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SEPTIC ARTHRITIS AND OSTEOMYELITIS
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Incidence and risk factors
Septic arthritis is a common consequence of bacteremia and septicemia in foals. In one study, septicemia was the most common cause of death (30%) in foals under 7 days of age. In the same study, septic arthritis was identified as the cause of death in 12.5% of foals aged 8 to 31 days. In adults, septic arthritis is the result of wounds, following joint injections, following surgery, or rarely, hematogenous. Establishment of infection depends on several factors including host defense, virulence of the organisms, and local joint factors. In foals, host defense is mainly associated with passively acquired immunity. Failure of transfer of passive immunity (FTPI) is the highest risk factor for development of septicemia in foals. Organism virulence is related to the ability to establish infection. Attachment factors, ability to resist phagocytosis, or resistance to cell killing all contribute to establishment of infection. Local joint factors that may predispose to establishment or maintenance of infection include low blood flow, particularly in end-loop capillaries, or poor blood supply, which is more a factor in bone. Certain intra-articular medication such as corticosteroids, hyaluronan, and polysulfated glycosaminoglycans have been associated with a higher risk for septic arthritis potentially by decreasing articular defense.

Pathogenesis
Articular blood supply is provided through a main arteriole that branches to the synovial membrane and epiphysis. Blood supply to the metaphysis is provided by the nutrient artery, but in young foals, transphyseal vessels exist that connecting the metaphyseal and epiphyseal blood supply. Intravenous injection of bacteria results in rapid inoculation of articular and peri-articular capillaries. Four types of hematogenous articular infection have been described in foals: Type S (synovial), where a septic arthritis resulting from inoculation of the synovial membrane is present; type E (epiphysis) where subchondral bone infection is present; type P (physis) where infection of the physis on the metaphyseal side of the growth plate is identified; and type T observed in premature foals, where infection of the small tarsal or carpal bones is seen. In young foals, functional transphyseal vessels allow communication of the metaphysis and epiphysis, such that bacteria localize preferentially in the synovial membrane and subchondral bone. Thus young foals suffer from predominantly from type S and E infectious arthritis. Closure of transphyseal vessels occurs approximately after 7-10 days of age, such that localization of infection to the metaphyseal vessel loops occurs in older foals. Although bone inoculation can occur simultaneously to synovial inoculation in young foals, identification can be delayed because of a delay in radiographic identification of lesions.

In adults, inoculation of the joint through a wound, joint injection or surgery will result in infection depending on inoculum size, concurrent use of drugs that decrease host defense, or inoculation by a particularly virulent bacterial strain. Once established, infection will persist because of sequestration within fibrin, and decreased blood flow because of effusion or capillary sludging. Articular cartilage proteoglycan depletion can
be identified within hours of infection.\textsuperscript{8} Gross cartilage lesions can develop in a few weeks, leading to joint instability and osteoarthritis.

\textbf{Diagnosis}

Septic arthritis, osteomyelitis, or physitis should be ruled out in any lame foal. Foals with septicemia are at high risk of developing septic arthritis, which generally is noted clinically hours to days after the initial signs of septicemia. Although owners often complain of external trauma, septic arthritis is the most common cause of lameness in foals. In young foals with types S and/or E arthritis, inoculation of the synovial membrane is the first event, which can be identified by the astute clinician as periarticular edema. Joint effusion rapidly follows. Multiple joint involvements are common, and identification of all affected joints is essential for successful management. Effusion of the shoulder, elbow, or hip joints is more difficult to discern, therefore arthrocentesis of these joints should be performed in any unidentified lameness. In the stifle, femoro-patellar joint involvement results in marked effusion. Femoro-tibial joint effusion is usually more difficult to discern. Because of the usual communication between the femoro-patellar and the medial femoro-tibial joint, both are usually involved concurrently. Lateral femoro-tibial infection is more subtle to discern and can occur separately. Distension of the long extensor pouch is often present in lateral femoro-tibial infection, and is a clue to involvement of that joint. In older foals (>7 days) physeal infection may be observed. The presence of concurrent synovial effusion depends on the intra or extraarticular localization of the growth plate. For example, distal metacarpal physeal infection results in periphyseal edema, initially without joint effusion. In septic arthritis in foals, laboratory data is consistent with infection, and includes a neutrophilic leukocytosis, and a high fibrinogen concentration.

In adults, any wound that has the potential for involvement of a synovial structure should be investigated. The joint (or tendon sheath) should be prepared aseptically at a site remote from the wound, and injected until distention is obtained. Identification of the injected fluid exiting the wound is evidence for joint communication. This step is critical and should be performed as early as possible when evaluating a wound. In one study,\textsuperscript{9} septic arthritis developed in 53% of horses with open joint injuries if joint involvement was identified within 24 hours to 92% if identification was delayed by 2 to 7 days. Arthrocentesis is the mainstay of diagnosis of septic arthritis.\textsuperscript{10} A high protein concentration (>2.5 g/dl), and a high leukocyte count are observed. Classic counts diagnostic of septic arthritis exceed 30,000 cells/\textmu L, with greater than 90\% neutrophils. Neutrophils are rarely degenerate. A gram stain is a useful diagnostic tool, as it may identify the etiologic agent in up to 25\% of cases where culture results are negative.\textsuperscript{11} In foals with a separate physeal infection, where the physis is extra-articular, a sympathetic joint inflammation and effusion can occur.\textsuperscript{12} This is manifested by a moderate increase in white blood cell count, with <90\% neutrophils. The presence of such should alert the clinician to the presence of physeal sepsis.

