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Polyneuropathy (PN) in the Alaskan malamute was first described at the 1982 Nordic Veterinary Congress. In 1997, a report was published documenting the disease in eleven affected Alaskan malamutes in the United States. In that report, the average age of affected malamutes was only 14 months old. Both male and female dogs were affected. In nine dogs, clinical signs progressed rapidly over approximately two to four months, to the point that all nine dogs were euthanized
because of the severity of their condition. In two dogs, signs remained static for two to three years despite experiencing an initial deterioration. In 2000, a report of 13 affected dogs was presented at the European Society of Veterinary Neurology, in which littermates, the sire and dam, as well as related dogs were studied. Since that report, few studies investigating PN in malamutes have
been published in the veterinary medical literature. As a result, our understanding of this devastating condition remains limited. This article attempts to summarize what we know about PN in malamutes and what we can learn from similar conditions in other breeds. Only through a
better understanding of PN will we be able to improve our ability to diagnose, determine a prognosis, and ultimately design treatment strategies to help affected dogs.

Despite its use in defining a disease, the term polyneuropathy is more of a pathological description rather than a specific disease process itself. Taken literally, the term polyneuropathy means poly “multiple” and neuropathy “pathology or disease of the nerve.” Although the term polyneuropathy is applied to many diseases, PN in Alaskan malamutes shares many commonalities with PN in other breeds of dogs.

In order to fully appreciate the clinical signs, an understanding of the anatomy and function of nerves is necessary. In general, nerves are involved in either creating movements (motor nerves) or in perceiving sensations (sensory nerves) such as touch, temperature, or pain. Regardless of their function, all nerves share a similar structure. Simplistically, nerve fibers can be thought of as insulated wires carrying electricity. An electrical charge or nerve impulse, called a depolarization, begins at one end of the nerve fiber and is conducted to the other end. For motor nerves, the depolarization begins in the spinal cord and is conducted down the nerve to the muscle it innervates and leads to a muscle contraction. Like an insulated wire, each nerve fiber (called an axon) is wrapped in insulation (myelin). On a microscopic level, PN is a degeneration of the axon and myelin. Without the axon, depolarizations are not conducted down the nerve and consequently, muscle contractions become diminished (demonstrated clinically as weakness) or absent (paralysis). Likewise, without myelin, the depolarization conducts more slowly, also resulting in reduced muscle function (weakness).

The clinical signs of PN are dominated by weakness. The degree of weakness reflects the severity of the condition. Mildly affected dogs may show few signs at all. Subtle signs of weakness may be exercise intolerance or a loss of endurance. In more severely affected dogs, the gait may become short-strided and have a stiff appearing, choppy quality. Affected dogs may have difficulty standing up from a prone position. Standing up may appear to be a strenuous activity. When standing, the posture may be crouched.

The stance in the back legs becomes plantigrade, which means standing with the hocks flexed so that the point of the hock is closer to the ground. The front legs may be pulled back along the trunk with the elbows rotated inwardly under the chest to help support weight. Severely affected dogs may be only capable of taking a few steps before having to sit or lay down. Often the hind legs are weaker than the front legs. Rarely, the nerves that innervate the larynx are affected. If they are, the character of the bark may be different, and the dogs may cough while drinking or eating. A loud and harsh sound may occur with panting or breathing heavily. Importantly, the clinical signs of PN are not specific. Many conditions can result in similar signs. For example, orthopedic conditions like severe arthritis can cause similar gait changes. One of the most important steps at arriving at a diagnosis of PN is to eliminate from consideration other conditions that may have a similar appearance, by thorough physical, orthopedic, and neurological examinations.

Diagnosing PN begins with a complete neurological examination, including careful assessment of the dog's gait from a side view as well as with the patient walking toward and away from the examiner. Position sense (proprioception) is then evaluated by tests called postural reactions. One common test is "knuckling," where the dog's foot is turned over so that the dog bears weight on the top of the foot; proprioception is gauged by how quickly the patient turns the foot over to the proper position. In some dogs with PN, the foot may be replaced in a normal position slowly or not at all. The most important finding on the neurological examination is reduced or absent reflexes. In the hind legs, the two main reflexes that are assessed are the patellar (knee jerk) and the flexor-withdrawal. As in humans, the patellar reflex is elicited by tapping on the patellar tendon with a reflex hammer and seeing that the knee extends (leg kicks out). The flexor-withdrawal test is performed by pinching the toes and seeing that the patient withdraws the limb by bending the limb at the hock, knee, and hip. As the dog withdraws the limb, the examiner holds the limb to assess the strength and completeness of the withdrawal. Often, dogs with PN do not flex their hock with appropriate strength and have a diminished patellar reflex. In the front legs, only the flexor-withdrawal reflex can be reliably assessed. Additionally, the patient may have muscle atrophy (muscle wasting). Given the thick coat of a malamute, it is imperative to palpate up and down the limb to feel for muscle loss, as atrophy can be easily missed by visual inspection alone.

