History
A 15-week-old 1.74-kg sexually intact male domestic shorthair cat was evaluated for an intermittent, shifting-leg lameness of 2 months’ duration. Right forelimb lameness was initially observed following mild trauma and resolved without treatment. Right forelimb lameness returned 1 month later after the cat jumped off a couch. One week later, the cat was reluctant to walk and unable to bear weight in the hind limbs bilaterally. Diet history included a combination of several dry and canned commercial diets formulated for kittens.

Clinical and Gross Findings
On physical examination, the cat had a thin body condition and moderate muscle atrophy of all 4 limbs. Ocular evaluation revealed no scleral abnormalities. The oral cavity showed normal dentition for a kitten. Orthopedic examination revealed bilateral, non-weight-bearing lameness in the hind limbs, bilateral antebrachial varus deformity, and a sharp bend in the tail. Neurologic examination revealed normal reflexes in all 4 limbs. Serum biochemical analyses revealed clinically normal total calcium concentration (9.9 mg/dL; age-adjusted reference range, 9.2 to 12.0 mg/dL), phosphorus concentration (6.4 g/dL; age-adjusted reference range, 6.0 to 10.4 mg/dL), and alkaline phosphatase activity (230 U/L; age-adjusted reference range, 37 to 333 U/L). Urine specific gravity was concentrated at > 1.050.

A serum parathyroid hormone (PTH), calcium, and vitamin D profile revealed a mildly high concentration of PTH (33 pg/mL; age-adjusted reference range, 1 to 28 pg/mL) and clinically normal concentrations of ionized calcium (1.31 mmol/L; age-adjusted reference range, 1.30 to 1.34 mmol/L) and calcidiol (25-hydroxyvitamin D; 120 nmol/L; age-adjusted reference range, 89.6 to 126.5 nmol/L). The mildly high PTH concentration was deemed inconsequential in combination with clinically normal ionized calcium and calcidiol concentrations.

Pelvic and hind limb radiography revealed severe, diffuse osteopenia, with thin cortices, double cortical lines, and apparent widening of the medullary cavities of all visualized long bones. The epiphyses of the femur and tibia had a coarse trabecular pattern bilaterally. There were chronic folding fractures of the proximal left tibia and distal right femur at the level of the metaphyses. The seventh lumbar vertebra was shorter than adjacent vertebral bodies. There were multifocal curved caudal vertebral bodies with sclerotic endplates. Due to the severity of clinical signs, the owner elected euthanasia.

At necropsy, the right femur had a complete fracture at its distal metaphysis, with an area of subcutaneous hemorrhage and edema overlying the fracture site. Callus formation was observed at the proximal metaphysis of the left humerus and distal metaphyses of both radii (Figure 1). The left radius was moderately curved medially at the distal callus. There was no widening of the growth plates visualized. All ribs had increased pliability. The calvarium was very thin,
with increased flexibility. The remainder of the necropsy findings, including histopathologic evaluation of the eyes, teeth, kidneys, thyroid glands, parathyroid glands, and skin, were unremarkable.

Formulate differential diagnoses, then continue reading.

**Histopathologic Findings**

Histologic evaluation of multiple long bones and ribs revealed marked reduction in thickness of woven bone forming the cortex, which was often lined by moderate numbers of osteoblasts and contained a thickened periosteum. Within the metaphyses, there was extension of primary spongiosa, with retention of cartilaginous cores and marked reduction in secondary spongiosa. Trabeculae of secondary spongiosa often contained reversal lines and frequent microfractures. Areas of microfracture were lined by osteoclasts. The grossly described calluses within the humerus and radii demonstrated multifocal, chronic, healing fractures with complete loss of normal cortical bone. Cortical bone was replaced by abundant and disorganized cartilage, with surrounding collagen, fibroblasts, and spicules of mineralized osteoid lined by osteoblasts and osteoclasts (Figure 2). No specific signs of a collagen disorder were noted; dentinogenesis and amelogenesis were normal. The periodontal ligament was widened due to bone loss, rather than abnormal formation.

**Morphologic Diagnosis and Case Summary**

Morphologic diagnosis: severe, diffuse osteopenia of long bones with lack of secondary spongiosa, accompanying fracture calluses and infraction lines (microfractures).

Case summary: lesions consistent with osteogenesis imperfecta (OI) in a cat.

