“Dixie’s Disko”

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Introduction

The canine spine is composed of the following vertebra: seven cervical, thirteen thoracic, seven lumbar, three fused sacral, and variable coccygeal. The vertebral bodies of C2-S1 as well as the coccygeal vertebrae are connected by an intervertebral disk.[1] The disk serves to transfer compressive forces between the vertebral bodies. The intervertebral disk provides structure and stability but also flexibility for the spine.[10] The intervertebral disk is composed of a nucleus pulposus, annulus fibrosus, transition zone and cartilaginous end plates.[1] The nucleus pulposus is located centrally within the disk and is a mucoid consistency. This portion does not have a direct blood supply. The annulus fibrosus surrounds the nucleus pulposus and is a dense, fibrous consistency. The outer layers of this portion have a minimal blood supply while the inner layers have no direct blood supply.[1] The transition zone changes from fibrous to cartilaginous material and connects the nucleus pulposus and anulus fibrosus. The cartilaginous end plates form the cranial and caudal margins of the disk.[1, 10] The end plates are stippled with pores that facilitate diffusion of nutrients to the remainder of the disk.[1] The end plates are supplied with blood via a capillary bed with decreased blood flow velocity. When infectious agents hematogenously spread to these areas, the minimal blood supply and pores present within the end plates create an excellent environment for infection to perpetuate. Infection of the intervertebral disc and the adjacent vertebral end plates is referred to as diskospondylitits.

History & Presentation

The literature reveals that diskospondylitis is overrepresented in large breed, male dogs.[2, 5] Presentation may vary greatly depending on location, severity and chronicity of infection. Clinical signs may range from mild spinal hyperesthesia to ataxia, proprioceptive deficits, paresis

or paralysis.[2, 5, 8] Cases most commonly present with moderate to severe spinal hyperesthesia.[2] Some patients may present with systemic signs such as fever, lethargy and anorexia.

Dixie, an approximately eight year old, female spayed mixed breed dog, presented to Mississippi State University College of Veterinary Medicine Veterinary Specialty Center on 12/18/20 for reluctance to stand, severe pain, and a non-weight bearing lameness of the right pelvic limb. The owners reported that Dixie had been lame in the right pelvic limb for the past few months. She was initially given fish oil as a supplement for joint health but this did not help the clinical signs. Approximately 2 weeks prior to presentation, Dixie had been playing outside with her housemate and she became acutely non-weight bearing lame in her right pelvic limb. She was noted to be painful and very reactive when touched in the hindquarters. The owners note that the right pelvic limb was held close to Dixie's body, and she frequently vocalized with even the slightest movement. On 12/3/20, Dixie was seen by her primary veterinarian. Radiographs were performed and she was diagnosed with diskospondylitis and possible intervertebral disk disease. She was tested for Brucella and the results were negative. At this time, Dixie was placed on the following medications: gabapentin (13 mg/kg PO Q8,) Tylenol IV (unknown dose), tramadol (2.2 mg/kg PO Q8), methocarbamol (22 mg/kg PO Q8), clindamycin (13 mg/kg PO Q12) and enrofloxacin (unknown dose). At the time of referral, the owners felt that Dixie was only slightly more comfortable on the medications and still severely affected by her lameness and pain. Dixie progressed and became unwilling to rise at all. Dixie was seen by a specialty hospital on 12/4/20 and 12/5/20 for severe pain, consistent vocalization and anorexia. Her medications were continued and Entyce was added (3 mg/kg PO Q24).

On presentation, Dixie was anxious but alert and responsive. She weighed 22.8 kg and had a body condition score of 5/9. She had a mildly elevated rectal temperature of 102.9^{o} F, a

pulse of 112 beats per minutes and respiratory rate of 36 breaths per minute. A grade III/VI right-sided systolic heart murmur was appreciated on auscultation. No crackles or wheezes were identified. An abrasion was noted on the lateral aspect of the left elbow, and erythema and alopecia were noted in the region of the left stifle. The inguinal region was also noted to be diffusely erythematous. The remainder of her general physical examination was within normal limits.

