Tumoral calcinosis in a dog with chronic renal failure

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ABSTRACT

A 2-year-old male German shepherd dog in poor bodily condition was evaluated for thoracic limb lameness due to a large, firm mass medial to the left cranial scapula. Radiography revealed several large cauliflower-like mineralized masses in the craniomedial left scapula musculature, pectoral region and bilaterally in the biceps tendon sheaths. Urinalysis, haematology and serum biochemistry showed that the dog was severely anaemic, hyperphosphataemic and in chronic renal failure. The dog was euthanased and a full *post mortem* performed. A diagnosis of chronic renal failure with secondary hyperparathyroidism was confirmed. The mineralised masses were grossly and histopathologically consistent with a diagnosis of tumoral calcinosis. Tumoral calcinosis associated with chronic renal failure that does not involve the foot pads is rarely seen.

Key words: canine, hyperphosphataemia, radiography, ultrasonography.

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INTRODUCTION

Tumoral calcinosis (TC) is an ectopic calcification syndrome characterised by single or multiple, irregular calcium deposits in juxta-articular tissues over pressure points[12,13]. Synonyms include calcinosis circumscripta, Kalkgicht, calcium gout, granulomatosis, apocrine cystic calcinosis, lipocalcinosis, tumoral lipocalcinosis and hip stone[5]. Tumoral calcinosis has been reported in the horse, cat and human[1,7,13,15]. In the dog the condition most commonly occurs in young, large breeds, particularly German shepherd dogs that are under 2 years of age[13,14]. Cases of TC affecting the tongue have also been reported in the dog and the cat[1,4]. There are several reports of TC occurring in association with renal failure in the dog[5,8,10,11,13]. In humans the condition is believed to be inherited and most patients have hyperphosphataemia with normal calcium levels[7,15]. The pathogenesis of TC in dogs remains unclear. This article reports an unusual presentation of a case of advanced TC associated with chronic renal failure and hyperphosphataemia and highlights its diagnostic imaging features.

CASE HISTORY

A 2-year-old male German shepherd dog was presented at the Onderstepoort Veterinary Academic Hospital, having been referred from a satellite clinic of the Faculty of Veterinary Science for further evaluation. The dog had a left forelimb lameness that was progressive over a 3-month period. The owner noticed a mass growing medial to the left scapula over this period. On examination the dog was in poor bodily condition with pale mucous membranes, halitosis and a large (250 × 200 mm), firm, non-painful, immobile, subcutaneous mass medial to the cranial part of the left scapula. The mass displaced the left shoulder laterally, with resultant adduction of the elbow and abduction of the paw. On fine-needle aspirate, cytology of the mass showed acellular, amorphous eosinophilic material. Haematology and serum biochemistry revealed the following abnormalities: severe normocytic, normochromic, non-regenerative anaemia; mild regenerative neutrophilia and stress leukogram; mild hypoalbuminaemia; markedly raised inorganic serum phosphate (SIP); and markedly raised urea and creatinine levels (Tables 1, 2). Total serum calcium levels were within normal limits. Faecal analysis was unremarkable. Urinalysis revealed a urine specific gravity of 1.010 with an inactive sediment and trace proteinuria on urine dipstick examination. The clinical pathological diagnosis based on these results was chronic renal failure with secondary renal hyperparathyroidism.

Radiographs showed several inhomogeneously mineralised masses of various sizes in the soft tissues around the thoracic inlet/caudal neck region (Figs 1, 2). The largest mass was a circular 120 × 115 mm, inhomogeneously mineralised structure seen in the region of the left caudal cervical spine and cranial thorax region. The mass extended from the level of the middle of the 4th cervical vertebra to the middle of the 2nd thoracic vertebra with its centre-point at the level of the spine. The margin of the mass was slightly irregular but well circumscribed and com-

