

## Gastric Bleeding Case Associated with Hypocalcemia in A Dog

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### ABSTRACT

The presented case report material was composed of a 4-year-old Golden Retriever dog brought to Afyon Kocatepe University Animal Hospital with complaints of weakness, anorexia, severe contraction and incoordination 1.5 months after giving birth. Due to biochemical analysis performed within the scope of anamnesis and clinical symptoms, serum calcium level was measured as 5.81 mg/dL and the patient was diagnosed with hypocalcemia (eclampsia). After the appropriate treatment procedure, all vital findings returned to normal, moderate hematemesi was observed 4 hours after the treatment. It was thought that the effect of hypocalcemia on the coagulation mechanism may cause gastric bleeding. In the biochemical measurement repeated 24 hours after the treatment, serum calcium level was determined as 7.70 mg/dL. In the subsequent follow-ups, no evidence of hematemesi was found and no recurrence was observed. The risk of bleeding disorders in dogs with hypocalcemia is significant and should be considered.

**Key Words:** Phosphorus, gastrointestinal bleeding, hypocalcemia, calcium, dog.

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### Bir Köpekte Hipokalsemi İle İlişkili Gastrik Kanama Olgusu

#### ÖZ

Sunulan vaka raporu materyalini doğum yaptıktan 1.5 ay sonra halsizlik, iştahsızlık, şiddetli kasılma ve inkoordinasyon şikâyeti ile Afyon Kocatepe Üniversitesi Hayvan Hastanesine getirilen 4 yaşlı Golden Retriever ırkı köpek oluşturdu. Anamnez ve klinik belirtiler kapsamında gerçekleştirilen biyokimyasal analiz sonucu serum kalsiyum düzeyi 5.81 miligram/desilitre (mg/dL) olarak belirlenen hastaya hipokalsemi (eclampsia) tanısı kondu. Uygun tedavi prosedürü sonrası tüm vital bulguları normale dönen hastada, tedaviden 4 saat sonra orta şiddetli hematemesis gözlemlendi. Gastrik kanamaya hipokalseminin pıhtılaşma mekanizması üzerindeki etkisinin neden olabileceği düşünüldü. Tedaviden 24 saat sonra tekrarlanan biyokimyasal ölçümde serum kalsiyum düzeyi 7.70 mg/dL olarak belirlendi. Sonraki takiplerde hematemesis bulgusuna rastlanmadı, nöks gözlenmedi. Köpeklerde hipokalsemi olgularında kanama bozukluğu riski önemlidir ve dikkate alınmalıdır.

**Anahtar Kelimeler:** Fosfor, gastrointestinal kanama, hipokalsemi, kalsiyum, köpek.

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## INTRODUCTION

Eclampsia is an acute disease with high mortality, characterized by a blood calcium level lower than 7mg/dL (hypocalcemia) in dogs. It is usually seen during pregnancy or between 1st and 3rd weeks of lactation. However, as stated in the presented case report, dogs that continue to breastfeed can still have the disease 1.5 months after birth (Dimitrov et al., 2016). Eclampsia is triggered by the increase in the need for calf calcium in the last period of pregnancy and the first milk release after birth, and the disease picture emerges as a result of the decrease in maternal blood calcium level. Since the calcium level in breast milk is kept at a normal level, offspring are not affected by hypocalcemia (Pathan et al., 2011). Animals that continue to breastfeed are highly susceptible to changes in blood calcium levels (Moe, 2008). Undiagnosed hypocalcemia causes clinical symptoms that require urgent treatment. Therefore, blood ionized calcium levels should be measured routinely in all suspected patients. Although this disease is usually seen in small breed dogs, it is also found in medium breed dogs with multiple puppies. Excessive calcium loss, atrophy of the parathyroid gland, and calcium deficiency play a role in the etiology of the disease (Drobatz et al., 2000). Eclampsia is an easy disease to diagnose with its typical clinical findings. At the onset of the disease, affected dogs are restless and nervous. In a short time, they start walking with difficulty and shaking. In the last phase of the disease, the legs contract and the dog becomes unable to walk. Severe muscle spasms, nystagmus and dyspnea may be seen. The patient's body temperature is often above 40°C. Accordingly, the respiratory rate also increases. Clinical symptoms sit very quickly, and ataxia, tremors and tetany are observed on average 12 hours after the first symptoms such as restlessness and aggression. Eclampsia is diagnosed by measuring blood calcium, phosphorus and glucose levels. Dogs with serum calcium levels below 7 mg/dL are diagnosed with eclampsia. At the same time, serum phosphorus level is generally determined to be low in these patients (Pathan et al., 2011). Apart from puerperal eclampsia, the most common causes of hypocalcemia in dogs are hypoproteinemia and hypoalbuminemia (Thomas et al., 1995). Calcium is responsible for blood

