Clinical Commentary

Septic osteitis and osteomyelitis in foals – are antimicrobials alone enough?

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Introduction

The case report by Lawrence and Fraser (2013) describes the successful management of 2 weanlings with septic osteitis of the proximal sesamoid bones, using prolonged (6 weeks) antimicrobial therapy alone. Doxycycline, an antimicrobial with excellent bone penetration properties, was deemed essential to treatment success. In contrast to the poor outcome in previously reported cases of septic sesamoid bone osteitis, the authors were able to show the value of a conservative approach over surgical debridement. The question is to what extent are we able to extrapolate this to the general treatment of septic osteitis and osteomyelitis in young horses?

Etiopathological, clinical, and diagnostic features

Septic osteitis (O; infection of bones lacking a medullary cavity) and osteomyelitis (OM) are common in foals up to age approximately 4 months and often involve adjacent synovial structures (Firth 1983; Neil et al. 2010). The source of bacteria, their species and the physiological and anatomical considerations that favour their growth at sites of predilection are summarised by Lawrence and Fraser (2013) and elsewhere in the literature (Firth 1983; Brewer and Koterba 1990; Schneider et al. 1993; Wilsin et al. 1999; Kay et al. 2012).

In mature horses, O/OM are usually associated with penetrating injuries or previous surgical interventions. In the report by Lawrence and Fraser (2013), 2 weanlings, aged 5 and 6 months, were affected by septic osteitis of the proximal sesamoid bones (PSB). In horses of this age haematogenous seeding of bacteria remains the most likely initiating cause in the absence of external injury, although a primary septic focus elsewhere in the body is rarely identified (Wisner et al. 1991; Dabareiner et al. 2001; Witte and Rodgerston 2005; Sherman et al. 2006). It is assumed that the relatively convoluted blood supply to the axial borders of the PSB and the interosseous ligament makes them predilection sites for haematogenous septic osteitis and desmitis in weanlings and mature equids (Wisner et al. 1991; Dabareiner et al. 2001; Barr et al. 2005; Sherman et al. 2006; Lawrence and Fraser 2013).

Lameness, focal pain and swelling (oedema and effusion) dominate the clinical picture of O/OM (Bramlage 1998). In cases with effusion, synovial fluid analysis as well as culture and sensitivity testing provide valuable information (Bramlage 1998; Sayegh et al. 2001). With the exception of an elevated body temperature, there is often a paucity of signs indicating a systemic response (Goodrich and Nixon 2004). Plasma fibrinogen concentrations and blood cultures, however, can be helpful in diagnosing O/OM (Sayegh et al. 2001; Newquist and Baxter 2009).

Radiography is most commonly used to confirm and follow a septic bone lesion. Bone lysis may not be recognised radiographically until at least 4–5 days post infection, at a time when the bone has lost 30–50% of more of its mineral content (Turner 1987; Bramlage 1998; Goodrich and Nixon 2004). In cases with concurrent infarction, this time lag may be as great as 2–3 weeks (Wegener and Alavi 1991; Bertone 1999). Delayed diagnosis and associated extensive lysis may result in pathological fracture, with a negative impact on prognosis (Fig 1). Advanced imaging (magnetic resonance imaging [MRI] or computed tomography [CT]) may allow earlier recognition (Sayegh et al. 2001; Easley et al. 2011) and provide information on the extent of the lesion (Fig 2). While the severity of the radiographic lesion does not necessarily appear to affect long-term outcome (Steel et al. 1999; Kay et al. 2012), its location is more likely to determine future soundness. Successful elimination of infection manifests radiographically as sharp delineation of the original defect and surrounding sclerosis (Fig 3). This being said, it can take many months for a defect to regain mineral density, if at all (Lawrence and Fraser 2013). Therefore, a positive clinical progression (decreased swelling and lameness) and improved results of repeated clinicopathological testing represent more important indicators of early success in treatment.

