# A CASE OF FIBROUS OSTEODYSTROPHY IN A DOG WITH SECONDARY RENAL HYPERPARATHYROIDISM

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**Summary**

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A clinical case of fibrous osteodystrophy in a dog with secondary renal hyperparathyroidism is described. Considerable deviations in blood biochemistry, radiological, ultrasonographic and ECG findings, as well as in histological examination of kidneys were observed. All these changes are considered as relevant and in our view, could be utilized for the proper diagnostics of this pathological state.

**Key words**: chronic renal failure, dog, fibrous osteodystrophy, hyperparathyroidism, parathyroid hormone

The parathyroid hormone (PTH) is a polypeptide composed of 84 amino acids. It is involved in the regulation of calcium-phosphorus homeostasis in the extracellular fluid together with 1,25-dihydroxy-cholecalciferol (Nagode & Chew, 1992; Kates & Sherrard, 1997).

Although secondary renal hyperparathyroidism and renal osteodystrophy are well known sequela of chronic renal failure (CRF), clinically important renal osteodystrophy is rarely seen in dogs and cats (Nagode *et al.*, 1996; Barber & Elliott, 1998). In dogs, it is most commonly manifested in young animals probably because metabolically active growing bone is more susceptible to the negative effects of hyperparathyroidism. So far it is not known why skull and jaw bones are the most affected and they could be demineralized to a degree such that tooth are mobilized and the mandible could be twisted without been fractured (rubber jaw syndrome). Facial bones could be deformed by the occurring significant proliferation of connective tissue. Barber & Elliott (1998) have found out that in cats, the skull and the mandible were not prone to renal osteodystrophy. Pathological fractures are rarely observed in dogs and cats with CRF (Roux, 2007). Other possible but rare clinical manifestations of severe renal osteodystrophy are decalcification of the skeleton, bone cysts, bone pain, and stunted growth. PTH has also other properties with negative effect of renal failure patients, so it is classified as uremic toxin (Slatopolsky *et al.*, 1980).

The toxic effect of PTH is at the background of CRF progress, manifested as accumulation of calcium salts in renal tubules and nephrocalcinosis.

PHT concentration could be reduced by the renal hormone calcitriol that delays the progressing of renal failure (Nagode & Chew, 1992), but this is not confirmed experimentally (Finco *et al.*, 1994).

The presented case of fibrous osteodystrophy is that of a female Caucasian shepherd dog at the age of 11 months, weighing 27 kg, owned by a private owner. The dog was referred to the Small Animal Clinic at the Faculty of Veterinary Medicine, Trakia University – Stara Zagora, on June 9, 2008. The history evidenced increased thirst, frequent and prolonged urination, fastidious appetite, weight loss and a general weakness. Three weeks before, the owner noticed a swelling in the regions of both jaws, difficulties in eating and chewing of food, frequent nasal bleeding, attempts to vomit and trouble in breathing.

The present status revealed a medium body constitution, emaciation and significant weight loss. The animal was strongly reluctant to move, got rapidly exhausted and frequently lied down. The skin elasticity was decreased, with marked enophthalmos. The visible mucous coats (conjunctivas) were markedly anaemic. The results from the clinical examination showed rectal body temperature of 37.1 ºC; heart rate of 132 min$^{-1}$ and respiratory rate of 37 min$^{-1}$. In auscultation, heart tones were clear and pure. The breathing was labial, very difficult in the inspiration stage, mainly abdominal. Profuse, bilateral haemorrhagic blood discharges from the nose, strong swelling and deformity of skull bones were observed (Fig. 1). The auscultation of lungs showed no pathological findings. When palpated, jaw bones were with elastic consistence and

marked teeth mobility. The appetite was fastidious with increased thirst and difficulties in chewing. The faeces were watery, dark-coloured and with unpleasant odour. The urination was frequent, and urine was clear, colourless, with low density (1.012) and of considerable volume – 4.7 mL/kg/m/h. Kidneys were not painful when palpated.



**Fig. 1.** Fibrous osteodystrophy of skull and jaw bones. On the radiograph, an increased transparency of jaw bones, thinned cortices and lacking alveolar bone plates are visible.

