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Cardiovascular system abnormalities in a dog with primary hypothyroidism*)

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Summary

The thyroid hormones have direct and indirect effects on the heart. Therefore, it is possible that depression of left ventricular functioning is associated with hypothyroidism. This article describes the case report of primary hypothyroidism in a dog with dominant clinical findings (clinical examination, ECG, echocardiography) associated with the cardiovascular system. Low heart rates, reduced R-amplitudes and bradycardic arrhythmias (first-degree AV block) were noted on an electrocardiogram before treatment. On the echocardiogram, the dog showed reduced contractility and reduced left ventricular wall thickness. The patient was re-examined after levothyroxine supplementation. Effects of treatment included increased heart rates, mildly increased R amplitudes, and the disappearance of bradyarrhythmias in ECG examination. The echocardiographic examination showed increased contractility and increased left ventricular wall thickness.

Keywords: dog, hypothyroidism, cardiovascular system

Hypothyroidism is a commonly recognized endocrinopathy in dogs. Immune-mediated destruction or idiopathic atrophy of the thyroid gland usually cause hypothyroidism (10).

A deficiency in the circulation of the thyroid hormone affects the metabolic functioning of almost all organ systems. Consequently, clinical signs can vary and as they are slow to develop, they are gradual and subtle. In the adult dog the most consistent clinical signs of hypothyroidism result from decreased cellular metabolism and the effects on the dog's mental status and activity. These signs include some degree of mental dullness, lethargy, exercise intolerance, unwillingness to exercise and a propensity to gain weight without a corresponding increase in food intake.

Additional clinical signs typically involve the skin, reproductive system and neuromuscular system. Alteration in the skin is the most common observable abnormality in dogs with hypothyroidism. The classic cutaneous signs include bilaterally symmetrical, nonpruritic truncal alopecia that tends to spare the head and distal extremities. The dermatological signs are the most common reason for the presentation of the dog. Other organ systems, such as the cardiovascular, ocular, hematological, gastrointestinal system, may also be affected with or without concomitant dermatological abnormality, but are rarely the reason for presenting the dog and present a challenge to the diagnostic approach for the clinician (3, 13, 14).

Our experience with the diagnosis of hypothyroidism is based on results obtained from the monitoring of 270 dogs of 42 breeds with chronic cutaneous lesions carried out at the I. Internal Clinic of Small Animals of the University of Veterinary Medicine in Košice between 1992-1998 (4).

The findings clearly pointed out that in practice with small animals, it is inevitable to recognize true hypothyroidism when the variable clinic symptoms in dogs are caused by a decreased functioning of the thyroid gland and to distinguish it from euthyroid syndrome where dermatological or other symptoms do not relate to the decreased function of the thyroid gland. The diagnosis of hypothyroidism is complicated by the lowering of serum thyroid hormone levels of total thyroxine (TT4) and free thyroxine (fT4) in diseased animals. The so-called „sick euthyroid syndrome" can occur in any serious disease or with other endocrinopathies that are associated also with low serum thyroid concentrations. The therapy of true hypothyroidism lies in supplementation of the missing thyroid hormone, however with sick euthyroid syndrome, therapy is contraindicated by L-thyroxine. The best way for distinguishing true hypothyroidism from the sick euthyroid syndrome is to obtain an accurate history, perform a thorough clinical examination, including endocrinological and biochemical laboratory tests (4, 10, 13).

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If the results of examinations of thyroid hormone concentrations in serum (TT4 and fT4) are low and increased canine TSH (cTSH) levels are found, the suspicion of the occurrence of true hypothyroidism increases, provided appropriate clinic symptoms are present. Moreover, concentrations of triodothyronine (TT3) are rarely decreased in dogs with true hypothyroidism because the body tries to preserve its levels in proper concentrations by the increased conversion of TT4 to a metabolically active hormone TT3 (3, 15).

Ultimately, the diagnosis should be based on the response to thyroid hormone replacement therapy. In case it is true hypothyroidism, L-thyroxine therapy should resolve all the signs of hypothyroidism (3, 13).

The aim of this article is to present a case report of an American cocker spaniel with primary hypothyroidism with no dominant dermatological symptoms, but with evidence of rare cardiovascular signs. Both laboratory and clinical findings changed after adequate L-thyroxine therapy.

Case report

An eight-year-old intact male American cocker spaniel was referred to I. Internal Clinic, University of Veterinary Medicine Košice with lethargy, apathy, decreased exercise tolerance and unwillingness to exercise of 6 months duration. The dermatological examination revealed dry hair coat and mild scaling of skin (fig. 1). Aggressive behaviour was observed and the owner also reported aggressive behavior in the home environment for no reason. Unreasonable aggression was also oriented against members of the owner's family.

