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Long-term follow-up of a cat with an undetermined osteoporotic bone disease managed with multiple intramedullary pins

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Abstract

Case summary Osteogenesis imperfecta (OI) is an inherited disorder related to the synthesis of type 1 collagen. Clinical signs of pain from the fracture of fragile bones are common. A 3-month-old male Chinchilla cat was presented for lameness and pain from a right femoral fracture. After surgical repair using intramedullary pins, and since repeated fractures occurred and there is little information about genes causing OI in cats, various examinations were performed to discriminate other diseases that could cause the pathological fracture. Primary hyperparathyroidism and nutritional or renal secondary hyperparathyroidism were ruled out through blood tests and ultrasonography. Quantitative CT confirmed low trabecular bone mineral density compared with normal cats. Radiography and histopathological examination revealed thin cortical bone. OI was tentatively diagnosed and long-term follow-up of the surgical repair was reviewed. Fractures were treated using intramedullary Kirschner wires. The same method of intramedullary pinning was then applied preventively to protect several other long bones by improving stress distribution and bending resistance. Follow-up was performed for 3 years until the patient's death due to undetermined reasons.

Relevance and novel information Although the patient underwent repeated fractures and bone unions, and needed medication for pain management sometimes, it was generally able to live as a companion cat. Therefore, palliative preventive intramedullary pinning could be used for long-term management of patients suspected of OI.

Keywords: Osteogenesis imperfecta; fracture; intra-medullary pins; long-term

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Introduction

Pathological fracture leading to bone abnormalities can occur due to primary hyperparathyroidism, nutritional or renal secondary hyperparathyroidism, and osteogenesis imperfecta (OI).[1] OI is a genetic disorder caused by mutation of *COL1A1* or *COL1A2* that leads to defects in type 1 collagen synthesis. Clinical signs of OI include malunion of bones during growth and repeated fractures causing limb deformity, often accompanied by blue sclera and dentinogenesis imperfecta.[2] As there is no cure for OI, in human medicine, treatments are based on the application of a brace or wheelchair, surgical correction, rehabilitation, pain management and prescription of vitamin C and/or bisphosphonate.[3–5] Surgical correction can be used for limb deformity and bone fracture using intramedullary pins, interlocking nails and others. Preventive intramedullary pinning can also be attempted to distribute the load on long bones.[6,7] However, owing to poor prognosis, euthanasia is often elected in veterinary medicine.[1] Thus, this case report aims to describe the long-term

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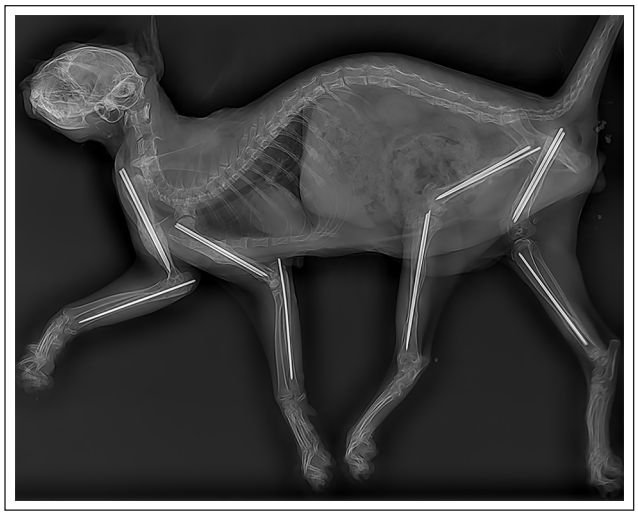

Figure 1 Radiographs of the 8-month-old cat showing pins inserted into the long bones and a spinous process fracture of thoracic vertebrae 6 months after the first operation

management of suspected OI by surgical repair using intramedullary pins in a cat.