Current treatment strategies in man and equids

In their ‘plea for general conservatism in the treatment of septic osteomyelitis of the skull and face’ Blair and Brown (1927) remind human practitioners of an old Italian proverb that states ‘He who goes slowly goes safely; he who goes quickly goes surely’. Unfortunately the question as to just how ‘safe’ or ‘sure’ a conservative approach is, remains unanswered in both human and equine medicine.

Current treatment recommendations in the equine veterinary literature include surgical debridement of bone as a primary course of action to address O/OM (Goodrich and Nixon 2004; Schneider 2006; McIlwraith 2007). In contrast, treatment of the human equivalent (acute haematogenous osteomyelitis [AHO] in paediatric patients) appears to focus on prolonged systemic antimicrobial therapy (Le Saux et al. 2002; Peltola et al. 2010). A recent prospective, randomised trial investigating appropriate antimicrobial treatment regimens found that extensive surgical interventions are rarely necessary in children (Peltola et al. 2010). The exception to this is the presence of an obvious abscess, from which...
purulent material is aspirated (Blyth et al. 2001; De Boeck 2005; Goergens et al. 2005). The continued emergence of multiresistant pathogens such as community-acquired methicillin-resistant Staphylococcus aureus in human patients has resulted in an increased necessity for surgical intervention (Darville and Jacobs 2004; Harik and Smeltzer 2010). Surgical exploration and debridement are also indicated if a patient does not respond to empiric antibiotic therapy within an appropriate time frame by showing persisting signs of pain and fever (Stanitski 2004; Goergens et al. 2005; Harik and Smeltzer 2010).

Closer analysis of the data presented in reports of O/OM cases in the veterinary literature (Witte and Rodgerson 2005; Neil et al. 2010; Kay et al. 2012; Lawrence and Fraser 2013) allows us to consider the value of an initial conservative approach in the equine case with lytic bone lesions. In a retrospective study of 108 foals, medical therapy alone was pursued in 9 (Neil et al. 2010), which were considered to have inoperable lesions due to extensive physseal involvement or surgically inaccessible locations such as the ilium or navicular bone. A conservative approach was therefore elected due to the morbidity likely to result from surgical intervention. Rather surprisingly, therefore, 7 of these 9 foals (78%), compared with 80 of the remaining 98 foals (82%) were reported to have a successful outcome (one foal was subjected to euthanasia without pursuing treatment).

Another recent report focused on the treatment of septic osteomyelitis of the patella (Kay et al. 2012). There, 6 of 8 foals (75%) made a full recovery. Notably, all surviving foals were treated without surgical debridement of the patellar lesion, but all received intralesional antimicrobials. Although numbers are small, these reports suggest that cases treated without bone debridement can have an equally successful outcome when compared to previous studies (Schneider et al. 1992; Vatistas et al. 1993; Axon et al. 1999). Figures 3-5 are further examples of cases treated successfully with antimicrobial therapy alone.
It is important to note that the term ‘conservative’ as used in this commentary refers to a lack of bone debridement and in no way discounts the value of lavage of adjacent synovial structures (whether by through-and-through needle lavage or arthroscopic techniques) in order to address sepsis or simply to reduce the burden of inflammatory mediators.

Empiric antimicrobial choice in the early management of O/OM

The goal of any antimicrobial treatment regimen is to achieve adequate tissue concentrations of an antimicrobial effective in eliminating the causative infectious agent. Although the most common pathogens involved in O/OM have been characterised, bone aspirates and/or synovial fluid samples for culture and sensitivity patterns should be obtained whenever possible. Prior to the availability of these results, however, choice of antibiotic should take the following into consideration: antimicrobial spectrum; capacity to penetrate affected tissues (including tissues with pathological milieu alteration); and commonly encountered antimicrobial resistances within the hospital population.

