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## **Title**

Skull pathology in ten cats with patellar fracture and dental anomaly syndrome

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## **Abstract**

### **Case series summary**

The aim of this case series is to describe the clinical and radiological features of mandibular and maxillary abnormalities in cats diagnosed with patellar fractures and dental anomalies, a syndrome that we have named 'Patellar fracture and Dental anomaly Syndrome' (PADS), also known previously as 'Knees and Teeth Syndrome'. Where available, clinical records, skull and/or intraoral radiographs, head CT images, microbiology and histopathology reports were collected, and follow-up was obtained. Ten cats with mandibular or maxillary abnormalities were identified. Common clinical features included multiple persistent deciduous teeth, gingivitis and swellings of the jaw. Skull radiographs were available for seven of ten cats and head CT images were available for one cat. Findings included marked bony and periosteal proliferation, hypodontia, root resorption, root malformation and unerupted permanent teeth. Where available, microbiology and histopathology results were consistent with osteomyelitis.

### **Relevance and novel information**

Mandibular and maxillary abnormalities are an additional unreported clinical feature of the rare condition that we have termed 'Patellar fracture and Dental anomaly Syndrome' (PADS). Radiologically, these lesions can have an aggressive appearance, which can mimic neoplasia. Medical management with antibiotic and anti-inflammatory therapy improves clinical signs in the short-term; however, surgical extraction of persistent deciduous and

unerupted permanent teeth, and debridement of proliferative and necrotic bone appear to be necessary for an improved outcome. Additional information on long-term outcome is required.

## **Introduction**

Cats with patellar fractures are a fairly rare presentation in veterinary practice. A survey of feline patellar fractures published in 2009 documented findings from 52 patellar fractures in 34 cats.<sup>1</sup> It was revealed that feline patellar fractures most commonly occur spontaneously in young adult cats at a mean age of 28 months. Over 50 percent of cats subsequently develop fractures of the contralateral patella with a median interval of three months from the first patellar fracture.<sup>1</sup> Fractures of the patella in these cases were consistently transverse and at the level of the mid to proximal third of the patella.<sup>1</sup> Radiological evidence of increased bone opacity of the fractured patella and contralateral non-fractured patella was demonstrated in the majority of cases, a finding suggestive of a response to repetitive mechanical stimulus and a feature of stress fractures.<sup>2</sup> In addition, cats with atraumatic patellar fractures often sustain fractures of other bones; the proximal tibia, acetabulum, ischium, humeral condyle and calcaneus being the most frequently reported bones affected.<sup>3,4</sup> It has therefore been postulated that these cats may be suffering from a primary bone disorder; the nature of which has not yet been identified.

The initial publication by Langley-Hobbs, 2009 centred investigations on patellar fractures as the presenting complaint; however, analysis of collated data revealed that five out of 34 cats with patellar fractures (15 percent) also had deciduous teeth persisting beyond six months of age.<sup>1</sup> Subsequent radiological evaluation has indicated that a number of these cats also have unerupted permanent teeth. The combination of patellar fractures

and dental abnormalities has led to the coining of the term 'Patellar fracture and Dental anomaly Syndrome' (PADS), also known previously as 'Knees and Teeth Syndrome'.<sup>5</sup>

Furthermore, from author experience, a small number of cats affected by this syndrome develop mandibular and maxillary abnormalities. The aim of this publication is to report the clinical and radiological features of mandibular and maxillary abnormalities in cats with 'Patellar fracture and Dental anomaly Syndrome'.

### **Case Series Description**

Databases of cats with patellar fractures (Patellar fracture and Dental anomaly Syndrome) from two authors (SLH and SB) were combined and searched for cases with a history of mandibular and/or maxillary abnormalities. Of the cases identified, all information submitted to the databases was collated and where possible, further case follow-up was performed. Where available, records of clinical history, skull and/or intraoral radiographs, head CT images, and microbiology and histopathology reports were included. All available radiographs and CT images were reviewed separately by specialists in veterinary diagnostic imaging (AM) and veterinary dentistry (MG), who were provided with a basic knowledge of case clinical presentation and treatments performed. The combined database had a total of 191 cats, 92 of which had recorded dental abnormalities. Ten cats with mandibular and/or maxillary abnormalities were identified. The results are summarised briefly in Table 1, and in more detail on a case by case basis below.

**Case one:** An adult male neutered domestic shorthair cat presented with a history of fractures of the patella, tibia, lateral humeral condyle and ischium, and a maxillary swelling.