On neurologic examination, Dixie was mentally appropriate. She was very reluctant to rise and ambulate with a non-weight bearing right pelvic limb lameness. Her cranial nerves were unremarkable. Postural reactions were challenging to assess due to severe patient discomfort. However, proprioceptive placing was normal in the thoracic limbs and left pelvic limb. The right pelvic limb was unable to be assessed due to a nerve root signature and non-weight bearing status. Her segmental reflexes were normal in all limbs and her perineal reflex was also normal. Discomfort was elicited on palpation of the cranial lumbar and lumbosacral regions and she became highly reactive and vocalized on gentle manipulation of the right pelvic limb.

Differential Diagnosis & Diagnostic Approach

Dixie originally presented to her family veterinarian for "hind limb lameness." At initial presentation, it would be important to consider all differentials for pelvic limb lameness. In a broad sense, they may be broken down into skeletomuscular and neurologic causes. Skeletomuscular differentials include: fractures/luxations, osteoarthritis, bone tumors and soft tissue injuries. The most important differential to rule out for hind limb lameness is rupture of the cranial cruciate ligament. A variety of neurologic differential diagnoses may be considered depending on the individual presentation. Possible differentials include intervertebral disc

disease, neoplasia, meningitis/myelitis, vertebral instability/subluxation, osteomyelitis, and lumbosacral stenosis.[5, 9]

Initial diagnostics for this presentation include thorough physical exam, orthopedic exam and neurologic exam. These assessments alone will help prioritize further diagnostic testing. Radiographs of the affected hind limb will likely be performed initially and show no abnormalities that explain the lameness. Spinal radiographs are the next indicated imaging modality.[5] These radiographs will most commonly display destructive and proliferative lesions.[12] Radiographic changes are reported to frequently be delayed approximately 2-6 weeks after onset of infection.[5] This may make early diagnosis difficult. Early changes may include lysis of vertebral end plates and narrowed disk spaces.[12] In more chronic cases, there may be marked osteolysis, vertebral fracture/luxation, and vertebral collapse. The most commonly affected site is L7-S1.[5] T13-L1 and C6-C7 are also reported in the literature.[5]

The following laboratory tests are indicated: complete blood count, chemistry panel, urine culture and sensitivity, blood culture and Brucella testing.[5, 8, 14] These may or may not be helpful in determining a diagnosis. The complete blood count may reveal an inflammatory leukogram or left shift. The chemistry panel may reveal abnormalities related to the underlying source of infection, such as the urinary tract. The urine culture and sensitivity and blood culture are considered part of the minimum database for diagnosis of diskospondylitis. It is reported that blood cultures are positive in approximately 45% to 75% of dogs with diskospondylitits.[9] Similarly, only 25% to 50% of dogs with diskospondylitits have a positive urine culture.[9] There is a positive serology for Brucella canis in approximately 10% of dogs with diskospondylitis.[14] Immunofluorescent assay (IFA) or Polymerase chain reaction (PCR) testes should be performed for confirmation of brucellosis.[9]

Further imaging, if available, may be indicated for confirmation of diskospondylitis. Computed tomography (CT) is a helpful diagnostic due to its detailed depiction of bone. CT findings are similar to radiographic findings and most commonly reveal irregular bone lysis of the affected vertebrae and adjacent end plates.[4, 14] Magnetic resonance imaging (MRI) may also be indicated but is less commonly used.[14] An ultrasound of the abdomen and heart may be helpful to determine the underlying cause of infection.[5] If no infectious organism is isolated, an ultrasound or CT guided aspirate of the disk space may be obtained.[14] This sample may be submitted for cytology and culture and sensitivity.

Dixie had lateral radiographs obtained of her right pelvic limb. No abnormalities were noted. Spinal radiographs were also performed at her primary veterinarian. They revealed narrowing of the intervertebral disc spaces at L2-L3 and L7-S1. There is also end plate lysis and adjacent sclerosis at these locations. Incidentally, there is also spondylosis deformans noted at these locations. We performed a minimum database including: complete blood count, neurochemistry panel, urinalysis, urine culture, blood culture and Brucellosis RSAT. The complete blood count was unremarkable and the only notable abnormality on the neurochemistry was a mildly elevated ALP of 165 (rr: 11-140). No bacteria were seen on urinalysis and the only abnormalities were trace protein and trace SSA. The urine culture revealed no growth after 48 hours. The blood culture revealed no growth after 5 days. The Brucellosis RSAT also returned negative. Dixie had a CT scan performed and severe diskospondylitis was noted at L2-3 and L7-S1. There was also a bulging disk at L7-S1.