coagulation, mineralization of the skeletal system, transmission between nerve cells, muscle contraction and intracellular communication. The role of calcium in blood plasma in coagulation is to convert prothrombin produced in the liver to thrombin. Thrombin, on the other hand, provides coagulation by converting fibrinogen to fibrin. Since the blood calcium level is low in an animal with eclampsia, prothrombin cannot turn into thrombin and fibrinogen cannot turn into fibrin, and coagulation metabolism is impaired (Dzik et al., 1988). Calcium ions are involved in the regulation of the coagulation process, which plays an important role in hemostasis (Varga-Szabo et al., 2009; Braun et al., 2011). Calcium ions are responsible for the full activation of various coagulation factors, including coagulation factor XIII, apart from platelet activation (Ambrus et al., 2001). The aim of this case report is to show that dogs with eclampsia can develop hematemeses and to emphasize the importance of this issue.

## CASE HISTORY

### Case Submission

The material of this case report was composed of a 4 year-old and 20 kg live weight Golden Retriever dog brought to Afyon Kocatepe University Animal Hospital. In the anamnesis, it was informed that the patient gave birth 1.5 months ago, had 6 puppies and the puppies are still sucking their mother. In the clinical examination of the patient who applied to our clinic with complaints of tremor, severe contraction and incoordination, her body temperature was measured as 42.5°C. Symptoms of hyperpnea (45 beats/minute), tachypnea (190 beats/minute) and agony were detected in the patient. Before the treatment complete blood count (Human, HumaCount80 TS) and calcium and phosphorus levels (Mindray BS120) were measured by blood samples taken from vena (V.) cephalica into anticoagulant and gel tubes (Tables 1-2). Whose serum calcium level was measured as 5.81 mg/dL in the dog and, it was diagnosed with hypocalcemia in the light of clinical findings. After the treatment, in order to control, blood samples were taken and serum calcium and phosphorus levels were detected (Table 2).

**Table 1.** Hemogram results before treatment (Fielder, 2015).

	RESULT	REFERENCE RANGE
WBC	19.13 10 <sup>3</sup> / $\mu$ l	5.0–14.1
LYM %	58.4 %	8–21
GRA %	40.9 %	62.0–87.0
LYM	11.18 10 <sup>3</sup> / $\mu$ l	0.4–2.9
GRA	7.83 10 <sup>3</sup> / $\mu$ l	3.00–12.00
Hb	12.9 g/dl	11.9–18.9
MCH	24.9 pg	21.0–26.2
MCHC	42.8 g/dl	32.0–36.3
RBC	5.16 10 <sup>3</sup> / $\mu$ l	4.95–7.87
MCV	58.3 fl	66–77
HCT	30.13 %	35–57
PLT	138 10 <sup>3</sup> / $\mu$ l	211–621
MPV	9.7 fl	6.1–10.1

**Table 2.** Serum Ca and P levels before and after treatment (Fielder, 2015).

	RESULT		REFERENCE RANGE
	Before Treatment	After Treatment	
Ca	5.81 mg/dL	7.70 mg/dL	9.1–11.7
P	-	2.85 mg/dL	2.9–5.3

### Diagnosis and Treatment

The diagnosis of the disease were made by anamnesis, clinical findings, serum biochemical analysis and evaluation of the response to treatment. The fact that the serum calcium concentration measured before the treatment is lower than 7 mg/dL confirms the diagnosis (Hall, 2015). The first symptom of eclampsia is usually restlessness. Later, the animal has gait disturbances and inability to walk, convulsions, hyperpnea, tachycardia and an increase in body temperature. The pupillary reflex is generally decreased and the pupils are dilated (Austad et al., 1976).

