



First Case Report of Recurrent Idiopathic Calcinosis Circumscripta in a Kangal Dog in Turkey: Clinical, Radiographic and Histopathological Observations

Musa GENÇCELEP¹ Serkan YILDIRIM² Yağmur KUŞÇU¹

¹Van Yuzuncu Yil University, Faculty of Veterinary Medicine, Department of Surgery, Van, Turkey

²Atatürk University, Faculty of Veterinary Medicine, Department of Pathology, Erzurum, Turkey

Received: 25.07.2018

Accepted: 16.12.2018

ABSTRACT

A 6 months old, male, 51 kg, Kangal race dog brought to Van Yuzuncu Yil University, Faculty of Veterinary Medicine, Department of Surgery constitutes the material of this case report. In patient's history, decreased appetite, stiff gait and lameness was reported. In clinical examination, hard, limited and painless swellings in both lateral side of tarsal joints were determined. In radiographic examination, presence of opaque areas in the masses were observed. Vicious and white fluid discharged was observed in operation. In histopathological examination, calcinosis circumscripta was determined. After 4 months, patient was brought to the clinic because of recurrent swelling in the same area. Histopathology results were the same again. It was concluded that the disorder was present in the idiopathic form. It is thought that this case should be considered important, because there is no report regarding the Kangal dogs and any presence of recurrence in the literature.

Keywords: *Calcinosis circumscripta, Dog*

ÖZ

Türkiye'de Bir Kangal Köpeğinde İlk Kez Karşılaşılan Tekrarlayan Özellikteki İdiyopatik Kalsinozis Sirkumskripta: Klinik, Radyografik ve Histopatolojik Gözlemler

Bu olgu sunumunun materyalini Van Yüzüncü Yıl Üniversitesi Veteriner Fakültesi Cerrahi Anabilim Dalı'na getirilen 6 aylık, 51 kg ağırlığında, erkek, Kangal ırkı köpeği oluşturmaktadır. Hastanın öyküsünde, iştah azalması, tutuk yürüyüş ve topallık bildirilmiştir. Klinik muayenede, tarsal eklemlerin her iki lateralinde sert, sınırlı ve ağrısız şişlikler tespit edildi. Radyografik incelemede kitlelerde opak alanların varlığı gözlemlendi. Operasyonda viskoz ve beyaz renkli sıvı gözlemlendi. Histopatolojik incelemede kalsinozis sirkumskripta olduğu tespit edildi. Dört ay sonra aynı bölgede tekrarlayan şişlik nedeniyle hasta tekrar kliniğe getirildi. Nüks materyalinin histopatoloji sonuçları aynı özellik göstermekteydi. Bozukluğun idiyopatik formda olduğu sonucuna varıldı. Literatürde Kangal ırkı köpeklerde herhangi bir rapora rastlanılmamış olması ve nüks olayının gözlenmesi klinik açıdan önemli bulundu.

Anahtar Kelimeler: *Kalsinozis sirkumskripta, Köpek*

INTRODUCTION

Calcinosis circumscripta is an ectopic mineralization syndrome in soft tissues, characterized by a tumor-like growth and local accumulation of calcium salts (O'Brien and Wilkie 2001; Szczepaniak et al. 2008; Tafti et al. 2005). The focal mineralized lesions are most frequently located in the region of extremity joints and subcutaneous tissues. Other sites such as mouth, gingiva, frenulum of the tongue, salivary glands, pinna, mandible, throat region and chest predispose other places where these lesions may develop (Howell and Ishmael 1968; Szczepaniak et al. 2008). Rarely, these pathological lesions can be formed in the intestines (Engel et al. 2014). This syndrome is most commonly found in large dog breeds and in younger dogs (particularly < 2 years of age), although dogs of all ages can be affected. German and Hungarian shepherd dogs are

predisposed. There is no predisposition according to gender (Tafti et al. 2005; Yumuşak et al. 2014).

Calcinosis circumscripta, which is not fully explained by ethiopathogenesis, is examined in its 4 forms (Szczepaniak et al. 2008).