Results and discussion

Upon physical examination obesity was observed (BCS 7/8) with body weight at 17 kg. CRT was under 2 seconds, weak pulse was palpated and scarcely palpable heart beat. Auscultation revealed decreased heart rate under 56/min and low intensity heart sounds. The results of CBC revealed leucocytosis (Le = 16.6 G/l) and mild anaemia (Ec = 5.3 T/l).

Serum biochemical abnormalities included mild hyperkalemia (K = 6.6 mmol/l) with a normal sodium level (Na = 143 mmol/l), mild hypercholesterolemia (Chol = 6.97 mmol/l), hyperlipidaemia (Tot. Lip. = 7.89 g/l), and an elevated activity of alkaline phosphatase (ALP = 4.2 µkat/l). Serum biochemical analyses were performed by spectrophotometric methods (Shimadzu UV 1601).

Endocrinological status was obtained by radioimmunoassay monitoring of thyroid hormone concentrations. The serum cTSH concentration was determined by use of an immunoradiometric assay. The total thyroxin serum concentration was low – TT4 < 8 nmol/l (reference range TT4 = 25-50 nmol/l), indicating hypothyroidism or euthyroid syndrome. Reference limit TT4 was judged according to the size of the breed and specifically corresponds to medium breeds with weight up to 27 kg (4). Low total triiodtyronin – TT3 = 0.84 nmol/l (reference range TT3 = 1.2-3.1 nmol/l), low free thyroxin – fT4 = 4.5 pmol/l (reference range fT4 = 11-33 pmol/l) and increased thyroid stimulating hormone level cTSH = 1.08 ng/ml (reference range cTSH = 0-0.41 ng/ml) suggested primary true hypothyroidism (2, 13, 16). The summary of the biochemical and endocrinological examination is found in tab. 1.

Fig. 1. Lethargy, apathy and obesity in a dog with hypothyroidism

Tab. 1. Hematological, biochemical and hormonal parameters before and after 6 months of treatment

	Reference range	Before treatment	After 6 months treatment
Leucocytes	6.0-11.0 G/l	16.6	10.6
Erythrocytes	5.5-10.0 T/l	5.3	6.4
K^+	3.5-5.1 mmol/l	6.6	4.6
Na^+	139-152 mmol/l	143	142
Cholesterol	3.25-6.5 mmol/l	6.97	4.72
Tot. Lipids	4.7-7.25 g/l	7.89	6.15
ALP	to 0.82 µkat/l	4.2	2.46
TT4	25-50 nmol/l	<8.0	27.5
fT4	11-33 pmol/l	4.5	11.5
TT3	1.2-3.1 nmol/l	0.84	1.6
cTSH	0-0.41 ng/ml	1.08	0.26

ECG examination revealed a heart rate of 70 beats per minute, sinus arrhythmia with I. degree AV block. Low voltage of R wave in the II. Lead (1.93 mV) was also noted. These findings supported our suspicion of possible hypothyroidism. ECG record is showed in fig. 2.

An echocardiogram was performed and showed myocardial hypocontractility and decreased left ventricular posterior wall thickness and decreased interventricular septum thickness. M mode evaluation (fig. 3) showed an increased left ventricular internal diameter in systole 26.9 mm (reference range 21-24 mm), the left ventricular internal diameter in diastole was within the reference range of 36.9 mm (reference range 34-38 mm). Fraction shortening was decreased

