PITUITARY DWARFISM IN A GERMAN SEPHERD-AKITA MIX DOG

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Abstract:*A 4 month old unneutered male German shepherd-Akita mix dog was presented at the Veterinary Teaching Hospital of Iasi for stunted growth in spite of a slightly increased appetite and adequate dietary intake. The dog underwent physical, routine and specific clinicopathological investigations. Physical examination revealed stunted growth, muscle atrophy, delayed dental eruption, woolly hair coat, fox-like facial features and underdeveloped testis. The owner did not report any other changes in the general state of the dog. Routine clinicopathological examination did not reveal any abnormalities. Considering the case history, age, breed and the physical appearance of the dog, the most probable suspected disease was hormonal deficiency. Special laboratory investigations revealed a low level of GH and FT4, confirming congenital pituitary dwarfism. The recommended treatment in this case was thyroid hormone replacement and medroxy-progesterone acetate at three weeks interval, than every six weeks. Four weeks post-diagnosis, the dog was brought back to the clinic with a three day history of profuse watery diarrhea, severe dehydration, anorexia and hypothermia and died shortly after admittance. The current paper describes a case of congenital pituitary dwarfism in a four month old German shepherd-Akita mix, a disease with a rare incidence in dogs.*

Keywords: *congenital GH deficiency, dog, hypothyroidism, pituitary dwarfism.*

INTRODUCTION

Pituitary dwarfism is the result of defects in the organogenesis of the pituitary gland and consecutive isolated or combined hormonal deficiency. In most cases, this endocrinopathy can occur as a consequence of cysts formation in the anterior pituitary lobe, followed by pressure on the adjacent tissue and atrophy or hypoplasia. Pituitary developmental deficits can occur due to an autosomal recessive inherited abnormality(Mooney and Peterson 2012). Congenital dwarfism has been reported with a higher incidence in German shepherds, 20% of dogs in this breed being estimated to carry the faulty gene. Both parents have to be carriers of a single copy of the gene and with a recessive gene to give birth to an affected dog. If two carriers are mated, almost 50% of their pups will be carriers and on average 25% of their offspring will suffer from pituitary dwarfism (Kooistra, Voorhout et al. 2000).

Pituitary dwarfism in German Shepherds is also associated to cysts development in Rathke`s pouch as consequence of underlying genetic defects, but it is not yet clear if the cysts are the cause of this endocrinopathy(Voorbij, Leegwater et al. 2010, Voorbij, van Steenbeek et al. 2011). Other predisposed breeds include wolfhounds and a series of pastoral breeds. Pituitary dwarfism occurs rarely in felines (Mooney and Peterson 2012).

The most important aspect of pituitary dwarfism is growth hormone (GH) deficiency and secondary hypothyroidism, the cause of most significant clinical signs. The secretion of GH takes action in a pulsatile fashion, under the stimulant effect of GH-releasing hormone and inhibitory action of somatostatin, both secreted by the hypothalamus. Growth hormone exerts

both catabolic and anabolic effects(Mooney and Peterson 2004). Catabolic actions include insulin antagonism, with consecutive increase of lipolysis, gluconeogenesis and reduced glucose uptake in the intracellular space. On the other hand, the anabolic effects are controlled by insulin like growth factor-1 (IGF-1), secreted mainly in the liver, under the direct influence of GH. The IGF-1 is involved in processes of protein synthesis, chondrogenesis, growth and body size. Impaired thyroid function is the consequence of combined pituitary hormone deficiency. The physiopathology in this form of secondary hypothyroidism is different from primary hypothyroidism, and instead of being elevated, the level of TSH is on the lower limit as a consequence of reduced pituitary function(Mooney and Peterson 2004, Rijnberk and Kooistra 2010).

The current paper describe a case of congenital pituitary dwarfism in a four month old German Shepherd-Akita mix.

MATERIALS AND METHODS

A four month old unneutered male German Shepherd-Akita mix dog was presented at the Veterinary Teaching Hospital of Iasi for stunted growth in spite of a slightly increased appetite and adequate dietary intake. The dog was well proportioned to his body size but as reported by the owner, he was three to four times smaller compared to healthy littermates, in spite of receiving the same care, including type and amount of food and routine deworming and vaccination procedures. The dog underwent physical, routine and specific clinicopathological investigations. Considering the reported clinical signs, age, breed and the physical appearance of the dog, the most probable suspected disease was congenital pituitary dwarfism. Diagnosis protocol included physical examination, clinical findings, routine organ function evaluation and specific determinations, such as IGF-1 and thyroid hormones.