Table 1: **Clinical biochemistry results.**

Parameter	Result	Normal range
TSP[a] (g/ℓ)	51.6	53–75
Albumen (A) (g/ℓ)	24.0	27–35
Globulin (G) (g/ℓ)	27.6	20–37
A/G	0.87	0.6 –1.2
ALT[a] (U/ℓ, 25°)	17.0	5–40
ALP[a] (U/ℓ, 25°)	40.0	40–190
Glucose (mmol/ℓ)	5.4	3.3–5.5
Na (mmol/ℓ)	143.0	140–155
K (mmol/ℓ)	4.14	3.6–5.1
Ca (Total)	2.39	2.2–2.9
SIP[a] (mmol/ℓ)	4.57	0.9–1.6
Urea (mmol/ℓ)	90.2	3.6–8.9
Creatinine (µmol/ℓ)	878.0	40–133
Ca mg/dℓ × SIP mg/dℓ[b]	165.0	<702

[a]TSP, total serum protein; ALT, alanine aminotransferase; ALP, alkaline phosphatae; SIP, serum inorganic phosphate.
[b]Conversion from SI to gravimetric units: Ca/0.2495, SIP/0.3229 (Bonagura and Kirk[2]).

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posed of a dense conglomerate of multiple mineralised irregular nodules up to 10 ×15 mm (but mostly smaller) – that gave the mass a distinct multilobular, cauliflower-like appearance. A similar round mass of 50 × 55 mm was seen superimposed on the tip of the manubrium. Also seen were linear clusters of mineralised irregular nodules at the cranial aspect of both shoulder joints.

Although closely associated with the bone, no periosteal reaction or any other bony changes were seen. Based on the irregular multilobular appearance of the mineralised masses, a radiological diagnosis of multifocal tumoral calcinosis was made. In addition, there were several areas of less well-defined mineralisation in the cranial thoracic epaxial and intercostal soft tissues, which are common sites of metastatic mineralisation.

On ultrasonography of the abdomen, the kidneys were diffusely hyperechoic (similar to the splenic echogenicity) with irregular capsular surfaces. The corticomedullary junctions were not discernible. Several intensely hyperechoic specks in the juxtapelvic region with streaks of clean shadowing emanating distally from them were seen in both kidneys. This appearance is consistent with focal areas of mineralisation. The right kidney measured 46 × 24 mm and the left 40 × 20 mm in the sagittal plane; both were subjectively judged to be small. The rest of the abdomen, including the gastric mucosa, was unremarkable. These ultrasonographic findings supported the diagnosis of chronic renal disease with nephrocalcinosis.

Owing to the poor long-term prognosis and financial constraints, the owner opted for euthanasia. On *post mortem,* the above-described mineralised masses identified by radiography were well demarcated macroscopically. They contained multiple deposits of chalky, gritty grey-white cheesy material embedded within a loose structure of fibrous tissue and muscle. White fluid oozed from multiple pockets within the mass after incising the surfaces (Fig. 3). The adjacent bones were unaffected. The larger mass was seen to compress the left brachial plexus. Mineralised masses were found bilaterally within the biceps tendon sheaths and shoulder joints. The kidneys were shrunken, pale and irregular with tightly adherent capsules and narrowed cortices. The parathyroid glands were markedly enlarged and greyish. No lesions within the foot pads were seen. Histopathology of the kidneys confirmed chronic, fibrotic, interstitial nephritis with foci of metastatic calcification in the tubular epithelium. There was no evidence of renal dysplasia. Histopathology also confirmed foci of mineralisation in the cranial intercostal muscles, endocardium of the left atrium and in the gastric mucosa, indicating metastatic calcification due to renal secondary hyperparathyroidism. Histopathology of the parathyroid glands was unfortunately not performed. Histopathology of the mineralised masses showed well-demarcated areas of calcification within the muscles and intermuscular fascia, surrounded by connective tissue and macrophages. There were, however, several foci within the muscle not associated with the calcification that showed immature fibrosis, fibre loss and attempts at muscle fibre regeneration.

