Osteosarcoma in a dog, 7 years after plate osteosynthesis for a femoral fracture

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Abstract

A 9-year-old, spayed, female dog presented with a complaint of acute left hindlimb lameness. Seven years prior to presentation, plate osteosynthesis was performed to stabilise a left femoral fracture. A radiographic examination performed under light general anaesthesia revealed osteolytic lesions of the left femoral diaphysis associated with the bone plate, consistent with osteosarcoma. There was no radiographic evidence of pulmonary metastasis.

A diagnosis of osteosarcoma was confirmed on histopathological examination of bone samples obtained surgically from the affected area. The affected limb was amputated by coxo-femoral disarticulation. The dog was managed post-operatively with oral meloxicam, tramadol, gabapentin, and cephalexin. Short-term outcomes were favourable. However, at three months postoperatively, the dog developed persistent soft tissue swelling and pain over and around the surgical site. Further histopathological examination of soft tissue samples obtained from the surgical site confirmed local invasion and infiltration with osteosarcoma.

Although implant-associated osteosarcoma is rare, this case highlights the importance of including it as a differential diagnosis in cases with a history of implantation of orthopaedic hardware where bone pathology is suspected. This case also highlights the locally invasive nature of osteosarcoma as described in the literature.

Introduction

Osteosarcoma (OSA) is a malignant tumour derived from primitive mesenchymal stem cells with the capacity to produce osteoid matrix (Fan & Khanna, 2015). OSA is characterised by local lytic or plastic processes and a high degree of metastases (Aminkov & Manov, 2005). This highly aggressive and locally invasive tumour most frequently occurs in the metaphysis of the long tubular bones such as the radius, humerus, femur, and proximal tibia (Longo et al, 2020).

OSA is the most common bone tumour, comprising up to 85% of all skeletal malignancies (Longo et al, 2020; Aminkov & Manov, 2005; Wouda et al, 2018; Gorza et al, 2019). Biologically, OSA originates within the intramedullary cavity of the metaphyseal bone (Fan & Khanna, 2015). The aetiology of OSA in dogs and humans is not fully understood, although various hypotheses and predisposing factors are cited, such as metal bone implants, neutering, phenotypic variation in interleukin-6, bone infarction, previous fractures, ionising radiation, viral infections, animal age and size, and, in humans, Paget's disease (Gorza et al, 2019).

The risk of OSA in giant breeds is approximately 150-fold higher than that in dogs weighing less than 10 kg (Aminkov & Manov, 2005). In dogs, OSA mostly affects giant and large breeds such as Rottweilers, Golden Retrievers, Labrador Retrievers, St. Bernards, Irish Red Setters, German Shepherd, and Doberman. The small-breed dogs most affected by OSA are Miniature Schnauzers, Cocker Spaniels, and Cairn Terriers (Gorza et al, 2019). Currently, a definitive diagnosis is obtained through histopathological examination, with tumour classification based on the formation of osteoid matrix. OSA can manifest as osteoblastic, fibroblastic, chondroblastic, telangiectatic, and combined subtypes (Boerman et al, 2012).

The development of OSA following orthopaedic fixation is a rare and devastating complication and occurs at the site of a previous fracture or fracture fixation between 9 months and 15 years after fracture fixation (Longo et al, 2020). The primary treatment for OSA in dogs is amputation of the affected limb or body part (Mauldin et al, 1988). Dogs with OSA that are treated with amputation alone have poor overall survival outcomes: median survival times are typically less than 5 months, with the majority suffering from metastatic disease (Boerman et al, 2012). The estimated annual incidence of osseous tumours of the appendicular skeleton in dogs is 7.9 cases per 100,000 dogs, with the risk substantially greater (61–185-fold) in dogs weighing more than 36 kg (Boudrieau et al, 2005).

Case Description, Management, and Outcomes

A 9-year-old, female, spayed, mixed-breed dog weighing 24 kg was presented at our practice with a complaint of left hindlimb lameness of a week's duration. There was a history of a fracture of the left femur managed by plate osteosynthesis 7 years prior to presentation.

Physical examination showed that clinical parameters were within normal limits. Because of the aggressive temperament of the dog, the rest of the examination was carried out under light general anaesthesia. Examination of the left hindlimb revealed a grade II/IV medial patellar luxation and negative cranial drawer sign of the stifle.

The remainder of the findings were unremarkable. Orthogonal radiographs of the pelvis and left hindlimb revealed osteolysis of the mid-diaphysis of the left femur, consistent with a high index of suspicion for appendicular OSA.

The plan to reach a definitive diagnosis involved explantation of the bone plate and screws, exploration of the mid-diaphysis of the left femur, and collection of bone samples for histopathological examination. The dog was treated with meloxicam at a loading dose of 0.2 mg/kg subcutaneously on the first day, followed by 0.1 mg/kg orally once per day on subsequent days.

