Management of MRSA septic B arthritis in a dog using a gentamicin impregnated collagen sponge

Methicillin-resistant Staphylococcus aureus septic arthritis occurred in a dog following elective joint surgery for cranial cruciate ligament rupture. Resolution of the infection was assisted by using a surgically implanted absorbable gentamicin-impregnated sponge. M. R. OWEN, A. P. MOORES* AND R. J. COE

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INTRODUCTION

Joint sepsis is a serious and potentially debilitating disease which can occur as a complication of articular surgery in dogs (Bennett and Taylor 1988, Marchevsky and Read 1999). The clinical signs of acute disease can result in severe disability; but the majority of joint infections in dogs are treated and have a good outcome, using appropriate orally administered antibactertial therapy, providing treatment commences before extensive joint damage has occurred (Bennett and Taylor 1988).

However, chronic infections and infected joints in which there is intra-articular non-absorbable suture material may require surgical intervention for resolution (Marchevsky and Read 1999).

The use of antibiotic-impregnated polymethyl-methacrylate (PMMA) beads has proved highly effective in the management of localised bone and soft tissue infections in humans (Henry and Galloway 1995), and in a single dog an indolent infection was successfully treated using gentamicin impregnated PMMA beads (Brown and Bennett 1988).

Using local antimicrobial drug delivery systems, high tissue concentrations of antimicrobials can be achieved without resulting in toxic levels (Dernell and others 1998).

However, a second surgery is usually necessary to retrieve the implants following resolution of infection (Tobias and others 1996). Biodegradable antimicrobial drug delivery systems have been evaluated in the management of orthopaedic infections (Wei and others 1991) and used clinically in humans. More recently, gentamicin-impregnated-collagen sponges (GIGS) have been used for the successful management of septic arthritis in cattle (Hirsbrunner and Steiner 1998, Steiner and others 1999).

While a variety of bacteria have been isolated from septic joints in dogs, the most commonly isolated causal agents are Staphylococcus intermedius and 3 haemolytic Streptococcus species (Bennett and Taylor 1988). Staphylococcus aureus is rarely isolated from canine joints but it is commonly isolated from infected joints in horses (Moore and others 1992) and, in a single horse

wound, infection with methicillin-resistant S aureus (MRSA) has been reported (Hartmann and others 1997).

In dogs, MRSA infection has previously been reported in only 11 cases from three teaching hospitals (Tomlin and others 1999); joint sepsis was a complication of surgery in three of these cases.

This case report describes the identification of MRSA infection in a dog following stifle surgery, and the successful elimination of the infection with the assistance of a GIGS.

CASE HISTORY

Four weeks after a stifle arthrotomy and the placement of an extracapsular mono- filament nylon suture for cranial cruciate ligament rupture, a four-year-old, female neutered English bull mastiff presented with marked right pelvic limb lameness. Routine haematology and biochemistry analyses performed prior to surgery had identified elevated urea (8.2 mmol/litre; reference range 2.0 to 7.0 mmol/litre), creatinine (156 pmol/litre; reference range 100 to 133 pmol/litre) and phosphate (1.46 mmol/litre; reference range 0.75 to 1.25 mmol/litre). On the basis of the serum biochemistry, and in the light of ultrasonographic findings, urinalysis and neeropsy findings of a sibling which had renal failure, a presumptive diagnosis of familial renal dvsnlasia was made.

NB It has not proved possible to reproduce the tables and illustrations that appeared with this article

On clinical examination, there was a pyrexia of 39•80C and the right stifle was effused and painful. Radiographs of the right stifle, obtained under sedation, identified periarticular soft tissue swelling and stifle effusion (Fig 1). A joint fluid sample (Fig 2) revealed a nucleated cell count of 60.8 X 109/litre, of which 92 per cent were neutrophils. Bacterial culture produced a scanty growth of Pseudomonas aeruginosa (Table 1). Systemic antibacterial therapy was instituted using 10 mg/kg enrofloxacm (Baytril; Bayer), orally once daily, and a postoperative course of oral meloxicam (Metacam; Boeinger Ingleheim) was continued at a dose rate of 0.1 mg/kg.

Following the institution of antibacterial therapy, there was an initial improvement in clinical signs. However, at re-examination two weeks later, marked lameness with stifel swelling and pain were again evident. A joint fluid sample taken under general anaesthesia was turbid with low viscosity. The cell count was 78.3 X 109/litre, of which 95 per cent were neutrophils, and intra- and extracellular cocci were identified on microscopic examination of the fluid. A subtotal synovectomy was performed and the extracapsular monofilament nylon ‘stabilising’ suture used in the original cranial cruciate ligament rupture surgery was removed.

