

Intravenous regional limb perfusions using erythromycin to treat septic physitis

Ali Mitchell

Introduction

Rhodococcus equi is a gram-positive facultative bacterium which is of global significance in foals and weanlings (Muscatello *et al.* 2007). The most common presentation of disease is pyogranulomatous pneumonia; however, haematogenous spread of the bacteria can result in extrapulmonary disease presentations including enteric and subcutaneous abscessation, septic osteomyelitis/physitis and uveitis (Bordin *et al.* 2022). *Rhodococcus equi* in foals is traditionally treated using a macrolide in combination with rifampin, typically rifampin and clarithromycin. Septic physitis caused by *Rhodococcus equi* carries a poorer prognosis compared to other causative organisms (Ruocco *et al.* 2020). Treatment choice includes the standard combination of systemic antimicrobials along with intravenous regional limb perfusions (IVRLPs) and surgical debridement. The use of erythromycin IVRLPs has only been described experimentally, and there is only one other case report in the literature detailing the use of erythromycin IVRLPs for the treatment of septic physitis caused by *Rhodococcus equi* (Kelmer and Hayes 2009).

Case history

A three-month-old Thoroughbred filly presented for signs of ill thrift and respiratory disease. Bloodwork revealed neutrophilic leukocytosis (white blood cell (WBC) count: $18.30 \times 10^9/L$, reference range (rr): $4.9\text{--}11.1 \times 10^9/L$; neutrophils: $14.56 \times 10^9/L$, rr: $2.5\text{--}6.9 \times 10^9/L$), elevated serum amyloid A (SAA) (1743mg/L, rr: 0–20mg/L) and hyperfibrinogenaemia (8.1g/L, rr: 0.5–4.0g/L). Serum biochemistry revealed increased aspartate aminotransferase (AST) (763 IU/l; rr 0–228 IU/l), lactate dehydrogenase (LDH) (3258 IU/l; rr 0–1830 IU/l) and γ -glutamyl transpeptidase (GGT) (145 IU/l; rr 0–71 IU/l). Ultrasonography of the chest showed diffuse comet tails bilaterally and two small areas of hyper-echogenicity consistent with abscessation. A trans-endoscopic tracheal wash was performed which yielded growths of *Escherichia coli* and a coagulase-negative *Staphylococcus* species. The foal was started on broad-spectrum antimicrobials (ceftiofur 2.2mg/kg IV Q12hr and gentamicin 6.6mg/kg IV Q24hr) based on culture and sensitivity results of the tracheal wash.

Two days later the filly presented for acute right hindlimb lameness (3/5 on the AAEP lameness grading scale). There was marked soft tissue swelling over the medial malleolus (figure 1), which was painful on palpation. Another blood sample was taken which revealed a mild reduction in SAA (1404mg/L) and fibrinogen (6.7g/L), however, WBC count was normal ($8.06 \times 10^9/L$). Radiographs showed lysis of the distomedial tibia including the growth plate. Synoviocentesis of the tibiotarsal joint yielded fluid with a total nucleated cell count (TNCC) of $1.75 \times 10^9/L$. A diagnosis of septic physitis without synovial involvement was made. Treatment with systemic gentamicin (6.6mg/kg IV Q24hr) was continued and IVRLPs with ceftiofur (1.1mg/kg IV Q24hr) were performed for five days. Repeat bloodwork after 5 days showed little improvement, a repeat synoviocentesis of the tibiotarsal joint yielded a TNCC of $3.96 \times 10^9/L$. Due to the lack of clinical response to the treatment and the tracheal wash culture and sensitivity results the filly was switched to marbofloxacin (3.5mg/kg Q24hr PO).

Figure 1A. Marked swelling over the medial malleolus. Figure 1B. The radiograph showing lysis of the distomedial tibia.



The filly was re-assessed 10 days later for pyrexia and 5/5 lameness in the right hindlimb. There was marked effusion of the tarsocrural joint with fluctuant swelling over the distomedial aspect of the tibia. Synoviocentesis of the tibiotarsal joint revealed a TNCC of $46.57 \times 10^9/L$, consistent with joint sepsis. The filly was then referred to MVS Equine Hospital for further treatment.

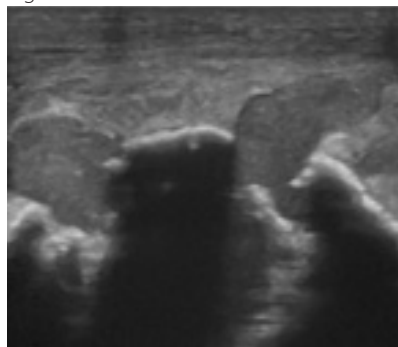
Presentation at clinic

At admission the foal was pyrexia ($39.4^\circ C$), tachycardic (92bpm) and tachypnoeic (64brpm) with harsh lung sounds. Repeat radiographs (figure 2) of the right tarsus showed an increase in the area of radiolucency seen in the distomedial tibia, extending from the medial physis proximally. The lucent area did not appear to extend to the joint. Ultrasound of the fluctuant swelling revealed an abscess (figure 3) with high cellularity, which communicated with the bone defect through a defect in the cortical surface of the distomedial tibia. Bloods at admission to the clinic revealed a normal WBC (9.71×10^9) with an elevated SAA (2523 mg/L) and fibrinogen (6.8 g/L). Serum chemistry abnormalities revealed elevated AST (847 IU/L), LDH (2519 IU/L), and GGT (155 IU/L) although bile acids and glutamate dehydrogenase (GLDH) were noted to be normal (GLDH 3U/L; rr: 1-8U/L, Bile Acids 7umol/L rr: 0-20umol/L).

