Use of a selective serotonin reuptake inhibitor for treatment of episodes of hypertonia and kyphosis in a young adult Scottish Terrier

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Case Description—A 2.5-year-old 12.4-kg (27.3-lb) castrated male Scottish Terrier was evaluated because of episodes of hypertonia and kyphosis for which a presumptive diagnosis of so-called Scottie cramp had been made when the dog was a puppy.

Clinical Findings—Findings of general physical, orthopedic, and neurologic examinations were within reference limits. Pelvic limb hypertonicity and kyphosis without signs of pain were induced with minimal exercise; ambulation returned to normal after a period of rest.

Treatment and Outcome—Fluoxetine, a selective serotonin reuptake inhibitor, was administered orally at a dosage of 1.2 mg/kg (0.55 mg/lb) once daily for 1 month. After this period of treatment, clinical signs of the disease were greatly reduced; the dosage of fluoxetine was changed to 0.8 mg/kg (0.36 mg/lb) twice daily, and response to treatment continued.

Clinical Relevance—Administration of benzodiazepines, vitamin E, or phenothiazines has been recommended for treatment of episodes of hypertonicity, but often does not result in control of clinical signs. It has been suggested that the pathogenesis of this disease is related to deficiencies in concentration or function of serotonin in the CNS; thus, a logical choice for treatment is administration of a serotonin reuptake inhibitor. In the dog of this report, fluoxetine resulted in good control of clinical signs. The use of an effective medication (other than a controlled substance) that is administered once or twice daily, has minimal adverse effects on the patient’s mental status, and is inexpensive may lead to better owner compliance and an improved quality of life for affected dogs. (J Am Vet Med Assoc 2009;235:168–171)

A 2.5-year-old castrated male Scottish Terrier for which a presumptive diagnosis of so-called Scottie cramp had been made when the dog was a puppy was admitted to the Veterinary Medical Center at Colorado State University for evaluation. Clinical history included episodes of kyphosis and pelvic limb spasticity that were elicited by exercise or excitement; these episodes had occurred within the last 6 months were also within reference limits. Clinicopathologic variables assessed were within reference limits. Pelvic limb hypertonicity and kyphosis without signs of pain were induced with minimal exercise; ambulation returned to normal after a period of rest.

On physical examination, the dog's mentation was considered normal. It weighed 12.4 kg (27.3 lb) and had a body condition score of 6 (on a scale of 1 through 9). There were no obvious physical abnormalities. Results of orthopedic and neurologic examinations were within reference limits. Clinicopathologic variables assessed within the last 6 months were also within reference limits. The dog's response to exercise was evaluated. Within 15 seconds of commencement of trotting and running, stiffening of the pelvic limbs became evident and the dog began to bunny-hop. During continued exercise, the dog's posture became kyphotic and spastic-

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5-HIAA  5-hydroxyindoleacetic acid

Abbreviation

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One month later, the dog was returned for progress evaluation. The owners reported that the dog could now walk for almost an hour with few, if any, exercise-induced episodes. However, during the latter part of the month, the owners had observed 3 episodes each of <10 seconds’ duration. Scottie cramp episodes no longer occurred during periods of excitement. As part of the reevaluation, the dog was exercised by running in the hallway of the hospital. No evidence of cramping occurred during 3 minutes of exercise and excitement.

The dosage of fluoxetine was adjusted to 0.8 mg/kg (0.36 mg/lb) administered orally twice daily, and the owners were instructed to return the dog for a follow-up examination after 1 month. At the 2-month recheck visit, it was evident that the dog continued to respond well to treatment with fluoxetine. A follow-up telephone conversation with the owners at 1 year revealed that the dog’s episodes continued to be well controlled.

**Discussion**

The term Scottie cramp refers to nonpainful disease that affects the posture and locomotion of Scottish Terriers and was first described in 1942. The classic feature of the disease involves a progression of signs with increasing levels of exercise or excitement. Initially, the thoracic limbs may become abducted or there may be arching or kyphosis of the lumbar portion of the vertebral column, followed by overflexion of the pelvic limbs. The neck may become extended with the nose pointing to the ground. With increasing activity, tonicity of the muscles increases; as the pelvic limbs become increasingly affected, the dog develops a goose-stepping or stringhalt gait. Increasing resistance to movement may cause walking in place, somersaulting, or falling. In a severely affected dog, forward progression of movement may become limited and respiratory and facial muscles may be affected; the patient may curl into a ball. After 10 minutes or less of rest, the hypertonicity usually resolves and the dog is able to ambulate more normally. This disease is not associated with a loss or change in mentation or with behavioral abnormalities. Scottie cramp does not alter life span, nor is it associated with neonatal deaths.

Clinical signs associated with Scottie cramp can be detected as early as 6 weeks of age and as late as 18 months. Severity of clinical signs can vary considerably among affected dogs, ranging from barely noticeable effects to severe incapacitating changes. It is thought that the differences in clinical signs are related to behavioral factors, environment, nutrition, and temperament of the affected dogs. The severity of the clinical signs in subsequent episodes rarely worsens. However, changes in the dog’s health and environment are believed to cause stressors that may result in onset of signs when they were not previously apparent.

