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CASE SERIES AND CLINICAL REVIEW

# Metaphyseal osteopathy in three Australian Kelpie siblings

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**Case report** Metaphyseal osteopathy (MO) was diagnosed in three Australian Kelpie puppies that were presented for veterinary assessment of lameness. The three puppies were siblings. Each was from a different litter by the same breeding pair. The puppy in case one was seen by the authors, and the puppies in cases two and three were patients at other veterinary hospitals. However, the medical records and radiographs were examined and reviewed for this report. Radiographic investigation of the lameness revealed pathognomonic appearance of MO affecting the metaphyseal region of the long bones in all three puppies. The diagnosis was confirmed on histopathology in one patient.

**Conclusion** MO is considered a disease of large and giant-breed dogs, being rarely reported in non-large-breed dogs, and has not been reported in the Australian Kelpie, which is considered a medium-breed dog. This case series suggests a previously unreported breed predisposition to MO in the Australian Kelpie.

**Keywords** Australian Kelpie; dogs; hypertrophic osteodystrophy; metaphyseal osteopathy

**Abbreviation** MO, metaphyseal osteopathy

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Metaphyseal osteopathy (MO) is a developmental bone disease of young dogs associated with painful swelling of the metaphyseal region of the long bones.[1,2] It is also commonly/historically referred to as hypertrophic osteodystrophy.

MO is traditionally considered to be a disease of rapidly growing large- and giant-breed dogs, with the Great Dane, German Shepherd, Weimaraner, Irish Setter and Irish Wolfhound considered to have increased risk.[1–5] MO has been reported to occur in more than 40 different breeds (including mixed breeds), with the only cases in non-large-breed dogs being single cases in the following breeds: Australian Cattle Dog, Bichon Frise, Cairn Terrier, Chow Chow, Wire-haired Fox Terrier, Maltese, Miniature Poodle, Soft-coated Wheaten Terrier and Shar-Pei.[4,6]

Clinical signs of MO typically occur at 3–4 months of age, with varying degrees of lameness, depression and inappetence. In more severe cases, systemic signs, such as gastrointestinal, respiratory and/or neurological signs, occur.[4,7,8] Physical examination reveals pain on palpation of the metaphyseal region of the long bones, often with pyrexia.[1,2] MO is typically a self-limiting disease that resolves around the time of skeletal maturity, with mildly affected animals considered to have a good to excellent prognosis. However, the prognosis is guarded for severely affected animals, in which recurrence of pain, pyrexia and inappetence results in severe debilitation, leading to death or euthanasia.[1,2]

A clinical diagnosis of MO is based on signalment, history, physical examination and characteristic radiographic changes in the metaphyseal region of the long bones, most notable of which is a radiolucent line in the metaphysis just proximal and parallel to a narrow zone of increased radiodensity adjacent to the physis.[2,9] The bones most commonly affected in MO are the distal radius, ulna and tibia, but it has also been reported to occur in the mandible, maxilla, skull, vertebra, scapula, humerus, femur and ribs.[1,4] Definitive diagnosis requires histopathology, with characteristic suppurative inflammation and extensive necrosis in the metaphyseal region of the long bones being seen. However, biopsy or necropsy is not typically performed, because of the pathognomonic radiographic changes and because many puppies recover from the disease before biopsy is considered.[2,7,10]

Treatment of MO involves anti-inflammatory/analgesic therapy generally by use of non-steroidal anti-inflammatory drugs. Supportive therapy in the form of intravenous fluids and assisted nutrition may be necessary in more severe cases.[2]

MO has not previously been reported in the Australian Kelpie, which is considered a medium-breed dog, with an average height of 47 cm at the withers.[11] We report three cases of MO in Australian Kelpie siblings, two of which were euthanased because of the severe or recurring clinical signs.

## Case reports

### *Puppy 1*

A 14-week-old male Australian Kelpie was presented for dullness and depression, slow gait and shifting lameness of 12-h duration. Approximately 10 days prior to presentation, the puppy had received its second vaccination with a combined, modified live vaccine containing canine distemper virus, adenovirus type 2, parvovirus type 2 and parainfluenza virus (Canvac® Puppy 4 Vaccine, Pfizer Australia, West Ryde, NSW, Australia). The initial vaccine dose had been administered 4 weeks earlier when the puppy was 8 weeks of age. An intestinal parasite all-wormer (Drontal Allwormer, Bayer Australia, Pymble, NSW, Australia) had been administered orally at 2, 4 and 6 weeks prior to onset of clinical signs.

