

Nutritional secondary hyperparathyroidism in a white lion cub (*Panthera leo*), with concomitant radiographic double cortical line

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ABSTRACT

A captive-bred white lion cub was presented with hindquarter pain, lameness and reluctance to move. Radiographs revealed generalised osteopaenia, multiple fractures, a severely collapsed pelvic girdle, bilateral lateral bowing of the scapulae and mild kyphosis of the caudal vertebrae. A double cortical line, a distinct sign of osteopaenia, was repeatedly seen on the pelvic limbs, most strikingly along both femurs. Based on radiographic findings and a history of an exclusive meat diet since weaning, a diagnosis of nutritional secondary hyperparathyroidism was made. The diet was changed to a commercial kitten food and the cub was given cage rest for 6 weeks. Signs of pain abated and the cub became more active. A guarded prognosis was given for full recovery, as changes to the pelvis were considered potentially irreversible.

Key words: calcium, double cortical line, lion, nutritional secondary hyperparathyroidism, osteopaenia, *Panthera leo*, phosphorous.

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INTRODUCTION

Skeletal diseases of metabolic origin in young companion animals were frequently diagnosed before balanced commercial pet foods became available. A commonly occurring condition was seen where skeletally immature cats (and less frequently, dogs) presented with various degrees of lameness, muscle pain and multiple fractures with no history of trauma. In the 1960s several researchers investigating this phenomenon established that an incorrect calcium to phosphorous (Ca:P) ratio in the diet was responsible for this condition^{11,13,17}. Symptoms were attributed to hyperparathyroidism secondary to a calcium-deficient diet¹³. Nutritional secondary hyperparathyroidism (NSH) became a clinically recognised syndrome and commercial diets were reformulated. Since then the incidence and severity of NSH in kittens and puppies has decreased, and is rarely seen. Other names that have been used to describe NSH include: juvenile osteoporosis, feline nutritional osteodystrophy^{16,20}, paper bone disease, Siamese cat disease and

osteogenesis imperfecta¹⁶. Osteogenesis imperfecta is a heritable condition in man (rare in animals) caused by a structural defect in type 1 collagen, which constitutes the majority of the non-mineral bone matrix. As a calcium imbalance is not involved, the term should not be used in describing NSH^{16,17}.

Normal skeletal development requires a Ca:P ratio for growth of 1:1 to 2:1^{5,9}. Beef and horse meat have ratios between 1:10 and 1:50^{1,16}. Diets based on the aforementioned meat result in a chronic calcium deficiency and relative phosphorous excess. When serum calcium concentration falls, parathyroid hormone is secreted into the circulation causing increased renal calcium re-absorption, phosphorous excretion, and increased renal synthesis of calcitriol (the active form of Vitamin D, also known as vitamin D 1,25-dihydroxycholecalciferol). This in turn stimulates more efficient intestinal absorption of calcium and phosphorous. Parathyroid hormone also mobilises calcium from bone in an attempt to maintain plasma calcium levels. Continued ingestion of a calcium-deficient diet results in the parathyroid gland secreting larger quantities of parathyroid hormone, resulting in a hyperparathyroid state^{3,9,20}. Vitamin D deficiency plays a minor role in NSH where adequate amounts are supplied by the diet^{3,5,9}.

The constant depletion of calcium from bone causes a generalised osteopaenia, muscle pain, and a predisposition to fractures. Occasionally seizures have been documented²⁰. Typical radiological signs of osteopaenia include generalised decreased bone opacity, thinned cortices and coarse trabeculation¹². Pathological fractures, spinal curvature changes and pelvic deformation are often a sequel to longstanding osteopaenia^{20,22}. A double cortical line is frequently seen in humans with various forms of osteopaenia but is a rare finding in small animals¹². The double cortical line is believed to result from intracortical bone resorption, which occurs secondary to osteopaenia. A study that looked at the occurrence of the double cortical line in small animals described 4 cases of which only 1 had NSH. However, in this case the double line was not very prominent¹².