Enteric Gram-negative organisms appear to predominate in bacterial isolates from bone lesions in foals (Firth 1983; Brewer and Koterba 1990; Orsini and Kreuder 1994; Baxter 1996; Neil et al. 2010). This is in contrast to AHO in children, where S. aureus is the most commonly isolated pathogen.
The role of chronicity in determining treatment and outcome

Chronic septic PSB lesions in the mature equine carry a poor prognosis when treated conservatively (Wisner et al. 1991; Dabareiner et al. 2001; Barr et al. 2005). Figure 1 is evidence of the authors’ negative experience with chronic sesamoid bone infections. This case was presented after a prolonged, unsuccessful attempt at medical management. Sherman et al. (2006) reported an isolated case of fungal ostelitis of the axial borders of the PSB that was successfully treated without surgical debridement.

Progression (and the inherent chronicity) of an osseous infection is an important determining factor as to whether or not a conservative treatment approach is going to succeed, irrelevant of antimicrobial choice. With time, avascular necrosis develops and changes in the tissue’s chemical milieu occur. Sequestration formation or the mere extent of the lesion will impede effective antimicrobial delivery, by whichever means. In these cases, surgical exploration for the removal of necrotic tissue and purulent material is mandatory (Fig 6). In cases with an insidious onset or a vague clinical history, it may be difficult to determine when this critical point is reached. Advanced imaging modalities such as nuclear scintigraphy, CT or MRI (Figs 1 and 2) may guide this decision as well as the approach. Rapid referral and appropriate treatment of the cases reported by Lawrence and Fraser (2013) undoubtedly contributed to a positive outcome with antimicrobials alone.

Doxycycline: spectrum of antimicrobial activity and other considerations

Lawrence and Fraser (2013) were successful with their use of doxycycline. This is a semisynthetic, bacteriostatic antimicrobial that reversibly binds to the bacterial 30s ribosomal unit and inhibits microbial protein synthesis. Less antimicrobial resistance and fewer toxic effects (nephrotoxicity) have been reported compared to other tetracyclines (Van Linthoudt et al. 1991; Joshi and Miller 1997). Its antimicrobial spectrum includes Staphylococcus spp. (including S. aureus), Streptococcus spp., Escherichia coli, Klebsiella spp., Salmonella spp., Pseudomonas spp., and anaerobic bacteria such as Bacteroides spp., Fusobacterium spp., Clostridium spp. and Actinobacillus spp. (Ensink et al. 1993; Joshi and Miller 1997); and it is therefore likely to be efficacious against most organisms commonly isolated from O/OM lesions (Firth 1983; Brewer and Koterba 1990; Schneider et al. 1992; Valitsta et al. 1993; Neil et al. 2010).

The value of tetracyclines in treating O/OM in foals is highlighted by Neil et al. 2010: Of the 107 foals for which choice of systemic antimicrobial used and treatment response were recorded, oxytetracycline hydrochloride (5–10 mg/kg bwt I.V. q. 12 h) was the antimicrobial most frequently associated with positive treatment responses. This was the case in 15/31 foals where it was used as the first choice antimicrobial and in a further 24 cases where it was either used as the second or third choice antimicrobial (Neil et al. 2010). Tetracyclines therefore compared favourably with all other single or combined antimicrobial choices reported in that study.

Further, doxycycline possesses anti-catabolic effects on cartilage and synovium (Haerdi-Landerer et al. 2007; Fortier et al. 2010; Schnabel et al. 2011) and has been used extensively in human medicine as an antimicrobial and

Fig 5: Skyline radiographic projection of the left stifle of a 6-month-old American Saddlebred. The weanling presented with acute left pelvic limb lameness and marked effusion of the femoropatellar joint. A lytic bone lesion at the lateral aspect of the patella (arrow) was present. Treatment consisted of a single intra-articular dose of amikacin (500 mg) into the femoropatellar joint and systemic oxytetracycline for 2 weeks. Full recovery was reported.

(Darville and Jacobs 2004; Hark and Smeltzer 2010). Thus, broad-spectrum antimicrobials, in particular the combination of an aminoglycoside and a β-lactam remain the first choice antimicrobials when treating O/OM. Amikacin is very commonly used for local antimicrobial delivery applications, due to its advantageous spectrum of activity for orthopaedic infections, and its concentration-dependent activity (Goodrich and Nixon 2004).

