A distinct Mendelian autosomal recessive syndrome involving the association of anotia, palate agenesis, bifid tongue, and polydactyly in the dog

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Abstract — A presumed genetic syndrome is described in a family of St. Bernards. Four identically affected littermates presented the association of palate agenesis, anotia, incomplete bifid tongue, preaxial hind paw polydactyly, and an extra thoracic vertebra and rib. Pedigree analysis is compatible with an autosomal recessive gene.

Résumé — Syndrome Mendélien autosomique récessif distinct chez le chien comprenant une association d'anotie, d'agénésie du palais, de langue bifide et de polydactylie. Un présumé syndrome génétique est décrite dans une famille de Saint-Bernard. Quatre individus d'une même portée affectées de façon identique présentaient une association d'agénésie du palais, d'anotie, de bifide incomplète de la langue, de polydactylie préaxiale à la patte arrière ainsi qu'un vertèbre thoracique et une côte supplémentaires. La présence d'un gène autosomique récessif est compatible avec l'analyse généalogique.

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A novel mutation of an autosomal recessive gene in a family of St. Bernards is reported. This mutant gene results in a fully penetrant syndrome, characterized by palate agenesis, anotia, an incomplete bifid tongue, preaxial hind paw (pes) polydactyly, and an extra thoracic vertebra and rib (Figures 1-B,C,D; 2-A,B,C,D).

Four (3 female, 1 male) puppies in a litter of 6 were similarly affected. The pedigree is shown in Figure 1-A. The affected animals were euthanized after birth by a veterinarian, at the owner's request. According to the owner, the studied litter was the 5th parity from the same pairing, with a progeny history of 22 normal and 6 affected individuals in the 4 previous litters. The parental dogs were not consanguineous, were healthy, and had had no anomalous antecedents. All 4 puppies had the same complex of malformations with only a few small differences. Three out of the 4 had 6 digits in the hind paws, classified as preaxial polydactyly (1) (Figure 1-B). All affected puppies lacked external ears (Figure 1-D), although puppy 3 had a very small auricular tag on the left side. The auditory canal was atresic, but the inner ear was normal, including the tympanic membrane and the auditory ossicles.

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All malformed animals had anomalies in the oral cavity. The tongue had a conspicuous, sagittal cleft along

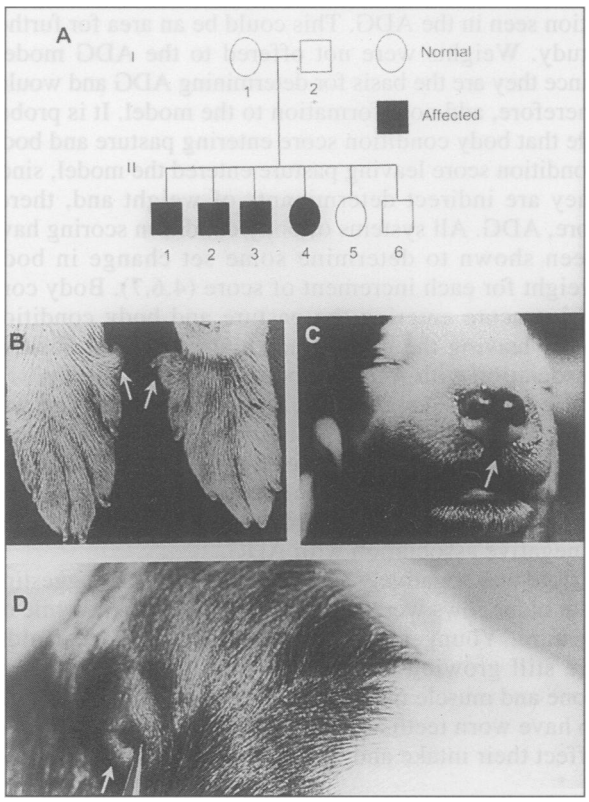

Figure 1. (A) The family pedigree and the identification of each affected individual. (B) Hind paws of puppy 2; arrows point to the extra digits. (C) Head of puppy 2; arrow points toward the harelip. (D) Right side of puppy 3's head; arrow indicates the anotia and auricular scar.