The radiography of jaw bones showed local cystic translucencies with increased transparency and thinned cortices. The roots of teeth were clearly visualized with
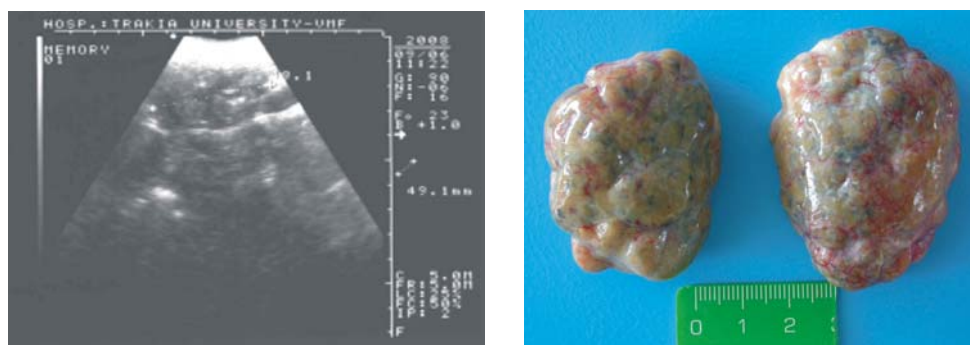
**Fig. 2.** Nephrosclerosis in the dog with fibrous osteodystrophy – ultrasonogram (left) and gross anatomy finding (right).

absent alveolar bone plates (Fig. 1).

The echography of kidneys showed that they were reduced in size, corrugated and with irregular margins. Hyperechoic alteration in the medulla and cortico-medullar junction was visible. The elements of the normal renal anatomy could not be clearly differentiated (Fig. 2).

ECG findings consisted in left ventricular hypertrophy with elevated R wave, increased duration of the QRS complex, deep ST segment and ventricular extrasystoles.

The morphology of blood showed severe erythropenia with hypochromaemia and reduced haematocrit (Table 1). Total leukocyte and thrombocyte counts were normal. There was a neutrophilia with a left shift. Blood biochemistry revealed hypocalcaemia (1.48 mmol/L) with marked hyperphosphataemia (7.03 mmol/L) and reduced serum potassium concentration. Significant deviations were observed in blood creatinine and urea that were very high as compared to reference values. Slight deviations were observed in blood glucose and liver transaminases ASAT and ALAT (Table 1).

The most significant deviations were observed in blood parathyroid hormone that was almost 20 times higher than nor-mal. Acid-base status was characterized with a severe metabolic acidosis: pH of 7.194, decreased bicarbonates, actual base excess and carbon dioxide partial pressure.

**Table 1.** Data from haematological, blood chemistry, electrolyte and acid-base analysis

| Parameter | Value |
|---|---|
| Haemoglobin, g/L | 30 |
| Erythrocytes, T/L | 1.33 |
| Haematocrit, % | 8.5 |
| Total leukocytes, G/L | 9.0 |
| Thrombocytes, G/L | 154 |
| St, % | 9 |
| Sg, % | 77 |
| Ly, % | 12 |
| Mo, % | 2 |
| Total protein, g/L | 55 |
| Blood glucose, mmol/L | 7.03 |
| Creatinine, μmol/L | 1812 |
| Urea, mmol/L | 28.58 |
| ASAT, U/L | 73 |
| ALAT, U/L | 67 |
| Ca, mmol/L | 1.48 |
| P, mmol/L | 7.29 |
| K, mmol/L | 3.36 |
| PTH, pg/mL | 180 |
| pH | 7.194 |
| $HCO_3$, mmol/L | 9.1 |
| ABE, mmol/L | −17.1 |
| $TCO_2$, mmol/L | 9.9 |
| $PaCO_2$, mmHg | 24.2 |

After the lethal issue, the patient was
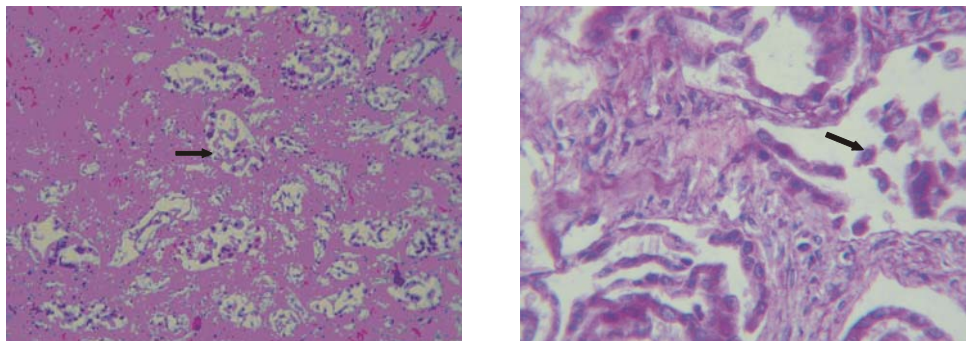
**Fig. 3.** Left: excessive growth of connective tissue and impaired renal structure. The enlarged renal tubules are visible (arrow). H/E, ×100; right: desquamation of renal tubules (arrow). H/E, × 400.
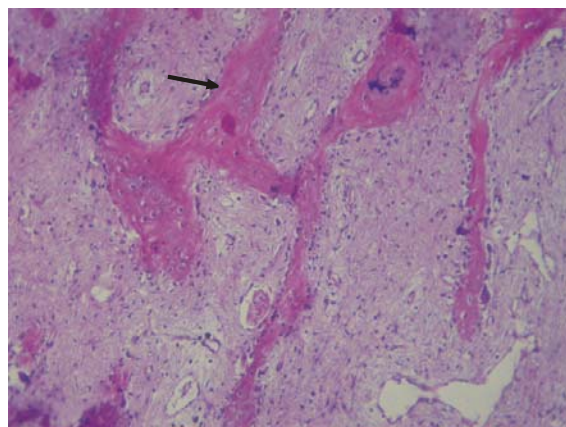


