

A case of canine *Salmonella* spp. osteomyelitis with secondary fracture following dog bite

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Abstract

An immature canine was attacked by another dog in a kennel facility and sustained multiple wounds to the lateral right forelimb and cranial right lateral thoracic region. General surgical and antimicrobial therapies were instituted immediately. The patient battled with recurrent infections and subsequent delayed healing. After approximately 35 days from the initial injury, the patient became acutely lame and febrile. The persistently open wounds were cultured and returned positive for *Salmonella* spp. Within the following days, the patient became painful, and the lameness progressed significantly. Radiographs confirmed pathologic humeral fracture, and the patient was referred for specialty evaluation. Zoonotic preventative protocols were adopted at the specialty facility upon arrival. Complete forequarter limb amputation was curative in this patient.

KEYWORDS

Exogenous Osteomyelitis, Pathological fracture, Salmonella, Zoonoses

1 | INTRODUCTION

Osteomyelitis refers to inflammation and concurrent infection of the periosteum, cortex and/or the medullary cavity of bone (Carlson, 1991; Rohilla et al., 2019; Siqueira et al., 2014). In human medicine *Salmonella* as an etiological agent in osteomyelitis is regarded as rare, with the microbe accounting for only 0.45% of all osteomyelitis cases (McAnearney & McCall, 2015; Santos and Sapico, 1998). *Salmonella* osteomyelitis itself accounts for as few as 0.8% of all *Salmonella* infections in human medicine (McAnearney & McCall, 2015; Rohilla et al., 2019). Haematogenous spread, which is extension from local soft tissue infections, and exogenous spread, which is via direct inoculation, are the two commonly reported pathways to osteomyelitis in human and veterinary literature (Johnson, 1994; Rohilla et al., 2019). Rohilla et al. (2019) reported that *Salmonella* osteomyelitis is extremely rare in humans generally, and even more so in apparently healthy individuals. These authors, as well as McAnearney and McCall (2015)

and Santos and Sapico (1998), also highlighted that haematogenous spread is far more predominant and is commonly seen in patients with haemoglobinopathies such as sickle cell disease or thalassemia, as well as immunocompromised individuals. Carlson (1991) and Gieling et al. (2019) reported that when haematogenous spread occurs in veterinary medicine, it predominates in juveniles more so than adults. Exogenous spread appears to be the most common form in veterinary medicine with notable examples of routes for direct inoculation including iatrogenic (surgical fixation of fracture), bite wounds, open fractures, gunshot wounds and foreign body penetration (Johnson, 1994). Emmerston and Pead (1999) were the first to describe a Weimaraner with a pathologic femoral fracture secondary to haematogenous osteomyelitis. Langley-Hobbs and Lascelles (2004) were the first to describe a Border Collie with a pathologic phalangeal fracture, following direct inoculation caused by a puncture wound. To the authors' knowledge this is the first report of a *Salmonella* osteomyelitis secondary to a dog bite wound, which ultimately resulted in a humeral pathologic fracture.

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2 | CASE PRESENTATION

A 21.6 kg, 6-month-old, fully vaccinated, male intact Labradoodle was attacked in a kennel facility by another fully vaccinated dog. The patient was current on monthly flea and tick preventatives and was being fed a commercial puppy diet. The patient sustained multiple, severe dog-bite wounds to the right lateral thoracic limb and cranial right lateral thoracic and axillary region. There was a 2-inch laceration to the right lateral shoulder, as well as four puncture wounds in the right axillary region. The patient was transported from the kennel facility to his primary veterinarian. On presentation, right forelimb and right thoracic lateral radiographs were obtained. Radiographs revealed no appreciable fractures or other orthopaedic abnormalities nor was there any sign of communication of wounds with the thoracic cavity. Extensive soft tissue trauma and emphysema to the right thoracic limb and axial region were present. The patient's wounds were clipped, irrigated, debrided, flushed and closed primarily without a drain. Analgesia was achieved via carprofen (Rimadyl) 2.2 mg/kg PO BID and tramadol (Ultram) 3 mg/kg PO TID/PRN. Antimicrobial coverage included cefpodoxime (Simplicef) 5 mg/kg PO BID and enrofloxacin (Baytril) 5 mg/kg PO SID for 7 and 10 days, respectively. The patient was discharged to owners the same day with a hard-plastic Elizabethan collar.