As alluded to above, a diagnosis is established by initially ruling out other conditions. Basic blood work, including a complete blood count, chemistry profile, and urinalysis should be performed in all dogs displaying clinical signs of weakness. Based on results, more specialized tests may be needed to exclude other disease processes. In dogs with PN, the blood work should be normal. In older dogs or those that display trouble breathing or swallowing, X-rays of the chest cavity may be warranted.

Unfortunately, there is no gold standard or definitive test to diagnose PN. However, one
helpful diagnostic tool is electrophysiological testing called electromyography (EMG)

and
direct evoked motor nerve potentials. As their names suggest, they are tests that directly
assess the “electrical” function of the muscles and nerves. The tests are performed with the
dog under general anesthesia using small needles, like those used for acupuncture, which
are inserted into the muscles and nerves to record electrical activity. EMG assesses the
muscle. The classical EMG findings in PN are the observation of muscles that spontaneously
depolarize (show electrical activity) called fibrillation potentials or positive sharp
waves. With direct evoked motor nerve potentials, the function of the nerves can be
directly assessed. In dogs with PN, the direct evoked motor nerve potential shows a
reduction in the number of functional nerve fibers, as well as a decrease in the speed
at which nerve fibers conduct electrical activity.

One eye-opening experience for me working with some affected malamutes has been
uncovering electrophysiological abnormalities in malamutes that did not display any
clinical signs of PN! This has also been observed by others. Another important
diagnostic step is a microscopic evaluation of a nerve biopsy specimen. Nerve biopsies
do carry some inherent risk of worsening the degree of weakness. However, if performed
by a skilled veterinarian using proper technique, nerve biopsies can be done with
little risk to the patient. Microscopic evaluation reveals a degeneration of the axon
(nerve fiber) and loss of myelin (insulation) resulting in an overall loss in the
number of nerve fibers. Often, the ends of the nerves toward the extremities undergo
more severe degeneration.

Unfortunately, a proven form of treatment is not available. Treatments with corticosteroids
or other immunosuppressive drugs have failed to help affected dogs. In other breeds with PN,
several nutraceuticals (nutritional supplements thought to have medicinal effects)
such as Lcarnitine, CoEnzyme Q10, and B vitamins have been advocated. To date, controlled studies
have not been performed, and success stories are limited to anecdotes related to an individual
dog’s success. In severely affected dogs, the progression of signs may continue to the point
where the dog is unable to walk and sadly often leads to euthanasia.

Without a doubt, more questions remain than are answered. Likely, PN in malamutes
demonstrates as a spectrum of disease spanning from those severely affected to those
with milder signs to even individuals that have abnormalities on electrophysiological testing yet
appear clinically normal. What will it take to find answers to questions like how is
the disease passed from one generation to the next? Are there genetic markers through
which blood tests can be designed so patients at risk can be identified? Are there
novel therapeutic interventions that can help affected dogs?

In humans, a polyneuropathy syndrome called Charot-Marie-Tooth syndrome (CMT; named after the physicians who first described the condition) encompasses a wide range of clinical disorders that may possess close similarities to PN in dog breeds. It is now possible to use genetic testing to help diagnose the various forms of CMT in people.

Like PN in malamutes, a more recent description of PN in the Leonberger dog has been reported. The disease process in the Leonberger dog appears to be genetic and as a result is passed from the sire and dam to their offspring. The basis of the inheritance is still under debate but may represent an X chromosome linked condition or may be a recessive condition. The importance of these reports lies in the lessons that can be drawn from the study of Leonbergers and applied to answering questions with PN in malamutes. What will it take? As in the Leonberger, the first step is identifying the prevalence of the condition (the number of affected dogs in the population). Since some dogs may appear normal yet be affected based on electrophysiology, it is necessary to evaluate both healthy appearing and clinically affected dogs. From such preliminary studies, it may be possible to identify potential genetic linkages. Now with the canine genome (DNA) having been sequenced, modern molecular genetic tests such as single nucleotide polymorphism (SNP; pronounced "snip") may help uncover a genetic defect that either causes or predisposes to the development of PN in malamutes. Once thought impossible, these state of the art diagnostic tools are being used today to study other genetic conditions in some breeds.

Likewise, until affected individuals can be identified, critical evaluation of novel therapies cannot be pursued. In the end, until there is clarity as to the genetics involved and improvements in the diagnostic tests used to identify dogs with PN, recommendations on how to truly eliminate PN will not come to fruition.