Brief Communication Communication brève

Suspect osteogenesis imperfecta in a male kitten

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Abstract — A 4.5-month-old, male domestic shorthair was presented with bilateral femoral fractures after falling from a low height. Radiographs revealed reduced radio-opacity and thin cortices of all long bones. A presumptive diagnosis of osteodystrophy, secondary to osteogenesis imperfecta, was made on postmortem examination.

Résumé — Suspicion de dysplasie périostale chez un chaton mâle. Un chat domestique à poil court, mâle, âgé de quatre mois et demi a été présenté avec des fractures fémorales bilatérales après une chute d'une faible hauteur. Les radiographies ont montré une opacité réduite aux rayons X et une substance corticale osseuse mince sur tous les os longs. Un diagnostic de présomption d'ostéodystrophie, secondaire à une dysplasie périostale, a été posé à l'examen post mortem.

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A 4.5-month-old, male domestic shorthair was referred to the Small Animal Clinic, Western College of Veterinary Medicine (WCVM), for evaluation of acute bilateral displaced femoral fractures after falling from a low height. The owners had obtained the kitten from a local farm at approximately 6 wk of age in apparent good health. There had never been any systemic signs of illness. Two months prior, however, a fall from a chair had resulted in right radial and ulnar fractures, which were treated by another veterinarian, using external splinting. The original owner of the kitten did not recall having administered any medications or supplements to the queen during pregnancy or to the queen and kittens after birth. Since being weaned at 6 wk of age, the kitten's diet had consisted of a dry commercial kitten food with no supplements or medications. The kitten was housed indoors, occasionally venturing outside on a harness into an enclosed backyard. There were no other animals in the house. The kitten had received 1 vaccination against *Feline rhinotracheitis virus, Feline calici virus,* and *Feline panleukopenia virus* 1 wk prior to presentation to the WCVM.

Case description

On admission to the WCVM, the kitten was responsive, but quiet, and in good body condition (1.9 kg). The rectal temperature was 38.9°C, the heart rate was 180 beats/min, and the respiratory rate was 40 breaths/min. Capillary refill time was 1 to 2 s and the mucus membranes were pink. Dorsopedal pulses were strong, synchronous with the heart beat, and regular. The kitten was nonweight bearing on both hind legs and gentle palpation revealed displaced femoral fractures bilaterally, with mild swelling adjacent to the fracture sites. No other abnormalities were noted on physical or neurologic examination.

A complete blood (cell) count (CBC) revealed a mild leukocytosis (19.6×10^9/L; reference range, 3.9 to 18.1×10^9/L), characterized by a neutrophilia (segmented neutrophils 16.5×10^9/L; reference range, 2.1 to 15×10^9/L) with a mild left shift (band neutrophils 0.59×10^9/L; reference range, 0.0 to 0.2×10^9/L). The serum chemical panel showed mild hyperglycemia (8.5 mmol/L; reference range, 3.5 to 8.1 mmol/L), consistent with stress. There were also moderate increases in serum alkaline phosphatase (ALKP) (189 U/L; reference range, 11 to 56 U/L) and creatinine kinase (CK) (1736 U/L; reference range, 75 to 471 U/L). The serum creatinine concentration (53 μmol/L; reference range, 78 to 178 μmol/L) was slightly decreased, probably related to age and low muscle mass. Serum total calcium (2.59 mmol/L; reference range, 2.26 to 2.86 mmol/L) and phosphorus (2.16 mmol/L; reference range, 1.08 to 2.21 mmol/L) were normal. The increased ALKP could have been secondary to increased bone isoenzyme due to growth or any disorder causing increased osteoblast action, such as periostitis, rickets, primary or secondary hyperparathyroidism, bone neoplasia, or fractures. The increase in CK was attributed to muscle trauma associated with the displaced fractures. The result of complete urinalysis was normal, with a urine specific gravity of 1.056. *Feline leukemia virus* antigen and *Feline immunodeficiency virus* antibody tests (Petcheck ELISA; IDEXX Laboratories, Westbrook, Maine, USA) were negative.

Limb radiographs revealed bilateral mid-diaphyseal displaced femoral fractures. There was also evidence of a previous fracture of the right femur and generalized thinning of all long bone cortices. These findings were most consistent with pathologic

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fractures related to bone abnormalities, possibly caused by primary hyperparathyroidism, nutritional or renal secondary hyperparathyroidism, or osteogenesis imperfecta. Serum calcium and phosphorus concentrations were normal. Samples were collected and submitted for parathyroid evaluation. Since the kitten had been fed a commercial diet without supplementation, nutritional secondary hyperparathyroidism was unlikely. The normal urine concentration and lack of azotemia made renal secondary hyperparathyroidism unlikely, as well. The kitten was managed overnight with analgesia and sedation: oxymorphone (Oxymorphone, Numorphan; Du Pont, Mississauga, Ontario), 0.1 mg/kg bodyweight (BW), and acepromazine (Atravet; Ayerst Laboratories, Montreal, Quebec), 0.06 mg/kg BW, q4h, and meloxicam (Metacam; Boehringer Ingelheim Vetmedica, Burlington, Ontario), 0.1 mg/kg BW, q24h.