As early as the 1800s, prior to the recognition of NSH, the above-mentioned symptoms were identified in zoo-reared lion cubs¹⁶. In the mid 1960s, NSH was diagnosed in several wild carnivores, including the bobcat, lion and tiger¹¹. The diagnoses were based on clinical signs and history of a solely meat diet. A recent case study reported multiple fractures in the forelimbs of a 10-month-old lion cub¹⁹. This was attributed to NSH based on radiographic evidence of osteopaenia and cortical thinning. Radiological examination of another 5-month-old cub revealed radiolucent bones with thin cortices and several greenstick fractures²¹. *Post mortem* and histopathology showed severe diffuse fibrous osteodystrophy leading to a diagnosis of NSH.

The purpose of this paper is to describe NSH in a hand-reared lion cub. Radiological abnormalities, including the presence of prominent double cortical lines are discussed. A comparison is made between lion cubs and domestic kittens with respect to the clinical and radiological presentation of NSH.

CASE HISTORY

A hand-reared male white lion cub was presented at 7 months of age with a history of lethargy and lameness. Signs

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had been mild at first, but gradually progressed over a 6-week period until presentation, whereupon the animal was recumbent and very painful over the pelvic limbs and hips. There was no history of trauma.

The cub came from a small lion safari park where young lions are used for educational purposes and need to be familiar with humans. Cubs selected for hand-rearing are routinely removed from the mother at 4 days of age and bottle-fed a commercial milk formula (Esbilac, Medpet) until the age of 3 months. They are weaned over a 3-day period onto horse muscle, liver and heart (fat and bones removed). Cheetah Supplement Powder (Hoedspruit Research and Breeding Centre) is added, but often below the manufacturer's recommended dosage. Cubs are kept in a cot until approximately 3 weeks of age and then moved to a 2 × 2 m outdoor enclosure during the day, spending nights in an indoor nursery. After their 1st vaccination at 3 months (against feline rhinotracheitis, calicivirus and panleukopenia) the cubs are moved to a display enclosure (15 × 15 m). The enclosure contains a fibreglass rockery and several large rubber tyres. In the late afternoon the cubs are walked back to the nursery for the night.

The only management change made with the cub in question was to cut down bottle-feeding duration from 3 months to 2 months. First signs of lameness appeared when the cub was 4 months old, but were very mild and presented as intermittent limping and walking more slowly than the other cubs in his group, progressing to inactivity and irritability when handled. These symptoms were not seen in age-matched cubs raised in outdoor camps by their mothers.

The initial clinical examination revealed severe constipation and pain on palpation and manipulation of the pelvic limbs. A complete blood count, urine and faecal analyses were normal. Clinical chemistry (Table 1) revealed a lowered total serum protein (TSP), raised alkaline phosphatase (ALP), low creatinine, low-normal total calcium (CaT) and low-normal serum inorganic phosphate (SIP). Follow-up chemistry run 6 weeks later showed minimal change in the TSP, and markedly reduced ALP, which was still slightly higher than normal. Creatinine was still low, but not as low as at presentation. Total calcium and SIP values had increased to within normal range.

Multiple radiographs of the scapulae, distal forelimbs, spine, pelvis, femurs and tibiae were made under sedation, using 0.4 mg medetomidine (Domitor, Novartis Animal Health), and repeated periodi-

Table 1: Summary of clinical chemistry results at presentation and 6 weeks later as compared with normal values of adult lions*.