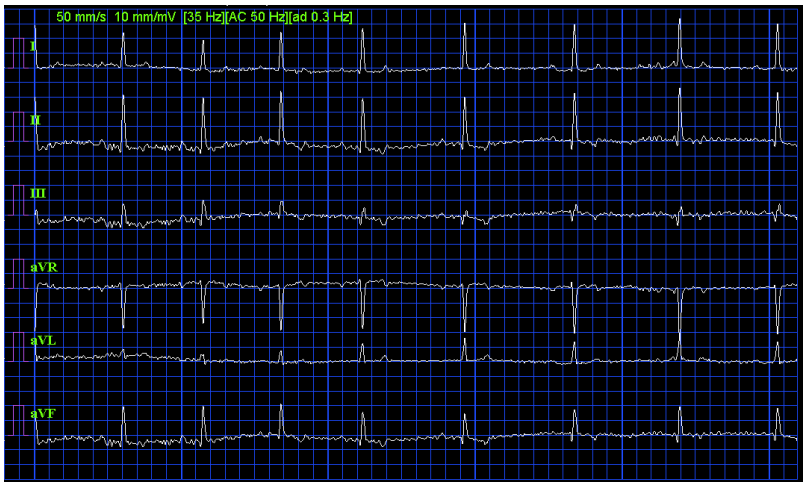

Fig. 2. ECG before treatment

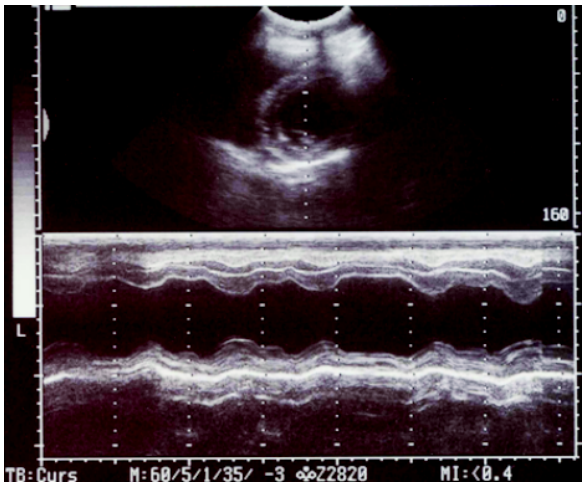

Fig. 3. Echocardiographic findings before treatment

– 27% (reference range 38-40%). Left ventricular posterior wall thickness was decreased – 7.6 mm (reference range 9 mm). Interventricular septum thickness was also mildly decreased 7 mm (reference range 8 mm), left atrium diameter was within the reference range of 18 mm (reference range 18-21 mm), aortic diameter was also in the reference range of 16 mm (reference range 16-20 mm) and left atrium aortic ratio was 1.12. Our reference levels correspond to values in literature (7).

The dog was treated with levothyroxine 100 µg twice daily and re-evaluated after 3 months of treatment. The owner reported an improvement in dog's temperament, he was less depressed and showed better exercise tolerance, and the unreasonable aggressive behavior was no longer noticed. Upon physical examination, we noticed a mild loss of weight (15.5 kg) and an improvement in cardiac rhythm, which was no longer bradycardic (104 beats per minute).

The total thyroxine serum concentration was TT4 = 18.8 nmol/l which was already increased, but still not in the reference range, the free thyroxine serum level increased fT4 = 9.2 pmol/l, but also was not in the reference range. ECG examination also revealed I. degree AV block, but P-Q interval was decreased (135 ms). ECHO re-evaluation showed a mild increase in LVDs and subsequently, an increased fraction shortening by 30%, but the other measured parameters remained unchanged. We increased the dose of levothyroxine to 150 µg twice daily. The dog was checked again 3 months after increasing the dose.

The serum biochemical profile revealed a decrease in serum level of alkaline phosphatase (2.46 µkat/l) compared to the level before treatment, but it was still a mildly increased serum level of ALP according to the reference range. Previously observed hypercholesterolemia, hyperlipidaemia, and hyperkaliemia were no longer present. Serum TT4 concentration (6 hours after pill administration) was slightly above the reference range (27.5 nmol/l) and serum fT4 level was also within the reference range. The results of hematological, biochemical and hormonal parameters before and after 6 months of treatment are summarized in tab. 1.

ECG revealed no AV block with P-Q interval 120 ms with a heart rate of 104/min and also a mild increase in R wave voltage (2.06 mV). The ECG record is