Pharmacokinetic properties of antimicrobials, especially bone penetration, are similar across species. Tetracyclines and most aminoglycosides have excellent bone penetration properties and are frequently used in equine practice (Dowling 2004). Chloramphenicol, with its very broad spectrum of activity and outstanding penetration of bone and synovial structures, is another good choice for the treatment of O/OM. Its application in animals, however, should be restricted to selected cases due to its association with idiosyncratic anaemia in man (Dowling 2004).

Regional variation in prevalence of bacteria and their ability to resist antimicrobial mechanism-of-action will influence and possibly restrict the choice of antimicrobial. Further, sound clinical examination and judgement should guide the choice of a specific antimicrobial protocol. An example of this is initiation of treatment with a macrolide/rifampin combination when O/OM results from extrapulmonary Rhodococcus equi infection. As emphasised in a recent case report by Close et al. (2010), lack of clinical improvement within 2–3 days of initiating antimicrobial therapy should prompt the clinician to reconsider the choice of antimicrobials used. This holds true, even when the choice of antimicrobial medications is based on results of culture and sensitivity analyses (Close et al. 2010).
therapeutic agent to address degenerative diseases, including osteoarthritis (Breedveld et al. 1990; Golub et al. 1991; Ryan et al. 1996). These properties, together with a bioavailability of 70% in horses after oral administration make doxycycline an excellent antimicrobial for treating O/OM in foals (Bryant et al. 2000).

Practical considerations with regard to duration and route of antimicrobial administration

Duration of treatment of AHO in human patients or O/OM in equids appears to be more empiric than evidence-based. Six weeks of oral treatment with doxycycline, as detailed by Lawrence and Fraser (2013), is in line with recommendations found in the human medical literature. However, a general consensus does not appear to exist and recent publications challenge current concepts on duration and initial route of administration (i.v. or oral) of antimicrobial therapy in AHO (Le Saux et al. 2002). Clinical, radiographic and clinicopathological findings should guide duration of treatment in the equine patient. Assuming acceptable tolerance of antibiotics, a period of 5–7 days following resolution of signs of infection provides an additional margin of safety.

Recent advances regarding the local delivery of antimicrobials are thought to be responsible for improved success rates when treating septic arthritis and O/OM in the horse (Ducharme and Mitchell 2004; Goodrich and Nixon 2004). Notwithstanding their positive impact in a large number of cases, their value and practicality need to be assessed on a case-by-case basis. Regional limb perfusion, for example, relies on a functional vasculature and the ability to effectively isolate the affected region. Such novel approaches should not be expected to compensate for poor choice of antimicrobial and this remains the main determinant over success when treating acute O/OM. As already mentioned, bone aspirates and/or synovial fluid samples for culture and sensitivity patterns should be obtained whenever possible. Depending on the patient and lesion site, sampling may necessitate short-term anaesthesia. At the same time, intralesional infiltration (as well as other methods of local antimicrobial delivery) and through-and-through lavage of concurrently affected synovial structures are readily performed. Finally, in cases where a primary source of infection is identified (e.g. infected umbilical remnants) this may be addressed in the same anaesthetic episode, if deemed necessary.

Conclusions

In agreement with the report by Lawrence and Fraser (2013), it is the authors’ opinion that a conservative initial approach, using systemic and local antimicrobial therapy alone, may be warranted in cases of acute septic O/OM. Success with this approach will reduce patient morbidity and costs associated with treatment.

Nonetheless, in accordance with current human medical guidelines, we propose the following indications for surgical lesion debridement: failure to show clinical improvement with conservative management in a timely manner (within 2–3 days); progression of a septic bone lesion (Fig 6); and evidence of abscess or sequestrum formation.

These factors must therefore be monitored closely to assess the response to treatment. Failure to respond not only justifies surgical intervention but should also prompt re-appraisal of the current antimicrobial protocol.
Authors' declaration of interests have been declared.

References


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