Parameters	Normal values	Results at presentation	Results 6 weeks later
Total serum protein (TSP) g/l	68–80	61.1	62.4
Globulin g/l	32–46	27.8	29.6
Albumin g/l	30–40	33.3	32.8
Alkaline phosphatase (ALP) U/l	0–51	491	65
Calcium (total) mmol/l	2.3–2.7	2.31	2.39
Serum inorganic phosphate (SIP) mmol/l	1.35–2.07	1.50	2.17
Creatinine µmol/l	167–372	66	99

*Reference ranges as used by the Section of Clinical Pathology, Department of Companion Animal Clinical Studies, Onderstepoort.

cally during the cub's 6-week hospitalisation period. A pelvic radiograph of an age-matched asymptomatic cub (from another game park) was made for comparison. Generalised osteopaenia (with the radiopacity of bones approximating that of soft tissues) as well as prominent double cortical lines were consistent features. Multiple greenstick and compression fractures (with no significant displacement of fracture ends) and marked collapse of the pelvic girdle were visible. Many fractures were found incidentally while investigating other suspected lesions. The physes were normal, with poor mineralisation of the adjacent zones of provisional calcification.

Caudocranial scapular views (Fig. 1) showed marked lateral bowing, resulting in shallow 'cupping' of the medial surfaces of the scapulae. What was visible of the right adjacent proximal humerus had

a fracture and a double cortical line. Moderate lumbosacral lordosis was present. Ribs seen on the spinal radiographs showed multiple fractures with associated focal callus formation. The pelvis revealed the most dramatic changes with marked narrowing of the pelvic canal in ventrodorsal views with virtual obliteration of the obturator foramina by the medially positioned ischia. Bilateral transverse fractures of the ilial shafts were present. There was some telescoping of the fragments with minimal immature callus present. Double cortical lines were seen on several pelvic bones. Proximal femoral diaphyseal fractures were present. Initially these were surrounded by poorly mineralised collars of callus (Fig. 2), which became more opacified after 3 weeks. After a further 3 weeks callus opacification had again diminished with remodelling of the fracture site



Fig. 1: CdCr view of scapula illustrating marked 'cupping' away from the body.

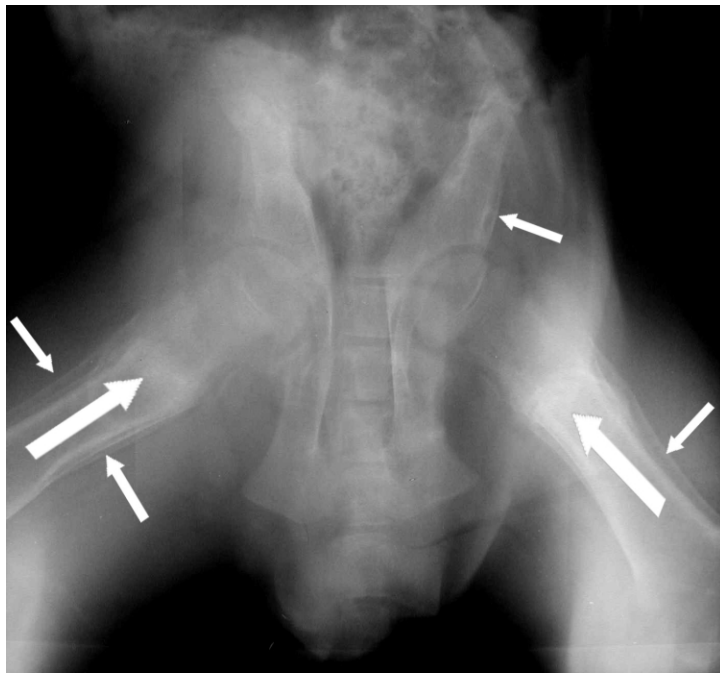


Fig. 2: VD extended view of the pelvis illustrating collapsed pelvic canal, bilateral fractures of iliac shafts and proximal femoral diaphyses with poor callus formation (large arrows) and double cortical lines (small arrows).

(Fig. 3). Prominent diaphyseal double to triple cortical lines were evident, which in some areas simulated a lamellated periosteal reaction. The right proximal tibial diaphysis had a similar fracture to the femurs, and both tibiae had extensive diaphyseal double cortical lines (Fig. 3). Double cortical lines were also seen along the metacarpal bones of the forelimbs.

