The Genetic Basis of a Kinetic Disorder of Scottish Terrier Dogs

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Transient episodes of muscular hypertonicity precipitated by exercise was first described in Scottish Terrier dogs in 1942.5 Later the term "Scotch or Scottie cramp" was introduced and is now used by most veterinarians and kennel owners when discussing the disease.15 The affected dogs appear normal when at rest or during short exercise periods. However, clinical signs are manifested with either strenuous exercise or excitement. Once manifested, the clinical signs progressively increase in severity during locomotor activity. Initially there is an arching of the back in the lumber region. Subsequently, a stiff-legged gait ensues with the hind limbs being overflexed and the front limbs markedly abducted while walking. Often when running they will "skip" with one or both legs flexed against the body. If activity continues, movement becomes progressively hindered until severely affected dogs are unable to walk. At this time the dog will be seen in a pillar-like stance. The increase in muscle tone is accompanied by an increase in electrical activity of the muscle. There is individual variation as some affected dogs will only have an arching of the back and an abnormal gait. At no time during an episode do they lose consciousness, nor do they appear to be in pain. If allowed to rest, there is complete remission of symptoms, but they will reappear if the inducing factors are not eliminated. The age at which the disease if first noted by the owner is variable, although generally it is noticed before the dog is 12 months old. We have personally observed dogs, and breeders have reported dogs who show signs of the disease at six weeks of age. The condition does not appear to shorten the life span of the dog.

There are several human diseases in which muscular hypertonicity can be precipitated by movement or exercise. McArdles disease6,7, myotonia congenita2,3 and a familial condition characterized by muscle cramping during exercise1, are all myopathies. The stiff-man syndrome is a neurologic disorder wherein painful muscle spasms are precipitated by a variety of sensory inputs, and the skeletal muscles show constant electrical activity even at rest12. Satoyoshi and Yamada13 described a condition of central nervous system (CNS) origin in two siblings, characterized by painful muscle spasms at the beginning of exercise. However, with continued exercise, the spasms became milder and less frequent.

This disease of Scottish Terrier dogs does not appear to have a homologue among the described human diseases based on the following studies. The histologic appearance of biopsied and post mortem muscle samples was normal.10 Myophosphorylase is present in normal amounts and no large glycogen stores have been demonstrated.9 Electrical stimulation of skeletal muscles in affected dogs following d-tubocurare administration did not induce a post stimulation electrical discharge of the muscle or muscular hypertonicity.9 Electrical stimulation of a peripheral nerve below a procaine nerve block did not elicit a post stimulation electrical discharge or a prolonged contraction.9 The symptoms of the disease can be effectively

suppressed with either diazepam, a commonly used CNS acting skeletal muscle relaxant and anti-anxiety drug, or by the promazine derivatives, chloropromazine and acepromazine.10
Pharmacologic evidence, obtained in a double blind study suggests that the clinical signs may be due to an abnormality in serotonin metabolism.8 Drugs which increased serotonin concentration, such as the monoamine oxidase inhibitor, nialamide, markedly decreased the severity of the clinical signs. Further, administration of p-chlorophenylalanine, a drug which decreases serotonin concentration, resulted in an increased severity of clinical signs. This data suggests the clinical signs may be a result of a functional deficiency of serotonin. This may be unique to serotonin since drugs affecting the catecholamines and acetylcholine were either ineffective, or changes in severity of the clinical signs could not be differentiated from the pharmacologic action of the compounds used.

While the etiology of this disease is obscure, a familial pattern has been noted in earlier reports.4, 5, 15 In this paper, evidence will be presented to show that "Scottie cramp" in Scottish Terrier dogs is an inherited trait with a recessive mode of transmission.

Pedigree Analysis

Most Scottish terrier breeders in the western United States and Canada who were registered with the Scottish terrier Club of America were contacted concerning litters in which at least one of the offspring was affected with "Scottie cramp". Data were used only from kennels where the owner was familiar with all offspring in litters having an incidence of "Scottie cramp" until they were 18 months of age, and where the litter was personally observed or the owner was entirely familiar with the disease.

Examination of the pedigrees of affected dogs indicated a familial pattern of the disease. Age of the sire and dam, number of previous litters, litter size, diet and climate did not appear to influence the occurrence of the disease. The dams generally had a normal gestation period and parturition.

Assuming that this disease is inherited, it would appear that it is transmitted as a recessive trait. The failure of the disease to be transmitted to offspring in successive generations, and the fact that affected offspring can arise from nonaffected parents negates the possibility of a completely dominant inheritance. In a pedigree studied, a dog was used as a sire six times; twice to closely related dams. The three offspring that resulted from matings of the two closely related dams were affected. The other four matings, were to unrelated dams. These four females did not have a previous history of "Scottie cramp" in their pedigree nor had they produced affected offspring in previous litters. These four matings resulted in more than 20 offspring, all of which were apparently normal. The four matings to unrelated dams provides additional evidence against a completely dominant inheritance. The transmission of the trait from an affected sire to his son rules out a dominant X-linked inheritance. From previously reported cases, breeding at Washington State University, and kennel records, there were 56 affected dogs where the sex was known. Of these, 30 were females and 26 were males.

Three matings of an affected male to an affected female at Washington State University resulted in one 5- and two 4-pup litters in which there was a total of 6 males and 7 females. One male died at birth and 2 females died before they were six weeks of age. ÍScottie crampÎ was observed in all 10 surviving offspring.