In the presented case report, caffeine (Kafedif®, Ceva, Turkey) at a dose of 5-15 mg/kg (0.8 ml) was applied subcutaneously (SC) for the first time in the treatment of the disease. In the patient 9 ml of calcium (Calcicaf, Provet, Turkey) and 250 ml of 5% dextrose solution were intravenous (IV) applied as diluted by 500 ml 0.9% isotonic sodium chloride solution. Upon the intense blood vomiting observed in the patient 4 hours after the treatment, 1.6 ml Ranitidine (Raniver, Osel, Turkey) Intramuscular (IM), 4 ml Metoclopramide HCl (Metpamid, Sifar, Turkey) IM, 2.5 ml Tranexamic acid (Transamine, Actavis, Turkey) IM and 2 ml vitamin K (Hemadur-K, Alke, Turkey) IM were administered. It was thought that this bleeding was caused by the effect of serum calcium level on the coagulation mechanism. 5% Dextrose (250 ml), Ranitidine, Metoclopramide HCl and Tranexamic acid treatment were continued at the defined doses for two days. In addition to this

treatment, the use of oral calcium preparations is also recommended in the treatment of the disease (Austad et al., 1976). Barbiturates and tranquilizers can also be used to relieve contractions in the treatment of eclampsia (Bloom, 1968).

### DISCUSSION

A decrease in blood calcium concentration below 7 mg/dL is defined as puerperal hypocalcemia (eclampsia) (Hall, 2015). Carlstrom measured the blood calcium level of 5-7 mg/dL in dogs with eclampsia for the first time in 1929 (Carlstrplm, 1929). According to a study by Bentinck-Smith in 1971, normal serum calcium level was determined as 9-11.5 mg/dL, Mg level 1.7-2.9 mg/dL, inorganic P level 2.5-5 mg/dL, glucose level 60-100 mg/dL in non-lactating female dogs. Similarly, in the presented case, the serum calcium level was measured as 5.81 mg/dL, initially. The main reason for this decrease in calcium levels is breastfeeding. The first urgent application in the treatment of the disease is to increase the falling blood calcium level. Calcium preparations used for this purpose are organic calcium compounds such as calcium barogluconate or calcium gluconate. The drug to be used is administered IV slowly until the contractions stop (Austad et al., 1976). In the general treatment protocol, 10% calcium gluconate (0.5-1.5 ml/kg) is administered at a dose. After the application, rapid clinical recovery and muscle relaxation are seen within

the first 15 minutes. In the presented case report, 0.5-1.5 ml/kg of calcium was administered to the patient by IV route and a decrease in the intensity of muscle contractions was observed in a short time. The determined dose of calcium gluconate can be given by diluting in 0.9% isotonic (Hall, 2015). The calcium preparation we gave in the treatment was diluted in 0.9% isotonic and used in our patient. Parathyroid gland hormones such as parathyroid hormone (PTH) are effective in regulating calcium metabolism in the body. In the deficiency of these hormones, neural symptoms along with muscle contraction and muscle spasm and convulsions are seen after a few days (McDonald, 1965). The oscillations of impulses in dogs occur at the neuromuscular junction in hypocalcemia, low blood calcium concentration decreases the activation level of sodium channels. The reason for this interaction is that calcium ions bind to the outer surface of sodium channels. Sodium channels are activated much less than normal levels, and this event facilitates the stimulation of nerve fibers. Sometimes nerve fibers are repeatedly stimulated without rest. In dogs with hypocalcemia, severe muscle contractions and muscle spasms occur when motor nerve fibers are stimulated spontaneously and repeatedly without rest (Hall, 2015).

Due to severe muscle contraction, an excessive increase in body temperature occurs. Extra antipyretic agents are not required for this increase in body temperature. Fever usually improves with hypocalcemia treatment (Hall, 2015). The body temperature of our patient in the case presentation was measured as 42.5 °C. After the first treatment of hypocalcemia, the body temperature of our patient was measured as 39.5 °C.

Too fast calcium administration may lead to bradycardia. During calcium administration, heart rate should be monitored in order to prevent bradycardia and arrhythmia. In the event of an arrhythmia, calcium therapy should be interrupted until the heart rhythm returns to normal (Hall, 2015). Our patient was continuously monitored during the treatment. No adverse events developed associated with caffeine injection.