Pathophysiology

Diskospondylitis is most commonly caused by hematogenous spread of bacterial infection.[9] The most commonly isolated infectious agents are staphylococcal organisms.[5] Other

common agents include: streptococcus, E. coli and B. canis.[5,8,9] Brucella canis is of special interest due to its zoonotic potential and public health concern.[5,8,9] In humans, Brucella canis may cause fever, chills, malaise, peripheral lymphadenomegaly and splenomegaly.[7] The following bacteria are less common but still reported in the literature: klebsiella, pseudomonas, proteus, actinomyces, Pasteurella and mycobacterium.[5] Diskospondylitis may less commonly be caused by fungal infection, including: candida and aspergillus.[5] These cases are usually more severe and the prognosis is worse.

The most common underlying source of infection causing diskospondylitis is a urinary tract infection.[5,8,9] Other common sources of infection may include: dental/oral, respiratory and endocarditits. Foreign body migration, penetrating wounds and abscesses have also been reported. Very few iatrogenic causes of diskospondylitis have been reported in veterinary literature.[3,11] These include diskospondylitis secondary to epidural injections and spinal surgery. There are several risk factors that have been identified for development of postoperative diskospondylitis (POD) in dogs. Dogs with disk protrusion are 4.5 times as likely to develop POD as dogs with disk extrusion.[3] German shepherds have been noted to be 9.8 times as likely to develop POD as other breeds.[3] Dogs over 8.8 years old and weighing over 20 kilograms are considered at risk for developing POD.[3] In human medicine, postoperative spondylodiskitits is reported to occur in 0.1% - 3% of patients.[3] Human postoperative spondylodiskitits (POS) and veterinary postoperative diskospondylitis (POD) refer to the same pathologic process.[3]

Treatment & Management Options

The mainstay of therapy for diskospondylitis is utilization of an appropriate antimicrobial for an appropriate duration of time. Cephalosporins provide excellent coverage for the most commonly implicated etiologies.[5] Therefore, these antibiotics are often used empirically while

awaiting culture/sensitivity results. The most commonly utilized first line therapies include: Cephalexin (20-30 mg/kg PO TID), Amoxicillin-clavulanate (12.5-25 mg/kg PO BID-TID), Oxacillin (15-25 mg/kg PO TID-QID) and Cefazolin (20-25 mg/kg IV, IM or SC QID).[5] In rare cases of fungal diskospondylitits, Ketoconazole (10 mg/kg PO BID) and Fluconazole (5 mg/kg PO BID) are recommended.[5] Canine Brucellosis is very difficult to treat and infected dogs are usually considered infected for life.[7] However, the recommended treatments include: Enrofloxacin (10-20 mg/kg PO SID), Doxycycline (20-25 mg/kg PO BID) or Tetracycline (10-20 mg/kg PO TID).[5] The other components of treatment may include: multimodal pain management, supportive care for underlying conditions (urinary tract infection, endocarditis, etc.), restricted activity and physical therapy.[5,8,9,14] In severe cases, surgical decompression may be necessary.[14]

On 12/18/20, Dixie was hospitalized and started on the following medications: lactated ringer solution (57 ml/hr), Fentanyl (3 mcg/kg/hr), Cefazolin (30 mg/kg IV Q8), Gabapentin (17.5 mg/kg PO Q8), Tylenol 4 (1.97 mg/kg PO Q8), and Trazodone (3.2 mg/kg PO Q8 PRN). She was pain scored every four hours and given a physical exam every 12 hours. Initial instructions were to walk Dixie with a sling every six hours but this was not possible due to her pain level. She urinated in the kennel through the evening and special care was taken to clean her and change her bedding. By the next morning, Dixie would tolerate gentle palpation of her right pelvic limb. However, she was still extremely painful and vocal when attempts were made to move her. She showed no interested in food or water. On 12/20/20, Diazepam (0.44 mg/kg PO Q8), Entyce (3 mg/kg PO Q24) and Carprofen (2.2 mg/kg PO Q12) were added. On 12/21/20, Amantadine (4.4 mg/kg PO Q24) was added and Trazodone was discontinued due to mild patient sedation. Fentanyl was decreased from 3 mcg/kg/hr to 2 mcg/kg/hr. Throughout the day, Dixie

