years).

The importance of having necropsies performed in any case of sudden death in an animal cannot be overstated.

Mode of inheritance

There are eight dogs with sudden death that likely had two copies of CLAM. Five were tested, and three were based on pedigree. These dogs died suddenly between 10 and 15 months of age. The identification of a dog with one copy of CLAM with cardiac fibrosis and sudden death at five years of age suggests that the mode of inheritance might not be a simple recessive. However, other risk factors may have contributed to this dog's death. Those risk factors could be genetic or environmental. In the two litters with multiple affected dogs, the age of onset was slightly different (First litter ten months and second litter 15 months), opening the possibility of environmental or genetic modification of the phenotype.

Dogs with two copies of CLAM have consistently exhibited sudden death as young dogs. Based on the histopathology of their hearts, this disease is not treatable. The heart muscle is replaced with scar tissue, and they likely have a severe abnormal rhythm that results in sudden death.

While there is a small potential risk in dogs with one copy, many dogs with one copy have lived completely normal lives.

Prevalence as of summer 2022

The North American heterozygote frequency was estimated using 300 NSDTR as 8.7%. The European heterozygote frequency was estimated by genotyping 422 dogs from mostly Switzerland as 0.2%. None of the 722 NSDTR had two copies of CLAM.

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