Hypoadrenocorticism in young related Nova Scotia duck tolling retrievers

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Abstract — Five cases of hypoadrenocorticism in young related Nova Scotia duck tolling retrievers are discussed. Two were littermates and the others shared one or more common ancestors. No specific mode of inheritance was determined. Clinical and laboratory findings typical of hypoadrenocorticism were observed. Further documentation will be required to confrim a breed predisposition.

Résumé — Insuffisance surrénale chez de jeunes Nova Scotia duck tolling retrievers apparentés. Cinq cas d'insuffisance surrénale chez de jeunes Nova Scotia duck tolling retrievers apparentés ont été étudiés. Deux cas provenaient de la même portée et les autres avaient un ou plusieurs ancêtres communs. Aucun mode spécifique de transmission génétique n'a été déterminé. Des signes cliniques et des résultats de laboratoire typiques de l'insuffisance surrénale ont été observés. Une documentation plus poussée sera nécessaire pour confirmer une prédisposition raciale.

(Traduit par docteur André Blouin)

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Hypoadrenocorticism is an uncommon condition that most frequently affects young to middle-aged female dogs (1,2). Familial hypoadrenocorticism has been recognized in standard poodles (3) and leonbergers (4). Recently, Great Danes, Portuguese water dogs, rottweilers, standard poodles, West Highland white terriers, and wheaten terriers were found to have significantly higher relative risks of developing hypoadrenocorticism (1). Breeds suspected of being predisposed to hypoadrenocorticism include Labrador retrievers (5), and bearded collies and Old English sheepdogs (6). Several cases of hypoadrenocorticism in young Nova Scotia duck tolling retrievers have recently been observed in eastern Canada. It is the purpose of this report to summarize these cases and alert practitioners to a possible breed predisposition to this condition.

Five cases of hypoadrenocorticism seen in the past 2 y at either the Atlantic Veterinary College, Prince Edward Island, or private practices in Nova Scotia and New Brunswick are included in this report (Table 1). The first author became aware of these cases through evaluation of diagnostic tests performed at the Atlantic Veterinary College or through personal communications. A survey of practitioners or breeders was not performed, so this report does not describe breed prevalence of this condition. Pedigrees were made available by the owners. Diagnosis of hypoadrenocorticism was made by necropsy findings of severe adrenal cortical atrophy or by demonstrating low to low-normal (0–20 nmol/L) baseline serum cortisol concentrations that failed to increase appreciably 2 h after IM administration of adrenocorticotrophic hormone (ACTH) gel. The atypical cortisol concentrations seen in the ACTH stimulation test in case 3 (Table 1) were considered to be due to assay interference by declining serum concentrations of prednisolone, as oral prednisone had been administered previously. Results of the remaining ACTH stimulation tests (cases 4,5) were similar to those reported for other dogs with hypoadrenocorticism (1,2).

Of the 5 dogs reported, 4 were very young (≤7 mo), and 1 was 3 years old. In a recent study of 225 cases of canine hypoadrenocorticism, the ages of affected dogs varied from 4 mo to 14 y, with the value for the 25th to 75th percentile being 2.5 to 6.5 y of age (1). Three of the dogs were male and 2 were female. Although higher percentages of female compared with male dogs have been reported with hypoadrenocorticism (1,2), the number of cases reported here is too low to make presumptions about sex predilection within this breed. All 5 dogs in this report had clinical signs consistent with previous reports of hypoadrenocorticism in dogs (2,4), including weakness (5/5), depression (5/5), vomiting (5/5), and diarrhea (5/5). Blood was present in the stool of 1 dog (case 3), possibly as a result of hypoadrenocorticism (7) or the administration of nonsteroidal anti-inflammatory medication. One dog (case 4) was bradycardic and 1 (case 3) had a normal heart rate; the information was not available for the others. Bradycardia or weak pulses have been reported in approximately 1/3rd of dogs with hypoadrenocorticism (2).

Two male littermates (cases 1,2) had unusual aspects to their history prior to the development of signs of hypoadrenocorticism at approximately 17 wk of age.