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On examination, the puppy was dull and reluctant to stand, with a rectal temperature of 40.7°C. Pain was elicited on palpation of the distal metaphysis of both tibiae, upon flexion of the elbows bilaterally and on flexion of the right carpus. At this examination, there was no appreciable swelling of the limbs or joints. No other abnormalities were detected on physical examination.

Further investigation at this stage was declined by the owner. Firocoxib (Previcox®, Merial, Parramatta, NSW, Australia) was administered at 5 mg/kg PO every 24 h and the puppy was admitted to hospital for overnight monitoring. The following day, its demeanour had markedly improved and the pyrexia had resolved. The lameness had lessened but not completely resolved. The puppy was discharged with a 4-day course of firocoxib and instructions for rest and restricted activity.

The puppy was re-presented 6 days later for recurrence of clinical signs. A marked improvement in clinical signs had been seen during treatment with firocoxib, but the dullness, depression and shifting lameness recurred after the treatment ceased. On physical examination, the puppy again showed pain on palpation of the distal tibial metaphyses, with the addition of bilateral distal radius and ulnar metaphyseal pain.

Complete blood count, serum biochemistry and urinalysis were performed. Radiographs were taken of all limbs and the thorax. Arthrocentesis of both carpal joints was also performed.

The haematological abnormalities included a mild anaemia (haematocrit 0.33; reference range, 0.37–0.55), mild leucocytosis ($15.4 \times 10^9$/L; reference range, 6.0–14.0) because of a mild neutrophilia ($11.6 \times 10^9$/L; reference range, 4.1–9.4) with a left shift (bands $0.3 \times 10^9$/L; reference, <0.1).

Biochemical abnormalities included low serum creatinine (20 µmol/L; reference range, 40–14), elevated alkaline phosphatase (204 U/L; reference range, 1–120), elevated phosphate (2.26 mmol/L; reference range, 0.8–2.0), elevated creatine kinase (900 U/L; reference, <401) and elevated cholesterol (11.7 mmol/L; reference range, 3.6–8.8). Urinalysis results were within normal reference ranges.

Radiographs of the distal radius, ulna and tibia revealed a radiolucent line in the metaphysis proximal to the growth plate bilaterally, with a line of increased opacity between them (Figure 1). Thoracic radiographs revealed no pulmonary or cardiovascular abnormalities, but there was a radiolucent line just proximal to the costochondral junction in each rib.

Carpal joint fluid was grossly clear and viscous, with no inflammatory cells seen on in-house cytological analysis. MO was diagnosed based on presenting clinical signs, physical examination and pathognomonic radiographic changes.

Because of the initial clinical response to firocoxib, the treatment was repeated at 5 mg/kg PO every 24 h. Again the puppy showed a rapid clinical response, but the lethargy and lameness recurred after 7 days despite ongoing treatment. Firocoxib treatment was discontinued at this stage.

Treatment with tramadol (Tramal® SR, bioCSL, Parkville, VIC, Australia) at 2.5 mg/kg PO every 12 h and amoxicillin/clavulanic acid (Noroclav, Norbrook Laboratories, Tullamarine, VIC, Australia) at 18 mg/kg PO every 12 h was commenced. After 48 h, treatment with prednisolone (1 mg/kg PO every 12 h; Prednisolone, Apex Laboratories, Somersby, NSW, Australia) was also started. The day after commencing prednisolone treatment, the puppy was bright, alert and responsive, with moderate improvement in gait, a return to normothermia and no discomfort on palpation of the metaphyses of the long bones. Continued improvement was seen, with resolution of all clinical signs 2 days after commencing the new treatment. After 5 days, the prednisolone dose rate was reduced to 0.5 mg/kg every 12 h and treatment with tramadol was discontinued. The antibiotic treatment was discontinued after a 7-day course. After 1 week, the prednisolone dose rate was further reduced to 0.5 mg/kg every 24 h, which continued to control the clinical signs for an additional 7 days, at which point the lameness and reluctance to stand recurred. The prednisolone dose rate was increased to 0.5 mg/kg every 12 h, with a subsequent resolution of clinical signs. Over the following 6 weeks, repeated attempts to wean the prednisolone resulted in the recurrence of clinical signs. It was at this point, given the difficulty in controlling the clinical signs, that the puppy's owners elected euthanasia.

