**Nocardia arthritidis** infection in the distal metaphysis of the metatarsal III and IV bone of a heifer

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**Case Description**—A 19-month-old 536.4-kg (1,180-lb) Brown Swiss heifer was referred for evaluation of a firm swelling over the distal aspect of the right metatarsal region and chronic lameness in the right hind limb.

**Clinical Findings**—Examination of radiographs of the right metatarsophalangeal joints revealed an expansile, smoothly margined, cyst-like lesion within the distal metaphysis of the metatarsal III and IV bone. Differential diagnoses included bone abscess, bone cyst, aneurysmal bone cyst, neoplasia, osteomyelitis, and metabolic bone disease. Aerobic microbial culture of the aspirate yielded moderate growth of branching, gram-positive, rod-shaped bacteria, which were presumptively identified as *Nocardia* spp. The isolate was subsequently identified as *Nocardia arthritidis* by 16S rRNA gene sequence analysis.

**Treatment and Outcome**—The lesion was surgically debrided, lavaged, and bandaged. Exercise was restricted, and systemic and local administration of antimicrobials was instituted. After a communication between the abscess and the metatarsophalangeal joints was iatrogenically created, the extralabel use of aminoglycosides was initiated. The heifer had noticable clinical improvement within 2 weeks after initial evaluation and reportedly had no evidence of lameness and minimal external blemishes 3 months after the second evaluation.

**Clinical Relevance**—To our knowledge, this is the first report on the diagnosis and management of a long-bone abscess attributable to *N arthritidis* infection in cattle. Complications encountered during treatment and the decision to engage in extralabel use of antimicrobial agents in the heifer described here may serve as a guide for food animal practitioners faced with the treatment of valuable cattle. (J Am Vet Med Assoc 2009;234:669–673)

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**ABBREVIATIONS**

<table>
<thead>
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<th>Abbreviation</th>
<th>Description</th>
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<tr>
<td>PMMA</td>
<td>Polymethyl methacrylate</td>
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<td>POP</td>
<td>Plaster of Paris</td>
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A 19-month-old 536.4-kg (1,180-lb) Brown Swiss heifer was referred to our veterinary medical teaching hospital for evaluation of a firm swelling lateral and immediately proximal to the right metatarsophalangeal joint. The heifer was pregnant (5 months of gestation). The swelling was first noticed by the owner 4 weeks prior to referral; however the heifer had been lame in the right hind limb for approximately 5 months. Acute onset of the lameness was reported after the heifer slipped and fell. After an initial evaluation by the referring veterinarian, the heifer was repeatedly treated with flunixin meglumine (1.1 mg/kg [0.5 mg/lb], IV), which resulted in temporary improvement of the lameness. The heifer had noticeable clinical improvement within 2 weeks after initial evaluation and reportedly had no evidence of lameness and minimal external blemishes 3 months after the second evaluation.

During physical examination, an obvious right hind limb lameness was evident when the heifer was walking. The heifer also bore minimal weight on the right hind limb when standing. No skin lesions were detected on the right hind limb. A firm swelling was evident on the lateral aspect of the distal metaphysis of the metatarsal III and IV bone expanding approximately 10 cm distally to the right metatarsophalangeal joint, with a palpably soft area over the center of the swelling. The heifer had signs of pain during manipulation of the swelling. The results of the remainder of the physical examination were unremarkable.

Radiography was performed on the right metatarsophalangeal joint. An expansile, smoothly margined, cyst-like lesion was detected within the distal metaphysis of the metatarsal III and IV bone (Figure 1). Moderate soft tissue swelling was evident in the region of the lesion. The bone lesion was approximately $3.5 \times 5.5$ cm. It was divided by thin bony septae and interrupted the plantarolateral cortical surface of the metatarsal III and IV bone. Based on the radiographic and clinical findings, the list of differential diagnoses included bone abscess, bone cyst, aneurysmal bone cyst, neoplasia, osteomyelitis, and metabolic bone disease.