On day 2, surgical stabilization of the bilateral femoral fractures was performed. Concerns regarding an underlying bone disorder, potentially making fracture stabilization and healing difficult, were discussed with the owners. The fractures were stabilized by internal bone plate fixation, using a 2.0-mm, 8-hole plate on the right femur and a 2.0-mm, 7-hole plate on the left femur. Manipulation of the right femur for reduction resulted in fissure formation and a small butterfly fragment with no soft tissue attachments. This fragment was removed for histopathologic examination. A bone biopsy from the left femur was also submitted. Postoperative radiographs revealed good alignment, reduction, and apposition of the left femoral fracture site. The right femur was noted to crack audibly during radiographic positioning. Radiographs showed a minimally displaced fracture, distal to the bone plate. This was repaired and satisfactory reduction and realignment was achieved by using 3 Kirschner wires and 3 cerclage wires. This fixation was tenuous; however, further manipulation of the bone to place a longer bone plate was considered highly risky of causing additional fracture, so this was not performed. Pain management was continued postoperatively, as previously described.

On day 3, the kitten was weight bearing on his left hind leg and eating, drinking, urinating, and defecating normally. The right hind leg was swollen and the kitten was nonweight bearing on this leg. Radiographs revealed a displacement of the right femur distal to the bone plate. After discussion with the owners, conservative management was selected. The kitten was discharged from the WCVM 48 h post surgery, with instructions to the owner for strict cage rest and continued analgesia.

Additional diagnostic results became available postoperatively. These revealed normal intact parathormone (2.2 pmol/L; reference range, 0 to 4 pmol/L), 25-hydroxy vitamin D (68 nmol/L; reference range, 65 to 170 nmol/L), and ionized calcium values (1.41 mmol/L; reference range, 1.0 to 1.4 mmol/L) values. These results, coupled with the normal serum total calcium and phosphorous levels, made a diagnosis of primary or secondary hyperparathyroidism unlikely, so therapy with calcium carbonate or calcitriol was not indicated. Histopathologic examination of both bone fragments submitted revealed thin trabeculae and a lack of osteoclasts. A tentative diagnosis of osteogenesis imperfecta was made.

The kitten was reevaluated at the WCVM 7 d postoperatively. His attitude, appetite, and gait were normal. A firm, nonpainful swelling was palpable over the right femoral fracture site, thought to be a callus secondary to healing. Oral examination revealed a slight pink discoloration of all teeth, which was suspected to be evidence of dentinogenesis imperfecta. Results from the remainder of the physical examiantion were normal. Based on the tentative diagnosis of osteogenesis imperfecta, therapy was initiated with vitamin C (75 mg/kg BW, PO, q24h). Treatment with an oral bisphosphonate (alendronate, Fosamax; Merck Frosst, Kirkland, Quebec), was also recommended, but declined by the owner. Continued confinement and exercise restriction were recommended.

The kitten was reexamined 45 d after the initial presentation, when it became acutely nonweight bearing on the right front leg after falling from a chair. Gentle palpation of the limb was suggestive of a fracture of the right humerus. Radiographs confirmed a mid-diaphyseal fracture and very thin bone cortices. The owners elected euthanasia and permission was granted for a complete postmortem examination.

The postmortem examination confirmed the radiographic findings, the prior stabilized femoral fractures, and the evidence of multiple additional sites of bone fractures. There was a fresh mid-shaft fracture of the right humerus and an old fracture of the distal end of the left humerus in the area of the medial malleolus. The femoral fractures repaired earlier were as described and showed little evidence of bony remodeling. Bone calluses were noted on the shafts of the 10th and 13th ribs, indicating previous fractures. In general, all bones appeared brittle and fractured easily. The parietal bone of the skull was thin, as were the teeth. All teeth had a distinct pink discoloration, the lower left canine tooth was loose, and the 3rd right upper premolar was fractured. The kitten was in good body condition and no abnormalities of any internal organs were detected.

On histopathologic examination, a reduction in the amount of mature cortical and trabecular bone, compared with that of a normal kitten of the same age and sex, was noted in all appendicular and axial bones examined. Epiphyseal bone was reduced to a few small spicules in some bones. Cartilage trabeculae of primary spongiosa were narrow and extended deep into the metaphysis and diaphysis. The trabeculae contained cores of cartilage with a layer of woven bone matrix. There appeared to be little osteoclastic resorption or formation of lamellar bone. Bone cortices were porous, consisting of trabeculae of primarily woven bone separated by loose connective tissue. There was an absence of well-developed osteons. A diagnosis of presumed osteogenesis imperfecta was made.