The largest wound over the right shoulder repeatedly dehiscid. This coincided with the discontinuation of enrofloxacin (Baytril). After a period of approximately 25 days of battling with delayed closure, the owners sought a secondary local opinion for the management of the patient's wounds. Culture and sensitivity samples were obtained from a visible draining track over the right lateral shoulder and were submitted to a verified veterinary laboratory for aerobic and anaerobic testing and urine samples were also collected and submitted for coccidioidomycosis, histoplasmosis and blastomycosis antigen (enzyme immunoassay) fungal panels. At this time, the patient had also begun to limp on the right forelimb. The patient's proximal humerus became very tender on palpation at 33 days post initial insult. The visible draining track was aseptically prepared and cleaned with chlorhexidine, and it was flushed with sterile saline. While culture results were pending, a honey tie-over bandage was placed. Analgesia in the form of tramadol (Ultram) 3 mg/kg PO BID and gabapentin (Neurotin) 10 mg/kg PO BID/PRN were prescribed. The patient was rechecked 4 days later, and the right forelimb lameness had progressed significantly. The patient was now lethargic and pyretic with a temperature of 104.0°F. The patient still had purulent exudate from the right lateral thoracic wound.

Two view right humeral radiographs were taken, and a minimally displaced proximal-diaphyseal transverse fracture of the right humerus was appreciated with significant periosteal reaction observed along the length of the bone. A presumptive diagnosis of humeral pathologic fracture secondary to osteomyelitis was made (Figures 1 and 2). Amoxicillin-clavulanate acid (Clavamox) at 13.75 mg/kg PO BID and enrofloxacin (Baytril) at 7 mg/kg BID PO were empirically prescribed pending culture results. Tramadol (Ultram) 3 mg/kg PO PRN/TID and deracoxib (Deramaxx) 2.2 mg/kg BID PO were prescribed for analgesia. Coccidioidomycosis, histoplasmosis and blastomycosis antigen

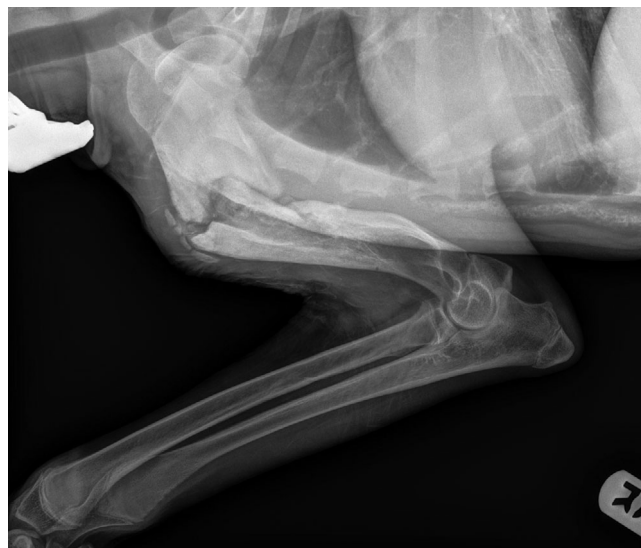


FIGURE 1 Right lateral radiographic projection of the right humerus including the radius and ulna at day 35 from the bite injury. Severe periosteal proliferation along the extent of the cortical humeral bone with a minimally displaced, transverse, proximal diaphyseal pathologic fracture of the right humerus, consistent with osteomyelitis, is present. The edges of the fracture site are rounded



FIGURE 2 Right cranio-caudal radiographic projection of the right humerus on day 35 after bite injury. Severe proximal periosteal proliferation of the humerus appreciated, resulting in superimposition over the distal aspect of the humerus. Slight cranial displacement of the distal humerus observed, supporting a diaphyseal humeral fracture. There is an increase surrounding tissue density associated with the right humerus and fracture site. Elbow and distal forelimb anatomy appear within normal limits

(enzyme immunoassay) fungal panels ran on a sample of urine from the patient were negative. Culture results confirmed heavy Gram-negative rod growth consistent with *Salmonella spp.*, sensitive to enrofloxacin (Baytril) and chloramphenicol (Chloromycetin), resistant to amoxicillin-clavulanate acid (Clavamox). The patient was transferred to our hospital later that day for an emergency surgical consultation; this was day 42 after the initial injury.

With the advanced knowledge that a *Salmonella*-positive patient was being transferred to our facility, discussions occurred with the front desk, nursing staff and overnight emergency doctors regarding the zoonotic potential. Upon arrival, the owners were greeted outside our facility by staff attired in personal protective equipment (PPE) with a gurney, so that the patient did not walk through the hospital. In addition to verbal communication, wall signs and emails were sent to staff to emphasise the importance of following infectious-disease protocols, and the added zoonotic potential of this patient's infection. PPE attire included disposable gloves and gowns, as well as the utilisation of foot baths. Several reminders of appropriate hand-washing were also posted, and all surface areas contacted by the patient was thoroughly disinfected.