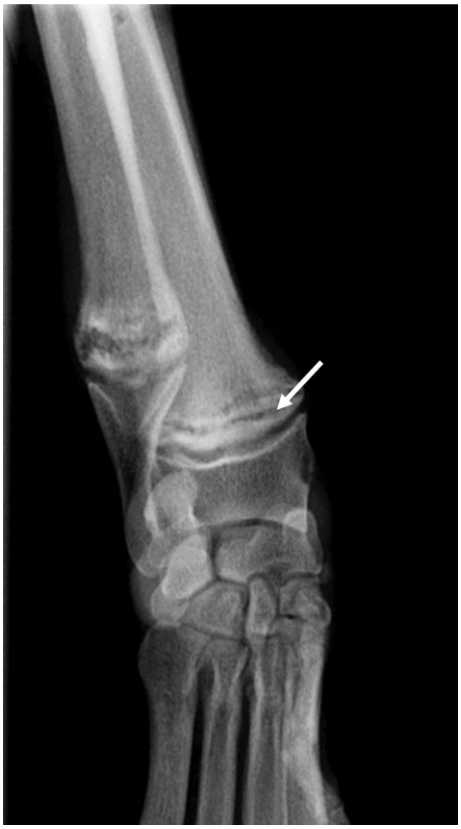

**Figure 1. Dorsoventral radiographic view of the distal radius/ulna and carpus. A line of radiolucency can be seen parallel and just proximal to the distal radial growth plate (arrow), which is the pathognomonic radiographic feature associated with metaphyseal osteopathy.**

Histopathological examination of bone samples from the distal radial metaphysis revealed a distinct lesion at the junction of the primary and secondary spongiosa. This was a line of brightly eosinophilic

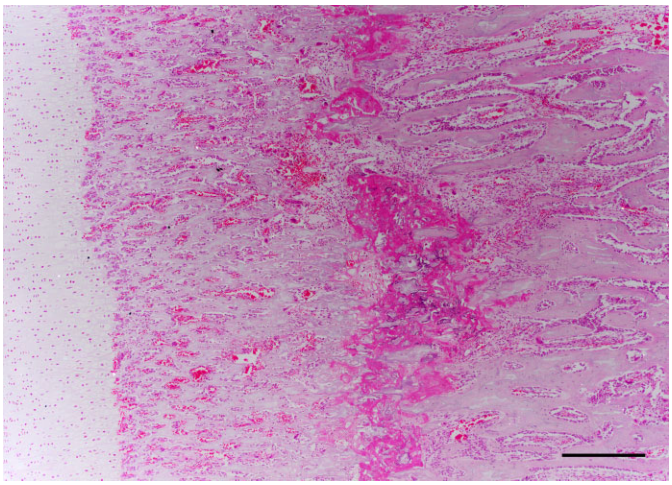

**Figure 2.** Radial metaphysis (physeal cartilage at the left). An eosinophilic band of necrotic debris including osteoid and cartilage is present at the interface between the primary and secondary spongiosa. At higher power it can be seen to be admixed with a loose mesenchymal proliferation (H&E, ×40; bar = 200 μm).

necrosis and associated debris, roughly parallel to the medullary aspect of the growth plate (Figure 2). The epiphysis and growth plate were unaffected. This finding was considered characteristic of MO, confirming the original diagnosis.

### *Puppy 2*

Puppies number 2 and 3 were identified after contacting the breeder of the puppy in case 1.

A 16-week-old male Australian Kelpie was presented for assessment of lethargy and lameness of 24-h duration. In the week prior to presentation, the puppy had received its third vaccination, with a combined, modified live vaccine containing canine distemper virus, infectious hepatitis virus, parvovirus, parainfluenza virus, *Bordetella bronchiseptica*, coronavirus, and *Leptospira* (Protech Duramune C7, Fort Dodge Animal Health, Fort Dodge, IA, USA). The same vaccine had been previously administered at 12 weeks of age, but a different vaccine containing modified, live canine distemper virus, infectious hepatitis virus, parvovirus and parainfluenza virus (Protech Duramune C4, Fort Dodge Animal Health) had been administered at 8 weeks of age.

On presentation, the puppy was alert and responsive with a good appetite, but reluctant to walk. It was pyrexic (rectal temperature 40.5°C), with pain and vocalisation on palpation of the distal antebrachial and tibial metaphyses. Radiographs of the distal forelimbs revealed pathognomonic changes of MO in each radius, with a radiolucent line parallel and adjacent to the distal growth plate. The puppy was subsequently diagnosed with MO and treated with tolfenamic acid (4 mg/kg SC; Tolfedine, Vetoquinol, Hastings, VIC, Australia) and amoxicillin/clavulanic acid (15 mg/kg SC; Noroclav, Norbrook Laboratories). The puppy was admitted to hospital for overnight monitoring. The following day, the puppy remained pyrexic, with a rectal temperature of 40.6°C. Because it was anorexic, laterally recumbent and consistently vocal, the owners decided not to pursue any further treatment and elected euthanasia.

