Infective Arthritis – Stepwise Approach - Diagnosis and Management

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Staphylococcus aureus, Neisseria gonorrhoeae, and other bacteria are the common causes of infectious arthritis. *Klebsiella pneumoniae, Pseudomonas, Fusobacterium necrophorum* infective arthritis also reported.[1-3] Various mycobacteria, spirochetes, fungi, and viruses also can infect joints. Since acute bacterial infection can rapidly destroy articular cartilage, all inflamed joints must be evaluated without delay to exclude noninfectious processes and to determine appropriate antimicrobial therapy and drainage procedures.

CLINICAL MANIFESTATIONS

The presentation of infectious arthritis varies with age. In infants, the symptoms are usually systemic rather than local.[4,5] Children develop high fever and are usually ill. The clinical features are more of systemic like fever rather than local arthritis. Older children may be febrile, unwell, but local signs are also prominent. Distension of joint capsule and increased intra-articular pressure contribute to joint pain. Joint is usually held in a position of flexion. Adults and elderly patients with osteoarthritis and rheumatoid arthritis are at a greater risk of acute septic arthritis. The lower extremities are more often affected, particularly hip and knee joints. Patients generally have severe pain and are reluctant to move and put weight on the joint. [6]

The joint capsule is distended, warm and often reddened and edematous. If infection is detected and treated during the first 2-3 days the outcome is favorable and there is no mortality.

The classic presentation of nongonococcal bacterial arthritis is the abrupt onset of a hot, painful, and swollen joint (Red-hot joint).[7-9] There will be an obvious joint effusion and marked restriction of active and passive movements. Nearly 10 to 20% are polyarticular. Polyarticular septic arthritis has an associated systemic illness, particularly RA.[7,10] The knee is the joint most often infected in adults, it is the site of more than 50% of all cases of nongonococcal bacterial arthritis. Hips are more often infected in children. A prior history of intravenous drug use, sexually transmitted disease, immunosuppression, or extraarticular signs of sepsis are suggestive of bacterial arthritis.

Acute bacterial arthritis present with fever, but it may be unimpressive. Shaking chills are unusual and are more common in patients with positive blood cultures. Prior episodes of acute monoarthritis suggest crystal-induced synovitis. A typical rash and potential tick exposure suggest Lyme disease. Viral arthritis, mycobacterial and fungal infections, acute traumatic and hemorrhagic arthritis, and acute presentations of systemic rheumatic diseases such as Reiter's syndrome and rheumatoid arthritis (RA) need to be considered, as differential diagnosis. Pseuodoseptic arthritis is most often caused by a single joint exacerbation of rheumatoid arthritis, although it has been reported in psoriatic arthritis and Reiter's syndrome. Other rheumatic disorders that may mimic bacterial arthritis include transient regional osteoporosis, polymyositis, polymyalgia rheumatica, and bacterial endocarditis. An indolent initial presentation of bacterial arthritis is more common in patients with preexisting rheumatic illness, those who are immunocompromised, and patients with rapidly fatal septicemia.

PATHOPHYSIOLOGY

In development of septic arthritis bacteria need to reach synovial membrane. This happens in several ways. First, bacteria reach the joint from a remote infectious focus (via the hematogenous route). Such foci are usually abscesses or infected wounds in the skin, teeth, upper or lower respiratory tract infections, urinary or intestinal tract infections or endocarditis. In few cases no obvious primary focus is noted, a common experience in septicemia. The bacteria reach the deep vascular plexus terminating in the looped capillary anastomosis (circulus articularis vasculosus).[11,12]

Second route, particularly common in small children, is a dissemination of bacteria from an acute osteomyelitic focus in the metaphysis or epiphysis. The vessels through the physis and epiphysis are not occluded as is usually the case above 1 year of age.[13] Above this age, spread of bacteria can occur from the metaphysis of the humerus and femur or in the elbow, where the joint capsule covers parts of the metaphysis, allowing bacteria to penetrate through the cortical bone and the periosteum to the joint cavity. In adults with closed growth plates there is a re-established connection between the metaphysis and the epiphysis and spread of infection to the synovial plexus is possible.

Third, an infection in the vicinity of the joint can progress to the joint or spread via the lymphogenic route. This is most often seen in non-penetrating traumatic and postoperative wound infection and in skin and soft tissue infection around the joints, particularly the knee joint.

A fourth possibility is iatrogenic infection caused by joint puncture for a diagnostic or therapeutic purpose. Although extremely rare, this has not yet been completely eradicated.

Lastly, penetrating trauma, usually caused by dirty objects or by animal or human bites, often gives rise to a severe infection because of the high inoculate of bacteria and the lacerated tissue. After joint surgery, perioperatively implanted bacteria can cause a postoperative infection.

In hematogenous infection, once the bacteria have reached the synovial membrane an inflammatory reaction starts. Leucocytes migrate to the focus and inflammatory proteins exude to the infectious focus. The synovial membrane proliferates and becomes tender, and the blood flow increases. Exudation of bacteria, cells and proteins into the joint cavity occur. Bacteria in the joint fluid can be killed by phagocytes. The joint becomes swollen and the joint pressure rises and can cause cartilage damage. The enzymes elastase and collagenase are liberated from polymorphonuclear leukocytes and synovial cells degrade the cartilage. The infection and inflammation can spread in the subchondral bone.[14] Joint cartilage loses its resilience, tolerating only about a third of the normal pressure. The tissue changes become irreversible, often in a few days.[15] A proliferating pannus tissue will often result from persistent infection.