Based on the history and the above findings a diagnosis of NSH was made. The diet was changed to a commercial kitten pellet (Hill's Feline Growth, Hill's

Pet Nutrition). Various organ meats with added Cheetah Supplement Powder were added at a maximum inclusion rate of 10 % of the pellet weight to improve palatability. This was supplemented with a teaspoon of calcium supplement (Calsuba Junior Powder, Group Laboratories) daily. The cub was painful on arrival, but non-steroidal anti-inflammatories were deemed inappropriate for a young feline and corticosteroids are contraindicated in NSH because they block calcium absorption from the gut and

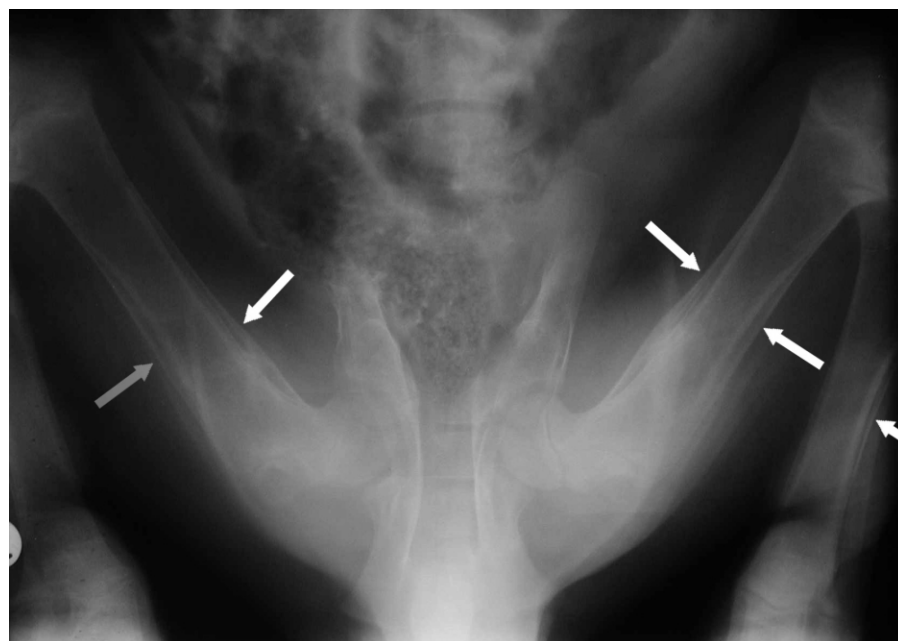


Fig. 3: VD flexed view of pelvis and femurs 6 weeks after presentation. The femoral fractures have remodelled but the diaphyseal double cortical lines are still very prominent (arrows).

inhibit calcium reabsorption in the distal tubule of the kidneys, resulting in further calcium loss from the body. A homeopathic product (Lapidar No. 9, Swiss Herbal Remedies) was used for pain relief. Lactulose syrup (Duphalac syrup, Solvay Pharmaceuticals) was given at a dosage rate of 10 ml/3 times daily to promote regular defaecation. The cub was cage rested for 6 weeks during which signs of pain abated and his gait improved.

DISCUSSION

The cub described in this report had been fed a diet consisting mainly of minced horsemeat. A paper describing the nutrient profile of horsemeat stated that horsemeat (muscle) has a calcium content of approximately 3.77 mg/kg and a mean phosphorous content of 231 mg/kg, yielding a calcium:phosphorous ratio of 1:61¹. Symptoms developed within 2 months of weaning. Kittens in pioneering experiments fed only red meat began to show locomotory disturbances after 41 days¹¹.

This lion cub represented an extreme example of NSH that presented with profound lameness and pain, but symptoms may be more subtle. Lameness may be intermittent or be of sudden onset, for example, following rough play with other cubs. The authors have seen a similar case where a cub developed lameness after doing a sudden turn around one foot. The lameness was found to be due to a greenstick fracture which resulted from the turn. Other symptoms which have been described with NSH but that were not seen with this cub include seizures and nasal stridor. Although uncommon, seizures have been reported in some animals, and are believed to result from hypocalcaemia^{13,20}. Muscle twitching and excitation have been seen in a cat²⁰. Nasal stridor and difficult breathing may be some of the first presenting complaints with NSH as a result of fractures of nasal turbinates and collapse of nasal passages¹³.