Radiographs of all affected joints are essential. The presence of osteomyelitis may affect prognosis, or at least dictate prolonged antibiotic therapy. Radiographs should be repeated on a weekly basis until resolution of clinical signs, or any time there is deterioration in the clinical condition.
Nuclear scintigraphy has been used to diagnose infectious foci in odd localization in foals. For example, vertebral and atlanto-occipital involvements have been diagnosed using this imaging modality. It is to be remembered that local bone infarcts will result in areas of decreased rather than increased uptake. Scintigraphy using technetium-99m labeled white blood cell or ciprofloxacin labels have potential uses in foals with multiple limb involvement, and warrant further investigation as imaging modality for septic arthritis. Newer imaging capabilities such as MRI or computed axial tomography may evolve as diagnostic modalities in septic arthritis.

Identification of the organism should be attempted in all cases of septic arthritis. Gram stains, culture of the synovial fluid collected in blood culture bottles, and of synovial biopsies have all been suggested to increase the likelihood of identification of the organism. In general, the positive culture rate from synovial fluid samples is approximately 50%, and synovial biopsy culture have a low yield to increase this figure. Because bacteremia or septicemia precedes the local signs, blood cultures should be obtained. In addition, culture of any other local sites of infection should be performed. In cases of septic physitis, needle aspiration of the affected bone under radiographic or fluoroscopic guidance should be performed.

Treatment

Septic arthritis is an emergency. Immediate assessment and institution of treatment should be performed. In foals, the systemic condition must be addressed. Management of failure of transfer of passive immunity, and all other problems associated with foal septicemia, should be done.

The principles of treatment of septic arthritis: systemic broad-spectrum antibiotics; local joint lavage and debridement; and local antibiotics. Initial antibiotic treatment should be based on knowledge of commonly isolated organisms. The most common organisms isolated in foal septic arthritis are: Actinobacillus sp; E.coli; Klebsiella sp; Pseudomonas sp; and Salmonella sp. In older foals, gram-positive organisms such as Strep sp may be isolated. In older foals with physeal lesions Rhodococcus equi or Salmonella sp are often involved. In young foals, systemic antibiotics should be effective against gram-negative organisms. A combination of a B-lactam and an aminoglycoside is a good choice, until results of culture are obtained. In older foals, gram stains of a physeal aspirate or of a trans-tracheal wash are helpful to identify R. equi. If present, appropriate therapy with erythromycin or azythromycin and rifampin should be instituted. The presence of osteomyelitis may warrant the use of an antibiotic combination that reaches effective bone levels. Rifampin is often used for that purpose. Other antibiotics that reach effective bone concentrations include tetracyclines, chloramphenicol, and cephalosporins. Third-generation cephalosporins should be used, as they are more effective against gram-negative bacteria. Fluoroquinolones should not be used in foals, as there is enough evidence of cartilage lesions developing in immature animals with the use of this class of drugs.

In adults, organisms that will be cultured from open wound injuries include Enterobacteriaceae (26%), gram positive organisms (Staph and Step), and importantly anaerobic organism (26%). Therefore broad spectrum antibiotic therapy should include antibiotics effective against anaerobic organisms such as metronidazole.
Local lavage can be performed by through-and-through needle technique, with the foal under heavy sedation or short-term intravenous anesthesia. This technique may be sufficient in joints where the diagnosis was made early, where the infection is not severe, and in simple joints (fetlock, carpus). In joints with multiple compartments (stifle, hock), in cases of severe infection, or in cases of longer duration or lack of response to joint lavage, arthroscopic debridement is indicated. Arthroscopy has several advantages over simple needle lavage. It allows thorough debridement, removal of fibrin and lavage of all compartments; and it allows evaluation and debridement of cartilage lesions. Arthroscopy may have prognostic value in cases where radiographic lesions are equivocal. Arthrotomies improve joint drainage and should be performed without hesitation if there is evidence of fibrin accumulation (which can be imaged by ultrasonography), recurrence of joint effusion, or if two subsequent daily needle lavage fail to improve the condition.

Intra-articular antibiotics are advocated for the management of septic arthritis. Aminoglycosides have been shown to maintain levels above MIC for 24 hours following a single intra-articular injection. Other local treatment modalities include antibiotic-impregnated polymethylmethacrylate (PMMA) beads, or biodegradable antibiotic-impregnated disks. PMMA implants are fabricated by mixing the desired antibiotic with the powder before adding the polymerizer. Tetracyclines do not elute from PMMA and should not be used. The implant is then molded into beads and strung on non-absorbable suture material. The implant is placed into the affected joint or bone, and elution usually persists for approximately 7 days, after which the implant is removed. Regional intravenous (RIP) or intraosseous perfusion (ROP) have recently been advocated for the treatment of septic arthritis complicated with osteomyelitis. The techniques are performed by placing a tourniquet above and below the region of interest. For RIP, a regional vein is catheterized whereas for ROP, an intraosseous screw is inserted. The antibiotic is then injected and the tourniquet is left insufflated for 30 to 45 minutes. Currently, there is no evidence of increased bone antibiotic delivery by these methods compared to intra-articular administration, but comparative studies in osteomyelitic bones have not been performed.

In the case of extensive physeal lesions, curettage, bone graft and external coaptation may be required. Angular limb deformities may result from growth disturbances, or collapse of the physis on the affected side.

Prognosis

Prognosis for septic arthritis should always be guarded. Elements that will influence prognosis are: systemic condition of the animal; number of joints involved; localization of joint involvement; severity of the infection; early vs delayed identification and institution of treatment; presence of osteomyelitis; and virulence of organisms. In one study, 73/93 (78%) of foals survived to discharge, but only a third reached racing performance. Isolation of Salmonella sp and multisystem diseases were negatively associated with survival and ability to race. Clients should be forewarned of the high cost of treatment.
References