

Is Canine Degenerative Cruciate Rupture a Consequence of Rheumatic Disease?

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Dr. Peter Muir said that while US pet owners spend billions each year on the health care of companion animals, only a small fraction of that amount is spent on research. As a result, very little data exists on canine cruciate rupture, and researchers are just now beginning to understand some aspects of the disease. A 2005 survey done by the University of Iowa showed that spending on the care of dogs with cruciate ligament rupture represents a large portion of total canine health care spending, indicating that this is one of the most common and important orthopedic conditions in dogs.

Arthritis usually is classified into two forms: rheumatic or inflammatory, and osteoarthritis, with the latter usually considered more important in dogs. Canine cruciate rupture is similar to ACL injury in humans, and is estimated to cause 20% of all lameness in dogs. Many large-breed dogs are affected with this condition, Dr. Muir said, and many dog owners do not recognize low-grade lameness. However, owners of hunting or agility dogs may see it earlier.

Dogs affected by cruciate rupture have prodromal lameness, and while the stifle or knee joint may appear stable, or exhibit only minimal instability, under radiographic examination it will show bilateral signs of arthritis. Ligaments may be frayed, Dr. Muir said, but are still attached to the femur and tibia. These conditions may persist for some time before a rupture finally occurs.

Histology of the collagen within the stifle joint of affected dogs suggests progressive mechanical overload of the ligaments, and radiographs show differences inside the stifle, including a roughening at the edges of the bone and a greater volume of fluid within the joint due to inflammation. Dr. Muir said this suggests the actual rupture and instability occur because of a pre-existing arthritis.

Affected stifle joints contain a mixture of inflammatory cells, including T lymphocytes, which are normally part of the body's defense against infection but also are associated strongly with immune-related rheumatic arthritis. "This cell is the central player in the development of persistent destructive inflammation," Dr. Muir said. Since the cruciate ligament gets most of its nutrition from joint fluid, the presence of inflammatory cells can cause irritation and have a profound effect on the tissue. This suggests that cruciate rupture is an oligoarthritis, which is defined as an inflammatory arthritis of four or fewer joints.

Traditionally, scientists have thought that inflammation and arthritis are the results of damage to the cruciate ligament, but Dr. Muir said his data suggests that the classical paradigm of relationship between inflammation and cruciate rupture is incorrect, and

that synovitis actually precedes cruciate rupture and the development of instability. Over time, this inflammation may cause the ligament to become overloaded, leading to cruciate rupture.

While a normal canine stifle does not contain bacteria, analysis of the synovial tissue and joint fluid of dogs with cruciate rupture shows that the stifle joints of about half of the dogs contain bacteria similar to those associated with arthritis in humans. This mixture of bacteria is not necessarily pathogenic, like the bacteria that cause Lyme disease and subsequently lead to arthritis, but it could be an important trigger for the immune system.

While these immune reactions may lead to chronic disruptive inflammation in dogs that are genetically susceptible, Dr. Muir said that is insufficient data to confirm a cause-and-effect relationship. However, this is a very active field of research in both human arthritis and other diseases associated with chronic inflammation, such as Crohn's disease.

The majority of cruciate rupture dogs have degenerative rupture, but normal physiological events may allow their ligaments to remodel and adapt successfully. This may be what happens in Greyhounds. However, most dogs are susceptible, and the combination of collagen degradation and trauma can lead to cruciate rupture during normal activity.

Goals for the management of cruciate rupture include gaining an improved understanding of the mechanisms that lead to cruciate rupture and the identification of biomarkers for prodromal oligoarthritis, which should lead to better tools to diagnose the condition while it is still in the arthritis phase. Current surgical treatments only address dynamic instability but do not help with passive instability or inflammation: while surgery may improve a dog's condition, it will not return the dog to normal. Comprehensive treatment is important and can be developed only with better understanding of the disease mechanism.

Discussion

A participant asked whether surgery is the only treatment option. Dr. Muir said it is too early to tell; while there is no question that joint inflammation is making dogs lame, treatments are also needed for other causes of lameness. The most effective current treatments offer pain relief, but do not reduce inflammation. There are many different drugs to treat inflammation in humans, but relatively few for dogs. Veterinarians want to move away from current surgeries that are ineffective, he said, creating pressure to conduct research that will improve medical and surgical treatment. While researchers are looking at tissue engineering, they should be looking more at ligament repair, Dr. Muir said.

Another participant asked whether Dr. Muir had reviewed other geographic areas where Lyme disease is not endemic, to compare research results. Dr. Muir said all his

research data comes from Madison, Wisconsin and that it would be relevant to collaborate with a group from another region where Lyme disease is not endemic, or for other institutions to take up some of their research to see if inflammation and potential for treatment is similar or different. However, such work remains to be done.

A participant asked whether there is an obvious direction for health professionals to take, in terms of looking at human anti-inflammatory treatments and drugs to see if they will transfer to canines. “Yes, absolutely,” Dr. Muir said. Cruciate rupture is a complex condition, and the current lack of information is a result of lack of funding.

Millions of dollars have been spent researching rheumatic arthritis, and yet the trigger is still not known. The condition is an economic burden to the country, Dr. Muir said, and determining how to bring more support to this program is very important.

Dr. Muir said research should continue to explore the idea of host/pathogen interactions. “In terms of therapy, what you say is right, and we’re developing that conversation with industry and looking for new collaborative trials to find new drugs for dogs.” Currently, the only available treatment for dogs is steroids. There is a pressing need for anti-inflammatory drugs to reduce inflammation without affecting the strength of collagen.