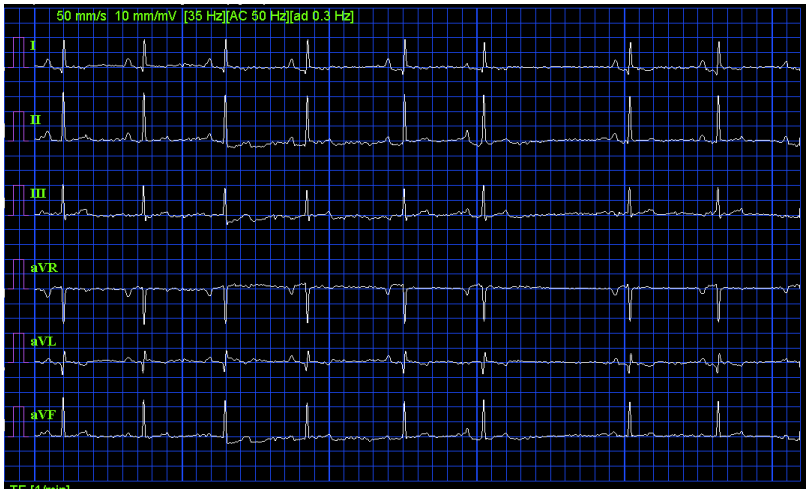

Fig. 4. ECG after 6 months of levothyroxine treatment

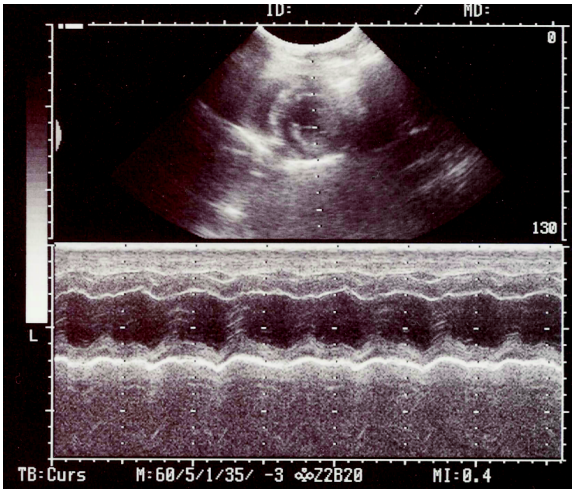

Fig. 5. Echocardiographic findings after 6 months treatment

showed in fig. 4. Echocardiogram results showed an improved fraction shortening of 37%, an increase in left ventricular posterior wall thickness and interventricular septum thickness slightly above the reference range (fig. 5). The other parameters remained unchanged. Results of ECG and echocardiographic measurements before and after 6 months of treatment are summarized in tab. 2. Current medication includes levothyroxine 150 µg twice daily and reexamination of hormonal status and cardiovascular function after six months.

After 6 months of L-thyroxine therapy, the owner confirmed an evident decrease in aggressivity against family members and the dog also behaved calmly in the veterinary ward.

Tab. 2. Results of ECG and echocardiographic measurements before and after 6 months of treatment

Measurements	Reference range	Before treatment	After 6 months treatment
ECG			
HR	80-140	70/min	104/min
P-Q interval	130 ms	143 ms	120 ms
R wave II lead	2.5-3.0 mV	1.93 mV	2.06 mV
Rhythm		AV block I. degree	Regular sinus rhythm
ECHO			
LVDs	21-24 mm	26.9 mm	23.3 mm
LVDd	34-38 mm	36.9 mm	36.8 mm
LVWd	9 mm	7.6 mm	9.8 mm
IVS	8 mm	7 mm	8 mm
LA	18-21 mm	18 mm	18.5 mm
Ao	16-20 mm	16 mm	16 mm
LA/Ao	1.3	1.12	1.15
FS	38-40%	27%	36.7%

Conclusion

Primary hypothyroidism is the most common cause of naturally occurring thyroid failure in adult dogs, accounting for more than 95% of hypothyroid cases.

Typical signs for hypothyroidism involve dermatological lesions, lethargy or obesity. The clinical symptoms in the reproductive and neuromuscular system are also frequently noted (10). Cardiovascular diseases connected with hypothyroidism occur less frequently. However, it is very important to distinguish them from cardiac diseases not caused by thyroid gland hypofunction, but represent part of euthyroid „sick" syndrome (3, 14, 15).

It is necessary to realize that true hypothyroidism affects several organ systems; therefore, the occurrence of more clinic symptoms supports this diagnosis to a greater degree than the finding of only one single symptom (3, 14). In our case, the patient displayed lethargy, apathy, mild obesity, dry seborrhoea, aggressive behavior and pronounced cardiologic difficulties. The diagnosis of hypothyroidism was confirmed by low laboratory findings of TT4, TT3 and fT4 together with high levels of cTSH. Most authors share the opinion that hypothyroidism is not confirmed by decreased TT4 concentration alone, which can occur with a non-thyroid disease, but primarily by low fT4 level findings and increased concentrations of cTSH (3, 10, 15, 16). In our patient, even a decreased TT3 concentration was observed, which is a rare finding (13-15).

Similarly, routine laboratory tests of hypercholesterolemia, hyperlipidemia and an increased concentration of alkaline phosphatase with mild anaemia may help to determine the diagnosis and it was valid for our case too (14). Finally, our diagnosis was also confirmed by test administration of L-thyroxine therapy, by which clinic symptoms and laboratory findings gradually improved. After six months of the therapy, even clinic symptoms improved on level of cardiovascular apparatus.

