Hereditary hypertrophic neuropathy in Tibetan Mastiff dogs

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ABSTRACT: Hypertrophic neuropathy in a family of inbred Tibetan Mastiff dogs is shown to be due to an autosomal recessive gene. The disease has an onset at 7 to 12 weeks of age and results in varying degrees of paralytic symptoms. Affected pups from carrier parents is as close to a 3:1 ratio as can be had with 62 pups (P = 0.15). The ratio of 47 normal to 15 affected is as close to a 3:1 ratio as can be had with 62 pups (P = 0.389, 1df, P < 0.5). This is consistent with a recessive mode of inheritance. The numbers of affected males and females (8 vs. 7) indicate that the trait is not sex-linked or sex-limited. The inbreeding in this family of dogs is a reflection of the rarity of the Tibetan Mastiff breed, which only recently has been introduced into the United States. Male G was mated to his sisters (D, E, F), and half sisters (H, I). His son J was bred to aunts (D, E, F), and half sisters (K, L). Another son of male G was bred to a granddaughter (N) of male G. This level of inbreeding resulted in the expression of the autosomal recessive defect. Bitch N, the most inbred of all, has an inbreeding coefficient of 0.375.

The clinical manifestations of hypertrophic neuropathies are motor and sensory impairment, slowed nerve conduction, and enlargement of nerves due to proliferation of Schwann cells following segmental demyelination of peripheral nerves. This report identifies autosomal recessive hypertrophic neuropathy in Tibetan Mastiff dogs.

Results and Discussion

Fifteen puppies (8 males and 7 females) showed clinical signs of generalized weakness, diminished reflexes, and loss of muscle tone. Severity of the signs varied from total recumbency to a less severe paresis characteristic of a shuffling gait. Affected pups began showing symptoms at 7 to 12 weeks old. These symptoms are compatible with hypertrophic neuropathy, and the disease was confirmed histologically in eight of the pups.

Parents of the affected dogs were identified, and all litters of pups from parents that had both produced an affected pup were identified. These litters contained 62 pups, 15 of which were affected. This includes 10 litters, 8 of which contained affected pups and 2 litters containing none but were from parents that had both produced affected pups. The ratio of 47 normal to 15 affected is as close to a 3:1 ratio as can be had with 62 pups (P = 0.389, 1df, P < 0.5). This is consistent with a recessive mode of inheritance. The numbers of affected males and females (8 vs. 7) indicate that the trait is not sex-linked or sex-limited.

The pedigree of the family of dogs is presented in Figure 1. All carriers of the trait in generation II are from the mating of A and B. Since the bitch, B, was also bred to male C with no known carriers resulting, it is most likely that the trait was introduced through male A; however, this can't be proven statistically.

Generation II bitches D and E were proven carriers by mating to males G or J. Bitch F produced 26 normal pups sired by male G, and four normal pups from male J. She is a noncarrier (P = 0.0005). The male, G, is proven to be a carrier by producing affected pups from both E and F. In generation III, male J is proven to be a carrier by string affected pups from bitches D, E, K, and L. These same breedings prove that bitches D, K, and L are carriers. Male J produced four normal pups when bred to his mother, F. One of the bitches of that litter, N, was proven a carrier by producing affected pups when bred to male M. The same litter also implicated male M as a carrier. Although the ratio of 47 normal to 15 affected pups from carrier parents is as close a fit to a 3:1 ratio as can be had, the distribution of pups in the litters does reveal some unlikely litters. One J × D mating produced 9 normal pups (P = 0.075). One E × G mating produced 1 normal and 4 affected pups (P = 0.15). The probability of these litters is not highly significant, but they are unlikely to occur.

The inbreeding in this family of dogs is a reflection of the rarity of the Tibetan Mastiff breed, which only recently has been introduced into the United States. Male G was mated to his sisters (D, E, F), and half sisters (H, I). His son J was bred to aunts (D, E, F), and half sisters (K, L). Another son of male G was bred to a granddaughter (N) of male G. This level of inbreeding resulted in the expression of the autosomal recessive defect. Bitch N, the most inbred of all, has an inbreeding coefficient of 0.375.

References