Schmidt's syndrome in a dog: a case report

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ABSTRACT: This report describes a clinical case and development of the polyglandular failure syndrome including hypothyroidism and hypoadrenocorticism in a 6-year-old female Black Russian Terrier. The bitch was presented because of hypothyroidism on the first occasion. Oral supplementation with sodium levothyroxine resulted in clinical improvement. Four months later, it was presented again with similar and rather vague clinical signs and diagnosed with adrenocortical deficiency both in mineralocorticoid and glucocorticoid functions. Indirect immunofluorescence to investigate the presence of circulating autoantibodies against the thyroid and adrenal glands revealed only anti-thyroid antibodies (microsomal pattern) at a dilution of 1:40. Since then, the bitch has been on hydrocortisone and fludrocortisone with no adjustments necessary for a year. The combination of two endocrinopathies and the episodic course of hypoadrenocorticism made the final diagnosis difficult, posed a diagnostic challenge and required the owner's compliance with diagnostic and therapeutic procedures.

Keywords: polyglandular failure syndrome; hypothyroidism; hypoadrenocorticism

A combination of primary hypothyroidism and primary hypoadrenocorticism, known as Schmidt's syndrome in humans, has already been recognised in the dog (Bartges and Nielson, 1992; Kooistra et al., 1995; Smallwood and Barsanti, 1995). Polyglandular failure syndromes characterised by the presence of autoantibodies against various glandular tissues are, however, uncommon in the dog. Each patient is therefore worth reporting (Bowen et al., 1986; Pedersen, 1999).

Case history

A 6-year-old female Black Russian Terrier was presented with a history of lethargy, decreased appetite, and disinterest in exercise. The above signs were gradual in onset, and most distinct in comparison with its daughter kept by the same owner. The bitch manifested locomotor problems including stiff gait causing an abnormal wear of nails on the thoracic limbs and was therefore examined to rule out the wobbler disease. The oestrous cycle was regular. However, alopecia due to hair clipping on the flank for purposes of ultrasonographic examination of reproductive organs, four months prior to the current presentation, was slow to re-grow. The results of other clinical physical examinations were unremarkable. Blood chemistry values are given in Table 1 – A. As shown, there was an increase in serum cholesterol and creatine kinase as well as a mild azotaemia. Parallel determination of total thyroxine (tT_4 < 12.87nmol/l) and canine thyrotropin (cTSH = 1.9 ng/ml) confirmed hypothyroidism because the low thyroxine associated with high TSH is very consistent with hypothyroidism (Kolevska et al., 2002). Oral supplementation with sodium levothyroxine (Euthyrox; Merck; 10 µg/kg twice daily) was commenced and the bitch made clinical improvement. Two months later, pre-pill tT_4 amounted to 55 nmol/l, so the dose was adjusted down to only 7.5 µg/kg twice daily.

The immunological part of the report was supported by the Ministry of Agriculture of the Czech Republic (Grant No. MZe 0002716201).

Table 1. Clinical chemistry data on hypothyreosis (A – the first clinical presentation) and hypoadrenocorticism (B – the second clinical presentation four months later) in a 6-year-old female Black Russian Terrier

	A	B
Total protein (g/l)	68	61
Albumin (g/l)	25.1	21
Total bilirubin (μmol/l)	4	5
Creatinine (μmol/l)	180.8	231
Urea (mmol/l)	12.3	23.0
Glucose (mmol/l)	5.2	2.5
Alkaline phosphatase (μkat/l)	0.24	0.83
Alanine aminotransferase (μkat/l)	0.32	0.24
Aspartate aminotransferase (μkat/l)	0.65	0.39
Creatine kinase (μkat/l)	9.46	–
Lactate dehydrogenase (μkat/l)	22.29	–
Cholesterol (mmol/l)	6.30	2.75
Triglycerides (mmol/l)	0.52	0.28
Calcium (mmol/l)	2.65	3.64
Inorganic phosphorus (mmol/l)	2.1	2.94
Sodium (mmol/l)	143.5	133.0
Potassium (mmol/l)	5.43	6.91
Chloride (mmol/l)	109.9	97.9

Four months after hypothyroidism had been diagnosed and the therapy started, the bitch was presented again with gradually worsening apathy, anorexia, weakness, weight loss and a slight increase in thirst. The signs deteriorated, then they improved over three weeks. The owner recalled the dog behaving oddly for a week prior to the onset of profound anorexia. It was unable to jump to its chair or it was found standing and staring at a wall. On physical examination, the dog was shivering, its body weight dropped from 43 kg to 37 kg in one month's time. The dog was coughing and, in the owner's opinion, it had problems when swallowing. Abdominal palpation provoked discomfort. Survey thoracic and abdominal radiographs were obtained because of the rather vague but serious clinical signs with no progress towards a diagnosis. Heart rate was 150 beats per minute and there were no electrocardiographic changes. The hypothyroidism status monitoring at that time resulted in finding nearly optimal