The stifle was lavaged with 5 litres of sterile saline using a pulsatile lavage system and a ‘closed system’ drain was placed within the stifle joint using fenestrated tubing (Bennett and Taylor 1988). Bacterial culture of the joint fluid produced a profuse growth of S aureus, and scanty growths of Escherichia coli and an anaerobic bacterial species that was not characterised further (Table 1).

Postoperatively, opioid analgesia was given for 24 hours in addition to meloxicam, as previously. Twice daily 20 mg/kg clavulanate potentiated amoxycillin (Synulox; Pfizer) was given orally, with 20 mg/kg oral metronidazole (Alpharma) once daily in addition to enrofloxacin, as previously. The stifle and the drainage system was managed with sterile dressings and, using sedation, the stifle was flushed with sterile saline once daily for five days. After an additional 10 days, there was minimal clinical improvement and repeat joint fluid analysis revealed a cell count of 144 X 109/litre (90 per cent neutrophils). Bacterial culture and sensitivity identified a multidrug-resistant S aureus (Table 1).

Further sensitivity testing of the isolate at the Public Health Laboratory, Bristol, identified methicillin resistance (Table 1). In order to deliver high levels antimicrobial agent to the joint, intra-articular antibacterial delivery was administered using a GICS (2 mg gentamicin) (Collatamp G; Schering-Plough).Joint fluid aspiration from the infected stifle revealed a large volume of turbid joint fluid. The joint was debrided and lavaged with saline prior to sponge placement. Postoperatively, systemic antimicrobial therapy was switched to 5 mg/kg gentamicin (Pangram; Bimeda), administered intravenously once daily for five days (Brown and Bennett 1988), while giving maintenance intravenous fluids and 10 mg/kg clindamycin (Antirobe; Pfizer), orally twice daily for four weeks.

For two days postoperatively, opioid analgesia was administered as needed, in addition to meloxicam for analgesia. Following institution of this treatment regimen, there was a progressive improvement in limb function. Systemic gentamicin therapy was discontinued after five days in order to reduce the chance of iatrogenic renal damage. Serum urea (6.3 mmol/litre) and creatinine (124 mmol/litre) indicated no evidence of drug-induced renal damage.

Barrier nursing methods (Bennett and others 1992) were used during the hospitalisation period in order to minimise risk to personnel and to other hospitalised patients. Four weeks later, the lameness was markedly improved and signs of stifle discomfort were completely resolved. Repeat joint fluid analysis revealed a cell count of 0.8>(109/litre consisting predominantly of mononuclear cells and lymphocytes). Bacterial culture was negative. Twelve months later, there had been no recurrence of clinical signs.

DISCUSSION

Infection is a potential complication of any surgical procedure and infection rates of 2.5 (Vasseur and others 1988) to 15.6 per cent for orthopaedic procedures (Whittem and others 1999) have been reported in veterinary teaching hospitals. Surgery is a risk factor for the development of septic arthritis, but larger breeds of dogs appear to be particularly predisposed to joint sepsis after arthrotomy (Bennett and Taylor 1988).

MRSA infection is a rarely reported cause of infection in companion animals (Hartmann and others 1997, Tomlin and others 1999). In humans, MRSA infections are a cause for concern because of increasing prevalence, the morbidity of infection and the costs associated with efficacious treatments (Wenzel and others 1991).

Furthermore, the treatment options available are decreasing as further resistance traits develop. Human clinical MRSA infections are usually preceded by colonisation that occurs without

adverse effects (Bonten and Weinstein 1996). MRSA infections in pet owners have been associated with MRSA colonisation in their pets (Scott and others 1988, Cefai and others 1994, Manian 2003) and, consequently, an MRSA-infected pet may potentially pose health risks to its owners.

The dog described in this case was hospitalised and barrier nursing methods were used to prevent transmission of MRSA (Bennett and others 1992) in order to reduce the risk of zoonotic spread of the disease to hospital staff or to the dog's owners. The source of this single case of MRSA infection at the University of Bristol Small Animal Clinic is unknown but chronically colonised hospital personnel can transmit MRSA (Mulligan and others 1993).

As this is the only MRSA infection identified in this clinic to date, it is probable that this infection was from a human source. In a study of 19 cases of septic arthritis, Marchevsky and Read (1999) identified the stifle as the joint most commonly affected in dogs. All 14 of the dogs in this study with stifle sepsis had undergone previous stifle surgery. It was proposed that the stifle joint may be predisposed to infection due to a combination of the large surgical incision frequently used, the long duration of surgery and the related potential for bacterial contamination, and the use of non-absorbable periarticular sutures.