Figure 2. Radiographs from time of admission at hospital.



Figure 3. Ultrasound of the fluctuant swelling at admission.



The swelling was lanced under general anaesthesia. A large amounts of purulent material was drained, and the bone defect was surgically debrided and irrigated using 1L lactated ringers. An IVRLP was performed using marbofloxacin (0.7mg/kg) diluted in 10ml of sterile water in the saphenous vein distal to the tarsus using proximal and distal Esmarch tourniquets, which were left in place for 20 minutes. A culture and sensitivity swab was taken from the bone, abscess and synovial fluid. The foal was placed in a Robert Jones-style bandage for recovery. The systemic antibiotics were stopped due to the concerns with hepatotoxicity. The filly was started on gastroprotectants (omeprazole 1mg/kg and sucralfate 20mg/kg), liver support including pentoxifylline (9mg/

kg PO Q12hr) and colchicine (30ug/kg Q24hr). Pain relief administered included meloxicam (0.3mg/kg Q12hr), morphine (0.2mg/kg Q12hr) and fentanyl (100ug/hr transdermally). The foal was anaesthetised for the next four days for marbofloxacin IVRLPs to be performed each day.

Culture and sensitivity results from the abscess and bone yielded a growth of *Rhodococcus Equi*. The culture and sensitivity from the synoviocentesis at admission revealed no growth. Systemic antibiotics were started again using clarithromycin (7.5mg/kg Q12hr PO) and rifampin (10mg/kg Q24hr PO). The IVRLPs were switched to using erythromycin as the antimicrobial choice. A 1g vial was dissolved in 60ml of sterile saline (0.9% NaCl). The IVRLPs were performed using an 18g insyte catheter, due to the large volume being infused. The catheter was placed each day and then removed. Repeat blood sample analysis revealed an elevated SAA (2146mg/L) and fibrinogen (7.8g/L), with a normal WBC count (7.37×10^9 /L). Serum chemistry revealed elevated AST (802 IU/L), LDH (2596 IU/L), GGT (122 IU/L); mild hyponatraemia (130mmol/L; rr:132–146mmol/L) and mild hypokalaemia (2.3mmol/L; rr: 2.4–4.7). Intravenous fluid therapy was initiated with 1L lactated ringers' solution Q6hrs for 48 hours to correct the electrolyte disturbances.

Within 24 hours of the change in anti-microbials the filly's pyrexia and tachycardia resolved. The lameness was markedly improved, and she began to bear weight on the limb. The volume of discharge draining from the wound also gradually decreased, as did the soft tissue swelling surrounding the tarsus. A total of four IVRLPs with erythromycin were performed. The filly was discharged after 10 days of hospitalisation. Repeat radiographs at discharge showed an increase in the area of radiolucency. Repeat blood sample analysis revealed an improvement in SAA (1401mg/L) and fibrinogen (6.3g/L), with a mild neutrophilic leukocytosis (WBC count: 11.14×10^9 /L; neutrophils: 7.64×10^9 /L). Serum biochemistry revealed elevated AST (969 IU/L), LDH (4380 IU/L), GGT (117 IU/L). The GLDH (58 U/L) and Bile Acids (29.6umol/L) were now increased. Following these results, vitamin E (500 IU Q24hr PO) was initiated. Due to the improvement seen in inflammatory markers the systemic antibiotics were stopped due to the concern of potential hepatotoxic effects of rifampin (Frank 1990).

The filly remained on strict box rest for the next four weeks. Repeat radiographs at that time showed a decrease in size of the lytic lesion in the bone and a slight increase in density of the lesion. The filly remained 3/5 lame. The bandage was decreased to a single layer bandage and the filly was allowed turn out into a small yard for two hours twice daily. The hock was re-radiographed again one month later – which was three months post hospitalisation (Figure 4). These radiographs showed a marked improvement in both the size of the lesion and radio-density.

Figure 4. Radiograph three months post discharge.



Discussion

As mentioned previously, the use of erythromycin as an IVRLP has been reportedly experimentally in horses and currently there is only one other case report detailing the treatment of septic phytitis associated with *Rhodococcus equi*. IVRLPs are a common ly used treatment method for deep wounds, septic synovial structures, and complicated deep tissue infections (Biasutti *et al.* 2021). They are an easy tool for veterinarians to use in the field, decrease the use of the antibiotic needed systemically and allow for higher concentrations of

antibiotic to be delivered to a specific area (Biasutti *et al.* 2021).

It is recommended that a maximum of 60ml volume is used for a saphenous or cephalic vein IVRLP in an adult horse, and the use of a 23g or 25g butterfly catheter is standard (Mirza *et al.* 2007). However, as the horse in this case was a foal there were concerns regarding the large volume needing to be infused, so an 18 gauge over the needle catheter was placed each time to help ensure vein integrity. Complications of IVRLPs include perivascular leakage of antibiotic, venous thrombosis, haematomas, cutaneous necrosis and cellulitis. The total volume was infused slowly over two minutes (Mirza *et al.* 2007). The most commonly antibiotics used in IVRLPs include gentamicin, amikacin, K-penicillin and ceftiofur sodium (Mirza *et al.* 2007). In this particular case, culture and sensitivity showed a heavy growth of *Rhodococcus equi*. This allowed targeted antimicrobial therapy. Access to intravenous macrolides is limited; therefore, intravenous erythromycin for the IVRLPs was sourced from the local hospital.

Overall, this case is a good example of the use of culture and sensitivity to guide antimicrobial therapy. It also demonstrates the use of IVRLPs for successful treatment of septic physisitis where the prognosis initially given was guarded to poor.

References

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