Radiographs of the skull demonstrated a unilateral, expansile and proliferative bony lesion of the maxilla (Figure 1). The lesion exhibited a region of marked periosteal proliferation without significant evidence of radiologically aggressive characteristics. Differential diagnoses based on radiographic appearance included; osteoma, osteochondroma, low grade osteomyelitis, with chondrosarcoma and osteosarcoma considered less likely. No follow-up information was available for this patient as the cat was euthanased following the diagnosis of a second patellar fracture.

**Case two:** A female neutered domestic shorthair cat presented at eight months of age with inappetence and a painful swelling of the right rostral mandible, which was most compatible with an abscess of unknown origin. Multiple persistent deciduous teeth were also identified on clinical examination. Purulent material from the mandibular swelling was cultured and *Pasteurella species* and anaerobes were isolated. A skull radiograph was unremarkable. A clinical improvement was observed following a two week course of oral marbofloxacin (2.75mg/kg PO q24h); the mandibular swelling reduced in size, but did not completely resolve.

At nine months of age the cat presented with right hind limb lameness and recurrence of the mandibular abscess and antibiotics were administered (as previously prescribed). At 10 months of age, the cat developed left hind limb lameness and radiographs revealed bilateral patellar fractures, which were managed conservatively. The cat subsequently sustained a fracture of the right proximal femur followed by a fracture of the left tarsus; both fractures were managed surgically.

Recurrence of the right mandibular swelling and generalised gingivitis were noted when the cat was six years of age and the cat was prescribed antibiotics (amoxicillin/clavulanic acid, 12.5mg/kg PO q12h). The cat subsequently sustained a luxation of the right coxofemoral joint and was euthanased.

**Case three:** A female neutered domestic longhair cat was re-homed as a young adult. The owner reported bilateral jaw abnormalities with skin defects and persistent deciduous teeth. Radiographs were not available for review; however clinical records reported the presence of unerupted permanent teeth on radiographs. Surgery was performed to debride the proliferative bone of the mandibular jaw and to close the skin defects. Following surgery, the owner reported that the cat made a satisfactory recovery with a good quality of life. The cat developed a patellar fracture in the following year. No further follow-up information was available.

**Case four:** A female neutered Siamese cross cat was re-homed from a rescue centre. Prior to being re-homed, a left unilateral mandibulectomy was performed to manage a presumed mandibular osteoma. Histopathology reports for this lesion were not available. At two years of age the cat developed left hind limb lameness. Persistent deciduous teeth and generalised gingivitis were noted at presentation. Radiographs of the left hind limb revealed a patellar fracture which was surgically stabilised. The cat was euthanased after sustaining a humeral condylar fracture in the postoperative period following patellar fracture stabilisation.

**Case five:** A male neutered domestic shorthair cat presented at one year and eight months of age with severe generalised gingivitis, multiple persistent deciduous teeth and failure of eruption of permanent dentition. Surgical extraction of all persistent deciduous teeth was performed. Within the same month, the cat sustained a right patellar fracture which was managed surgically. Five months following the right patellar fracture, a left patellar fracture was diagnosed and managed conservatively. At this time, the cat also presented with a recurrence of gingivitis and development of left mandibular swelling. Radiographs revealed marked irregular periosteal proliferation of the left mandibular body (Figure 2a & 2b). The lesion was classified as radiologically aggressive due to the active periosteal reaction, and differential diagnoses included osteomyelitis, osteosarcoma, chondrosarcoma and multi-lobular tumour of bone. There was evidence of malformed, unerupted permanent maxillary canine teeth and unerupted permanent maxillary incisor teeth (Figure 2c).

The mandibular swelling persisted despite medical management with antibiotics and non-steroidal anti-inflammatory drugs and the lesion was biopsied. Histopathological findings were consistent with osteomyelitis. A staged surgery was performed to extract the unerupted permanent mandibular teeth. The swelling gradually reduced in size over a period of six months with continued medical management of antibiotics and non-steroidal anti-inflammatory drugs; however, following development of a pelvic fracture the cat was euthanased.

**Case six:** A female entire domestic shorthair cat was re-homed at four months of age from a rescue centre. Left hind limb lameness was noted at five months of age and radiographs demonstrated coxofemoral luxation; a femoral head ostectomy was performed. Sixteen months later the cat developed right hind limb lameness and bilateral patellar fractures were diagnosed on radiographs; both were managed conservatively.