The prognosis for resolution of joint infection is generally good if appropriate antimicrobials, based on bacterial culture and sensitivity, are used (Bennett and Taylor 1988) and if previously placed non-absorbable suture material is removed (Marchevsky and Read 1999). In the case described in this report, indolent bacterial infections occurred despite surgical joint lavage and debridement. In order to improve the chances of eliminating the MRSA infection once it had been identified, intra-articular local antimicrobial delivery was used in addition to appropriate systemic antibacterial therapy, based on culture and sensitivity testing.

Local antimicrobial delivery using PMMA beads achieves higher drug concentrations in the tissue at the site of infection than those achieved using systemic therapy alone and, despite high target tissue concentrations, serum levels do not reach toxic levels (Walenkamp and others 1986). Successful outcomes have been reported using antibiotic-impregnated PMMA beads in indolent joint infections in horses (Holcombe and others 1997), cattle (Butson and others 1996) and in a single dog (Brown and Bennett 1988), but in most cases a second surgery is necessary to retrieve the PMMA beads.

In contrast to PMMA beads, GIGS are absorbed and, in humans, absorption occurs between nine days and three months after implantation (Stemberger and others 1989). Because the gentamicin is neither mechanically nor chemically bound in the Collatamp preparation, its release depends on the rate of collagen breakdown. The relatively rapid rate of gentamicin release which therefore occurs prevents subinhibitory local antibiotic concentrations, which can occur using PMMA beads, and which contribute to bacterial resistance problems (von Hasselbach 1989).

Hence, the GIGS results in prolonged antimicrobial release without the need for future implant retrieval (Steiner and others 1999). Furthermore, the sponge is simple to insert and does not interfere with joint motion. The efficacy of using GIGS alone in the management of joint sepsis is yet to be evaluated and it is currently normal clinical practice to give systemic antibacterial

therapy in addition to local antimicrobial delivery (Brown and Bennett 1988, Holcombe and others 1997, Dernell and others 1998, Steiner and others 1999).

Clindamycin was used systemically in the case described here because sensitivity tests indicated susceptibility to macrolides, such as erythromycin and lincomycin. The dog had previously suffered adverse gastro intestinal responses to erythromycin and lincomycin but not to clindamycin. Because the dog in the present report was client-owned and because the bacteria responsible for the infection were sensitive to drugs that could be safely administered systemically, it was not possible to evaluate the efficacy of the GIGS used alone. Further studies of GIGS for the management of indolent joint sepsis in dogs are justified.

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References
BENNETT. 0. & TAYLOR, D. I. (1988) Bacterial infective arthritis in the dog. Journal of Small Animal Practice 29, 207-230

BENNETT, M. E., THURN, J. R., KLICKER, R., WILLIAMS, C. 0. & WEIlER, M. (1992) Recommendations from a Minnesota task-force for the management of persons with methicillin.resistaflt Staphylococcus aureus. American Journal of In faction Control 20, 42-48

BONTEN, M. J. M. & WEINSTEIN, R. A. (1996) The role of colonization in the pathogenesis of nosocomial infections. In faction Control and Hospital Epidemiology 17, 193-200

BROWN, A. & BENNETT, 0. (1988) Gentamicin-impregnated polymethylmethacrylate beads for the treatment of septic arthritis. Veterinary Record 123, 625-626

BUTSON, R. J., SCHRAMME, M. C., GARLICK, M. H. & DAVIES. i. V. (1996) Treatment of intrasynovial infection with gentamicin-impregnated polymethylmethacrylate beads. Veterinary Record ±38, 460-464

CEFAI, C., ASHIJRST, S. & OWENS, C. (1994) Human carriage of methicillin-resistant Staphylococcus aureus linked with pet dog (Letter). Lancet 344, 539-540

DERNELL, W. S., WITHROW, S. J., STRAW, R. C., POWERS, B. E., WEMBER, E. W., JAMESON. V. J.1 WILKINS, R. M. & ALLEN, R. F. (1998) Clinical response to antibiotic impregnated polymethyl methacrylate bead implantation of dogs with severe infections after limb sparing and allograft replacement — 18 cases (1994-1996). Veterinary and Comparative Orthopaedics and Traumatology 11, 94-99

HARTMANN, F. A., TReSTLE, S. S. & KLOHNEN, A. A. 0. (1997) Isolation of methicillin-resistant Staphylococcus aureus from a postoperative wound infection in a horse. Journal of the American Veterinary Medical Association 2±1, 590-592

HENRY, S. L. & GALLOWAY, K. P. (1995) Local antibacterial therapy for the management of orthopedic infections — pharmacokinetic considerations. Clinical Pharmacokinetics 9, 36-45

HIRSBRIJNNER, G. & STEINER, A. (1998) Treatment of infectious arthritis of the radiocarpal joint of cattle with gentamicin-impregnated collagen sponges. Veterinary Record ±42, 399-402