### *Puppy 3*

A 14-week-old female Australian Kelpie was presented for assessment of lethargy and a forelimb lameness of 24-h duration. Eight days prior to onset of clinical signs, the puppy had received her second vaccination with a combined, modified live vaccine containing canine distemper virus, infectious hepatitis virus, parvovirus and parainfluenza virus (Protech Duramune C4, Fort Dodge Animal Health). The same vaccine had been administered 4 weeks earlier.

On physical examination, the puppy was quiet but responsive and had a rectal temperature of 40.1°C. There was bilateral forelimb lameness with discomfort on palpation of the distal antebrachial metaphyses. Radiographs of the forelimbs revealed a transverse radiolucent line in the distal metaphysis parallel and just proximal to the growth plate in each radius and ulna. The puppy was subsequently diagnosed with MO and treated as an outpatient with carprofen (2 mg/kg every 12 h PO; Rimadyl, Pfizer) for 5 days, then 2 mg/kg every 24 h for 5 days. The dull demeanour and lameness resolved 24 h after commencing treatment. The puppy remained clinically well and at discontinuation of the carprofen, there was no recurrence of clinical signs. No further follow-up was available.

The breeder had not been informed of any other affected puppies, with at least one puppy from each of the three litters being still known to the breeder and apparently unaffected. Not all owners of the puppies from these litters were contactable, so the prevalence of the disease in the offspring of this breeding pair could not be determined.

## Discussion

We describe the first reported cases of MO in the Australian Kelpie breed. Although the puppies in cases 2 and 3 did not have histopathological confirmation of the diagnosis, the radiographs of all three animals contained pathognomonic changes consistent with a diagnosis of MO, which was confirmed by a specialist radiologist's review.

The exact aetiopathogenesis of MO remains to be elucidated, but the acute histological lesions affecting the radius and ulna, and sometimes all fast-growing bones, are well reported and considered characteristic of the disease. These include the presence of a zone of intense suppurative inflammation and subsequent necrosis between the primary and secondary spongiosa parallel to the growth plate in the metaphysis.[1] This area of inflammation and necrosis corresponds to the metaphyseal radiolucent line seen on radiographs. The histopathology report for the puppy in case 1 included necrosis predominantly, with little active inflammation. The absence of inflammation was most likely related to both the timing of bone sampling being 2 months after the initial clinical signs, with the inflammation having progressed to necrosis, and to the anti-inflammatory treatment.

The aetiology of MO remains unknown, with the previously proposed theories of vitamin C deficiency and over-nutrition having not been proven.[1,4] An infectious cause, with bacterial (*Escherichia coli*) or viral (canine distemper virus) aetiology, has been suggested,[12–14] but other

studies, including a large case series of more than 130 dogs, have failed to identify an association with infectious agents.[4] Despite this, an infectious aetiology is still considered likely by some, because of the suppurative nature of the early inflammatory lesions and the presence of lesions at the metaphyses, epiphyses and osteochondral junctions, similar to the lesions typically seen in dogs with confirmed haematogenous bacterial osteomyelitis.[1]

In most breeds MO occurs sporadically, with only single animals affected. In the Weimaraner, the disease has been reported to occur in littermates and also closely related animals.[9,10] It has been reported that Weimaraner puppies with MO that have an affected littermate are more likely to have relapses of the disease.[9] These observations have led to a general acceptance that there is a significant inheritable component of the disease in this breed, but the mode of inheritance remains unknown.[4,8–10,15]

The literature commonly reports the development of MO within several weeks of vaccination.[3,4,8–10,15,16] However, only one study has been conducted to investigate the link between recent vaccination and the onset of MO. That study investigated whether there was an association between the canine leucocyte antigen DQ1A allele of the major histocompatibility complex and the development of clinical MO in Weimaraners, but no association was found.[16]

In the current report, all three puppies had received a vaccination within the 2 weeks prior to development of clinical signs. Although this might suggest a possible vaccine association, it must be noted that the typical age of onset of MO is 3–4 months of age, and that vaccines are routinely administered at 2, 3 and 4 months of age, so there is likely always to be a temporal association between the development of MO and recent vaccination in all affected breeds. Although some have speculated that there is a link between vaccination and the development of MO,[8,9,15] without evidence from a controlled trial no conclusions can be drawn.