RESULTS AND DISCUSSIONS

Physical and clinical examination indicated a wide range of data. Musculoskeletal system evaluation revealed stunted growth, muscle atrophy, thin skeleton, delayed dental eruption and fox-like facial features, all characteristic signs of pituitary dwarfism. Also, on dermal examination, a series of specific features have been noted, such as thin skin, seborrhea sicca, woolly hair coat and retention of the lanugo hairs. Reproductive system was also affected, the dog was not cryptorchid as usually expected with pituitary dwarfism, but presented underdeveloped testis. No other changes of the general state of the dog were observed. Routine clinicopathological examination did not reveal any abnormalities regarding the kidney function, which is most often impaired in dwarfs due to the abnormal development of the glomeruli and reduced glomerular filtration rate(Mooney and Peterson 2012).

Basal IGF-1 level was well under the lower end of the reference parameters 12.57 nmol/l or 95.9 ng/ml (reference: 26.2-104.8 nmol/L or 200-800 ng/ml), confirming the suspicion of pituitary dwarfism. Secondary hypothyroidism was also diagnosed, based on a free thyroxine level of 8.8 pmol/l (reference: 10-45 pmol/l).

Figure 1: *Stunted growth, muscle atrophy, thin skeleton, fox-like facial features, woolly hair coat and retention of the lanugo hairs in a confirmed case of pituitary dwarfism*

Other recommended diagnosis procedures include determinations of basal specific GH, CT or MRI examination and pituitary function tests (Mooney and Peterson 2012). Even if directly affected by the disease, GH level is not always indicated as a sole diagnosis test. First, specific GH holds a low worldwide availability to clinicians and its determination usually requires shifting samples over borders. Also, GH is secreted in a pulsatile fashion and it can appear decreased in normal healthy dogs. However, GH determinations can be used within the pituitary function test, which is a definitive diagnosis procedure. The test is based on the administration of GH stimulants, such as GH-releasing hormone (GHRH) 1µg/kg i.v., alpha-adrenergic drugs, like clonidine 10 µg/kg i.v. or xilazyne 100 µg/kg i.v, followed by GH determinations at zero hours and then at 30 minutes. The expected response in a healthy dog is a two to four fold increase of the GH level, while a reduced increase is specific for pituitary dwarfism. Intracranial imaging by MRI or CT can reveal cysts and/or reduced volume (hypoplasia) of the pituitary gland (Meij, Mol et al. 1996, Hamann, Kooistra et al. 1999).

Life expectancy in these cases does is 3 to 5 years old and by this age the dogs usually develop a series of complications secondary to progressive loss of the pituitary function, increasing volume of the pituitary cysts and chronic kidney disease. Even if treated properly, the prognosis remains guarded. Treatment protocol relies on hormonal replacement. Canine GH is not currently available, but porcine GH can be used as a treatment option, as the amino acid sequence is similar in both species. Human GH on the other hand cannot be used in dogs due to the different structure of the hormone between humans and dogs, which can lead to antibody formation (van Herpen, Rijnberk et al. 1994). Porcine GH can be administered subcutaneously in doses of 0.1 – 0.3 IU/kg, three times a week. Long term frequency of porcine GH administration can be reduced, based on the IGF-1 plasma concentration. Overdosing can lead to insulin resistance, thus blood glucose level should also be monitored along with the IGF-1. When GH is not available, progesterone can be used to induce the expression of the GH gene in the mammary gland of the dog, a process followed by GH secretion to the systemic circulation. Medroxiprogestesterone acetate 2.5-5 mg/kg can be administered subcutaneously every three weeks, and then every six weeks, resulting in increasing of body size and hair growth (Knottenbelt and Herrtage 2002). Progesterone can also lead severe side effects including insulin resistance, acromegaly, pyoderma, development of mammary tumours and cystic endometrial hyperplasia. Thus, all female dogs should be spayed before progesterone administration. Secondary hypothyroidism should be addressed with levothyroxine, 10 to 44 µg/kg administered orally every 12 h, based on free T4, total T4 and TSH (Mooney and Peterson 2012).

In the current case, the dog was presented back to the clinic, with a four day history of profuse diarrhea, anorexia, severe dehydration and lethargy and died shortly after admission. The owners did not agree to necropsy examination, thus confirming if there was pituitary hypoplasia or cysts, was not possible, nor the cause of death.

CONCLUSION

The current case presented a wide variety of clinical signs, all indicative for pituitary dwarfism. The German shepherd mix breed was also an indicative clue for the diagnosis. Although the physical features of pituitary dwarfism seemed obvious, the final diagnosis was based on low levels of IGF-1 and thyroid hormones determination. Treatment and hormonal replacement needs to be life-long. As medication on its own can lead to a series of complications protocol also requires periodical monitoring of hormone plasma levels. As in the current case, pituitary dwarfs have a low expectancy of life and even with proper treatment the long term survival rate does not exceed four to five years of age.

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