Some dogs can learn to self-modify their activity, which can lead observers to believe that remission of the disease has occurred. Results of pedigree analyses and inbreeding and outcross matings have suggested that this is an inherited autosomal recessive disorder. To explain the variability in clinical signs among dogs, it has been proposed that other genes may be associated with the defective gene and that those other genes modify or influence the clinical expression of the disease. Diagnosis is made primarily on the basis of signalment and clinical signs. Tests performed in 10 affected Scottish Terriers in the late 1960s and the early 1970s did not reveal any biochemical, hematologic, or radiographic abnormalities. In other affected dogs, gross and histologic examinations of skeletal muscles, peripheral nerves, and connective tissues did not reveal lesions, and no cardiovascular, endocrine, respiratory, digestive, or CNS abnormalities were detected. In addition, blood lactate and pyruvate concentrations in affected dogs were comparable to values in control dogs without the disease (Scottish Terriers and other breeds). Electromyographic investigations of dogs with Scottie cramp have revealed increased interference patterns during episodes but no abnormal spontaneous discharges at rest.

A considerable amount of experimental work has been performed in an attempt to understand the underlying pathogenesis of Scottie cramp. In those studies, Scottie cramp was compared with previously reported diseases of muscle. McArdle disease (a glycogen storage disease that is caused by a deficiency of the enzyme glycogen phosphorylase) was ruled out by evidence of apparently normal muscle glycogen stores and normal function of myophosphorylase in affected dogs. Core myopathy was ruled out because core structures were not detected during histologic examination of skeletal muscle specimens. Myotonic myopathy is characterized by prolonged muscle contraction upon voluntary contraction or can be initiated by mechanical (percussion), pharmacologic, or electrical stimulation. Results of electromyographic investigations have indicated that abnormal relaxation is responsible for myotonic myopathy; because myotonia is maintained even after neuromuscular block with procuring, and spinal anesthesia, the abnormality appears to be at the level of the myomembrane. In attempt to determine whether the defect in Scottie cramp was at the level of the muscle, neuromuscular junction, or peripheral nerve, Meyers et al performed a series of tests to inhibit function of these structures in affected dogs. Affected Scottish Terriers were anesthetized and administered tubocurarine as a neuromuscular blocking agent, and the quadriiceps femoris, biceps femoris, gastrocnemius, biceps brachii, supraspinatus, deltoideus, and pectoralis muscles were both mechanically and electrically stimulated. Poststimulation discharge of the muscle could not be elicited. The function of the muscles was also evaluated following epidural administration of procuring; this treatment also blocked electrical activity. From these experiments, the authors proposed that the Scottie cramp defect is not in the peripheral nervous or muscular system, but within the CNS; they postulated that the abnormality was related to abnormal physiologic functioning of a neurotransmitter. On the basis of results of pharmacologic experiments, it was suggested that the disease was related to mechanisms of serotonin within the CNS. When amphetamine or parachlorophenylalanine (a noncompetitive inhibitor of tryptophan hydroxylase involved in serotonin synthesis) was administered to affected dogs, the severity of clinical signs increased. Furthermore, administration of tryptophan typically amelio-
ated the effects of parachlorophenylalanine. Administration of nialamide, a selective monoamine oxidase inhibitor that prevents catabolism of serotonin, prevented the onset of signs or substantially reduced the severity of an episode. In addition, administration of methysergide, a selective serotonin receptor blocker, increases clinical signs in a dose-dependent manner and has been used as a provocative test for purposes of diagnosis. Following administration of methysergide at a dose of 0.1 to 0.3 mg/kg (0.045 to 0.14 mg/lb), clinical signs can be provoked and maintained for as long as 2 hours.

Another study was undertaken to further define the nature of the serotonin abnormality within the CNS and other body systems. In that study, the concentration of the serotonin metabolite 5-HIAA was measured in urine collected over 24-hour periods for 3 days and in a minimum of 3 CSF samples that were collected at least 1 week apart from Welsh Terriers and affected and unaffected Scottish Terriers. No significant differences in 5-HIAA concentrations in urine and CSF were identified among groups. Concentrations of serotonin were also measured in whole blood samples and multiple areas of the brain and the lumbar portion of the spinal cord from affected and unaffected Scottish Terriers, and there were no significant differences between those groups. Probenecid blocks the amino acid transport mechanism that removes 5-HIAA from the brain and allows 5-HIAA accumulation in the cisternal pool of CSF and in brain tissues. When probenecid was administered to the Welsh terriers and the affected and unaffected Scottish Terriers, the overall turnover rate was not significantly different among groups. From these findings, it was proposed that the biochemical defect was unlikely directly related to serotonin concentrations. Later, studies revealed that the turnover of serotonin in the CNS of affected dogs is decreased following an episode of Scottie cramp, which suggests that neuronal function is normal at rest but there may be a functional deficiency during periods when clinical signs are apparent.