Case description

A 3-month-old male Chinchilla cat weighing 0.8 kg was admitted for pain in the right hindlimb. Radiographs revealed an oblique diaphyseal fracture of the right femur. After closed reduction, two Kirschner (K)-wires of 1.5 mm diameter were inserted in a normograde fashion. The inserted K-wires were removed 1 month after the surgery. Several days after removing the implants, the patient was presented with a fracture of the distal metaphysis of the right tibia after falling from a low height. Surgical repair was performed in the same way using two K-wires 1.6 mm in diameter. After the second operation, as additional fractures occurred owing to unknown reasons or suspected slipping events, several additional surgeries were carried out inserting K-wires into intact long bones to aid stress distribution on those bones. K-wires with a diameter of 1.2 to 2.0 mm were used and applied in a normograde fashion after closed reduction (Figure 1).

Blood tests were performed to identify other diseases that could cause pathological fractures. Complete blood count revealed no particular abnormality. Serum total calcium, serum total phosphorus, ionised calcium, parathyroid hormone and 25-hydroxy vitamin D levels were all normal (Table 1). As blood urea nitrogen and creatinine levels were within the reference intervals and renal ultrasonography confirmed no specific findings, secondary renal hyperparathyroidism was deemed improbable. Trabecular bone mineral density was measured from the 12th thoracic vertebra (Figure 2a) and the fourth lumbar vertebra (Figure 2b) using CT (Hi Speed QX/I; GE Medical). Relatively low trabecular bone mineral density was confirmed in the patient (219.8 Hounsfield units [HU] at the 12th thoracic vertebra and 169.46 HU at the fourth lumbar vertebra), compared with normal cats of a similar age. Bone biopsy was performed from the patient's humerus during surgery and the sample was submitted for histopathological examination. Irregular and thin cortical bone with increased diameter of Haversian canals and replicated cement lines was identified (Figure 3). Based on these results, OI was tentatively diagnosed.

Table 1 Results of serum chemistry, ionised calcium, parathyroid hormone and 25-hydroxy vitamin D levels

Measurement	Patient value	Reference interval
Calcium (mg/dl)	10.6	8.2–10.8
Phosphorus (mg/dl)	7.9	2.4–8.2
Blood urea nitrogen (mg/dl)	20	18–33
Creatinine (mg/dl)	0.7	0.7–1.8
Ionised calcium (mmol/l)	1.23	1.0–1.4
Parathyroid hormone (pmol/l)	1.97	0–4
25-hydroxy vitamin D (ng/ml)	24.93	26.0–68.0

Radiography was performed for follow-up or when the patient showed clinical signs. Follow-up radiographs were taken for 2 years. The patient showed spinous process fractures on several thoracic vertebrae 3 months after the first operation. After 5 months, the patient showed fractures on the ribs. As alignment was unchanged, no additional surgery was performed. Seven months later, a pelvic fracture not disrupting the pelvic cavity was revealed. The patient showed a fracture of the proximal ulna which had the K-wire inserted, luxation of thoracic vertebrae 4–5, changes in the morphology of the thoracic cavity and a fracture of the canine tooth of the right mandible, implying dentinogenesis imperfecta 1 year after surgery. Loosening of an inserted pin often occurred and irritated the adjacent joint and soft tissues, which then required cutting of the pin and/or re-insertion. The last radiographs taken 2 years postoperatively suggested repeated fractures and bone unions (Figure 4).

Follow-up complete blood count and serum chemistry, except parathyroid hormone and 25-hydroxy vitamin D, were performed regularly but failed to reveal any abnormalities. During the 3-year follow-up period, although the patient often showed lameness or ataxia due to fractures and required medical management using tramadol (Tridol 2 mg/kg q12h; Yuhan Corporation) and/or meloxicam (Metacam 0.05 mg/kg q24h; Boehringer Ingelheim), it was able to walk until it died due to undetermined reasons.