Metastatic calcification: Secondary mineralized local areas are formed due to disorders in serum calcium and phosphor levels in both humans and animals (Szczepaniak et al. 2008). The most common cause of metastatic calcinosis cutis in dogs is overproduction of adrenal hormones (corticosteroids or steroids). This may be due to cancer or overgrowth of the pituitary or adrenal glands. In some susceptible dog breeds, it may also progress from steroid hormones that are used for therapy (Ferguson 1996).

Dystrophic calcification: In this form, serum calcium and phosphor levels are normal (Engel et al. 2014). Local calcium deposits can be formed in regions where tissue damage is caused by pathological processes such as recurrent impact, necrotic tissue, inflammation (mechanical, chemical), and apocrine gland degeneration, which may impair blood flow and nutrition (Engel et al. 2014; Mumba et al. 2014; Szczepaniak et al. 2008; Tafti et al. 2005).

Iatrogenic calcification: It can also be classified as dystrophic calcification. In some cases; iatrogenic calcification has been reported to be associated with co-injections of medroxyprogesterone and proligestone, the use of polydioxanone suture material and previous surgical interventions (Davidson et al. 1998; Ferguson 1996; Ginel et al. 1992; Kirby et al. 1989; O'brien and Wilkie 2001; Szczepaniak et al. 2008, Tafti et al. 2005). At the same time, it is also formed in the subcutaneous calcinosis circumscripta at the site of a proligestone injection of a Burmese breed cat (O'brien and Wilkie 2001).

Idiopathic calcification: This form is common in animals. There is no tissue damage or systemic metabolic disorder. Its cause is unknown. Breed and familial predilection can occur (Engel et al. 2014). It is thought that a mutation in the type II protocollagen gene plays an important role in the etiology of this disease, both in animals and humans (Szczepaniak et al. 2008). Calcinosis circumscripta has never been reported in a Kangal dog previously. As it was observed that there was a recurrence, the situation has also got a clinical importance.

CASE DETAILS

A 6-month-old, male dog (51 kg) of the Kangal race was brought to the surgical clinic with complaints of lameness and with lateral bulging of the right and left tarsal joints. The pet owner declared that he knew the mother, father and uncle of the pet, in which there had been no such problems.

Clinical examination showed lameness and stiffness. On palpation, it was determined that lateral masses were hard and painless. The masses were connected to the skin. The left mass moved in all directions independently of the subcutaneous tissues and the mobility of the right mass was very limited. Ulcerated field on left mass was determined. On direct radiography (AP) of the tarsal joints, high intensity opaque areas were observed in the masses (Fig. 1). Some values were analyzed in the blood serum (Table 1). These masses were extirpated from the regions under dissociative anesthesia. During the excision of the masses, a crepitation and white colored viscous fluid were seen. Biopsy samples were sent to laboratory for histopathological examination.

On the 4th month after the surgery, the patient was brought back to the clinic because of swelling of the same fields. Clinical examination showed no lameness. The same findings from the first examination were observed again on palpation. On direct radiography, a low intensity opaque field was detected only in the right mass. These masses were extirpated from the region under dissociative anesthesia. Biopsy samples were sent to laboratory for histopathological analysis.

Macroscopically, masses from stated regions were weighed as 95 and 20 gr and diameters were 3x2x1, 5x2x1 and 2x1x1 cm. The preparations were prepared with a thickness of 4 µm after decalcification (Merc, HC313331,

Germany) of a large number of masses, which are determined to be having different sizes of cystic structures filled with calcium inside, on the cross-section. The preparations that were prepared for the histopathological examination were examined with light microscope (Leica DM 1000) after being stained with hematoxylin-eosin (HE), with Masson's trichrome and immunohistochemically (CD31, CD34, CK, EMA, Actin) (Fig. 2).



Figure 1. Preoperative and radiographic appearance of left mass. (A): Ulcerated field on left mass. (B): A / P radiography

Table 1. Some serum biochemical parameters

Parameters	Dog's parameters	Normally parameters
ACTH	11.6 pg/ml	10-70 pg/ml**
Cortisol	0.4 µg/dl	1.0-6.0 µg/dl**
Calcium	10.1 mg/dl	9.1-11.7 mg/dl**
Phosphor	4.9 mg/dl	2.9-5.3 mg/dl***
Creatinin	1.27 mg/dl	0.5-1.7 mg/dl***
BUN	12.50 mg/dl	8.0-28.0 mg/dl***

; Khan and Line 2011; *: Maden and Cuhadar 2013.