Upon intake examination, the patient was stable. Temperature, pulse and heart rate were all within normal limits. His baseline bloodwork was unremarkable aside from a mildly elevated ionised calcium of 1.47 mmol/L (reference range 1.12–1.4 mmol/L), which was consistent with the patient's juvenile status. The owners were very interested in preserving the right forelimb with an external fixator device, but also desired a 'guaranteed' resolution to the problem. After thorough discussions with the owners, a complete forequarter limb amputation was approved as the best approach for the patient, while achieving the resolution goals of the client, simultaneously.

The surgical procedure was performed successfully the following day under general anaesthesia with hydromorphone (Dilaudid) 0.1 mg/kg, IM, midazolam (Versed) 0.2 mg/kg IM, famotidine (Pepcid) 1 mg/kg IV and maropitant (Cerenia) 1 mg/kg IV for premedication. Propofol (PropoFlo) at 6 mg/kg IV, titrated to effect was used for induction, and isoflurane anaesthetic gas was used. Enrofloxacin (Baytril) at 10 mg/kg IV was given pre-operatively. Hydromorphone (Dilaudid) 0.1 mg/kg IV QID and enrofloxacin (Bayril) 10 mg/kg IV SID were administered post-operatively. The patient recovered uneventfully and was discharged 2 days later. Tramadol (Ultram) 3 mg/kg PO TID and gabapentin (Neurotin) 10 mg/kg PO TID were prescribed for analgesia. He was initially prescribed ciprofloxacin (Cipro) 12.5 mg/kg BID PO pending intra-operative culture results.

The right forequarter limb was submitted for histopathology, which confirmed osteomyelitis of the humerus with subsequent pathological humeral fracture. Aerobic and anaerobic culture of soft tissue swab and bone piece were submitted for analysis as well, which returned a heavy Gram-negative growth of bacteria, identified as *Salmonella* spp., sensitive to ciprofloxacin and chloramphenicol, while now being resistant to enrofloxacin. After reviewing human literature and consultation with a veterinary infectious disease expert, ciprofloxacin (Cipro) 12.5 mg/kg BID PO and chloramphenicol (Chloromycetin) 50 mg/kg BID PO were prescribed for four weeks.

Recheck and suture removal with primary care veterinarian at 10 days post-amputation showed continued improvement with complete healing at surgical site. As recommended by the veterinary infectious disease expert, a swab of the patient's oral, incisional and rectal region was obtained at eight weeks post-operatively to ensure that the patient was not a carrier for *Salmonella*; the culture was negative. At the

time of this report submission, approximately 1-year post surgery, the patient continues to do well.

3 | DISCUSSION

Osteomyelitis is a challenging condition across all animal species and is often caused by prior or persistent infection with pyogenic organisms (Carlson, 1991; Gieling et al., 2019). Osteomyelitis typically occurs by two means as mentioned earlier, haematogenous or direct inoculation (exogenous) spread of the inciting pathogen (Carlson, 1991; Dodwell, 2013; Johnson, 1994). Haematogenous osteomyelitis in humans has a reported incidence of 8–10 per 100,000 in developed countries, such as the United States (Dodwell, 2013; Jaramillo et al., 2017). In contrast, haematogenous osteomyelitis has been reported in veterinary medicine to a much lesser extent (Emmerson & Pead, 1999). The most common cause of osteomyelitis in veterinary medicine is via direct inoculation (exogenous); predominately with open fractures and surgical fixation of closed fractures (Braden, 1991; Caywood et al., 1978; Jackson & Pacchiana, 2004; Johnson, 1994). Other reported sources of exogenous infections in veterinary medicine include bite wounds, gunshot wounds and foreign body penetration (Braden, 1991; Caywood et al., 1978; Johnson, 1994). This patient's bite wounds were immediately closed without a drain by the first veterinarian and empirical antimicrobial therapy was instituted. This practice should be exercised with extreme caution and may have contributed to the negative outcome (i.e., loss of limb) of this case. Despite an extensive literature search, osteomyelitis due to direct inoculation of *Salmonella* spp., secondary to a bite wound from another dog that resulted in a pathologic fracture, could not be found.