HOLCOMRE, S. J., SCHNEIDER, R. K., BRAMLHGE, L. R. & EMBERTSON, R. M. (1997) Use of antibiotic impregnated polymethyl methacrylate in horses with open or infected fractures or joints: 19 cases (1987- 1995). Journal of the American Veterinary Medical Association 2±1, 889-893

MANIAN, F. A. (2003) Asymptomatic nasal carriage of mupirocin-resistant, methicillin-resistant Staphylococcus aureus (MRSA) in a pet dog associated with MRSA infection in household contacts. Clinical Infectious Diseases 36, E26-E28

MARCHEVSKY, A. M. & READ, R. A. (1999) Bacterial septic arthritis in 19 dogs. Australian Veterinary Journal 77, 233-237

MOORE. R. M., SCHNEIDER, R. K., KOWALSKI, J., BRAMLAGE, L. R., MECKLENBURG, L. M. & KOHN, C. W. (1992) Horses with musculoskeletal infection during 1979- 1989. Equine Veterinary Journal 24, 450-456

MULLIGAN, M. E., MURRAYLEISURE, K. A., RIBNER, B. S., STANDIFORD. H. C., JOHN, J. F., KORVICK, J. A., KAUFFMANN, C. A. & Yu, V. L. (1993) Methicillin-resistant Staphylococcus aureus — a consensus review of the microbiology, pathogenesis, and epidemiology with implications for prevention and management. American Journal of Medicine 94, 3 13-328

SCOTT, G. M., THOMSON, R., MALONELEE, J. & RIDGWAY, G. I. (1988) Cross-infection between animals and man — possible feline transmission of Staphylococcus aureus infection in humans. Journal of Hospital In faction 12, 29-34

STEINER, A., HIRSBRUNNER, G., MISEREZ. R. & TSCHUDI, P. (1999) Arthroscopic lavage and implantation of gentamicin-impregnated collagen sponges for treatment of chronic septic arthritis in cattle —14 cases (1995- 1997). Veterinary and Comparative Orthopaedics and Traumatology ±2, 64-69

STEMBERGER, A., SORG, K. H., MACHKA, K. & BLüMEL, G. (1989) Technologische und biochemische aspekte von kollagen-implantaten. In: Kollagen als Wirkstofftrager. Eds A. Stemberger, R. Ascher, F. Lechner and G. BIümel. Schattauer, Stuttgard, New York. pp 17-29 Toelss, K. M. S.,

SCHNEIDER, R. K. & BESSER, T. E. (1996) Use of antimicrobial-impregnated polymethyl methacrylate. Journal of the American Veterinary Medical Association 208, 841-845

TOMLIN. J., PESO, M. J., LLOYD, 0. H., HOWELL, S., HART- MANN, F., JACKSON, H. A. & MUIR, P. (1999) Methicillinresistant Staphylococcus aureus infections in 11 dogs. Veterinary Record ±44, 60-64

VASSEUR, P. B., LEVY, J., Dowo, E. & ELIOT, J. (1988) Surgical wound-infection rates in dogs and cats — data from a teaching hospital. Veterinary Surgery ±87, 60-64

VON HASSELBACH, C. (1989) Klinik und pharma-kokinetik von kollagen-gentamicifl als adjuvante lokaltherapie knocherner infektionen. Unfallchirurg 92, 459-470

WALENKSMP, G. H. I. M., VREE, 7. B. & VANRENS, 7. J. G. (1986) Gentamicin-PMMA beads — pharmacokinetic and nephrotoxicological study. Clinical Orthopaedics and Related Research 206, 171-183

WEI, G. X., KOTOURA, Y., OHS, M., YAMAMURO, T., WADA, R., HYON, S. H. & IKRDA, Y. A. (1991) Bioabsorbable delivery system for antibiotic-treatment of osteomyelitis — the use of lactic-acid oligomer as a carrier. Journal of Bone and Joint Surgery — British Volume 73, 246- 252

WENZEL, R. P., NETTLEMAN, M. 0., Josis, R. N. & PFALLER, M. A. (1991) Methicillin-resistaflt Staphylococcus aureus — implications for the 1990s and effective control measures. American Journal of Medicine 91 (Supplement 3b), 5221-5227

WHITTEM, T. L., JOHNSON, A. L., SMITH, C. W., SCHAEFFER, 0. J., COOLMAN, B. R., AVERILL, S. M., COOPER, T. K. & MERKIN, G. R. (1999) Effect of perioperative prophylactic antimicrobial treatment in dogs undergoing elective orthopedic surgery. Journal of the American Veterinary Medical Association 215, 212-216