**Comments**

The most common metabolic causes of diffuse osteopenia and pathologic fractures in dogs and cats are nutritional or renal secondary hyperparathyroidism.\(^1,4\) Nutritional or hereditary (type 1 or type 2 vitamin D–dependent rickets) vitamin D deficiency and hypophosphatemic rickets can also cause similar clinical signs.\(^1,4–6\) Nutritional vitamin D deficiency is uncommon in dogs and cats receiving an age-appropriate, balanced diet, and hereditary vitamin D deficiencies are rare diseases in dogs and cats.\(^5,6\) Measurement of serum creatinine, urea nitrogen, ionized calcium, phosphorus, vitamin D, and PTH concentrations, as was performed for the cat of the present report, screens for the aforementioned metabolic conditions. If these measurements are within the age-adjusted reference ranges, OI should be considered.

Osteogenesis imperfecta is an inherited bone disorder that is extremely rare in dogs and cats.\(^1,7,8\) In humans and dogs, OI most commonly results from gene mutations in type 1 collagen (\textit{COLIA1}, \textit{COLIA2})\(^7,9–14\); however, recent studies have shown mutations in \textit{SERPINH1} causing OI in Dachshunds.\(^11,15\) Normal type I collagen forms the scaffold for bone mineralization, with abnormalities leading to lack of bone mineralization and extreme bone fragility.\(^16\) In dogs, there are no known sex predilections, but breed predispositions have been suggested in Beagles.\(^11,13,17\) Collies,\(^17–19\) Dachshunds,\(^9,11,15,20\) and Golden Retrievers.\(^11–13,17\) Although there have been individual case reports of clinically suspected OI in cats,\(^8,21\) the underlying gene mutations or breed predispositions are unknown.
Affected dogs and cats typically develop clinical signs by 10 to 18 weeks of age. Common clinical signs are nonspecific and include lethargy, lameness, and signs of pain. Physical examination findings include blue-colored sclera, bone fractures without history of trauma, angular limb deformities secondary to fractures, and in severely affected dogs and cats, dyspnea and paresis or paralysis. Dentinogenesis imperfecta is a possible concurrent disorder that causes thin, roughened, discolored teeth due to thinning of the dentin layer.

Clinicopathologic analyses are unremarkable in dogs and cats with OI when reference ranges are adjusted for the animal’s age. Hyperphosphatemia and high alkaline phosphatase activity, based on adult reference ranges, may be observed in puppies and kittens but are indicative of a developing animal. Most notably, age-adjusted serum concentrations of total calcium and ionized calcium are normal, and azotemia is not observed. Urine specific gravity is adequately concentrated for the age of the patient. Further hormonal testing, including assessments of concentrations of PTH, calcidiol, and calcitriol should be within age-adjusted reference ranges in dogs and cats with OI. Although calcitriol is the metabolically active form of vitamin D, serum calcidiol is routinely measured in human medicine to evaluate for vitamin D deficiency. Diagnostic imaging with radiography or CT demonstrates diffuse osteopenia, acute or chronic pathologic fractures, and angular limb deformities. Lack of wide, cupped growth plates or enlarged growth plates, which are commonly observed in dogs and cats with vitamin D deficiency, further supports a diagnosis of OI.

Definitive diagnosis of OI requires genetic testing for defects in type 1 collagen genes. As the genetic defect is unknown in cats, the combination of compatible clinicopathologic, diagnostic imaging, and ultimately, histopathologic features are necessary. In the case presented, absence of hypocalcemia, absence of biochemical evidence of renal disease, and normal calcidiol concentrations excluded other metabolic causes. The age of a cat is an important consideration when performing metabolic testing, as calcidiol concentrations vary in clinically normal, developing kittens. Notably, the serum calcidiol concentration was slightly low in comparison to the laboratory reference range in the cat of the present report. However, calcidiol concentration was clinically normal when adjusting for the cat’s age, and in combination with a clinically normal ionized calcium and absence of radiographic changes associated with vitamin D deficiency, type 1 and type 2 rickets were considered unlikely.

Histopathology confirmed changes reported secondary to OI in the presented case, including decreased cortical bone, decreased secondary spongiosa, and callus formation at fracture sites. Accurate diagnosis is critical, as successful treatment of OI in cats is not described; clinical signs and pathologic changes secondary to nutritional or hereditary vitamin D deficiency may improve with treatment. Attempts to surgically correct pathologic fractures secondary to suspect OI have not been successful due to diffuse bone fragility and lack of healing. Bisphosphonates are prescribed to human patients with OI and may provide palliation in dogs and cats; efficacy has not been reported. Vitamin C has been prescribed to cats with suspected OI due to effects on collagen growth; however, clinical signs did not improve in 1 report. Palliation with pain medication may improve quality of life in the short term, but prognosis for long-term survival is poor.

Acknowledgments

No third-party funding or support was received in connection with this case or the writing or publication of the manuscript.

References