At two years of age the cat presented with a left mandibular swelling and multiple persistent deciduous teeth were noted. Skull radiographs showed marked periosteal reaction with aggressive characteristics affecting the left mandibular body (Figure 3a). Differential diagnoses included; osteomyelitis, osteosarcoma, chondrosarcoma and multilobular tumour of bone. Multiple unerupted permanent mandibular teeth were also observed. The cat was prescribed antibiotics (amoxicillin/clavulanic acid, 12.5mg/kg PO q12h and enrofloxacin, 5mg/kg PO q24h) and surgery was performed to debride the proliferative bone and extract the unerupted teeth (Figures 3b & 3c). *Escherichia coli*, *Enterococcus species* and *Serratia marcescens* were isolated on bacterial culture of the excised tissue. Bone biopsies were submitted for histopathological examination which revealed periosteal woven bone proliferation and suppurative inflammation, findings consistent with osteomyelitis.

Following surgery, the mandibular swelling persisted and the cat developed an area of exposed necrotic mandibular bone and a left total mandibulectomy was performed. The left mandibular body was submitted for histopathology which revealed marked, chronic pyogranulomatous osteomyelitis with bony proliferation. Treatment for this cat is ongoing.

**Case seven:** A female neutered Maine Coon cross cat presented at 10 months of age with multiple persistent deciduous teeth (Figure 4a), gingivitis and ventral mandibular swellings. Skull radiographs confirmed the presence of persistent deciduous teeth and unerupted permanent teeth (Figure 4b). Bilaterally the mandibular bodies were thickened with a loss of normal corticomedullary definition. Multiple persistent deciduous teeth and unerupted permanent teeth were surgically extracted. Necrotic mandibular bone was debrided and samples submitted for histopathological examination. Histological findings were consistent with secondary osteonecrosis and suppurative osteomyelitis. The mandibular bone also exhibited features suggestive of a diagnosis of osteopetrosis, such as areas of increased bone density with abnormal organisation.

Amoxicillin/clavulanic acid (20mg/kg PO q12h) and robenacoxib (2mg/kg PO q24h) were prescribed. Five months later, the cat developed left hind limb lameness and radiographs demonstrated a chronic left patellar fracture with a fibrous union, which was conservatively managed.

Eight months following the initial presentation, a fluctuant swelling developed over the right side of the head. Intraoral examination of the right caudal mandible revealed areas of exposed necrotic bone, severe inflammation and a draining tract. The swelling was surgically incised, drained and flushed and the area of necrotic bone was debrided. Abscess material was cultured, *Pasteurella* and *Actinomyces species* were isolated and antibiotic therapy was initiated (amoxicillin/clavulanic acid, 20mg/kg PO q12h and metronidazole, 5mg/kg PO q12h). The areas of necrotic bone persisted despite antibiotic therapy and a CT scan of the head was performed. CT images demonstrated an aggressive, proliferative lesion of the right mandible, most consistent with osteomyelitis (Figure 4c). Multiple teeth were

absent and several small hyperattenuating fragments were present within the right mandibular body, consistent with small foci of sequestered necrotic bone. Bilateral mandibular and medial retropharyngeal lymphadenomegaly was detected and considered reactive; however cytological examination was not performed. The right parotid salivary gland was also enlarged, a possible indication of right parotid sialoadenitis. Further debridement of necrotic bone was performed and antibiotic therapy was continued. A resolution of the intraoral inflammation and exposure of necrotic bone was observed, and treatment is ongoing.

**Case eight:** A female neutered domestic shorthair cat presented at 15 months of age with right hind limb lameness. Multiple persistent deciduous teeth were noted on clinical examination. Non-steroidal anti-inflammatory drugs (Meloxicam 0.05mg/kg PO q24h) were prescribed and a mild improvement in lameness was observed. At 18 months of age the cat presented with left hind limb lameness. Radiographs of the stifles revealed bilateral patellar fractures which were surgically managed.

At eight years of age the cat sustained fractures of the pelvis; including a right ilial body fracture which was surgically stabilised.