Table 2: **Haematology results.**

Parameter	Result	Normal range
Haemoglobin (g/ℓ)	43	
Red cell count (no./ℓ)	1.68×10^{12}	5.5–8.5
Haematocrit (ℓ/ℓ)	0.117	0.37–0.55
MCV[a] (f/ℓ)	69.7	60–77
MCHC[a] (g/dℓ cells)	36.9	32–36
RDW[a] (%)	14.6	
White cell count (no./ℓ)	18.6×10^9	6.0–15.0
Mature neutrophils (no./ℓ)	14.7×10^9	3.0–11,5
Immature neutrophils (no./ℓ)	0.19×10^9	0.0–0.5
Lymphocytes (no./ℓ)	2.08×10^9	1.0–4.8
Monocytes (no./ℓ)	1.51×10^9	0.15–1.35
Eosinophils (no./ℓ)	0.04×10^9	0.10–1.25
Basophils (no./ℓ)	0.07×10^9	0.00–0.10
Thrombocytes (no./ℓ)	190×10^9	200–500
Anisocytosis	2+	
Reticulocytes	0.84 % of red cells	
Myeloblasts	1+	

[a]MCV, mean corpuscular volume; MCHC, mean corpuscular haemoglobin concentration; RDW, red cell distribution width.

DISCUSSION

The signalment in this case was typical as TC is most commonly reported in young, large-breed dogs, particularly German shepherd dogs, under 2 years of age[13,14]. The aetiology of TC remains enigmatic. One proposed mechanism of TC is

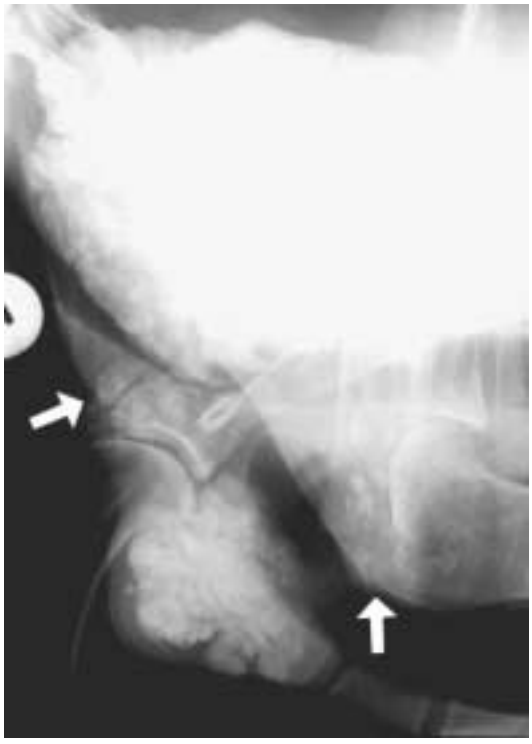

Fig.1: **Left lateral radiograph of the caudal neck region with the left forelimb pulled cranially. The bony detail of the vertebrae is obscured by the huge superimposing mineralised mass. Note the mineralised deposits bilaterally within the biceps tendon sheaths** (arrows) **and around the manubrium.**

dystrophic mineralisation, which occurs under conditions of normal calcium and phosphorous metabolism due to injury or necrosis of tissue. Tumoral calcinosis occurs more commonly over pressure points and sites of possible trauma[14]. One report describes TC developing in the thoracic wall following a thoracotomy in the repair of a patent ductus arteriosus[6]. It has been reported to occur following the use of polydioxanone suture material[9]. Tumoral calcinosis associated with chronic renal failure has been reported most commonly to occur in the footpads of dogs[5,8,10,11,13]. In a retrospective study of 130 cases where none of the dogs had chronic renal disease, it was concluded that TC occurring in sites other than the footpads is usually not associated with presently recognized inciting factors[14]. Similar to this case, only 2 other reports describe TC associated with renal failure at other anatomical sites without foot pad involvement (referred to below as Case 1 and Case 2)[5,10].

Case 1 was an 11-month-old Samoyed-cross bitch. The TC masses were located in 3 separate sites, namely: bilaterally over the trochanteric fossae and within the synovial membranes of the coxofemoral joints, measuring up to 50 mm in diameter; and deep to the cranial border of the left shoulder joint, measuring 50 ×40 × 40 mm[5]. Although the kidneys appeared small on radiography (dimensions not reported), ultrasonography was not performed. A histopathological diagnosis of severe bilateral nephrosclerosis was made on *post mortem.* There was no evidence of other vascular or visceral organ mineralisation. The parathyroid glands were not evaluated, and serum parathyroid hormone levels were not determined. Case 2 was a 3-year-old German shepherd bitch. The TC mass was located over the left lateral metatarsus, measuring 60 × 4 × 20 mm, and had an ulcerated, exudative surface[10]. Ultrasonography of the kidneys showed dilated renal pelves and thin cortices. Neither a renal biopsy nor a *post mortem* was performed. As with the 1st case, hyperparathyroidism was not confirmed because serum parathyroid hormone levels were not determined.

