

Primary Hypoparathyroidism in one Cat and Two Dogs

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ABSTRACT

Background: Primary hypoparathyroidism (PH) is an endocrine disorder characterized by decreased production and/or release of parathyroid hormone (PTH). Dogs and cats are rarely affected, and typical clinical signs include an abrupt onset of neurological and neuromuscular signs. The diagnosis is based on the history, clinical signs, and laboratory findings of hypocalcaemia, as well as the exclusion of other causes of tetany. Treatment involves stabilization of serum calcium with specific therapy. This study aimed to report three cases of PH: two canine cases and the first feline case in Brazil.

Cases: 1) A 8-year-old male Yorkshire terrier was brought to the clinic with a history of tetanic crisis. The owner reported that the animal had been previously diagnosed with epilepsy and since treated with phenobarbital. The physical examination revealed hyperthermia, tachypnea, tachycardia, salivation, and ataxia with hyperextension of the anterior and posterior limbs. Emergency treatment included intravenous (IV) administration of calcium gluconate, and the animal showed clinical improvement within an hour. Overall, the complete blood count was within the normal range, but the calcium and PTH levels were below the normal ranges. Therefore, PH was confirmed. Calcium carbonate and vitamin D3 supplementation were prescribed, and the treatment with phenobarbital was suspended. During the following year, the dog suffered three episodes of hypocalcaemia, even with appropriate administration of medication by the owner. In the last crisis, the animal died, probably because of acute renal failure (ARF). 2) A 7-year-old male Pinscher was presented for veterinary care with a history of 15 days of tetanic and seizure crises. The physical examination revealed hyperthermia, seizure activity, and hyperextension of the anterior and posterior limbs. Levels of total calcium and PTH were below the normal ranges. The animal showed clinical improvement with IV administration of calcium gluconate. Therefore, PH was diagnosed from the clinical signs, response to emergency treatment, and values of calcium and PTH. Calcium carbonate and vitamin D3 supplementation were prescribed. The owner had trouble purchasing calcitriol, and the animal died before the follow-up appointment. 3) A 14-year-old female mixed-breed cat was brought to the clinic with a history of anorexia and vomiting. From the results of the complete blood count, serum biochemistry, and electrocardiogram, the cat was diagnosed initially with hypertrophic cardiomyopathy with hepatic lipidosis due to prolonged anorexia. However, the serum ionized calcium and PTH levels were below normal ranges. Thus, on the basis of the clinical symptoms and serum calcium and PTH levels, the animal was diagnosed with PH. Treatment consisted of ongoing supplementation with vitamin D3 and calcium carbonate, and the existing treatment for heart disease was continued. The treatment did not result in any clinical improvement, and the animal was euthanized.

Discussion: The two dogs presented with the classic symptoms reported in the literature. However, the cat with the same pathology had different clinical signs. In the three cases, the diagnosis was confirmed according to the procedure described in the literature, ie, clinical symptoms, serum calcium and PTH levels below normal ranges, and response to treatment. The stabilization of the serum calcium concentration with calcium and vitamin D3 supplementation corroborates the literature. None of the study patients survived: the first dog probably died because of ARF due to excessive crises; the second dog died because of the advanced stage of the disease and the difficulty in purchasing the drugs prescribed; the cat was euthanized because it did not show any response to treatment, perhaps because it had more than one disease concurrently.

Keywords: calcium disorders, parathyroid, tetany.

INTRODUCTION

Primary hypoparathyroidism (PH) is an endocrine disorder characterized by decreased production or release of parathyroid hormone (PTH), which results in hypocalcaemia and mild to moderate hyperphosphatemia [2]. PH can occur spontaneously or iatrogenically [2], and rarely affects dogs [2] and cats [4].

The clinical course of the disease is characterized by an abrupt onset of neurological and neuromuscular disorders. The owners of affected animals usually report signs of tetany such as focal muscle spasms, muscle tremors, generalized tonic muscle spasms, and rigid walking [10]. Other abnormalities observed include seizures, weakness, hyperventilation, disorientation, dementia, hyperexcitability, anxiety, and aggression [10], as well as intense licking and biting of the paws [4]. Abdominal pain, vomiting, appetite loss [9], and hyperthermia [9,10] have also been reported.

The diagnosis of PH is based on the history, clinical signs, and laboratory findings of hypocalcaemia, as well as exclusion of other causes of tetany [6,8,9].

The treatment of PH is based on stabilization of serum calcium [1]. Emergency therapy consists of slow intravenous administration of calcium gluconate 10%. Later maintenance is performed with supplementation with vitamin D2 (ergocalciferol); vitamin D3 (calcitriol) or diidrotaquisterol; and gluconate, lactate, chloride, or carbonate salt of calcium administered orally [4]. With specific therapy, the prognosis is excellent [4].