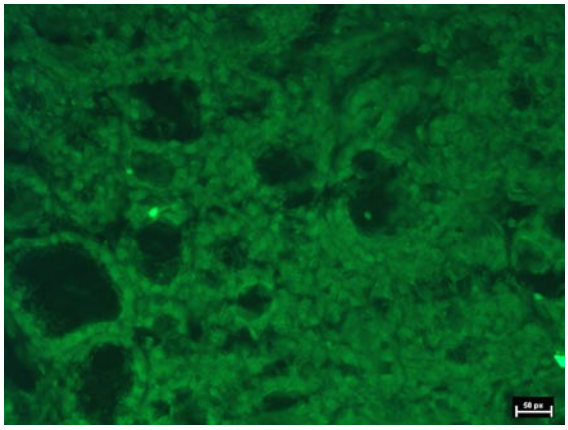

Figure 1. Indirect immunofluorescence positive for the presence of circulating autoantibodies against the thyroid gland components (microsomal pattern). Thyroid gland sections prepared from an unrelated dog were used for the testing of the patient's serum; magnification 400×

thyroxine supplementation (tT_4 = 19.7nmol/l; cTSH = 0.31 ng/ml; pre-pill blood collection) and ruled out a possibility of thyrotoxicosis. Samples of blood and urine were taken for laboratory examination three times during the period of developing problems; twice with inconclusive results. Blood chemistry values of the last collection are given in Table 1 – B. They indicated hypoglycaemia, azotaemia, hyponatraemia, hyperkalaemia, hypochloraemia, hypercalcaemia, and hyperphosphataemia. The sodium/potassium ratio was 19.25. Differential leukocyte count revealed eosinophilia (14%). Urine specific gravity was 1.025. The suspected diagnosis of hypoadrenocorticism was confirmed by low plasma cortisol prior to and after ACTH stimulation test (< 5.5 nmol/l). Two days of infusion therapy using physiologic saline solution and hydrocortisone (Hydrocortison; Jenapharm; 5 mg/kg body weight *i.v.*) resulted in rapid clinical improvement of the bitch. Since then, the bitch has been on hydrocortisone (20 mg twice daily *per os*) and fludrocortisone (Fludrocortison; Squibb; 0.2 mg twice daily *per os*) and electrolyte assessments every other week revealed normal concentrations of sodium and potassium with no adjustments necessary.

Since patients with metabolism dysregulation for different reasons, including hypothyreosis, can be affected by immunodepression, a panel of immunological tests including lymphocyte subset enumeration using flow cytometry (Faldyna et al., 2001a), assessment of lymphocyte activity in a lym-

phocyte transformation test and phagocytizing activity in the test of ingestion and respiratory burst detection (Faldyna et al., 2001b) was performed to evaluate the immune status. These tests showed no alteration of immune functions when compared with normal healthy dogs. Thyroid and adrenal gland sections prepared from an unrelated dog were used to investigate the presence of circulating autoantibodies against the glands in the patient's serum by indirect immunofluorescence. Double blind reading revealed only anti-thyroid antibodies at a dilution of 1:40 (cf. Figure 1).

DISCUSSION

Polyglandular endocrinopathies may pose a diagnostic challenge due to the insidious onset of a slowly progressive disease. As described above, the presenting signs of hypothyroidism and hypoadrenocorticism were vague and quite the same in the Black Russian Terrier bitch. Moreover, the episodic course of hypoadrenocorticism with several inconclusive blood examinations made the final diagnosis difficult. In most affected dogs, each endocrinopathy is manifested separately, with additional disorders ensuing one by one after variable periods of time. In our case the period between the clinical presentations of both diseases was four months and mild azotaemia was the only sign that might have been due to hypoadrenocorticism on the first occasion (Table 1 – A). The ACTH stimulation test, however, was not performed at that time and azotaemia disappeared with thyroxine supplementation. Diagnostic tests and treatment are directed at each disorder as it is recognized because it is not possible to reliably predict or prevent any of these problems (Nelson, 2003). Considering the breed predisposition, the Black Russian Terrier originates from Rottweilers, Giant Schnauzers and Airedale Terriers, which are at greater risk of developing both hypothyroidism (Nelson, 2003) and hypoadrenocorticism (Peterson et al., 1996). Contrary to Kooistra et al. (1995) reporting primary hypothyroidism and only glucocorticoid deficiency in a female Boxer dog, our bitch was deficient both in the mineralocorticoid and glucocorticoid functions. Bartges and Nielson (1992) and Fritzen et al. (1996) described a rare finding of reversible megaoesophagus associated with hypoadrenocorticism in a dog with concurrent hypothyroidism. Though the megaoesophagus was not found on survey radiographs in our patient, the signs possibly associated with oesophageal weakness resolved with therapy. It is not always possible to confirm autoantibodies in polyglandular syndromes. For example, Kooistra et al. (1995) detected no circulating autoantibodies in their Boxer dog, while Bowen et al. (1986) found both adrenocortical and thyroid ones. It is known that endocrinopathies develop over time due to the gradual immune-mediated glandular destruction (Nelson, 2003). Initially, adrenocortical functions may become inadequate during periods of stress only. The relative overdose of thyroxine (tT_4= 55 nmol/l) observed two months after the start of supplementation might have been such a stressor hastening the development of hypoadrenocorticism in our patient.

Acknowledgements

Authors would like to thank the laboratory technicians (Mrs. Kudlackova and Leva and dr. Samankova) from the Department of Immunology of Veterinary Research Institute for their skilful assistance.

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Received: 2007–03–14
Accepted after corrections: 2007–07–16

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