Surgery was performed 7 days after the initial examination. On the day of surgery, the dog was treated peri-operatively with cefazolin at 22 mg/kg intravenously, meloxicam at 0.1 mg/kg subcutaneously, and butorphanol at 0.2 mg/kg intravenously. General anaesthesia was achieved using xylazine premedication at 1 mg/kg intramuscularly, followed by anaesthesia induction with sodium thiopentone administered intravenously to effect, achieving a

August 2024

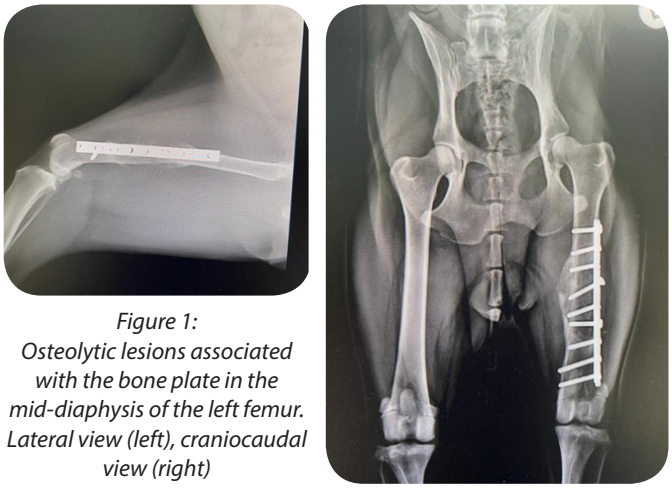

Figure 1:
Osteolytic lesions associated with the bone plate in the mid-diaphysis of the left femur. Lateral view (left), craniocaudal view (right)

cumulative dose of 14.6 mg/kg. Anaesthesia was maintained with a gaseous mixture of isofluorane and 100% oxygen as needed, administered intratracheally via a preplaced endotracheal tube. The left femoral diaphysis was accessed using a cranio-lateral approach as described by Piemattei and Johnson (2004). Explanation of the bone plate and screws resulted in the exposure of the mid-diaphysis of the left femur, revealing diaphyseal cortical bone with a soft and spongy consistency, consistent with extensive osteolysis due to OSA.

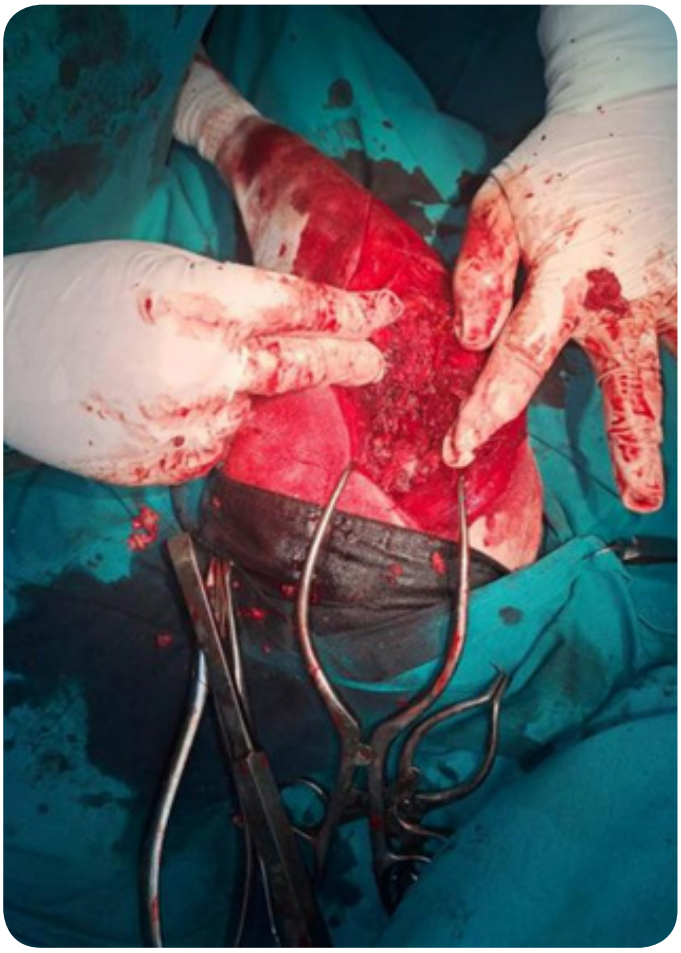

Figure 2:
Intraoperative appearance of the mid-diaphysis of the left femur following explantation of the bone plate and screws. The spongy appearance of the bone in this region was readily observed.