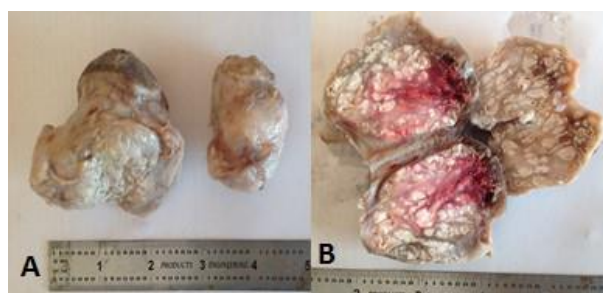


Figure 2. (A): Macroscopic view of the masses, (B): Macroscopic view of the cross section of the masses.

Microscopically, multiple granulomatous lesions surrounded by a fibrous capsule were observed. These granulomas were found to be surrounded by lymphocytes, plasmocytes, macrophages, giant cells and fibrous capsules, which were found to be filled with the various sizes of the eosinophilic granular mass in the middle part (Fig. 3A). This inflammatory zone was found in multiple vascular networks and giant cells (Fig. 3B). In the regions, where these masses were tightest, it was observed that connective tissue was converted to chondrocytes by metaplasia (Fig. 3C). The density of the vascular network around the granulomas was determined by immunohistochemical staining with CD31, CD34 and smooth muscle actin. The EMA and CK stained only the epidermis layer of the skin and smooth muscle actin

stained only smooth muscles around the arterial vessels (Fig. 3D).

Masson trichrome staining showed that the real structure of the stroma was a connective tissue, and the cartilage tissue became more visible (Fig. 4A). Similar findings were observed in the histopathology of recurrent masses (Fig. 4B). The number of giant cells was smaller. There was a higher cartilage density. According to histopathology results, it was determined that calcinosis circumscripta.

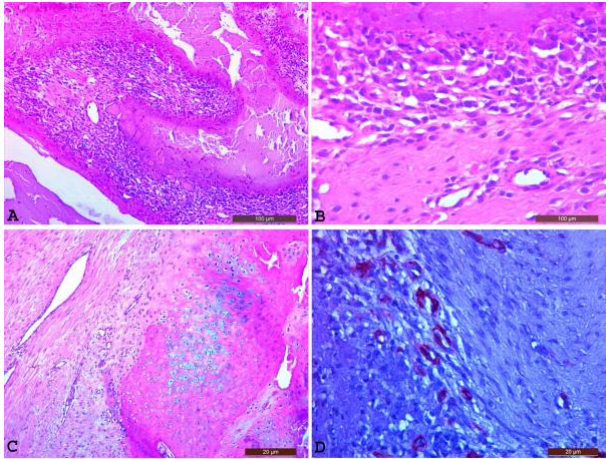


Figure 3. (A): A necrotic calcifying mass in the middle, a dense vein network around it, and a granulomatous lesion surrounded by a large number of foreign-body giant cells and an outwardly fibrous capsule, H & E, Bar: 100µm. **(B):** Lymphocytes, plasmacytes, macrophages and giant cell infiltration around the granulomas, H & E, Bar: 100µm, **(C):** Fibro-ossification cartilage structure, H & E, Bar: 100µm, **(D):** Anti-actin positive smooth muscle cells, immunoperoxidase, Bar: 20µm.

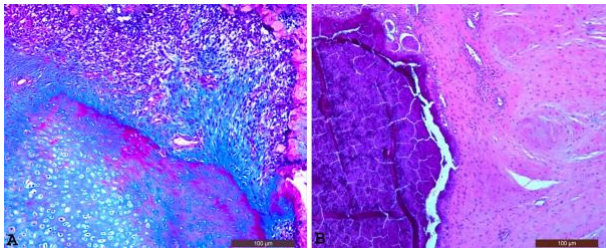


Figure 4. (A): Recurrent masses, connective tissue and cartilage tissue, Masson Trichrome, Bar: 20µm, **(B):** Recurrent masses, granuloma dark blue-purple calcification in the middle, foreign body giant cells around, H & E, Bar: 20µm.