Ultrasonography revealed that the lesion was irregularly shaped and consisted of numerous confluent, round cavities filled with echoic debris. Blood flow could not be detected within the lesion during examination with spectral wave form, color flow, or power Doppler ultrasonography.
The heifer was sedated with xylazine hydrochloride (0.05 mg/kg [0.023 mg/lb], IV) and positioned in left lateral recumbency on a tilt table. The area was aseptically prepared, and a fine-needle aspirate was obtained with a 16-gauge, 1.5-inch needle by entering the cavity through the aforementioned soft area. A cream-colored, odorless, gelatinous material was collected and submitted for fluid analysis, microscopic examination after application of Gram stain, and aerobic and anaerobic bacterial culture. An additional dose of xylazine hydrochloride (0.05 mg/kg, IV) was administered to the heifer. Three milliliters of a 2% lidocaine solution was infiltrated SC over the soft area of the swelling, and a 3-cm vertical incision was made to penetrate into the lesion. By use of sterile curettes, approximately 100 to 200 mL of the gelatinous material was removed from the cavity, and the fine bony septae were removed by blunt disruption. The cavity was lavaged and packed with 10 ceftriaxone-impregnated PMMA beads prior to placing a sterile bandage over the wound. Fluid analysis of the aspirate revealed abundant necrotic cellular debris and also rare intact neutrophils and macrophages. Examination of the Gram-stained material revealed large numbers of filamentous, gram-positive, beaded, rod-shaped bacteria embedded in necrotic cellular debris. The heifer was started on penicillin G procaine (22,000 U/kg [10,000 U/lb], IM, q 12 h) and discharged to the owner. Instructions were that the heifer be confined to a stall and monitored for signs of increased lameness and that administration of penicillin G procaine be continued until culture results became available. The distal portion of the right hind limb was to be maintained in a clean bandage with a recommendation for bandage changes until a scheduled reevaluation in 2 weeks.

Pending culture results, additional special staining was performed on the aspirate, including the use of periodic acid–Schiff, modified Kinyoun acid-fast, and partial acid-fast stains. The filament did not stain with the periodic acid–Schiff or modified Kinyoun acid-fast stains. However, the structures did stain with the partial acid-fast stain, which was suggestive of Nocardia spp. Aerobic culture yielded a moderate growth of gram-positive, rod-shaped bacteria identified as Nocardia spp. The isolate was submitted to a veterinary diagnostic laboratory for speciation and was identified as Nocardia arthritidis by 16S rRNA gene sequence analysis. Antimicrobial susceptibility testing was not performed. On the basis of the identification of the isolate, systemic treatment with sulfonamides was recommended. The daily treatments with penicillin G procaine were discontinued, and the heifer was given a dose of sulfamethazine (330 mg/kg [150 mg/lb], PO), which was repeated again 3 days later.

The heifer was reevaluated at our facility 15 days after the initial examination. With regard to the lameness condition, the heifer had improved substantially with only a subtle right hind limb lameness still apparent when walking. The owner reported that little discharge was observed during bandage changes, but 2 ceftriaxone-impregnated PMMA beads had come out of...
the incision by the time of the first bandage change. In addition, the owner indicated that the heifer had been improving daily. After physical examination, the heifer was sedated with xylazine hydrochloride (0.05 mg/kg, IV) and positioned in left lateral recumbency on a tilt table. Radiographs were acquired to assess healing and assist with the removal of the previously placed PMMA beads. During removal of the PMMA beads by use of curettes and sponge forceps, the abscess was repeatedly flushed with sterile saline (0.9% NaCl) solution by use of a bulb syringe. During the lavage procedures, it was observed that the dorsal pouches as well as the plantaromedial and plantarolateral pouches of the third and fourth metatarsophalangeal joints, respectively, were distended with saline solution, which was suggestive of a direct communication with the abscess. Radiographic imaging was performed by use of positive-contrast medium. Communication between the abscess and third and fourth metatarsophalangeal joints was confirmed. Although communication between the third and fourth metatarsophalangeal joints is normal in cattle, communication between the abscess and the metatarsophalangeal joints may have been iatrogenic during bead removal and saline solution lavage.

A single PMMA bead was left in place to minimize further disturbance of the bony separation between the abscess and metatarsophalangeal articulations. Because of the apparent joint involvement and considering the risk of septic arthritis, the decision was made to use amikacin-impregnated POP beads. The lesion was thoroughly lavaged with 2 L of sterile saline solution, and the abscess was packed with amikacin-impregnated POP beads. The amikacin-impregnated POP beads had been constituted with 30 g of calcium sulfate hemihydrate, 4 mL (1 g) of amikacin solution, and 5 to 10 mL of PBS solution. A sterile bandage was applied, and the heifer was removed from the tilt table.