**Fig. 4.** Fibrous osteodystrophy. Severe reduction of bone tissue (arrow) and its replacement by connective tissue is clearly seen. H/E staining, magnification ×100.

necropsied. Material for histological examination was obtained from kidneys and jaw bones.

The gross anatomical appearance of kidneys showed that they were reduced in size, with grey-whitish to yellow colour, and nodular surface, corrugated at some areas (Fig. 2). Their consistency was hard, and the cut surface – greyish, with sclerotic areas. The cortex and core of kidneys were reduced, with indistinct border between.

Histologically, the structure was severely impaired. Consequently to the growth of connective tissue, the liver parenchyma was highly damaged. The nephrons were atrophied, the renal tubules – with cystic enlargements and the renal glomeruli – sclerotic (Fig. 3).

Macroscopically, jaw bones were soft, elastic and easily cut with a knife. Histologically, the amount of bone tissue was reduced and replaced with connective tissue (Fig. 4). The process was so advanced that only a small part of bone tissue has remained.

The pathogenesis of hyperparathyroidism is rather contradictory (Felsenfeld,

1997). The observed osteodystrophy with secondary renal hyperparathyroidism was associated with hyperphosphataemia, reduced serum calcium levels and decreased bone resistance against the calcaemic effect of PTH. Felsenfeld (1997) has shown that in early and moderate renal failure, the specific factors responsible for hyperparathyroidism could be hardly distinguished. It is assumed that the relative or complete deficiency of calcitriol had a primary role in its development (Chew & Nagode, 1993; Martinez *et al.*, 1997). Calcitriol, the active form of vitamin D, is formed by 1-α-hydroxylation of 25-hydroxycholecalciferol in the cells of renal tubules (Slatopolsky *et al.*, 2005). In the beginning of the CRF, the accumulation of phosphate inhibits renal tubular 1-α-hydroxylase activity and limited calcitriol synthesis (Takahashi *et al.*, 2002; García-Rodrígues *et al.*, 2003). PTH stimulates the activity of renal 1-α-hydroxylase and calcitriol formation. On its turn, calcitriol inhibits PTH synthesis by a negative feedback mechanism (Nagode *et al.*, 1993).

In more advanced renal failure, only serum calcium correlates with serum PTH activity (Kates & Sherrard, 1997). The decreased intestinal calcium absorption, related to low serum calcitriol, has probably a crucial role in hyperparathyroidism occurring in dogs and cats with advanced renal failure. In cats with CRF, Barber & Elliott (1998) reported that over 50% of animals in the final stage of CRF were hypocalcaemic.

The observed severe erythropenia and hypochromaemia confirmed the findings of Eschbach *et al.* (1990), Nissenson *et al.* (1991) and Cowgill (1992) in dogs and cats with CRF. It is believed that the main cause for hypoproliferative anaemia in men and animals with CRF is erythropoietin deficiency (Hocking, 1987; Nissen-

son *et al.*, 1991; King *et al.*, 1992). Other clinically important causes for anaemia in dogs and cats with impaired renal function are iron deficiency, chronic gastrointestinal bleeding, reduced survival of erythrocytes and decreased glutathione level (Chandra *et al.*, 1988; Cook & Lothrop, 1994).

The azotaemia, observed in this and other studies, is a sequel of the compromised ability of kidneys to excrete protein catabolic products consequently to the decreased glomerular filtration rate (Mitch & Walser, 1991).

Metabolic acidosis in a well known sign of CRF, resulting primarily from the limited capacity of damaged kidneys to excrete hydrogen ions and secondarily, from disturbed ammoniagenesis, reduced filtration of phosphates and sulfates, the loss of bicarbonates and the reduced secretion of protons from renal tubules (Kimmel, 1998). The observed signs of anorexia, nausea, vomiting, lethargy, weakness and weight loss are probably effects of metabolic acidosis (DiBartola *et al.*, 1987; Lemieux *et al.*, 1990; Lulich *et al.*, 1992). The severe acidemia could reduce the cardiac output, arterial blood pressure and serum potassium (Androgue & Madias, 1998). Hypokalemia could be a cause for the observed altered heart electrical activity (Dow & Fettman, 1992; Lulich *et al.*, 1992; DiBartola, 1994).

The presented case adds to the clinical experience with regard to fibrous osteodystrophy, secondary to renal hyperparathyroidism in dogs and cats.

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