To ascertain if a condition is indeed recessively inherited, the type of genetic test used depends upon how the families were selected. In this study, families were selected through their offspring, thus families without affected offspring would be excluded. This is referred to as incomplete selection which can be divided into three methods of ascertainment: truncate, single, and multiple selection.11, 16 Due to the random means by which the families with affected offspring were found, families with many affected

offspring were no more likely to be found than families with only one affected offspring. This method of ascertainment is termed truncate selection.11,16 Assuming truncate selection, the expected number of affected offspring resulting from nonaffected parents in a sibship of size(s) was calculated by the a priori method14 (see Table I). For the recessive hypothesis to be confirmed there should be a close agreement between the observed and the calculated or expected number of affected dogs. As seen in Table I, the close agreement between the total number of affected dogs observed (24) and calculated (23.5) suggests that "Scottie cramp" is recessively inherited.

At this time, since we do not have a crucial mating (i.e., an affected female bred to a nonaffected male producing either all affected males or at least one nonaffected male), we cannot state definitely that the disease is due to an autosomal gene. However, the distribution of the trait among the sexes suggests that it is due to an autosomal gene.

Specific knowledge concerning the frequency of occurrence of the gene in the Scottish Terrier breed is lacking. However, this trait is distributed throughout the United States and is readily recognized as a clinical entity by many veterinarians. This suggests that the gene occurs quite frequently.

Summary

A brief clinical description and a pedigree analysis of Scottish terrier dogs having a neurologic disorder known as "Scottie cramp" is presented.

Environmental factors did not appear to account for the incidence of the disease. General pedigree analysis indicated that the condition was recessively inherited as it generally appeared only when the dam and sire were related, and affected to affected matings resulted in all affected offspring. Further affected males bred to nonaffected females did not generally produce affected offspring. If an affected offspring was produced from such a mating the female was either related to the male, or was related to dogs whose offspring had an incidence of "Scottie cramp". The recessive hypothesis was further advanced by the close agreement between the total expected and observed number of affected dogs, as calculated by a priori method, for offspring resulting from nonaffected parents. These data suggest that the disease is a recessively inherited trait.

Literature Cited

1. BETHLEM, J., J. VAN GOOL, W.C. Hullsman and A.E. F. H. MEYER. Familial nonprogressive myopathy with muscle cramps after exercise Brain 89: 569-587. 1966.
2. BROWN, G.L. and A.M. HARVEY. Congenital myotonia in the goat, Brain 62:1-18. 1941.
3. BUCHTHAL, F. And S. CLEMNESEN. Electromyographical observations in congenital myotonia. Arch. Psychiat. 16:389-403. 1941.
4. JOSHUA, J.C. Scottie cramp. Vet. Rec. 68:411-412. 1956.
5. KLAVENBEEK, A., S. KOOPMANS, and J. WINSSER. Een Aanvalsgewijs Optredende Stoornis in de Regulatie van de Spiertonus Waargenomen bij Schotsche Terriers. Tijdschr Diergeneesk. 69:14-21. 1942.
6. McARDLE, B. Myopathy due to a defect in muscle glycogen breakdown. Clin. Sci. 10:13-33. 1951.
7. MAMMAERTS, W. F., H. M. ILLINGWORTH, and C.M. PETERSON. A functional disorder of muscle associated with the absence of phosphorylase. Proc. Nat. Acad. Sci. 45:791. 1959.
8. MEYERS, K. M. and W. M. DICKSON. Indolealkylamines and hyperkinetic episodes in Scottish Terrier dogs. Fed. Proc. 28:794. 1969.
9. --------, J. E. LUND and J. T. BOYCE. Muscular cramping of central nervous system origin in Scottish Terrier dogs. Fed. Proc. 27:611. 1968.

10. --------, J. E. LUND, G. A. PADGETT, and W. M. DICKSON. Hyperkinetic episodes in Scottish Terrier dogs. J.A.V.M.A. 155:129-133. 1969.
11. MORTON, N. E. Genetic tests under incomplete ascertainment. Am. J. Human Genet. 11:1-16. 1959.
12. OLAFSON, R. A., D. W. MULDER, and f. M. HOWARD. ÍStiff-manÎ syndrome: A review of the literature, report of three additional cases and discussion of pathophysiology and therapy. Proc. Staff Meet. Mayo Clin. 39:131-144. 1964.
13. SATOYOSHI, E. and P. YAMADA. Recurrent muscle spasms of central origin. Arch. Neurol. 16:254-264. 1967.
14. SLOME, D. The genetic basis of amaurotic family idiocy. J. Genet. 27:363-372. 1933.
15. SMYTHE, R. H. Recurrent tetany in the dog. Vet. Rec. 57:380. 1945.
16. STEINBERG, A. G. Methodology in human genetics. J. Med. Educ. 34:315-334. 1959.

Table I. Occurrence of affected and nonaffected offspring from families where both parents were normal

Sz of sibship (s)	No. of sibships of size (s)(ns)	Size (s) with no. of aff. offspring (r) (1)	(2)	(3)	Total no. of offspring in r=(s)(ns)	Total no. of affected in sibship (rs)	Exp no. of affected in (ns) sibships(cs)
1	3	3	-	-	3	3	3.0
2	1	1	-	-	2	1	1.1
3	3	3	-	-	9	3	3.9
4	6	4	-	2	24	10	8.8
5	3	1	2	-	15	5	4.9
6	1	-	1	-	6	2	1.8
Total		59			24	23.5	

*There was not a sibship of size (s) with more than three affected offspring, thus a (r) of 4, 5 or 6 was not included