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Both had developed bilateral diffuse corneal edema at 13 wk of age, which slowly resolved following treatment with ophthalmic corticosteroid medication. Later, postmortem examination of 1 of these pups (case 2) revealed bilateral neutrophilic keratitis and lymphocytic conjunctivitis. Another dog (case 3) had multiple white punctate corneal lesions present diffusely over the cornea of both eyes when examined at 7 mo of age.

In addition to the ophthalmic changes, 1 of the male littermates (case 2) had also experienced 3 seizures in a 24-hour period at approximately 16 wk of age. No laboratory evaluation was performed at that time, so hypoglycemia could not be ruled out. Hypoglycemia can be associated with hypoadrenocorticism in dogs and is occasionally severe enough to result in seizure activity (8). However, this particular pup died 1 wk later and postmortem examination revealed lymphocytic meningitis, in addition to the findings of severe bilateral adrenal cortical atrophy and the keratitis-conjunctivitis described above. Therefore, the previous seizure activity could have been due to meningeal inflammation, hypoglycemia, or an unrelated cause. The other male littermate (case 1) died at approximately the same time (17 wk). Postmortem examination revealed bronchointerstitial pneumonia, necrotizing polyarteritis, and severe bilateral adrenal cortical atrophy. The bronchointerstitial pneumonia was suspected to be due to aspiration of oral cavity contents. The necrotizing polyarteritis was present in medium-sized arteries of the epicardium, and was characterized by infiltration of moderate numbers of lymphocytes, macrophages, and neutrophils within and around the vessel walls.

In those patients in which serum biochemical data were available (4/5 cases), hyponatremia, hyperkalemia, hypochloremia, and an Na/K ratio below 23 (Table 1) were present. This finding is consistent with that of the majority of cases of hypoadrenocorticism (1,2). Hypoglycemia (2.1 mmol/L, reference range: 3.3–5.6 mmol/L) was present in 1 dog (case 1), and, in a recent study, had been observed in 16.7 % of dogs with hypoadrenocorticism (1). Azotemia was noted in 4 dogs, whose serum urea concentrations ranged from 15.4 to 63.6 mmol/L (reference range: 3.0–10.5 mmol/L). Serum creatinine concentrations were also increased (327 to 593 umol/L, reference range: 60–140 umol/L) in 3 dogs; 1 dog had a value at the upper limit of normal (136 umol/L). Serum phosphorus concentrations were increased in the 3 dogs (cases 1,3,5) in which they were measured (2.15–4.52 mmol/L, reference range: 0.82–1.87 mmol/L). Bone growth likely contributed to the increased phosphorus concentration in the 2 younger dogs (cases 1,3). Concurrent urine specific gravity (1.030) was available for 1 dog (case 3) and was considered to be inappropriately low for a dehydrated patient. Low urine specific gravity values can be seen in hypoadrenocorticism; severe hyponatremia impairs the ability of the kidney to concentrate through medullary solute washout (2). Differentiation from primary renal disease is not possible in these cases without performing an ACTH stimulation test and assessing whether values for urine specific gravity, serum creatinine concentrations and serum urea concentrations normalize following therapy for hypoadrenocorticism. Three of the 4 dogs for which data were available had increased serum creatine kinase (CK) concentrations, ranging from 804 to 1036 U/L (reference range: 0–300 U/L). Mild muscle cellular leakage secondary to hypovolemia is one possible explanation, but other mechanisms (trauma, immune-mediated myositis) cannot be ruled out. One dog (case 1) demonstrated hypercalcemia (5.72 mmol/L, reference range: 2.24–3.04 mmol/L). Approximately 1/3rd of dogs with hypoadrenocorticism are hypercalcemic at the time they demonstrate hyperkalemia (2).

Complete blood count results were available for 4 dogs. No abnormalities were found in 2 dogs (cases 1,5). One dog (case 4) had a mild lymphocytosis (7.86×10^9/L, reference range: $1.0–4.8 \times 10^9$/L). One dog (case 3) had leukogram changes, consistent with stress attributed to previous prednisone administration. This same dog also had a mild nonregenerative anemia (RBC: 4.45×10^{12}/L, reference range: $5.5–8.5 \times 10^{12}$/L) and a mild thrombocytopenia (160×10^9/L, reference range: $200–900 \times 10^9$/L). These findings were attributed to recent gastrointestinal blood loss.