The myocardium is particularly sensitive to the effects of thyroid hormone and increased or decreased concentrations of circulating thyroid hormone may produce clinically significant changes in the cardiovascular system. The major physiologic action of thyroid hormone on the myocardium is a direct positive inotropic effect, stimulation of myocardial hypertrophy and increased responsiveness to adrenergic stimulation. The most commonly reported cardiovascular signs in hypothyroid dogs include a weak cardiac apex beat, bradycardia, and cardiac arrhythmias (3, 6). Manifestations of cardiac symptoms in dogs with primary occurring hypothyroidism are variable. Our presented dog had a weak cardiac apex beat and barely auscultable heart sounds. Stephan (17) reported weak apex heart beat and low intensity heart sounds in 60% of dogs with primary hypothyroidism before L-thyroxine supplementation. In all dogs the intensity of the heartbeat increased after L-thyroxine treatment. Increased heart beat strength was also observed in our presented patients. The explanation of this finding may be an increase in strength of heartbeat as well as a decrease in body weight after treatment.

Changes in the electrocardiogram are usually only evident with severe hypothyroidism. In humans, electrocardiographic changes associated with hypothyroidism include sinus bradycardia, conduction disturbances, low QRS complex voltage, deviation of mean electrical axis, prolongation of the QRS complex interval and flattened or inverted T waves (1). In dogs with spontaneous primary hypothyroidism, the most frequently observed ECG abnormalities are low QRS voltage, inverted T waves and sinus bradycardia (6). Despite the influence of stress during ECG recording in our case, we noticed a decreased heart frequency

that was either below or in the lower reference range. Panciera (12) found bradycardia in 11 hypothyroid dogs and Stephan (17) reported a heart frequency of 70-120 bpm with an average frequency of 102/min in 10 dogs with hypothyroidism. In five dogs after L-thyroxin treatment, an increase in heart frequency was noticed with an average heart frequency of 120/min (12, 17). In our reported case, the heart frequency after levothyroxine supplementation increased to within the reference range.

In dogs with experimentally induced hypothyroidism, prolongation of the PR interval suggests abnormalities of the atrioventricular nodal conduction (5). In his study, Stephan (17) reported the presence of I. and II. degree AV block in 3 dogs with naturally occurring hypothyroidism. Nijhuis (11) reports reversibility in these abnormalities with thyroid hormone supplementation and suggests a direct correlation between the electrocardiographic changes and the severity of thyroid deficiency. Our patient had a severe thyroid deficiency: we noted rhythm abnormalities and also I. degree AV block. In our case, after hormone supplementation, we noticed an improvement in cardiac rhythm and reversibility of AV conduction abnormality. Stephan (17) reported low R amplitude voltage in all investigated dogs with hypothyroidism. Panciera (12) identified an R amplitude voltage below 1.0 mV that was significantly higher after L-thyroxine supplementation in 58% cases of spontaneous hypothyroidism. In our presented case, the R amplitude was below 2.0 mV and we noticed only a mild increase in R amplitude voltage after hormonal treatment.

Myocardial changes induced by the hypothyroid state are measurable *in vivo* and *in vitro* as reduction in the velocity of contraction, in the force developed during contraction, and in the rate of relaxation. A reduced left ventricular pump function has been demonstrated in dogs with experimentally induced hypothyroidism (9). Abnormal echocardiographic findings in hypothyroid dogs include a mildly increased end-systolic left ventricular dimension, a slightly reduced shortening fraction (FS), thinning of the left ventricular posterior wall and septum and decreased posterior wall excursion that are concluded to be reversible with hormone supplementation (12). Stephan (17) reported decreased myocardial contractility in 80% of spontaneously hypothyroid dogs with decreased FS between 22-26% before treatment and improvement in all cases after hormonal supplementation. In our case, we noticed an increase in FS of more than 9% after 6 months of supplementation therapy; moreover, LVW thickness and septum thickness increased after hormone supplementation. Abnormal electrocardiographic and echocardiographic findings are reported to be quite frequent in dogs with decreased thyroid functioning but they vary in their expression in different cases. Although studies have confirmed that thyroid hormone deficiency is associated with reversible myocardial failure, it remains uncertain whether hypothyroidism alone causes clinically important myocardial failure and congestive heart failure in dogs (3, 8).

Based on these observations, the treatment of primary hypothyroid in the dog with standard replacement of levothyroxine and current monitoring of thyroid functioning appeared to improve all clinical findings associated with the cardiovascular system.

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