Discussion

OI is an inherited disorder caused by genetic mutation of *COL1A1* and *COL1A2*. *CRTAP, LEPRE1, PPIB, SERPINH1,*

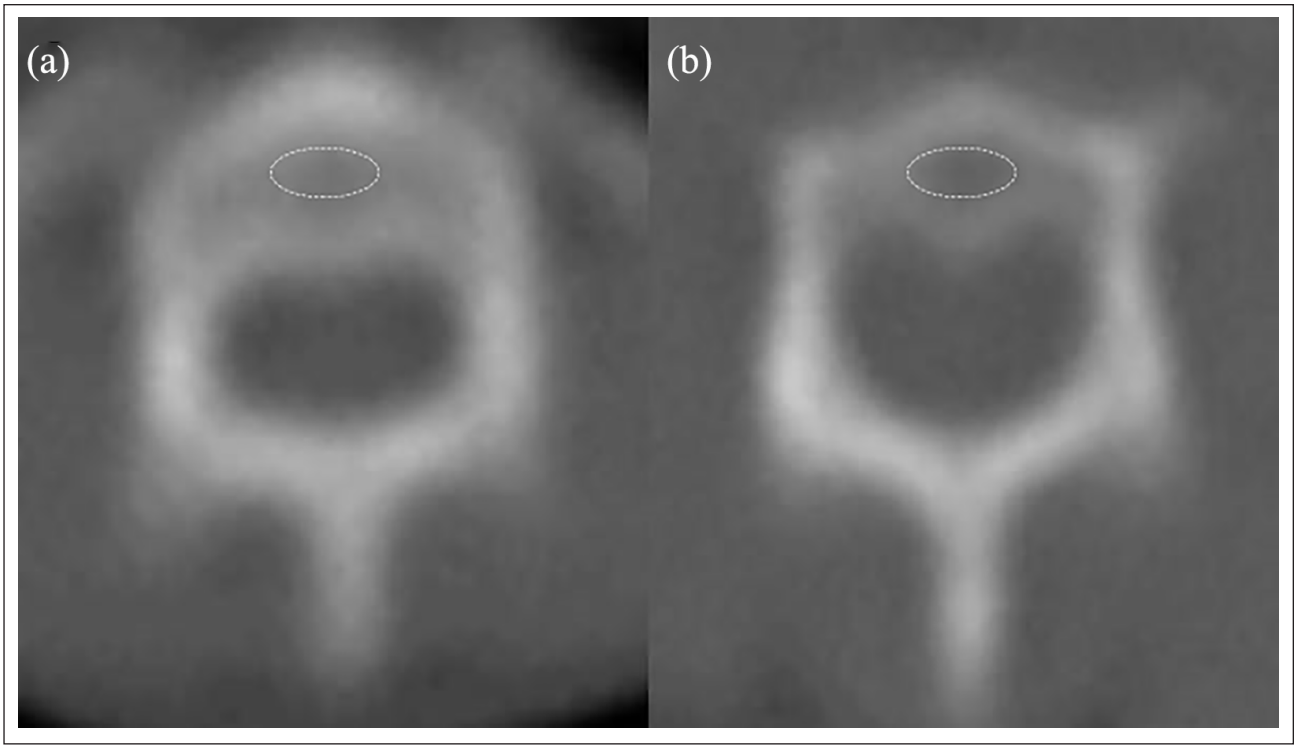

Figure 2 Measurement of mean Hounsfield unit (HU) values for the region of interest (circled) at the level of (a) the thoracic vertebra and (b) the lumbar vertebra via CT. Mean HU values at the level of the 12th thoracic vertebra and the fourth lumbar vertebra were lower than those in normal cats of similar age, implying lower trabecular bone mineral density