Discussion

Osteogenesis imperfecta is a disorder leading to bone fragility. This disorder is most commonly caused by a mutation in 1 of the 2 genes coding for type 1 collagen (1–4); which is the most abundant structural component of skin, bone, cartilage, tendons, and ligaments. This structural collagen defect leads to bone fragility and pathological fractures. Osteogenesis imperfecta is a well-characterized heritable disorder in humans and can vary in severity (4). In humans, there are several distinct clinical

variants of the disease, with greater than 90% of the cases caused by autosomal dominant mutations in the genes coding for type 1 collagen (1–4). All types are characterized by fragile bones that shatter spontaneously or secondarily to minimal trauma. Osteogenesis imperfecta has been documented in the dog (1–3) and there is a single report of presumed osteogenesis imperfecta in a cat (5).

The clinical features of osteogenesis imperfecta in small animals have typically included lameness and multiple fractures occurring with minimal or no associated trauma (1–3,5). Onset of clinical disease is most common in puppies and kittens between 10 and 18 wk of age (1–3,5). Most of the fractures have been reported to occur when young animals jump to the floor from a low height, as from a bed or a chair (1–3). Radiographs reveal long bone cortices that are less opaque than normal and with pathological fractures. It is not uncommon to find concurrent evidence of old healing fractures. Hematologic values, serum chemical, and measured hormone concentrations are normal, making metabolic disorders, such as primary and secondary hyperparathyroidism, unlikely.

Because the organic matrix of dentine is composed primarily of type 1 collagen, animals with osteogenesis imperfecta also commonly have abnormal dentine development in the teeth, leading to dentinogenesis imperfecta (3). The teeth in these young animals have severe thinning of the dentine layer, leading to a translucent appearance, pink discoloration, and multiple tooth fractures (1–3,5). This appears quite distinct from the brown, yellow, or gray staining that can occur with tetracycline administration (6). Not all dogs with osteogenesis imperfecta have had dentinogenesis imperfecta at the time of initial presentation for pathologic fractures (1). This may develop later in the course of disease, as in the kitten reported here.

No clinical dermatologic abnormalities are noted in humans and animals affected with osteogenesis imperfecta, and microscopic examination of skin is normal, despite the abundance of type 1 collagen present in skin (1–5,7). Analysis of type 1 collagen obtained from cultured skin fibroblasts can, however, be used to achieve a definitive diagnosis (1,2). This test was unavailable at the time this kitten was evaluated.

Once a diagnosis of osteogenesis imperfecta was suspected in this kitten, therapy was initiated using vitamin C, which is essential in collagen formation and tissue repair (6,7). Initiating therapy with alendronate, was also recommended, since bisphosphonates are synthetic analogs of inorganic pyrophosphate that inhibit osteoclast activity, thus decreasing bone resorption (1,8,9). They may also promote architectural changes in cancellous bone, reducing fracture risk (8,9). These drugs have been effective in some post menopausal women with osteoporosis, increasing mineral density and decreasing pathological fractures (1,8,9). Their use is also being investigated in the treatment of hypercalcemia of malignancy and the treatment of lytic skeletal metastases in dogs (9). Bisphosphonates administered to children with osteogenesis imperfecta over a 2-year period were effective in increasing bone mineral density and decreasing the frequency of fractures (1). The effectiveness of bisphosphonates in treating osteogenesis imperfecta in dogs and cats has not been evaluated.

Although osteogenesis imperfecta is rare in cats and dogs, it should be considered as a differential diagnosis whenever a puppy or kitten is presented for multiple pathological bone fractures. Historical and biochemical evaluation can be used to rule out other causes of multiple fractures or bone fragility. Clinical evidence of concurrent dentinogenesis imperfecta can raise the index of suspicion of this disorder; however, definitive diagnosis requires analysis of cultured skin fibroblasts, a test that is not readily available. CVJ

References

1. Lazar T, deHaan JJ, Peck JN, et al. Osteogenesis imperfecta in three dogs from a single litter. Vet Comp Orthop Traumatol 2000;13:23–7.
2. Campbell BG, Wootton JAM, Krook L, DeMarco J, Minor R. Clinical signs and diagnosis of osteogenesis imperfecta in three dogs. J Am Vet Med Assoc 1997;211:183–187.
3. Seelinger F, Leeb T, Peters M, et al. Osteogenesis imperfecta in two litters of Dachshunds. Vet Pathol 2003;40:530–539.
4. Rowe DW, Shapiro JR. Osteogenesis imperfecta. In: Avioli LV, Krane SM, eds. Metabolic Bone Disease, 3rd ed. London: Acad Pr, 1998:651–695.
5. Cohn L, Meuten D. Bone fragility in a kitten: An osteogenesis imperfecta-like syndrome. J Am Vet Med Assoc 1990;197:98–100.
6. Plumb DC. Veterinary Drug Handbook, 3rd ed. Ames: Iowa State Univ Pr, 1999:476–477,53–54.
7. Guyton AC, Hall JE. Textbook of Medical Physiology, 10th ed. Philadelphia: WB Saunders, 2000:812.
8. Ding M, Day JS, Burr DB, et al. Canine cancellous bone microarchitecture after one year of high dose bisphosphonates. Calcif Tissue Int. 2003;6:72:737–744.
9. Milner R, Farese J, Henry CJ, et al. Bisphosphonates and cancer. J Vet Intern Med 2004;18:597–604.