The case reported in this paper differs from the 2 described above in several respects, namely: the size of the TC masses; the nature of the renal and renal-associated changes; confirmation of hyperparathyroid hyperplasia; the magnitude of the calcium–phosphorus ratio; and evidence of previous muscle injury.

The size of the largest TC mass (up to 120 mm long) in this case is, to the best of the author's knowledge, the largest yet reported in the literature. There are several conditions that manifest radiologically as mineralisation of soft tissues in and around joints[12]. The bilateral shoulder masses seen in this case appeared closely associated with the biceps tendon. Differential diagnoses for mineralisation at this site include synovial osteochondromatosis and calcifying tendinopathy[12]. However, these differentials are not associated with multiple masses as were seen in this case. Myositis ossificans is the formation of non-neoplastic heterotopic bone and/or cartilage in striated muscle. It usually forms within a single muscle or muscle group following trauma[12]. Myositis ossificans was discarded as a differential in this case as it tends to develop in alignment with the specific muscle and has sharply defined margins.

Chronic renal failure with nephro-

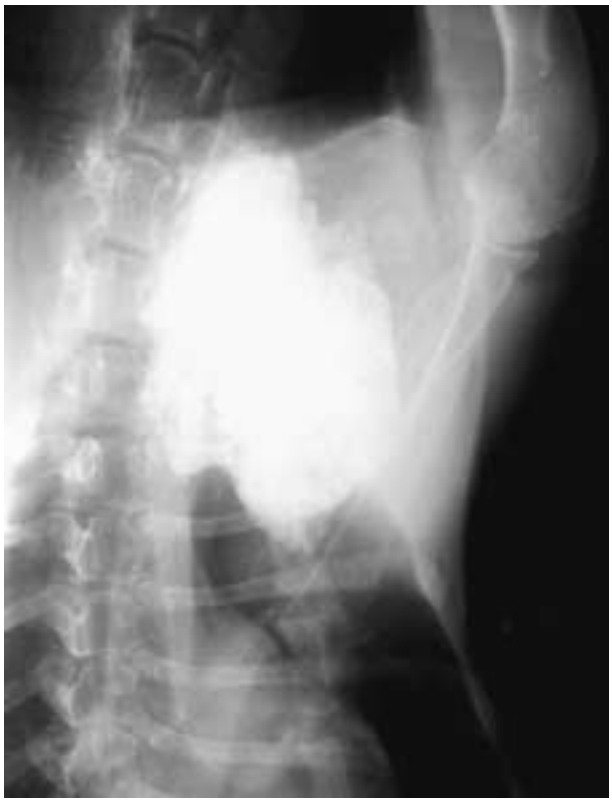

Fig. 2: **Ventrodorsal oblique view of the left scapula region. The large size of the mineralised mass caused marked lateral displacement of the left scapula and shoulder joint.**