There is an increasing number of reports in the literature regarding the superior improvement in clinical signs in Weimaraner puppies with MO attributed to use of corticosteroid treatment versus treatment with non-steroidal anti-inflammatory drugs. Based in part on these findings, the variable severity of clinical signs and the multisystemic involvement in puppies with MO, it has been hypothesised that MO may be a multifactorial immune-mediated/hyperinflammatory syndrome.[8,9,15,16] Further investigation into the involvement of the immune system in the development of MO, such as studying alleles other than those investigated by Crumlish et al, would be required to confirm this theory.

The fact that all three puppies in this case series were from the same bitch and sire cross, but were raised in different households suggests the possibility of a hereditary component to the disease in the Australian Kelpie. As there are no reports of immunological deficiencies in kelpies, it may be that this is idiopathic or it may be an environmental factor(s) that the bitch was exposed to during pregnancy that contributed to the later development of MO in the puppies.

In these three cases of MO in Australian Kelpie puppies, there are definite similarities to the disease described in the Weimaraner breed. These include the more severe clinical signs and the apparent superior response to prednisolone therapy observed in case 1. Given this, it is possible that MO in the Australian Kelpie is associated with an immune-mediated process, as has been proposed for the Weimaraner. This warrants consideration for the use of corticosteroids such as prednisolone for controlling the clinical signs of MO in the Australian Kelpie.

If presented with a pyrexic Australian Kelpie puppy with lameness and/or metaphyseal pain, MO should be considered as a differential diagnosis, as well as other conditions that can result in similar clinical signs, such as septic polyarthritis, trauma, retained cartilaginous cores, nutritional secondary hyperparathyroidism and hypertrophic osteopathy.[5]

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## References

1. Thompson K. Inflammatory diseases of bones. In: Grant Maxie M, editor. *Jubb, Kennedy & Palmer's pathology of domestic animals*. 5th edn. Elsevier, St Louis, 2007;92–105.
2. Tobias KM, Johnston SA, editors. *Veterinary surgery small animal*. Vol. 1. Elsivier, St Louis, 2012;117–118.
3. LaFond E, Breur GG. Breed susceptibility for developmental orthopaedic diseases in dogs. *J Am Anim Hosp Assoc* 2002;38:467–477.
4. Munjar TA, Austin CC. Comparison of risk factors for hypertrophic osteodystrophy, craniomandibular osteopathy and canine distemper virus infection. *Vet Comp Orthop* 1998;11:37–43.
5. Slatter D, editor. *Textbook of small animal surgery*. 3rd edn. WB Saunders, Philadelphia, 2003;2251–2252.
6. Appeldoorn AM, Schrauwen EMJ. Hypertrophic osteodystrophy in a toy breed. *Vet Comp Orthop* 1995;8:210–212.
7. Watson ADJ, Blair RC, Farrow BRH et al. Hypertrophic osteodystrophy in the dog [Case Report]. *Aust Vet J* 1973;49:433–439.
8. Abeles V, Harrus S, Angles JM et al. Hypertrophic osteodystrophy in six Weimaraner puppies associated with systemic signs. *Vet Rec* 1999;145:130–134.
9. Safra N, Johnson EG, Lit L et al. Clinical manifestations, response to treatment, and clinical outcome for Weimaraners with hypertrophic osteodystrophy: 53 cases (2009–2011). *J Am Vet Med A* 2013;242:1260–1266.
10. Woodard JC. Canine hypertrophic osteodystrophy: a study of the spontaneous disease in littermates. *Vet Pathol* 1982;19:337–354.
11. Australian National Kennel Council. Australian Kelpie. 2013. http://www.ankc.org.au/Breed_Details.aspx?bid=133. Accessed August 2013.
12. Schulz KS, Payne JT, Aronson E. *Escherichia coli* bacteremia associated with hypertrophic osteodystrophy in a dog. *J Am Vet Med A* 1991;199:1170–1173.
13. Mee AP, Gordon MT, May C et al. Canine distemper virus transcripts detected in the bone cells of dogs with metaphyseal osteopathy. *Bone* 1993;14:59–67.
14. Baumgartner W, Boyce RW, Alldinger S et al. Metaphyseal bone lesions in young dogs with systemic canine distemper virus infection. *Vet Microbiol* 1995;44:201–209.
15. Harrus S, Waner T, Aizenberg I et al. Development of hypertrophic osteodystrophy and antibody response in a litter of vaccinated Weimaraner puppies. *J Small Anim Pract* 2002;43:27–31.
16. Crumlish PT, Sweeny T, Jones B et al. Hypertrophic osteodystrophy in the Weimaraner dog: lack of association between DQA1 alleles of the canine MHC and hypertrophic osteodystrophy. *Vet J* 2006;171:308–313.

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