became more painful. That evening, she did begin eating but still appeared very painful. Her Fentanyl was increased back to 3 mcg/kg/hr. During the night, Dixie displayed aggression and seemed more painful. A Ketamine CRI was started at 5 mcg/kg/min. That evening, she was monitored for an elevation in temperature. It remained within within normal limits. At this point, Dixie was not responding to therapy as strongly as we had anticipated. On 12/22/20, she was changed from Cefazolin to Cefpodoxime (9 mg/kg PO Q24). All other medications remained the same, including the Ketamine CRI. Her temperature was monitored every six hours and remained within normal limits. On 12/23/20, Trazodone was restarted at (3.2 mg/kg PO Q12 PRN) and Amantadine was increased from once daily to twice daily. Dixie was now eating more consistently and appeared more comfortable. The Ketamine CRI was discontinued at 8 pm. Dixie remained comfortable and her Fentanyl CRI was discontinued at 2 am.

On 12/24/20, Dixie was discharged to be managed and monitored at home. She was discharged with the following medications: Cefpodoxime (9 mg/kg PO Q24) for approximately 6 months. Instructions were given for tapering schedule of Gabapentin at (17.5 mg/kg PO) Q8 for 21 days, Q12 for 7 days, Q24 for 7 days and then discontinue. Tylenol IV (1.97 mg/kg PO Q8), Diazepam (4.4 mg/kg PO Q8) and Carprofen (2.2 mg/kg PO Q12) were given for 14 days. Amantadine (4.4 mg/kg PO Q12) was given for 7 days. Entyce (3 mg/kg PO Q24) was given for 5 days. Trazodone (3.3 mg/kg PO Q12) was instructed to be given as needed. The owners were instructed to keep Dixie strictly rested for the next 4-6 weeks. If Dixie did well over this time, we discussed that she should be gradually returned to normal activity after this rest period. We recommended a recheck examination at 4 weeks from discharge.

Case Outcome

Approximately 2 weeks after discharge, Dixie's owners called to report that she was very comfortable at home and did not appear painful at this time. We recommended a gradual decrease in her pain medications but emphasized that her antibiotic could not be discontinued at this time. Dixie responded well to her pain medications being discontinued. Dixie did not return for her recommended recheck exam at 4 weeks after discharge. At approximately 4 months after discharge, Dixie is still doing well at home. She remains on her antibiotics but is comfortable without any pain medications. She is now ambulating normally and appropriately around her home.

Discussion

Prior to presentation, Dixie had a several month history of lameness of the right pelvic limb. Her pain level was severe and further complicated by its chronicity. Multimodal pain management was an essential aspect of her treatment. The chronic and potentially neuropathic component of her pain proved to be challenging to control. In addition to an opioid and nonsteroidal anti-inflammatory, Dixie was started on Gabapentin, Amantadine and Ketamine. There is minimal research on chronic pain in veterinary medicine but these medications are considered valuable options. Gabapentin's mechanism is not entirely understood but it is understood that it decreases neurotransmission by binding to and blocking presynaptic, voltage-activated calcium channels.[6] Amantadine is an antiviral N-methyl-D-aspartate (NMDA) antagonist.[6] When used alone, it is not considered effective. However, there are reports of effective analgesia when used in combination with opioids and/or NSAIDs. Ketamine is a dissociative NMDA receptor antagonist.[15] The NMDA receptors in the spinal cord contribute to wind up pain and make NMDA antagonists valuable options for multimodal therapy.[15]

It is well understood that antibiotic treatment must be continued long term. However, there is no clear description in the literature of exactly how to determine this length of treatment. One study cited the mean treatment time as approximately 13.5 months.[5] The most common recommendation is to treat several weeks past the resolution of clinical signs. However, it is also recommended to recheck radiographs every 4-8 weeks until radiographic signs have resolved.[5,13] One study found that dogs less than one year of age showed radiographic resolution within 4-6 weeks.[13] However, mature dogs took several months to show radiographic resolution. Many of these adult dogs showed a delay between time to clinical improvement and radiographic resolution. For clients that are open to pursuing every option available, radiographic monitoring would be ideal. In Dixie's case, recheck examination was declined.

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