Three of the dogs (cases 3,4,5) were successfully stabilized on medical therapy, consisting of oral fludrocortisone acetate (Florinef, Squibb, Bristol-Myers-Squibb, Montreal, Quebec) at an initial dose of 0.01–0.02 mg/kg bodyweight (BW), q12h, and oral prednisone (Apo-prednisone, Apotex, Toronto, Ontario) at initial dose of 0.15–0.2 mg/kg BW, q24h or q12h.

Primary idiopathic hypoadrenocorticism in dogs is presumed to be an immune-mediated disease (2,9), based on the histologic findings of lymphoid and plasma cell infiltration in the adrenal cortex of some patients (9), as well as the presence of anti-adrenal antibodies reported in the serum of 2 patients (9). It is not possible to determine if the hypoadrenocorticism seen in these 5 Nova Scotia duck tolling retrievers was immune-mediated. In 1 dog (case 2), the significant lymphocytic infiltration of the adrenal cortex was supportive of an immune-mediated cause. It is interesting to speculate that the corneal opacity seen in 3 of the dogs, as well as the necrotizing arteritis in 1 dog and the lymphocytic meningitis in another dog, could have an immune-mediated basis.

All 5 dogs reported here are related (Table 1). While cases 1 and 2 are closely related (littermates), the remaining dogs shared 1 or more common distant ancestors. No one ancestor was common to all 5 dogs and no specific mode of inheritance could be determined. As the hypoadrenocorticism occurred in both male and female dogs, a sex-linked mode of inheritance is unlikely.

In summary, the 5 Nova Scotia duck tolling retrievers had similar clinical signs and laboratory findings to those seen in other cases of hypoadrenocorticism. Although the number of cases reported here is very low, the dogs were younger than the age in which hypoadrenocorticism is most often diagnosed. Because very young dogs commonly present with vomiting and diarrhea due to dietary indiscretions or infectious gastroenteritis, it was not surprising that most of the cases included here initially received a possible diagnosis of gastroenteritis. Tentative diagnosis of hypoadrenocorticism requires a careful history, physical examination,

Table 1. Signalment, laboratory findings, sequelae, necropsy findings, and pedigree information for 5 Nova Scotia duck tolling retrievers with hypoadrenocorticism

Case	Sex	Age	Clinical Signs	Electrolyte Concentrations (mmol/L)	Other Laboratory findings	Cortisol (nmol/L) 1. Baseline 2. Post-ACTH	Sequelae	Necropsy	Pedigree Available	Comments
1	M	4 mo	Weakness Depression Vomiting Diarrhea Previous corneal edema Dehydration	Na: 127 K: 8.0 Cl: 94 Na/K: 16	Azotemia Increased CK concentration Normal CBC Hyperkalcemia	1. 4.2 nmol/L 2. N/A	Died	Severe bilateral adrenal atrophy. Bronchointerstitial pneumonia. Necrotizing polyarteritis.	Partial	Littermate to case 2. Shares same G sire on dam's side as on dam's side of case 3.
2	M	5 mo	Weakness Depression Diarrhea Previous corneal edema Previous seizuring	—	—	—	Died	Severe bilateral adrenal atrophy and lymphocytic infiltration. Keratitis. Conjunctivitis. Meningtitis.	Partial	Littermate to case 1. Shares same G sire on dam's side as on dam's side of case 3.
3	F	7 mo	Weakness Depression Vomiting Diarrhea (bloody) Dehydration	Na: 116 K: 7.1 Cl: 87 Na/K: 16	Azotemia Mild thrombocytopenia Mild nonregenerative anemia Stress leukogram[a]	1. 51 nmol/L[a] 2. 21 nmol/L[a]	Stabilized on therapy	—	Yes	Shares same G sire on dam's side as on dam's side of cases 1 and 2. Shares same GGGG sire on sire's side as on sire's side of case 5. Shares same GGG sire on dam's side as on dam's side of case 5.
4	M	3.5 mo	Weakness Depression Inappetence Dehydration Bradycardia	Na: 138 K: 7.7 Cl: 100 Na/K: 18	Azotemia Moderate lymphocytosis	1. 1.4 nmol/L 2. 8.6 nmol/L	Stabilized on therapy	—	Partial	Shares same G sire on sire's side as on sire's side of case 5. Shares same GGG sire on dam's side as the GGG sire on sire's side of case 5.
5	F	3 yr	Weakness Vomiting Diarrhea Dehydration	Na: 134 K: 7.1 Cl: 96 Na/K: 19	Azotemia Increased CK concentration	1. 7.7 nmol/L 2. 7.2 nmol/L	Stabilized on therapy	—	Yes	Shares same GGGG sire on sire's side as on sire's side of case 3. Shares same GGG sire on dam's side as on dam's side of case 3.