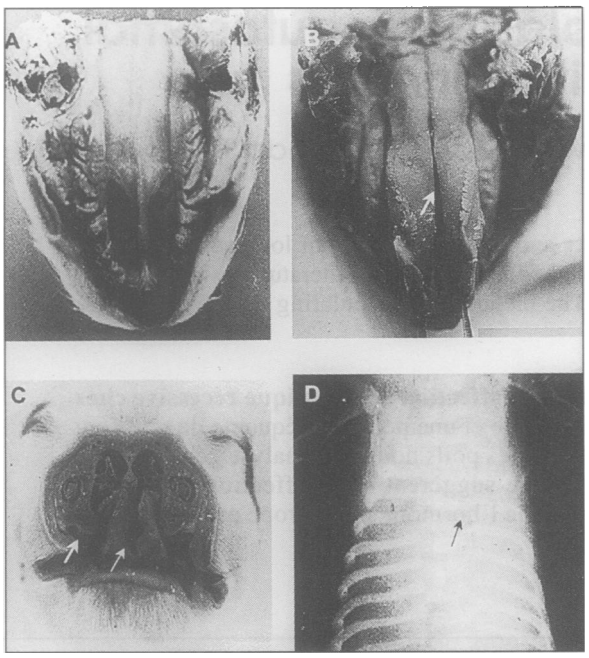

Figure 2. (A) Ventral view of the oral cavity of puppy 2 showing the absence of the palate and the communication with the nasal cavity. (B) Dorsal view of the tongue from puppy 2; arrow indicates the median cleft dividing the tongue. (C) Transverse section of the nasal and maxillary regions of puppy 3's head; thick arrow indicates the border of the gum where the palate ceased developing; narrow arrow indicates the ventral surface of the tongue left intact by the median cleft. (D) Radiographic view of puppy 4's thorax; arrow points toward the 4th bifid rib.

its dorsal surface, running from the root toward the apex to form an incompletely bifid tongue (Figure 2-B,C). The cleft was deeper at the apex, without reaching the lower surface. The palate was completely absent, so that the oral and nasal cavities coalesced (Figure 2-A,C) and puppies 2 and 4 had a slight harelip (Figure 1-C). Thoracic radiographs showed 14 ribs and their corresponding vertebrae in 3 of the affected animals, but puppy 4 had 14 ribs on the right side and 13 on the left, because the 4th rib was bifid and articulated with both the 4th and the 5th vertebrae (Figure 2-D). No gross internal anomalies were observed on postmortem examination of the abdominal and thoracic cavities.

Genetic databases (2,3) were screened in a search for similar genetic entities. The search rendered negative results in humans and animals.

Although most of the traits were highly constant in the different affected animals, it is difficult to be certain if the polydactyly is really part of the syndrome. In many breeds of dogs, and also wolves and jackals, there are 5 digits on the front feet and 4 on the hind feet. In addition, some breeds have a vestigial 1st digit, which is usually referred as the dewclaw. However, some large breeds, such as St. Bernard and Newfoundland, sometimes have a 6th digit, the "double-clawed" condition (4). This might be experimentally defined, if the putative mutant gene were introduced in a different breed background.

The occurrence of the same syndrome in 4 littermates of different sex and, apparently, in several individuals from previous litters by the same parents can be considered as strong evidence of the action of a fully penetrant, Mendelian autosomal recessive mutant gene. The identity of the putative mutant gene is unknown, and the proposal of a candidate gene is not possible, because no equivalent genetic pathology has been described previously in man or other species.

The availability of molecular genetic resources in dogs, such as DNA genetic markers like microsatellites (5), opens the possibility of genetic mapping by linkage analysis and eventual cloning of the putative mutant gene. In this context, the conservation and study of canine families with gene mutations is highly relevant, in order to contribute to gene identification, gene function, and the understanding of the processes of development.

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