The present work aimed to report three cases of PH, the second reported case of hypoparathyroidism in dogs and the first case in a cat in Brazil.

CASES

1) A 8-year-old male Yorkshire terrier, weighing 5.0 kg, was presented for veterinary care with tetanic signs in May 2010.

During anamnesis, the owner reported that the animal had displayed seizures when submitted to physical activity and was initially diagnosed with epilepsy one year after first exhibiting signs. Since then, the dog had received 0.8 mg/kg SID of phenobarbital sodium (Gardenal®)¹. In addition to medication, the owner submitted the animal to a cold bath in moments of crisis to lower its body temperature. The crises usually occurred at night and on days when the animal was

left alone; in the latter situation, the dog scratched at the door of the house all day.

The physical examination showed hyperthermia (39.9°C), tachypnea (168 mvm), tachycardia (216 bpm), drooling, and ataxia with hyperextension of the hind and forelimbs.

By these clinical signs, hypocalcaemia due to hypoparathyroidism was suspected, and a blood sample was collected for determination of complete blood count and levels of serum calcium, PTH, amylase, lipase, and serum albumin.

Emergency treatment consisted of intravenous administration of calcium gluconate (Glucafós®)² at a dose of 100 mg/kg over 4 h [6]. During the administration, the heart rate was monitored to avoid bradycardia. Within 1 h, the animal showed clinical improvement: a body temperature of 39°C, normopnea (32 mvm), normal cardiac rate (104 bpm), decreased drooling, normalized gait, and normal flexion of the members.

The blood count and biochemical tests showed values within the normal ranges. The results for calcium and PTH levels were below the normal values (Table 1).

On the basis of the clinical signs, response to emergency treatment, and levels of calcium and PTH, the dog was diagnosed with PH.

The day after the initial attendance, the animal was prescribed ongoing oral supplementation with calcium carbonate and vitamin D3 (Caps D Cal®)³ at a dose of 35 mg/kg twice a day and 500 IU/kg once a day, respectively. And treatment with phenobarbital was suspended. It was also recommended to avoid situations that could expose the animal to agitation or stress.

During the following year, there were three other hypocalcemic crises, even with correct administration of medication by the owner. These crises were always associated with the absence of the owner during his working hours and the fact that the dog kept scratching at the door during this time. In the third crisis, the animal presented with anuria, and even with treatment support such as fluid therapy and intravenous calcium gluconate, the patient died, possibly because of acute renal failure (ARF).

2) A 7-year-old male Pinscher, weighing 5.0 kg, was presented for veterinary care in October 2014 with tetanic signs and seizures for the previous 15 days. The owner had taken the dog to another

veterinarian because of the clinical signs, and the final diagnosis was ehrlichiosis with cardiopathy. Because of these previous diagnoses, the dog was being medicated with doxycycline (Doxitec®)⁴, furosemide (Lasix®)¹, enalapril maleate (Enalaprev®)⁵, and phenobarbital, but there was no clinical improvement, and the tetany and seizures were becoming more frequent.

The physical examination revealed hyperthermia, tetany, and seizure activity, and the dog was medicated with 25 mg/kg BID of dipyron (Novalgina®)¹, 1 mg/kg BID of diazepam (Diazepam®)⁶, and NaCl 0.9% intravenously.

Blood was collected for determination of complete blood count and biochemical and serological parameters. Urinalysis was also performed.

The complete blood count showed neutrophilic leukocytosis. The leukocyte count was of 50,600/mm³ and the neutrophil count was of 41,492/mm³. Urinalysis revealed the presence of struvite crystals and pyocytes (30 per field). Ehrlichia serology was negative. Because of these preliminary results, the antibiotic therapy was changed to 5 mg/kg SID of enrofloxacin (Baytril®)⁷ and 15 mg/kg BID of amoxicillin-potassium clavulanate (Agemoxi CL®)⁶.

The results of the biochemical tests showed normal values for urea and creatinine, while aspartate transaminase (AST) and alanine aminotransferase (ALT) levels were above normal ranges. The calcium level was below normal range (Table 2). The owner did not authorize PTH measurement at this point.

The dog was diagnosed with hypocalcaemia, and, as the patient was hospitalized, calcium gluconate was administered at a dose of 100 mg/kg over four hours. The next day, the dog showed clinical improvement and was sent home with a prescription for enrofloxacin and amoxicillin-potassium clavulanate at the same dosage it was receiving in the hospital. Calcium carbonate, vitamin D3 (Caps D Cal® - 50mg/kg SID), and 50 mg/kg TID of vitamin C (Vita-Vet C®)⁸ were also prescribed, as well as a urinary therapeutic diet to help control struvite crystals.