Siqueira et al. (2014) retrospectively evaluated canines with bacterial appendicular osteomyelitis. Of the 52 canines evaluated, 78% of the cases were due to vehicular trauma, 17% were secondary to dog bites and 5% were caused by pododermatitis infections. According to these authors, the tibia, femur, radius/ulna and humerus were infected in 31%, 28%, 25% and 16% of cases, respectively. The likely explanation for the humerus being the least affected can be attributed to the fact that it has significant circumferential musculature. In the dog in the presenting report, who suffered a direct bite wound to the humeral aspect of the forelimb, a minor disturbance of the cortical bone or periosteum could have occurred at the time of injury that was not detectable on initial radiographs, or the chronic infection could have gradually caused a cortical disturbance. Based upon the history, it was surprising to the authors that a sequestrum was not observed. A boarded radiologist later reviewed our radiographs and confirmed absence of a bony sequestrum.

Although imaging techniques such as radiographs, fistulograms, ultrasonography and computed tomography can be used to detect bone abnormalities, the gold standard for diagnosis of osteomyelitis remains culture and sensitivity carried out by a verified laboratory (Siqueira et al., 2014). Radiographs were obtained initially after the injury and then again after the patient began limping and became

pyretic, confirming the proximal–diaphyseal right humeral fracture. The diagnosis of *Salmonella* osteomyelitis in this case was made via culture and sensitivity results. Prior to referral to our facility, initial culture sample was obtained from a draining tract over the lateral right humerus. This sampling technique is more likely to reveal incidental bacterial contaminants rather than the cause of any deep-seated bony infection and is not recommended. A bone culture or sampling from the fracture site is the best practice (Johnson, 1994; Walker et al., 1983). Culture samples were obtained from the fracture site post amputation of the right thoracic limb, which did support the preliminary diagnosis of *Salmonella* osteomyelitis.

Bacterial osteomyelitis remains the most common cause of osteomyelitis in veterinary medicine (Bubenik, 2005; Carlson, 1991; Langley-Hobbs & Lascelles, 2004). Caywood et al. (1978) and Walker et al. (1983), reported that the most commonly isolated aerobic bacteria included *Staphylococcus* spp. and *Escherichia coli*, followed by *Streptococcus* spp., enteric bacteria and *Corynebacterium* spp. Fungal osteomyelitis, though less common, has rarely been reported in the veterinary literature (Brearley & Jeffery, 1992). In a case series of 52 canines, approximately 42% ($n = 21$) of bacterial osteomyelitis infections were mixed infections. *Salmonella* spp. was isolated in 3.8% of those 52 cases ($n = 2$); however, *Salmonella* spp. was never isolated in conjunction with any other bacteria, that is polymicrobial infections (Siqueira et al., 2014). Lending to the thought that when *Salmonella* spp. is isolated from an osteomyelitis lesion, there is a high likelihood of it being the sole causative agent.

Similarly, in human medicine, *Salmonella* spp. has been linked as the causative organism in only 0.45% of osteomyelitis cases, occurring mainly in patients with hemoglobinopathies such as sickle cell disease. *Salmonella* osteomyelitis itself accounts for as few as 0.8% of all *Salmonellae* infections (McAnearney & McCall, 2015; Rohilla et al., 2019). Although most human cases are self-limiting (Wright et al., 2005), *Salmonella* spp. is estimated to infect 1.4 million people annually in the United States. Recent epidemiological human studies have additionally reported an overall 2.8-fold increase in osteomyelitis cases over the past 20 years (Dodwell, 2013). Public health experts have long been concerned about the serious illnesses that stem from *Salmonella* infections, as well as their zoonotic potentials (Lenz et al., 2009; Reimschuessel et al., 2017). Lenz et al. (2009) and Chomel (2014) documented *Salmonella* related infections as a re-emerging zoonotic disease, particularly amongst dogs and cats across the United States. Although raw food diets have historically been linked as a primary source of contracture in our companion animals (Lenz et al., 2009; Reimschuessel et al., 2017), commercial diets contaminated with *Salmonella* have been emerging as a more frequent source of exposure. In 2015, the United States Food and Drug Association reported that greater than 70 commercial pet food recalls between January 2012 and December 2015 were secondary to *Salmonella* spp. contamination. In 2020, they also reported that approximately nine commercial pet foods (or treats) were recalled as a result of potential *Salmonella* contamination. The diet of the attacking dog is unknown in this case, and thus, diet related involvement cannot be substantiated.