Reference ranges are as follows: sodium (Na): 144–162 mmol/L, potassium (K): 3.6–6.0 mmol/L, chloride (Cl): 106–126 mmol/L, baseline cortisol concentration: 14–180 nmol/L, post-ACTH cortisol concentration: 231–571 nmol/L.
G: grand. GGG: great great grand. GGGG: great great great grand. ACTH: adrenocorticotrophic hormone
[a]Atypical results attributed to declining serum concentrations of prednisolone

and complete laboratory screening. Definitive diagnosis is made based on the results of ACTH stimulation testing or, unfortunately, through postmortem examination. The confirmation that a true breed predisposition to hypoadrenocorticism exists in Nova Scotia duck tolling retrievers will require documentation of further cases and comprehensive surveys of practitioners and breeders. At present, however, it is wise for any practitioner faced with clinical signs of depression, vomiting, or diarrhea in a young Nova Scotia duck tolling retriever to consider the possibility of hypoadrenocorticism and to test accordingly.

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Addendum

Two of the treated dogs (cases 3,4) developed clinical and laboratory findings consistent with immune-mediated hemolytic anemia within 1 y following diagnosis of hypoadrenocorticism. CVJ

References

1. Peterson ME, Kintzer PP, Kass PH. Pretreatment clinical and laboratory findings in dogs with hypoadrenocorticism: 225 cases (1979–1993). J Am Vet Med Assoc 1996; 208: 85–91.
2. Hardy RM. Hypoadrenal gland disease. In: Ettinger SJ, Feldman EC, eds. Textbook of Veterinary Internal Medicine-Diseases of the Dog and Cat, 4th ed. Philadelphia: WB Saunders, 1995: 1579–1593.
3. Shaker E, Hurvitz AI, Peterson ME. Hypoadrenocorticism in a family of Standard Poodles. J Am Vet Med Assoc 1988; 192: 1091–92.
4. Smallwood LJ, Barsanti J. Hypoadrenocorticism in a family of Leonbergers. J Am Anim Hosp Assoc 1995; 31: 301–305.
5. Feldman E, Nelson RW, Lynn RC. Desoxycorticosterone pivalate (DOCP) treatment of canine and feline hypoadrenocorticism. In: Kirk RW, Bonagura JD, eds. Current Veterinary Therapy XI: Small Animal Practice. Philadelphia: WB Saunders, 1992: 353–355.
6. Aronson L. Hypoadrenocorticism (letter). J Am Anim Hosp Assoc 1996; 32: 90.
7. Medinger TL, Williams DA, Bruyette DS. Severe gastrointestinal tract hemorrhage in three dogs with hypoadrenocorticism. J Am Vet Med Assoc 1993; 202: 1869–1872.
8. Levy JK. Hypoglycemic seizures attributable to hypoadrenocorticism in a dog. J Am Vet Med Assoc 1994; 204: 526–530.
9. Schaer M, Riley WJ, Buergelt CD, *et al.* Autoimmunity and Addison's disease in the dog. J Am Anim Hosp Assoc 1986; 22: 789–794.

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