After two days at home, the patient returned with tetany. The blood calcium test was repeated, and the result was 3.7 mg/dL. The animal was hospitalized again and received NaCl 0.9% and calcium gluconate intravenously at the same dose as that in the initial care.

A PTH test was performed and yielded a result of 3 pg/mL, which is below the normal range (5-25 pg/mL).

The dog stayed at the hospital for four days and received calcium gluconate (Glucafós®), NaCl fluid, and the antibiotics prescribed and showed clinical improvement. After these four days, the dog was discharged with the same prescription in addition to 0.05 µg/kg SID of calcitriol (Rocaltrol®)⁹, and the owner was advised not to expose the dog to stress or intense exercise. The local drug stores did not have calcitriol in stock, so the owner had to buy it online. Unfortunately, the dog died the day after it went home because of a seizure crisis.

3) A 14-year-old female mixed-breed cat, weighing 5.5 kg, with a history of anorexia and vomiting, was presented for veterinary care in December 2010. The owner reported behavioral changes such as urination and defecation outside the litter box, failure to cover feces in the litter box, polyuria, and lack of grooming.

The physical examination revealed only pale mucous membranes. Complete blood count and biochemical tests were performed. The hematocrit at 25% was close to the minimum acceptable value (normal range, 24-45%), and biochemical tests showed no abnormalities in liver, pancreatic, or kidney parameters.

During the cardiac assessment, an enlarged cardiac silhouette was found on radiography. An electrocardiogram revealed electric axis deviation (-120°), which suggested right chamber overload or right bundle branch block. The diagnosis on the Doppler echocardiographic report was hypertrophic cardiomyopathy. The cardiac alterations justified the clinical signs, and treatment with furosemide (Lasix® - 2 mg/kg BID) and 0.25 mg/kg BID of benazepril (Fortekor®)¹⁰ was prescribed. After seven days of treatment, there was no improvement in the clinical signs, and new biochemical tests were performed, which showed an increase in the enzyme ALT (Table 3).

Throughout this period, the patient refused food from any source. Because of the prolonged anorexia and the increased ALT, an esophageal feeding tube was placed to prevent or reverse a possible hepatic lipidosis disorder.

After three months of medication for heart disease and administration of food via the esophageal feeding tube, there was no clinical improvement. In addition to the initial clinical signs, there were weakness

in the limbs and neck ventroflexion. Laboratory tests were repeated, and these showed no changes in the blood cell count and in the renal, hepatic, and pancreatic parameters. However, the serum ionized calcium level was below normal range. A PTH test was performed, and the value was also below normal range (Table 4).

On the basis of the clinical symptoms and levels of serum calcium and PTH, PH was diagnosed. Treatment was initiated with vitamin D3 and calcium carbonate (Caps D Cal®) at the dosages of 0.03 µg/kg and 1 g/5.5 kg, respectively, once a day, and the treatment for heart disease was continued.

In March 2011 (approximately four weeks after the beginning of the use of calcium carbonate and vitamin D3), the owner reported that the animal was lying in the water and requested euthanasia for the animal, but the owner was asked to continue the treatment.

In June 2011, the patient was returned to the clinic with generalized weakness, listlessness, muscle tremors, neck ventroflexion, 8-10% degree of dehydration, and urinating and defecating while lying down. The cat was hospitalized for 48 h with a saline infusion and feeding via an esophageal feeding tube. All previous treatment was continued.

The clinical picture worsened after two days of hospitalization, and the cat was euthanized with prior authorization of the owner and referred to necropsy.

At the necropsy, cardiac hypertrophy was seen. The parathyroid glands and thyroids were collected for histopathological evaluation, but no changes were detected. It remained undetermined whether the PH was due to decreased production of PTH, which usually occurs because of C-cell atrophy.

Table 1. Values for biochemical parameters of dog 1 with hypoparathyroidism.

Parameter	Values
Serum calcium	3.5 mg/dL (9-11.3 mg/dL)
PTH	1 pg/mL (5-25 pg/mL)
Amylase	904 IU/L (300-2000 IU/L)
Lipase	28.9 IU/L (25-750 IU/L)
Serum albumin	3.3 g/dL (2.3-3.8 g/dL)

Table 2. Values for biochemical parameters of dog 2 with hypoparathyroidism.