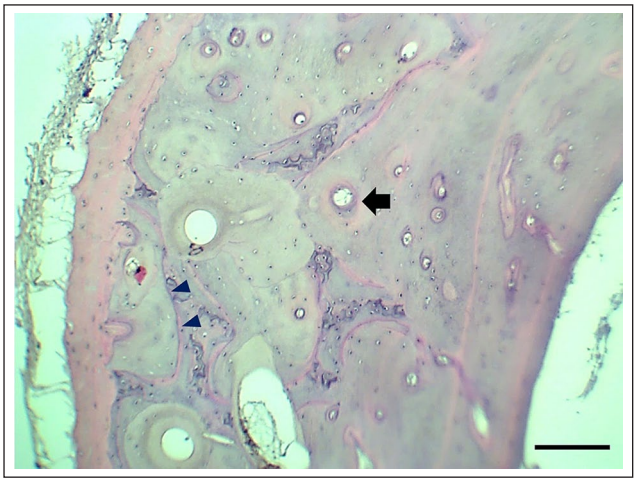

Figure 3 Thin cortical bone with increased diameter of the Haversian canals (arrow) and replicated cement lines (arrowheads) was revealed in some fractured bone particles by histopathological examination (haematoxylin and eosin, ×100; scale bar 100 µm)

Figure 4 Radiographs of the 32-month-old cat showing multiple fractures of thoracic vertebrae, ribs and pelvis 2 years and 6 months after the first operation

FKBP10, PLOD2, SP7 and *SERPINF1* mutations have also been identified as causes of OI in human medicine.[8] Several genes, such as *COL1A1, COL1A2* and *SERPINH1*, related to OI in dogs have been discovered.[9–11] However, little is known about these genes in cats. Thus, for a tentative diagnosis, the patient was investigated for other diseases that could cause pathological fracture. Blood tests related to primary and secondary renal hyperparathyroidism were normal. Ultrasonography did not confirm kidney disease. As the patient was fed a standard commercial diet containing adequate amounts of calcium

and phosphorus, and showed normal total calcium, ionised calcium, phosphorus and parathyroid hormone levels, nutritional secondary hyperparathyroidism was improbable. Trabecular bone mineral density, which is used to assess for bone disorders in cats, was measured using quantitative CT. Compared with normal cats of a similar age (315 HU at the 12th thoracic vertebra and 274.8 HU at the fourth lumbar vertebra), the patient showed relatively low trabecular bone mineral density, implying a bone disorder.[12,13] Previous histopathological studies of OI found thin trabeculae of woven bone with microfractures, few osteocytes, an absence of secondary spongiosa and osteoblasts containing cytoplasmic vacuoles.[1,9,11] The patient in the present study showed similar histopathological results and a tentative diagnosis of OI was made after excluding other possible diseases with similar clinical signs.

Owing to the poor prognosis, euthanasia is performed in most patients with OI after diagnosis.[1,11] Even with surgical repair in a male kitten with suspected OI, which is described in a separate report, the owner went on to elect euthanasia after further fractures were found.[14] Unlike veterinary medicine, various treatments, including surgical repair, are carried out in human medicine to improve quality of life. Intramedullary fixation is often recommended for fracture repair.[3,6–8] For this patient, as the owner and veterinarian attempted a different approach, K-wires were used for fracture repair of the long bones. K-wires were also inserted into the intact long bones to distribute stress. Although pain management was sometimes needed for repeated fractures and pin migrations,[15] the patient was able to live an ordinary life as a companion animal without severe limb deformity. Further research is needed on the remaining problems such as fracture of the spine or pelvis.

Conclusions

Although surgical repair using intramedullary pins in patients with OI is a palliative treatment, as in human medicine, and it is challenging to deal with repeated fractures, it is an option for possible long-term management of OI patients in veterinary medicine.

Conflict of interest The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical approval This work involved the use of non-experimental animals only (including owned or unowned animals and data from prospective or retrospective studies). Established internationally recognised high standards ('best practice') of individual veterinary clinical patient care were followed. Ethical approval from a committee was therefore not necessarily required.

Informed consent Informed consent (either verbal or written) was obtained from the owner or legal custodian of all animals(s) described in this work for the procedure(s) undertaken. For any animals or humans individually identifiable within this publication, informed consent (either verbal or written) for their use in the publication was obtained from the people involved.

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