With our companion animals being potential carriers of *Salmonella*, and with the staggering increase in companion animals per household in the past two decades, the transmittance of the disease has increased (Chomel, 2014; Wright et al., 2005). *Salmonella* is commonly shed in faecal material and contact with such material can result in zoonotic transmission, whether pets are clinical or not (Lenz et al., 2009; Reimschuessel et al., 2017). Transmission can also occur via contact with infected bodily excretions, such as purulent exudate from the draining tracks in our patient. With this knowledge and the diagnosis of *Salmonella* osteomyelitis in mind, the zoonotic risk was of paramount importance, and appropriate hospital protocols were instituted. The zoonotic potential of the infection was also shared with the owners, and they were strongly advised to consult with their family physician.

Wright et al. (2005) reported that the occurrence of several *Salmonellosis* outbreaks documented across the United States were all traced back to three companion animal veterinary clinics and an animal shelter between 1999 and 2000. Over 45 individuals became infected including employees, clients and client-owned pets. Various state health department investigations surmised that all four outbreaks were due to multidrug-resistant *Salmonella typhimurium*. This further highlights the need for judicious antimicrobial usage, as well as strategically targeted therapy via early culture and sensitivity when warranted. Though empirical antimicrobial therapy is often prescribed in many post-traumatic injuries, early consideration for the potential of multi-drug resistant etiological agents should be explored in non-healing wounds such as was seen in this case. This is highlighted in Siqueira et al. (2014), where a significant portion of the study group had high resistance panels to common empirical antimicrobials, such as clindamycin (59%), penicillin (59%) and azithromycin (80%). This information reinforces the importance of obtaining cultures of non-healing post-traumatic wounds with laboratory evaluation for microbial identification and sensitivity panels, so that target antimicrobial therapy can be instituted earlier rather than later. In addition, extended-spectrum sensitivity panels may be beneficial and should be considered. When it comes to the management of exogenous bacterial osteomyelitis, medical and surgical therapies are typically incorporated together to achieve lasting results, as seen in this case (Bubenik, 2005; Carlson, 1991; Harari, 2013). This approach is warranted due to the general pathophysiology of osteomyelitis, where the infected bone usually becomes surrounded and buried by a mass of dense fibrous connective tissue (Carlson, 1991). The treatment of chronic osteomyelitis usually follows the surgical principles of debridement, sequestrectomy, drainage and irrigation (Johnson, 1994). However, in this case, after discussions with the owners, it was determined that a right forequarter amputation would be a more certain method of obtaining complete resolution, which was desired by the clients. It is of paramount importance in veterinary medicine that potent zoonotic pathogens such as *Salmonella* spp. are aggressively and appropriately treated (Banky et al., 2002; Bubenik, 2005; Gieling et al., 2019; Kiflu et al., 2017; McAnearney & McCall, 2015).

Due to the chronicity prior to presentation, severe bacterial resistance was suspected in the dog in this case report. The second

culture and sensitivity panel from intra-operative samples confirmed isolation of *Salmonella* spp. There was also now, documented resistance to enrofloxacin that was not noted 10 days earlier on culture sample obtained from the patient's draining tracks. The intraoperative culture and sensitivity panel also showed sensitivity to ciprofloxacin and chloramphenicol, as well as amikacin. These findings, in addition to recommendations obtained from the consulting veterinary infectious disease expert, confidently directed our post-amputation therapeutic management of the case. The combination of ciprofloxacin and chloramphenicol was deemed most appropriate based on adequate bone penetration, as well as efficacy to eliminating the specific infection (Santos and Sapico, 1998; Wright et al., 2005). As seen in human medicine, when there is documented osteomyelitis and a potential degree of sepsis in an otherwise non-compromised patient; antimicrobial therapy in this patient was instituted for a 1-month duration. Rechecks were performed by the primary veterinarian due to distance from our hospital. At two months post-amputation, a recheck culture and sensitivity of mucocutaneous swab samples showed no evidence that the patient was a *Salmonella* carrier. To the authors knowledge the patient continues to do well 1-year post-amputation.

4 | CONCLUSION

Exogenous osteomyelitis is the most prevalent form of osteomyelitis reported in veterinary medicine, with bacterial pathogens being the most frequently isolated culprits. Nonetheless *Salmonella* spp. osteomyelitis is a profoundly uncommon veterinary diagnosis. Its presentation may result in diagnostic and therapeutic challenges as seen in this case that may terminate in devastating skeletal conditions as well as the potential for zoonosis. *Salmonella* spp. should be considered as a differential, in suspected or confirmed osteomyelitis cases to allow effective management and limit human exposure.

AUTHOR CONTRIBUTIONS

Elroy Williams: writing original draft, writing review and editing.
Heather Ann Marie Towle: writing review and editing.

PEER REVIEW

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