At nine years of age the cat presented with halitosis, gingivitis and a necrotic lesion on the ventral aspect of the left mandible. Persistent deciduous teeth associated with the localised area of gingivitis were extracted. Twelve months later the cat developed additional necrotic lesions, gingivitis and a swelling of the right mandibular ramus. Non-steroidal anti-inflammatory drugs (Meloxicam 0.05mg/kg PO q24h) and antibiotics (Cefovecin 8mg/kg SC)

were administered. The necrotic lesions improved, however swelling of right mandible remained. Skull radiographs showed both persistent deciduous teeth and unerupted permanent teeth, with evidence of tooth resorption in multiple arcades. Bony changes comprised mild thickening of the mandibular cortices and periosteal reaction. These changes were considered relatively non-aggressive, most likely reflecting reactive inflammatory change, with marked osteomyelitis considered less likely. Abnormal dentition was surgically extracted and the necrotic bone debrided. Follow-up was performed four weeks after surgery and a persistent discharging sinus was reported; treatment is on-going.

**Case nine:** A female neutered domestic shorthair cat presented at 11 months of age with difficulty walking. Persistent deciduous teeth were noted on clinical examination. Radiographs demonstrated bilateral olecranon fractures, a right patellar fracture and multiple rib fractures. Generalised increased radio-opacity and a lack of cortico-medullary definition of the long bones was identified on radiographs. Haematology and serum biochemistry were within normal limits. The cat was managed conservatively with non-steroidal anti-inflammatory drugs and significantly improved over a period of three months.

At 20 months of age, the cat developed a swelling of the right mandible. Radiographs of the skull demonstrated smooth, well defined periosteal proliferation along the ventral aspect of the right mandibular body with differential diagnoses including inflammatory/reactive change or low grade chronic osteomyelitis. There was generalised increased opacity of the osseous structures; including the calvarial bone, mandibular cortices, vertebral bodies and the hyoid bones (Figure 5).

**Case ten:** A female neutered domestic shorthair cat was re-homed at approximately two years of age and presented with right hind limb lameness three days following re-homing. Persistent deciduous teeth were noted on clinical examination. Radiographs demonstrated a right patellar fracture which was managed conservatively with non-steroidal anti-inflammatory drugs (Meloxicam 0.05mg/kg PO q24h).

At two years and two months of age the cat developed a draining mandibular abscess and was prescribed non-steroidal anti-inflammatory drugs (Meloxicam 0.05mg/kg PO q24h) and antibiotics (Clindamycin 5.5mg/kg PO q12h) for one week. An improvement was noted; however the abscess recurred three months later. A mandibular molar tooth associated with the abscess was extracted and antibiotics (Clindamycin 5.5mg/kg PO q12h) were prescribed. Four weeks later, the cat presented with a mandibular swelling at the same site, together with halitosis and gingivitis. A six week course of antibiotics (Clindamycin 5.5mg/kg PO q12h) was prescribed, however the mandibular swelling remained. Radiographs were obtained but were not available for review. Reports indicated the presence of persistent deciduous teeth and changes consistent with osteomyelitis and antibiotics were continued.

At three years and six months of age, the cat developed left hind limb lameness and radiographs demonstrated pelvic fractures which were managed conservatively. At four years and six months of age, the cat developed a right humeral condylar fracture which was surgically stabilised. At nine years of age the cat sustained a right calcaneal fracture and was euthanased.

## **Discussion**

Mandibular and maxillary abnormalities in cats with patellar fractures and persistent deciduous teeth ('Patellar fracture and Dental anomaly Syndrome'), also known as Knees and Teeth Syndrome, have not previously been reported. In cats, the process of exfoliation of primary teeth and eruption of permanent teeth is usually complete by six months of age.<sup>6</sup> Unlike dogs, deciduous teeth persisting beyond six months of age are rarely reported in the feline population and as such the incidence is poorly documented. One study describing dental pathology of adult feral cats from an inbred population on a Sub-Antarctic island found the incidence of persistent deciduous teeth to be two percent.<sup>7</sup> Whilst collating data from initial investigations on feline patellar fractures in 2009, it was found that 15 percent of cats with patellar fractures had persistent deciduous teeth.<sup>1</sup> Additionally, of the cases included in the initial survey, it was noted that a small number of these cats also presented with mandibular and maxillary abnormalities, prompting further investigation of this clinical presentation.

A key objective of this case series was to report the radiological features of mandibular and maxillary abnormalities in cats with this syndrome. Marked bony and periosteal proliferation was a common feature, with lesions being classified as radiologically aggressive in several cases. Osteomyelitis was considered a key differential diagnosis for these radiographic lesions, alongside neoplasia. Interestingly, one of the cats in this case series had previously undergone a unilateral mandibulectomy for management of a suspected osteoma. No radiographs or histopathology reports were available for this cat. However, considering the subsequent history of a patellar fracture, mandibular

osteomyelitis would be a reasonable alternative differential diagnosis for the mandibular lesion. Dental abnormalities identified on radiographs included persistent deciduous teeth, hypodontia, root resorption, root malformation and unerupted permanent teeth. Head CT images were available for one cat and demonstrated findings consistent with ongoing osteomyelitis despite surgical extraction of persistent deciduous and unerupted permanent teeth. Small hyperattenuating fragments were also identified within the most affected mandible and are suspected to be foci of sequestered necrotic bone acting as a nidus for infection.