Parameter	Values
Urea	51 mg/dL (21.4-59.9 mg/dL)
Creatinine	0.3 mg/dL (0.5-1.5 mg/dL)
AST	136 U/L (8.2-57U/L)
ALT	226 U/L (8.2-57 U/L)
Total Calcium	2.0 mg/dL (9-11.3 mg/dL)

Table 3. Results of biochemical tests in the second evaluation of the patient.

Parameter	Values
ALT	200 (10-80 IU/L)
Direct Bilirubin	1.1 (0-0.3 IU/L)
Indirect Bilirubin	2.32 (0-0.5 IU/L)
Total Bilirubin	3.42 (0.1-0.6 IU/L)
Creatinine	1.5 (0.8-1.8 mg/dL)
Urea	39 (10-30 mg/dL)
Total protein	8.2 (5.9-8.5 g/dL)

Table 4. Biochemical tests of the cat diagnosed with hypoparathyroidism.

Parameter	Values
Serum calcium	4 mg/dL (6-10.2 mg/dL)
PTH	3 pg/mL (15-19 pg/mL)
Creatinine	1.9 (0.8-1.8 mg/dL)
Urea	45 (10-30 mg/dL)
Phosphorus	7.2 (1.8-6.4 mg/dL)
Potassium	4.2 (3.8-4.5 mEq/L)
Sodium	144 (147-156 mEq/L)

DISCUSSION

The present report is important because there is only one article in the Brazilian literature on PH in dogs, reporting the case of a Schnauzer [5], and no articles about the pathology in cats. In addition, there are no reports on the involvement of this disease in Yorkshire terrier and Pinscher dogs, as well as domestic cats [1,2,4,9].

Despite PH being considered an uncommon hormonal disorder in dogs [2] and cats [4], the two dogs reported were male and aged 7-8 years, corroborating the literature [2,4]. However, the age and sex of the cat reported does not corroborate the literature, because this disease most frequently affects young or middle-aged male cats [1,4].

In the case of the first dog, the patient presented with the classical signs reported in the literature: muscle tremors, ataxia, hyperthermia, tachycardia, tachypnea, and rigid walking, which is called tetany. The second dog presented with tetany, hyperthermia, and seizures [9]. The cat exhibited different clinical signs for the same pathology, because behavioral changes and muscle weakness were the only signs observed.

The diagnostic process in the case of the two dogs was performed according to the literature, and was based on clinical symptoms, serum calcium and PTH levels below normal ranges, and responsiveness to emergency treatment [6,9]. However, the diagnosis of the cat was delayed by the unusual signs; thus, calcium and PTH levels were investigated only three months after the first veterinary consultation, which resulted in the clinical deterioration of the animal. As was the case with the dogs, PTH and calcium levels were below normal ranges, and PH as the cause of hypocalcemia was confirmed in all the animals.

The goal of treatment is stabilization of the serum calcium concentration, and the literature recommends medication with diidrotaquisterol or calcitriol (D3) to increase blood calcium level [1,6,7]. The chosen treatment was supplementation with calcium carbonate and vitamin D3.

As part of the treatment of the two dogs, it was also recommended to avoid situations that promote agitation or stress, because these occasions demand more muscle calcium and can trigger hypocalcemic crises.

None of the animals in the cases survived. In the first case, it was hard for the owner to keep the dog from getting stressed or agitated, because the dog suffered from severe separation anxiety when the owner was away from home and scratched at the door incessantly. The agitation culminated in new crises, leading to ARF and anuria. Prolonged hyperthermia may lead to intrinsic ARF, as occurs in cases of heat-stroke. In these cases, kidney damage occurs when the body temperature of the dog reaches 41°C, leading to direct thermal cytotoxicity and a complex cascade of responses to endotoxin, inflammatory cytokines, endothelial cell activation, and change in coagulation with microvascular thrombosis [3]. The first dog was presented with tetany at the last veterinary consultation with a body temperature higher than 40 °C, which certainly justifies the kidney damage after several ongoing crises.

The second dog died the day after the medication was prescribed. According to the initial levels of calcium, the disease was possibly more advanced. In addition, there was an infection, which could have further aggravated the clinical case.

The cat was euthanized because it did not respond appropriately to the treatment. The lack of response might have been due to complications asso-

ciated with heart disease hindering adequate clinical improvement.

Some authors [4] report that the prognosis for PH is excellent with appropriate therapy as well as owner cooperation and clinical monitoring. In the present three cases, the first patient lived for about one year after the diagnosis. This patient might have survived longer if the anxiety situation could have been controlled. Unfortunately, the other two patients had concurrent diseases, which might have impaired improvement of the endocrine disease.

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