Consequent to these intra-operative findings, the left hindlimb was amputated by coxofemoral disarticulation as described by Johnson and Dunning (2005). Samples of bone from the affected femoral diaphyseal area were obtained and submitted to a reference laboratory for histopathological examination. The muscle, fascia and subcutaneous tissues were routinely closed in a simple continuous suture pattern using monofilament PGA-PCL 2/0. The skin was closed using nylon 3/0 in a simple interrupted suture pattern.

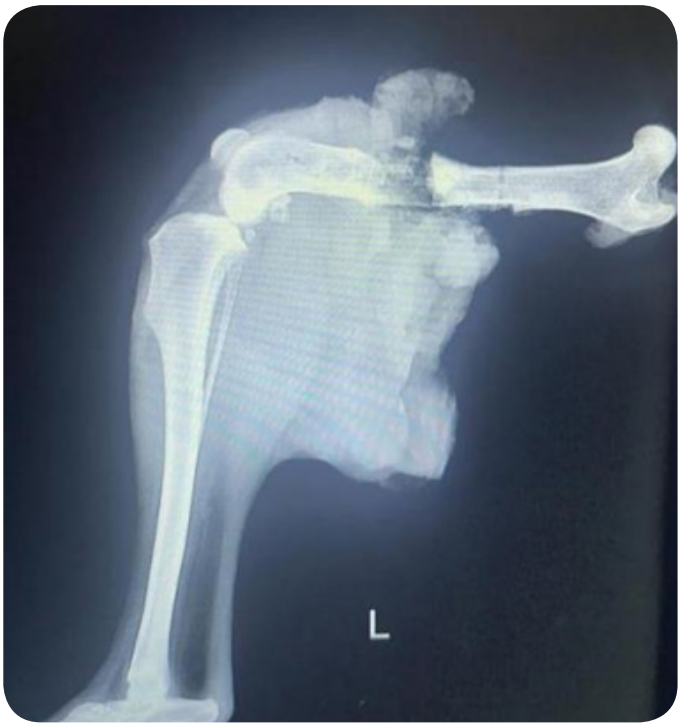

Figure 3:
Lateral radiograph of the left pelvic limb following plate and screw explantation and amputation by coxofemoral disarticulation. The osteolytic lesions and loss of the normal bone architecture in the mid-diaphysis of the femur can be readily appreciated.

Orthogonal thoracic radiographs were obtained in the immediate postoperative period and were unremarkable.

The dog was discharged on cephalexin at 20.8 mg/kg orally twice per day for 7 days, tramadol at 3.1 mg/kg orally three times per day for 7 days, gabapentin at 12.5 mg/kg orally twice per day long-term, and meloxicam at 0.1 mg/kg orally once daily long-term. Histopathological examination of bone samples obtained from the mid-diaphyseal area of the left femur revealed tissue composed of sheets of densely packed, pleomorphic, polygonal to plump spindle-shaped cells associated with a variable amount of amorphous pink matrix consistent with osteoid. These findings led to a diagnosis of minimally productive, osteoblastic, appendicular OSA. The dog presented 3 months later with a complaint of persistent and diffuse soft tissue swelling and inflammation at the surgical site that was sub-optimally responsive to non-steroidal anti-inflammatory (NSAID) therapy.

Histopathological examination of tissue samples from the surgical site confirmed soft tissue infiltration of this region with minimally productive, osteoblastic OSA. The owners were advised of the poor prognosis associated with locally infiltrative and metastatic disease, along with the expected survival times. Palliative treatment with meloxicam and gabapentin was continued.

Discussion

In dogs, OSA development has been described subsequent to fractures and elective orthopaedic procedures such as tibial plateau levelling osteotomy (TPLO), tibial tuberosity advancement (TTA), triple pelvic osteotomy (TPO), total hip replacement (THR), and cortical bone allograft (Selmic et al, 2018; Wouda et al, 2018; Longo et al, 2020). Other neoplastic histotypes associated with previously implanted orthopaedic hardware have been described, including undifferentiated sarcoma, histiocytic sarcoma, fibrosarcoma, and malignant mesenchymoma (Sinibaldi et al, 1976).

The ability of biomaterials or their breakdown products to be carcinogenic is of increasing concern in the medical device field (Woud et al, 2018; Aminkov & Manov, 2005). Factors proposed to increase the risk of fracture-associated OSA include chronic inflammatory reaction to the implant, surgical site infection, and implant corrosion (Selmic et al, 2018, Sinibaldi et al, 1976). A recent study reported the release of metallic ions from Slocum TPLO implants. According to the authors, this release was caused by implant corrosion (Sprechter et al, 2018 cited in Longo et al, 2020; Wouda et al, 2018). Although canine orthopaedic procedures such as TPLO and fracture repair are commonly performed in modern-day veterinary practice, mesenchymal tumours of the bone associated with metallic implants remain rare. However, the actual incidence is unknown.