The cause of NSH is chronic dietary calcium deficiency. Both absolute calcium content and a balanced calcium to phosphorous ratio is essential for normal skeletal development⁸. In normal animals blood ionised calcium (the physiologically active form of calcium) is regulated in narrow limits, principally by the effects of parathyroid hormone. This is because normal ionised calcium concentration in extra-cellular fluid is essential for normal neuromuscular, secretory and enzyme functions⁹. Persistently decreased calcium intake will lead to chronic parathyroid stimulation, with increased parathyroid hormone secretion². As a result of these

compensatory mechanisms, blood calcium levels will appear normal despite severe deficiency^{6,16}. In this case, initial total plasma calcium levels were at the lower range of normal, but rose after hospitalisation. Mild hyperphosphataemia compared with adult cats is considered a normal finding in growing animals as a result of rapid bone metabolism²⁰. However, with NSH a hypophosphataemia may be encountered. This is because all meat diets, despite providing very high phosphorous relative to the calcium content, are actually low in phosphorous²⁰. Again, initial SIP values were in the low-normal range, but rose to a more 'normal' hyperphosphataemic level. The ALP values were raised 9 times the top normal value. High ALP values are consistent with active bone remodelling and calcium mobilization and may be up to 3 times above normal in young animals that is attributable to active growth⁷. The ALP levels dropped during hospitalization, to within levels acceptable with bone growth. Creatinine values were significantly lower than normal, but adult reference values are being compared with those of a young animal, so this may not be abnormal in a cub. Creatinine values are influenced by muscle injury, breakdown and level of activity⁷ and the lower levels may be attributed to the cub having been non-ambulatory and anorexic for several days. Creatinine values also improved over this period. A mild hypoglobulinaemia was noted. The authors speculate that this may be as a result of waning maternal antibodies (F Reyers, Department of Companion Animal Studies, Onderstepoort, pers. comm., 2003).

As calcium and phosphorous are continuously mobilised from the bone, osteopaenia eventually results. There are various causes for generalised osteopaenia, which should be differentiated from NSH. Bone disease which occurs with secondary renal hyperparathyroidism results from a complex of metabolic derangements including phosphate accumulation, decreased production of 1,25-dihydroxycholecalciferol by the kidneys and impaired tubular resorption of calcium². Although osteopaenia follows, young animals typically develop hyperostotic osteodystrophy, usually noted over the jaw, with loss of the lamina dura around the teeth^{3,9}. Clinical chemistry will differentiate this condition from NSH. Primary hyperparathyroidism features a sustained hypercalcaemia^{3,9}.

Rickets, an extremely rare condition, is caused by a Vitamin D deficiency. Typical radiographic findings include metaphyseal flaring and widened physes.

Other causes of osteopaenia include hyperparathyroidism due to glucocorticoid excess and pseudohyperparathyroidism, both of which can be differentiated from NSH on the basis of history, signalment and clinical findings^{3,9}, and are unlikely in a young cub.