In addition to the amikacin-impregnated POP beads, the heifer was started on a 7-day course of gentamicin (6.6 mg/kg [3 mg/lb], IM, q 24 h) and penicillin G procaine (22,000 U/kg, IM, q 12 h). There was a thorough discussion with the owner about the potential for prolonged tissue residues of aminoglycosides. The owner signed an agreement that the heifer would not enter the food supply chain at the time of death or euthanasia and that her milk would be tested for antimicrobials for use in the treatment of nocardiosis has been sulfonamides (with or without trimethoprim). Trimethoprim-sulfamethoxazole was not used in this heifer because ruminants rapidly eliminate this drug. Instead, sulfamethazine was prescribed because it can be conveniently administered by farm personnel and may be used in an extralabel manner in dairy cattle < 20 months old. To avoid tissue residues, the owner was cautioned that the heifer was not to be slaughtered within 8 days after the last treatment, as specified in the package insert of the product that was used.

The treatment of animals with nocardiosis usually involves the use of antimicrobials in conjunction with surgical debridement and establishment of drainage when necessary. Traditionally, the first choice of antimicrobials for use in the treatment of nocardiosis has been sulfonamides (with or without trimethoprim). Other species that cause disease in dairy cattle include Nocardia farcinica and Nocardia neoardiniensis. The treatment of animals with nocardiosis usually involves the use of antimicrobials in conjunction with surgical debridement and establishment of drainage when necessary. Traditionally, the first choice of antimicrobials for use in the treatment of nocardiosis has been sulfonamides (with or without trimethoprim). Trimethoprim-sulfamethoxazole was not used in this heifer because ruminants rapidly eliminate this drug. Instead, sulfamethazine was prescribed because it can be conveniently administered by farm personnel and may be used in an extralabel manner in dairy cattle < 20 months old. To avoid tissue residues, the owner was cautioned that the heifer was not to be slaughtered within 8 days after the last treatment, as specified in the package insert of the product that was used.

Antimicrobial susceptibility testing was not pursued for the isolate of N. arthritidis. Although antimicrobial treatment is ideally supported by results from culture and susceptibility testing, it was not considered practical for this patient. To culture and test the susceptibility pattern of N. arthritidis, lengthy intervals of

Discussion

Results of radiography were used to rapidly provide an answer regarding the size as well as the characterization of the lesion in the lame heifer described here. Differential diagnoses of lytic lesions in long bones that were considered included several plausible ones, such as bone abscess, aneurysmal bone cyst, or neoplasia, and less likely diagnoses, such as osteomyelitis, metabolic bone disease, or bone cyst. With the exception of bone cysts, all of the listed differential diagnoses could result in localized swelling and signs of pain, such as lameness. Bone cysts usually do not cause clinical signs of disease unless a pathologic fracture occurs. Doppler ultrasonography was performed to differentiate between the most strongly considered differential diagnoses of bone abscess, aneurysmal bone cyst, and neoplasia. Lack of blood flow in the lesion made an aneurysmal bone cyst or hemangioma less likely as the cause of the underlying pathologic change. After retrieving copious amounts of white, creamy material from the fine-needle aspirate, the morphologic diagnosis of a bone abscess was made.

Long-bone abscesses in small ruminants have been reported. The bacterial organism in both of those reports was Corynebacterium pseudotuberculosis. To our knowledge, the heifer described here represents the first reported case of N. arthritidis infection in an animal. Nocardia spp are aerobic, gram-positive actinomycetes that are widely distributed in the environment. Most infections with aerobic actinomycetes appear attributable to contact (through trauma or inhalation) with a contaminated environmental source. Nocardia infections are usually opportunistic and have been reported in cattle, small ruminants, pigs, horses, cats, and other domestic animals. Systemic infections, cutaneous and subcutaneous abscesses, and mastitis are the most frequently reported forms of nocardiosis in animals. Nocardia asteroides is the species most frequently isolated from humans and other animals. Other species that cause disease in dairy cattle include Nocardia farcinica and Nocardia neoardiniensis.
several weeks are typically required. In addition, there are no Clinical and Laboratory Standards Institute interpretation guidelines available for antimicrobial susceptibility testing for *N. arthritidis* infections in cattle. Therefore, susceptibility information, even a minimum inhibitory concentration, would not necessarily have been useful in predicting clinical efficacy. Rapid speciation of the isolate and appropriate antimicrobial treatment in accordance with published antimicrobial susceptibility patterns for *N. arthritidis* were regarded as the most time- and cost-efficient approach for this particular patient. However, it must be emphasized that whenever possible, antimicrobial treatment should be based on a susceptibility pattern for the isolate. Prolonged intervals for culture and susceptibility testing, as expected for this particular organism, cannot be used as a rationale for extralabel use of antimicrobials.