Among OSA cases in dogs, the reported incidence rates of those associated with fracture repair are 1.0–4.5% (Arthur et al, 2016 & Li et al, 1993 cited in Wouda et al, 2018; Sinibaldi et al, 1976). Approximately 1.4–28% of dogs diagnosed with implant-associated OSA have secondary lesions at the time of diagnosis (Selmic et al, 2018). In one study, the interval between operative intervention for fracture repair and the appearance of neoplastic growth was 7.5–8.3 years (Aminkov & Manov, 2005) whereas in another study, the median interval was 5.5 years (Burton et al, 2015). The previously reported average interval between bone fracture and the appearance of fracture-induced OSA was 6.3 years (Brodey et al, 1969 cited in Aminkov & Manov, 2005).

The interval between fracture repair and the appearance of neoplastic lesions associated with the orthopaedic implants was 7 years in our case, which was consistent with the findings of previous studies. In a recent study in which treatment with amputation alone was compared with treatment involving amputation and adjuvant chemotherapy using doxorubicin and cisplatin, none of the dogs treated with amputation alone survived beyond 16 months (Mauldin et al, 1988). In another study, the average survival time after amputation alone was 4-5 months (Brodey et al, 1977 cited in Aminkov & Manov, 2005). In yet another study, the median survival time after treatment with amputation alone was 6 months (Burton et al, 2015).

Following amputation and treatment with carboplatin chemotherapy for appendicular OSA, the median survival time was 9 months (Saam et al, 2011). However, the optimal protocol for adjuvant chemotherapy has not been determined (Saam et al, 2011; Mauldin et al, 1988). Although implant-associated OSA is a rare and devastating complication in dogs, the findings in the described case were mostly consistent with those obtained in previous studies of OSA. These observations may suggest that implant-associated OSA has the same biological behaviour as naturally occurring OSA in dogs.

In dogs, OSA carries a poor prognosis, as it is associated with a high incidence of metastatic disease and local infiltration at the time of diagnosis. Although implant-associated OSA is a very rare complication, it may be worth discussing this with owners at the time of fracture fixation and/or implantation of orthopaedic hardware and to consider this condition as a differential diagnosis where bone pathology is suspected in cases in which orthopaedic hardware has been implanted.

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QUESTION 1

What is osteosarcoma (OSA)?

a. A benign neoplasm commonly affecting the bones of the skull and vertebral column, and capable of producing osteoid matrix.
b. A malignant neoplasm commonly affecting the bones of the skull and vertebral column, and not capable of producing osteoid matrix
c. A benign neoplasm commonly affecting the long bones, and capable of producing osteoid matrix.
d. A benign neoplasm commonly affecting the long bones, and not capable of producing osteoid matrix.
e. A malignant neoplasm commonly affecting the long bones, and capable of producing osteoid matrix.

QUESTION 2

What percentage of skeletal tumours comprises OSA?

a. 25%
b. 45%
c. 65%
d. 85%
e. None of the above

QUESTION 3

Which large/giant breed dogs are commonly affected by OSA?

a. Rottweiler
b. St Bernard
c. Doberman Pinscher
d. German Shepherd
e. All of the above

QUESTION 4

Which small breed dogs are commonly affected by OSA?

a. Miniature Schnauzer
b. Cocker Spaniel
c. Cairn Terrier
d. All of the above
e. A and C only

QUESTION 5

What is the typical survival time for dogs treated for OSA with amputation alone?

a. Less than 5 months
b. 5 months - 1 year
c. 1-2 years
d. 2-3 years
e. None of the above

QUESTION 6

Implant-associated OSA has been described following which orthopaedic procedures?

a. TPLO (tibial plateau levelling osteotomy)
b. THR (total hip replacement)
c. TTA (tibial tuberosity advancement)
d. TPO (triple pelvic osteotomy)
e. All of the above

QUESTION 7

What other implant-associated tumour types have been described in dogs?

a. Undifferentiated sarcoma
b. Histiocytic sarcoma
c. Fibrosarcoma
d. Malignant mesenchymoma
e. All of the above

QUESTION 8

What is the average interval between operative intervention and the appearance of implant-associated OSA in dogs?

a. 6 years
b. 2 years
c. 1 year
d. 6 months
e. None of the above

QUESTION 9

Which adjuvant chemotherapeutic agents are commonly used to treat OSA in dogs?

a. Doxorubicin
b. Cisplatin
c. Carboplatin
d. Vincristine
e. A, B and C only

QUESTION 10

OSA in dogs carries a poor prognosis because:

a. There is a high incidence of metastatic disease and local infiltration at the time of diagnosis
b. It occurs in older dogs near the end of their lifespan
c. OSA interferes with normal GIT function
d. Hypoproteinaemia secondary to a protein-losing enteropathy is common in OSA
e. None of the above

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