Recommended treatment options for Scottie cramp have included drugs that act on the CNS to facilitate muscle relaxation. Chlorpromazine was evaluated initially because of its ability to antagonize the effects of amphetamine, which was shown to promote episodes of Scottie cramp. Following IM injection of chlorpromazine, clinical signs of Scottie cramp resolved within 15 minutes in 2 affected dogs. Acepromazine maleate (0.1 to 0.75 mg/kg [0.045 to 0.34 mg/lb], IM) has been used to treat dogs in clinical settings. Treatment with IM injection of diazepam during an acute episode of Scottie cramp results in reduction of clinical signs. Chronic usage of oral diazepam has been used to reduce the severity and number of episodes.

Both of these treatments present a challenge to practical management of affected dogs by clients. For a dog that has an episode of Scottie cramp once daily or more frequently, treatment via injection would likely not be tolerated for long by the patient, assuming that the client was able and willing to perform the injections. Also, acepromazine can cause profound sedation, an undesired effect. Although diazepam can also cause mild sedation, its status as a controlled substance also complicates its use, especially when required on a lifelong basis. Diazepam has a short duration of action, which necessitates administration 3 times daily, and recommended dosages of diazepam are fairly high (0.5 to 1.5 mg/kg [0.23 to 0.68 mg/lb], PO, q 8 h). These facts, coupled with the cost, potentially decrease the likelihood of compliance by owners to medicate their pets. It has also been suggested that vitamin E administered orally at doses >125 U/kg/d (36.8 U/lb/d) may be effective in reducing the likelihood of episode occurrence but not the severity of an episode.

An ideal treatment for Scottie cramp would be an effective medication (other than a controlled substance) that is administered orally no more than twice daily, that has minimal adverse effects, and that is inexpensive. The selective serotonin reuptake inhibitor fluoxetine is generally used for behavior modification in animals. It has a wide safety margin and minimal adverse effects. Because fluoxetine is now available as various generic products, it can also be obtained inexpensively from pharmacies. Once ingested, fluoxetine is detectable in the CNS within 1 hour. The half-life of the drug is approximately 2 to 3 days, allowing for a once- or twice-daily administration. Selective serotonin reuptake inhibitors prevent uptake of serotonin by presynaptic neurons; thus, the extracellular concentration of serotonin increases for use by postsynaptic neurons. Given that the pathogenesis of this disease appears to be related to deficiencies in concentration or function of serotonin in the CNS and that clinical improvement is associated with experimentally induced increases in serotonin concentration, it seems likely that maintenance of higher serotonin concentrations would decrease the severity and frequency of the episodes of Scottie cramp, thereby allowing affected dogs to have more normal lives.

In the dog of this report, the dosage of fluoxetine administered was within the recommended range. The dog’s clinical signs were greatly reduced, and it was able to lead a more normal life, including accompanying its owners on walks for longer than a few minutes. Treatment with fluoxetine is inexpensive and appears to be effective and associated with few adverse effects when administered once or twice daily, compared with several other treatment options. On the basis of the apparent success of fluoxetine treatment in the dog of this report, the use of and response to this medication in dogs with Scottie cramp warrant further investigation.

References

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Comparison of tepoxalin, carprofen, and meloxicam for reducing intraocular inflammation in dogs
Margi A. Gilmour and Terry W. Lehenbauer

Objective—To compare effects of orally administered tepoxalin, carprofen, and meloxicam for controlling aqueocentesis-induced anterior uveitis in dogs, as determined by measurement of aqueous prostaglandin E₂ (PGE₂) concentrations.

Animals—38 mixed-breed dogs.

Procedures—Dogs were allotted to a control group and 3 treatment groups. Dogs in the control group received no medication. Dogs in each of the treatment groups received an NSAID (tepoxalin, 10 mg/kg, PO, q 24 h; carprofen, 2.2 mg/kg, PO, q 12 h; or meloxicam, 0.2 mg/kg, PO, q 24 h) on days 0 and 1. On day 1, dogs were anesthetized and an initial aqueocentesis was performed on both eyes; 1 hour later, a second aqueocentesis was performed. Aqueous samples were frozen at ~80°C until assayed for PGE₂ concentrations via an enzyme immunoassay kit.

Results—Significant differences between aqueous PGE₂ concentrations in the first and second samples from the control group indicated that aqueocentesis induced uveitis. Median change in PGE₂ concentrations for the tepoxalin group (10 dogs [16 eyes]), carprofen group (9 dogs [16 eyes]), or meloxicam group (9 dogs [16 eyes]). Median changes in PGE₂ concentrations for dogs treated with meloxicam or carprofen were lower but not significantly different from changes for control dogs.

Conclusions and Clinical Relevance—Tepoxalin was more effective than carprofen or meloxicam for controlling the production of PGE₂ in dogs with experimentally induced uveitis. Tepoxalin may be an appropriate choice when treating dogs with anterior uveitis. (Am J Vet Res 2009;70:902–907).