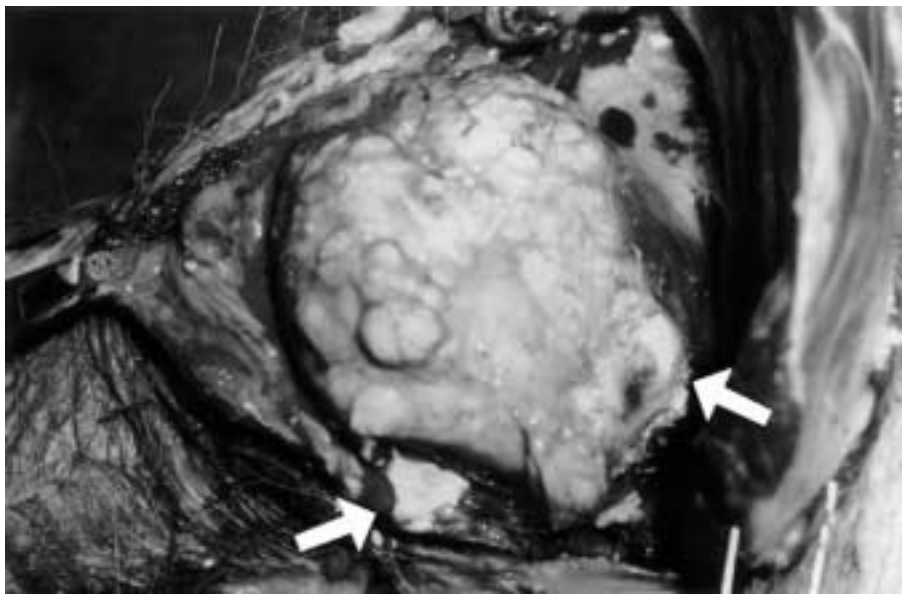

Fig. 3: **Left axilla region at *post mortem.* The lobular subscapular mass has been exposed after reflecting the scapula. Note the white fluid that has oozed from the cut surfaces** (arrows)**.**

calcinosis was strongly suspected based on the ultrasonographic findings and confirmed at *post mortem* in this case. Owing to the chronic nature of the renal lesions, a definitive diagnosis was impossible. However, with the primary lesion located in the interstitium, a previously resolved pyelonephritis is speculated to be the most likely cause. The renal changes seen on histopathology in this case were mainly located in the interstitium with minimal glomerular changes, whereas there was a strong additional glomerular component (dilated and cystic glomerulae) reported in case 1. Although no histopathology was performed on case 2, the reported ultrasonographic findings of dilated renal pelves would be consistent with pyelonephritis or hydronephrosis, neither of which was evident in this case.

Severe hyperphosphataemia attributed to chronic renal failure was found in this dog. Causes of hyperphosphataemia include dietary imbalance, hypervitaminosis D, hypoparathyroidism, decreased renal function, osteolytic bone disease, haemolysis of the blood sample or delayed processing of the blood sample, and severe tissue necrosis or trauma. Young animals may have mildly elevated serum inorganic phosphate (SIP) levels as a normal finding. Although parathyroid hormone assays and histopathology were not performed in this dog, the parathyroid glands were markedly enlarged macroscopically, indicating renal secondary hyperparathyroidism. The mechanism of renal secondary hyperparathyroidism and hyperphosphataemia in chronic renal disease is well described and documented in dogs[3]. The diagnosis of secondary renal hyperparathyroidism in this case was strengthened by the findings of mineralisation of the gastric mucosa, intercostal muscles, kidney tubular epithelium and endocardium of the left atrium – all typical sites of metastatic calcification. The calcium-phosphorus product (with units in mg/dℓ) in this case was 165, well in excess of the 70 threshold where metastatic mineralisation is hypothesized to occur in dogs in renal failure[3]. The calcium-phosphorus product in the 2 previously reported cases detailed above was 125 in Case 1 and 145 in Case 2[5,10]. Interestingly, Case 1 did not show any evidence of visceral or vascular mineralisation consistent with metastatic mineralisation at *post mortem* (Case 2 was not necropsied).

The low total serum protein (TSP) found in this dog was due to low serum albumin. Although a trace proteinuria was found on urine dipstick examination, the protein loss in the urine was not quantified. It was thought that the low albumin in this case was probably due to a combination of anorexia and urinary loss.

There was no history of trauma in this case. However the areas of fibrotic muscle with regeneration in the medial scapula region that were not associated with the mineralisation are indicative of some previous muscle injury. It can be speculated that the dog may have previously injured the shoulder region, potentiating the deposition of minerals in the area. The high levels of circulating minerals may have accelerated the dystrophic mineralisation thereby providing some explanation of the unusual clinical manifestation.

This case emphasises that renal disease with hyperphosphataemia due to secondary renal hyperparathyroidism appears to be an important aetiological factor in TC. All dogs with clinical and radiological evidence of TC (even those without involvement of the foot pads) should be evaluated for underlying renal disease.

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