Research is currently ongoing for cats with 'Patellar fracture and Dental anomaly Syndrome' to establish a genetic cause for the disorder. Biopsies of mandibular bone from one case demonstrated histological features of osteopetrosis. Osteopetrosis in humans is a rare genetic disorder characterised by reduced osteoclast-mediated bone resorption, leading to a net increase in bone density.<sup>8,9</sup> Human patients with osteopetrosis have also been reported to suffer from persistent deciduous teeth and pathological fractures. Generalised increased bone opacity is not a common feature of this syndrome; but was observed for one case in the series, in which radiographs demonstrated increased radio-opacity of multiple skeletal structures including long bones and bones of the skull. Furthermore, a recent case report documented how a cat receiving long-term oral bisphosphonates (inhibitors of osteoclastic bone resorption) developed bilateral patellar fractures in association with sclerosis of both patellae.<sup>10</sup> A degree of increased bone density can also be present without an abnormal radiological appearance.

Bone from patients with osteopetrosis is thought to have a reduced vascular supply and is therefore more prone to osteomyelitis.<sup>8</sup> In one human study, nearly two-thirds of

patients with osteopetrosis autosomal dominant type II had oral manifestations, including mandibular osteomyelitis (11 percent).<sup>11</sup> In humans, mandibular osteomyelitis has been shown to be a destructive process requiring repeated surgeries and multiple courses of antibiotics.<sup>11</sup> For this cases series, positive bacterial cultures were obtained for all cats where microbiology reports were available, and histopathology findings were consistent with osteomyelitis and osteonecrosis.

Treatment protocols were extremely variable for the ten cats included in this case series; however, antibiotics and non-steroidal anti-inflammatory medications were administered in the majority of cases. Initial improvement of clinical signs was often observed, however complete resolution of clinical signs was not a common feature for cats receiving solely medical management.

Deciduous teeth may persist for many years if their permanent counterparts are not present.<sup>12</sup> Physiologic root ankylosis and resorption and tooth exfoliation often results.<sup>12</sup> Surgical extraction of unerupted permanent teeth is often recommended to prevent complications such as the development of dentigerous cysts<sup>13, 14</sup>. Interestingly, none of the cases reported here showed radiographic or histological signs of cystic development. Surgery was performed for seven of ten cats in this case series. Surgical procedures included; extraction of persistent deciduous teeth, extraction of unerupted permanent teeth, debridement of proliferative and necrotic bone and in two cases a unilateral mandibulectomy.

Unfortunately, due to the rarity of this condition, a limitation of this case series is the small number of cases included. Other limitations include the retrospective nature of the case series and variability of information in the case notes, particularly relating to details

about specific tooth involvement. Furthermore, treatment protocols and quality of available images were variable. Long-term follow-up on surgical outcome was not available for many of the cats in the series, as cats were either lost to follow-up, euthanased following development of multiple limb or pelvic fractures or treatment was on-going at the time of data acquisition. Overall, the reported short-term outcome following surgery appears to offer an improved outcome, however further research in this area is required.

### **Conclusion**

In summary, mandibular and maxillary abnormalities are an additional clinical feature of this disease that we have named 'Patellar fracture and Dental anomaly Syndrome'. It is therefore recommended that a thorough oral examination is performed in every cat diagnosed with atraumatic patellar fractures. Radiologically, these lesions can exhibit aggressive characteristics, which due to the rarity of this condition may be misinterpreted as neoplastic disease. Additional diagnostic tests, such as microbiology and histopathology are recommended to distinguish osteomyelitis from neoplasia. Treatment of osteomyelitis with targeted antimicrobial agents and anti-inflammatory medication is associated with short-term improvement of clinical signs. However, surgical extraction of persistent deciduous and unerupted permanent teeth, and debridement of proliferative and necrotic bone appears to be associated with an improved outcome. Aggressive surgical management such as mandibulectomy is not recommended as a first line treatment but could be considered for cases where osteomyelitis is unresponsive to treatment.

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