Radiographic findings of osteopaenia include decreased bone opacity, thin cortices, coarse trabeculation and pathological fractures^{11,12}. Bone mass loss of 30–50 % is necessary before osteopaenia will become evident radiologically. Exposure factors also play a role in how osteopaenia will be interpreted. High kV values will 'induce' osteopaenia as bone will become less radiopaque relative to the soft tissues. Therefore, signs other than generalised osteopaenia need to be recognised to improve radiographic diagnostic sensitivity. Bone changes resulting from NSH include greenstick and complete fractures of long bones, pelvic collapse and spinal deformations such as scoliosis, kyphosis and lordosis, which may cause spinal cord compression¹³. Pathological fractures have been reported in another lion where NSH was diagnosed¹⁹. Scapular cupping, as seen in this lion cub, was a common clinical finding in kittens with NSH in the 1960s and considered virtually pathognomonic for NSH¹⁷. This is a feature that has previously not been seen by the authors and has only been recently described in 2 cats with NSH²⁰. One article described deformation and medial bowing of the scapula on macropathology in a 5-month-old lion cub that had been artificially raised²¹. The double cortical line has been well described by Lamb¹² but is only rarely seen in domestic animals. It results from intra-cortical bone resorption due to generalised and midcortical osteopaenia and may be seen in the diaphyseal cortex or subchondrally. The latter was not a feature in this cub. The intracortical bone resorption may result in up to 3 cortical lines, causing the bones to take on the appearance of a lamellar periosteal reaction. In this case no other underlying focal osseous pathology or asymmetry was associated with the reaction, thus excluding this possibility. The authors have seen radiographs of other cubs with NSH which demonstrated similarly prominent double cortical lines and this may thus be a more common presentation in the lion than in domestic cats. Double cortical lines have not previously been reported in lions, and were not noted on reproductions of radiographs seen in the literature. Pelvic collapse was marked in this cub.

There are some basic differences in the growth rates of domestic kittens and

puppies, and lion cubs. It is important to abide by correct weaning times, and not to extrapolate this from domestic animals, but rather from observations of the appropriate species in its natural environment. Domestic kittens and puppies are naturally weaned at about 6–10 weeks⁵ whereas lion cubs are completely dependent on the mother until 3 months of age, and are usually weaned by 6–7 months. The cubs are then fully dependent on adults for food until 16 months and are not capable of surviving on their own until at least 30 months of age^{8,14,18}. Time of physeal closure can be used as a guideline for cessation of growth of an animal. In puppies the last growth plates to close (femoral head and trochanter major) do so by 18 months^{4,15}. In cats, most growth plates are closed by 16 months, except for the distal ulnar epiphysis and proximal epiphysis of the humerus which may take up to 24 months to close¹⁵. A recent radiographic study of lions in the wild¹⁰ has demonstrated that physes take up to 66 months to close, which is in stark contrast to the above. This is of clinical significance as the presentation of NSH symptoms in a 5-month-old kitten implies the animal is adolescent, but symptoms in a cub aged between 5 and 7 months implies the animal is relatively much younger and in a more active phase of growth. At 6 months of age a cub weighs approximately 20–30 kg, and must attain an adult weight of 150–250 kg (males) and 120–182 kg (females)^{8,18}, that is, grow at least a further 5 times in size. Lesions such as pelvic girdle or vertebral collapse at a young age may not be compatible with life at the adult weight. A 5-month-old cat may, in contrast, at best double or triple in size.

In this case study, the cub was weaned almost instantly onto meat at the age of 2 months and symptoms were evident from as early as 4 months of age. From the time of diagnosis he was cage rested and had his diet altered. Over the 6 week hospitalisation period signs of pain abated, the animal became ambulatory and regular bowel movements returned. The transition from meat to pelleted feed initially resulted in some weight loss, but the cub adapted well to the new diet. At the time of discharge his gait was normal, but due to the severe pelvic narrowing he was given a guarded prognosis for full recovery.

Other tests that may have been useful tools in the diagnosis of NSH were calcitriol levels (raised with NSH) and parathyroid hormone levels. Parathyroid hormone levels have proved to be useful for the diagnosis of NSH in domestic cats^{2,6}. Parathyroid hormone levels were

not tested because samples require special handling, there were no age-matched control samples available and the test has not been validated in lions.

In conclusion, NSH in lion cubs yields very characteristic radiological changes. Diagnosis can be made based on radiological findings and history alone, but clinical chemistry tests such as ALP, calcium and SIP levels may corroborate the diagnosis. The authors believe that NSH is a common problem which has been under-diagnosed in captive bred lions and if not managed correctly may have future consequences in adult animals and possibly on the future of captive prides.

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