Severe hyperpnea findings can also be seen in the disease. Hyperpnea causes respiratory alkalosis. Respiratory alkalosis, on the other hand, promotes the binding of serum calcium to proteins, causing exacerbation of hypocalcemia (Hall, 2015). Similarly, when the patient, who was the subject of the case report, applied to our hospital, a respiratory rate of 45/min hyperpnea was detected.

In a study conducted by Moretti et al in 2016, it was stated that calcium is an important cofactor of the coagulation mechanism and may play a role in the pathophysiology of intracerebral hemorrhage. Hypocalcemia was diagnosed in 229 of 2103 patients with intracerebral hemorrhage included in this study. Hypocalcemia is associated with the degree of

bleeding in patients with intracerebral bleeding. Calcium plays a role in vascular reactivity. Hypocalcemia causes higher blood pressure due to increased arterial vascular tone (Morotti et al., 2016). A certain level of calcium is required in the blood coagulation mechanism. Since prothrombin cannot turn into thrombin and fibrinogen in the absence of calcium in the blood, impairments occur in coagulation metabolism and bleeding occurs in various organs or parts of the body (Dzik et al., 1988). Similarly, in this case report, it was evaluated that gastrointestinal system bleeding was observed in our patient due to a possible effect of calcium deficiency on the blood coagulation mechanism.

In a study conducted by Drobotz et al. in 2000, various abnormal clinical findings were detected in 29 of 31 dogs with eclampsia. Multiple abnormal clinical signs were reported in most dogs affected in this study. According to the study, typical eclampsia symptoms such as tremors, spasm, gait disturbance, and nystagmus were observed in 23 of the 29 dogs. Further, in this study, hyperpnea in 15 animals, behavioral disorders in 14 animals, weakness in 6 animals, vomiting in 3 animals, diarrhea in 3 animals and aggression in 2 animals (Drobotz et al., 2000). Similarly, a significant part of these findings were detected during the preliminary clinical examination in the presented case report.

While Mayer (1968) emphasized that eclampsia develops due to calcium and vitamin D deficiency during pregnancy and breastfeeding. Nesvadba (1971) stated that overfeeding with animal proteins such as egg and meat may cause impairment of calcium metabolism and hypocalcemia. Vitamin D supplements increase the absorption of calcium from the intestines. Vitamin D supplementation administered at a dose of 0.03-0.06 mcg/kg to dogs with eclampsia may play a role in preventing hypocalcemia (Hall, 2015). Again, phytate compounds bind ionized calcium to make it biologically unusable and are recommended as a support for hypocalcemia treatment (Resnick, 1964). For patients who will continue breastfeeding after hypocalcemia, the use of oral calcium preparations at a dose of 25-50 mg / kg 3-4 times a day has been recommended. If the puppies are large enough, they should be weaned. Puppies should not be allowed to suckle for 24 hours after an eclampsia attack to prevent relapse (Wikstrom, 1974). In this case, the puppies were prevented from sucking.

## CONCLUSION

In the presented case report, hypocalcemia due to calcium deficiency was diagnosed in our patient due to prolonged breastfeeding. Breastfeeding was discontinued in the patient whose general condition improved after treatment, and the patient's diet regimen was changed. A proprietary formula containing calcium and vitamin D and phytate-

containing cereals (soybean, legume) was proposed. The patient was prescribed a balanced feed supplement (VMP tablet) containing vitamins, proteins and minerals. No recurrence was detected. Feeding is important in dogs in the post-pregnancy period. In order to avoid possible cases of hypocalcemia and serious complications such as GIS bleeding, attention should be paid to maternal feeding during this period. During the lactation period, the use of a balanced and period-appropriate diet and feed supplement and etc. should be recommended. The risk of bleeding disorders in dogs with hypocalcemia should not be clinically ignored and taken into account by veterinarians.

**Ethics Committee Information:** This study is not subject to the permission of HADYEK in accordance with the “Regulation on Working Procedures and Principles of Animal Experiments Ethics Committees” 8 (k). The data, information and documents presented in this article were obtained within the framework of academic and ethical rules.

**Conflict of Interest:** The authors declared that there are no actual, potential or perceived conflicts of interest for this article.

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