DISCUSSION

This type of lesion has been reported to be seen in cats and some dog breeds (Tafti et al. 2005; Yumuşak et al. 2014), however, such a lesion has not been identified in a Kangal dog previously. Mineralized lesions are formed in subcutaneous tissues close to the joints and over bony prominences, where the tissue is especially susceptible to injury. Metastatic calcification is reported in both humans and animals, with mineralized foci occurring secondarily

to derangement in blood serum calcium and phosphor levels (Szczeplaniak et al. 2008). In the case of the Kangal dog brought to the clinic, the lesions were located laterally in both tarsal joints. Since the levels of serum Ca and P were in physiological limits, it was determined that the lesion was not metastatic. The lesions recurred after surgical resection in a cat with renal hyperparathyroidism (Tafti et al. 2005). Despite the absence of renal insufficiency according to clinical examination and the biomarkers in our material, recurrence was observed in the same region. Six months after the removal of the recurrent masses by surgery, the clinical examination revealed that both regions were normal.

The disorder may be classified into four major types according to the etiology. So that, the histopathologic and radiographic findings couldn't give an idea for classification of the calcinosis. However, biochemical markers can partially be contributing to the etiologic distinction.

According to the anamnesis, there was no damage in the sites with lesions before the calcification was formed. No surgical procedure or treatment was administered to the area. In addition, blood values were normal. According to these findings, etiologic factors could not be revealed, and it was concluded that a disorder was present in the idiopathic form.

REFERENCES

- Davidson EB, Schulz KS, Wisner EK (1998). Calcinosis circumscripta of the thoracic wall in a German Shepherd dog. *J Am Anim Hosp Assoc*, 34, 153-156.
- Engel S, Randall EK, Cuddon PA, Webb BT, Aboellail TA (2014). Imaging diagnosis: multiple cartilaginous exostoses and calcinosis circumscripta occurring simultaneously in the cervical spine of A dog. *Vet Radiol Ultrasound*, 55(3), 305-309.
- Ferguson JF (1996). What is your diagnosis? (Calcinosis circumscripta in a dog). *J Small Anim Pract*, 37, 447-452.
- Ginel PJ, Perez J, Rivas R, Novales M, Rodriguez JL, Mozos E (1992). Calcinosis circumscripta associated with medroxy-progesterone in two Poodle bitches. *J Am Anim Hosp Assoc*, 28, 391-394.
- Howell JM, Ishmael J (1968). Calcinosis circumscripta in the dog with particular reference to lingual lesions. *Path Vet*, 5, 75-80.
- Khan CM, Line S (2011). The Merck Veterinary Manual. Whithouse Station, NJ, Merck & Co, 10th Ed.
- Kirby VM, Knolls JS, Manley PA, Millier LM (1989). Calcinosis circumscripta associated with polydioxanone suture in two young dogs. *Vet Surg*, 18, 216-220.
- Maden M, Cuhadar F (2013). Laboratory diagnosis of endocrine diseases in dogs and cats. *J Vet Sci*, 4, 3, 35-60.
- Mumba C, Squarre D, Mwase M, Yabe J, Shibahara T (2014). Calcinosis circumscripta in a captive African cheetah (*Acinonyx jubatus*). *Asian Pac J Trop Biomed*, 4, 10, 832-834.
- O'Brien CR, Wilkie JS (2001). Calcinosis circumscripta following an injection of proligestone in a Burmese cat. *Aust Vet J*, 79 (3), 187-189.
- Szczeplaniak AE, Orzelski M, Śmiech A (2008). Canine calcinosis circumscripta-retrospective studies. *Medycyna Wet*, 64(12), 1397-1400.
- Tafti AK, Hanna P, Bourque AC (2005). Calcinosis circumscripta in the dog: A retrospective pathological study. *J Vet Med*, A, 52, 13-17.
- Yumuşak N, Alçıgır ME, Çaliskan M, Kutsal O (2014). Calcinosis circumscripta in a dog. *Vet J Ankara Univ*, 61, 153-154.