At the time of reexamination of the heifer and the discovery of a communication between the abscess and metatarsophalangeal joints, antimicrobial treatment was reevaluated. Facing the substantial risk of septic arthritis from *N. arthritidis* as well as other pathogens, a treatment decision had to be made that balanced the intended use of the heifer with the most effective antimicrobial treatment for septic arthritis. Septic arthritis and its sequelae could preclude use of the heifer as a show animal, which was a high priority for the owner. In the context of AMDUCA, the therapeutic plan was designed to do everything reasonably possible to avoid septic arthritis or provide an appropriate treatment for that condition.17 In return, the owner agreed that the heifer would never be slaughtered for human consumption and that her milk would be tested for residues before it would be sold.

The choice of the most efficacious antimicrobial treatment was based on the isolation of *N. arthritidis* and on the risk of secondary infection of the metatarsophalangeal joints from other potential pathogens commonly associated with septic arthritis in cattle, including *Enterobacteriaceae* spp, *Staphylococcus* spp, and *Arcanobacterium* spp. Alternatives to sulfonamides, including amikacin and imipenem, are efficacious against most *Nocardia* spp.15,19,20 Amikacin is highly effective against most *Nocardia* spp15,19,20 and is highly effective against a broad range of gram-negative bacteria. Therefore, amikacin-impregnated beads were placed in the abscess. Systemic treatment with the combination of penicillin and gentamicin was added to obtain adequate serum concentrations and to broaden the antimicrobial spectrum against various pathogens that can potentially cause septic arthritis. It needs to be emphasized that aminoglycosides should not be used in food-producing animals except in the rarest of situations. Their use in this particular patient was justified because of the potential detrimental consequences of septic arthritis to the heifer’s main intended use as a show animal. The use of aminoglycosides was only considered after obtaining the owner’s signed agreement to ensure that products containing antimicrobial residues as a result of treatment would not enter the human food chain.

Antimicrobial-impregnated beads or collagen sponges can be successfully used to treat cattle with septic arthritis.21,22 The bioabsorbable properties of calcium sulfate, which is a component of POP, made POP beads our preferred choice as the local depository device. Because of the osteoconductive qualities of calcium sulfate, POP beads provide a scaffold for new bone formation and may contribute to faster healing of a large bone defect.23,24

To our knowledge, this is the first report of the diagnosis and management of a long-bone abscess attributable to *N. arthritidis* infection in cattle. The clinical, radiographic, and ultrasonographic findings in this heifer may provide valuable information for the diagnostic evaluation of expansile bone lesions in large animal patients. The complications encountered during treatment and the decision to engage in extralabel use of antimicrobial agents in this heifer may serve as a guide for food animal practitioners faced with the treatment of valuable cattle.

a. Marshfield Clinic Laboratories, Veterinary Diagnostic Services, Marshfield, Wis.
b. SulfaSure SR Cattle Bolus, Boehringer Ingelheim Vetmedica Inc, St Joseph, Mo.
c. MD-76 R, Mallinckrodt Inc, St Louis, Mo.

References


17. US FDA Web site: Animal Medicinal Drug Use Clarification Act
Identification of potential on-farm sources of Listeria monocytogenes in herds of dairy cattle
Hussni O. Mohammed et al

Objective—To elucidate the ecology of Listeria monocytogenes on dairy cattle farms by determining the prevalence of the organism in various samples.

Sample Population—Dairy cattle operations in central New York State.

Procedures—A repeated cross-sectional study design was used. Various samples were obtained from cattle (feces, composite udder milk, and udders), their environment (silage, feed bunks, water troughs, and floor bedding), inline milk filters, and bulk tank milk from 50 dairy farms. Samples were tested for the presence of L monocytogenes by use of a PCR assay with 2 steps of bacterial enrichment. Data were analyzed with mixed-effect logistic regression to control for the potential clustering of L monocytogenes on particular farms.

Results—L monocytogenes was detected in composite milk, udder swab samples, and fecal samples at prevalences of 13%, 19%, and 43%, respectively. There was no significant clustering of the pathogen by farm. Listeria monocytogenes was more common in samples obtained from cattle and the environment during winter and summer versus the fall. The prevalence of L monocytogenes was twice as high in samples obtained from feed bunks, water troughs, and bedding, compared with that in samples obtained from silage (65%, 66%, 55%, and 30%, respectively).

Conclusions and Clinical Relevance—L monocytogenes was more prevalent in samples obtained from dairy cattle and their environment than in milk samples. Strategies to control the pathogen in dairy operations should focus on cow hygiene and sanitary milk harvesting on the farm. (Am J Vet Res 2009;70:383–388)

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