DIAGNOSIS

Synovial Fluid Examination and Culture

Infective arthritis needs to be differentiated from gout and diffuse chondrocalcinosis.[16]

The definitive diagnosis of bacterial arthritis can be made only by visualizing bacteria on a Gram stain smear or by culturing the organism from the synovial fluid. Whenever there is a suspicion of bacterial arthritis, the initial and most important diagnostic procedure is an arthrocentesis and synovial fluid examination. If a patient has not been on antibiotics before the joint aspiration, synovial fluid cultures are positive in 70 to 90 percent of cases of nongonococcal bacterial arthritis.[7, 9] The yield of positive synovial fluid culture varies from 10 to 50 percent for patients with suspected gonococcal arthritis.

Aspirated synovial fluid should be brought directly to the microbiology laboratory and immediately placed on conventional broth and solid media or into aerobic and anaerobic blood culture bottles. Specimens suspected of containing *Neisseria* or *Haemophilus* should be placed in chocolate agar and incubated in an environment of 5 to 10 percent carbondioxide. If fluid cannot be aspirated or if it is impossible to be certain whether a joint effusion is present, further attempts at aspiration must be pursued. Flouroscopic or computed tomographic (CT)-guided aspirations have been helpful, but an open surgical procedure may be required to obtain synovial fluid. This is especially true in joints such as the sternoclavicular joint or in suspected prosthetic hip infection.

Occasionally the synovial fluid may be sterile, but microorganisms may be recovered from a culture of the synovial membrane.[12] Synovial membrane cultures have routinely provided a better recovery rate than synovial fluid in fungal and tuberculous arthritis. However synovial membrane cultures have not been commonly performed in culture-negative bacterial arthritis.

Synovial fluid leucocyte count more than 50,000 cells/mm^3 with more than 80 percent PMN cells suggests bacterial arthritis. Synovial fluid glucose and lactate dehydrogenase levels have not provided much additional useful diagnostic information. Determination of bacterial fatty acid levels has not proven to be reliable and practical enough for diagnostic utility. Polymerase chain reaction (PCR) techniques have been used predominately in gonococcal arthritis but may be useful in other suspected bacterial joint infections.[14]

Blood Culture and other tests

Nearly 50% of patients with nongonococcal bacterial arthritis have positive blood cultures, and sometimes the blood culture is positive when the synovial fluid culture is negative.[7] Every patient should be carefully examined for possible extra-articular infection, especially cutaneous, respiratory, and genitourinary sites, and appropriate cultures should be taken. 67% of patients with acute bacterial arthritis have a peripheral blood leucocytosis, almost all patients manifest an elevated erythrocyte sedimentation rate (ESR) and positive C reactive protein (CRP), but these tests provide little useful diagnostic utility in the setting of an acute inflammatory synovitis.

Radiologic Evaluation

Plain X-ray films should be obtained to provide a baseline assessment of the infected joint and to exclude possible contiguous osteomyelitis. Definitive radiological changes of bacterial arthritis usually appear often within couple of days.[7,15,17] Earliest findings reveal the presence of a joint effusion with displacement of the fat pads. Periarticular osteoporosis is evident during the first week of bacterial arthritis. Joint space narrowing and erosions may be detectable within 7 to 14 days. Rapidity of changes depends on the virulence of the organism. Few radiologic features of bacterial arthritis are diagnostic. Gas formation within the joint suggests infection, especially from *Escherichia coli* or anaerobes. However intra-articular gas may be secondary to a prior arthrocentesis or to an infection that communicates with the skin or viscera. The radiographic features of septic arthritis resulting from a contigous osteomyelitis include prominent epiphyseal destruction or metaphyseal periostitis and osteolysis. The radiologic findings in a suspected infected prosthetic joint are difficult to distinguish from mechanical loosening of the prosthesis because both may cause zones of radiolucency at the bone-cement interface.[17] In such situations arthrography with hip aspiration may be helpful to document pathologic bone and cement separation and to demonstrate synovial hypertrophy and abscess formation.

In joints that are particularly difficult to evaluate clinically or that have a complex anatomic structure, CT, radionuclide imaging, or magnetic resonance imaging (MRI) are most useful.[7,15-18] CT may demonstrate early bone erosions, reveal soft tissue extension and facilitate arthrocentesis of shoulders and hips. CT and MRI are especially useful in detecting septic sacroiliitis. Bone scan has been useful for detecting axial joint infections.

MANAGEMENT

Appropriate antibiotics of parental and well-absorbed oral formulations with sufficient penetration of joint structures determine success of therapy.[19] The antibiotics should be instituted

within 2-3 days of onset of the clinical symptoms.[20] Early and aggressive therapy is imperative to prevent destruction of cartilage, especially in childhood,[21] and mortality high in elderly patients with RA or diabetes mellitus.

Isoxazolyl penicillins in suspected Gram–positive infection and a cephalosporin in suspected Gram-negative infection are effective in the ordinary acute case. Parental cloxacillin 2g tid or 100 mg /kg/day in Gram-positive infections, and cefuroxime 1.5g tid or 75-80 mg/kg/day in Gram-negative infections are recommended. The duration of parenteral therapy should be 7-10 days and thereafter oral drugs, flucloxacillin 1.5g t.i.d. or 78-80mg/kg/day or a cephalosporin, are given for a total of up to 6 weeks.[19]

Joint Drainage

Adequate drainage of purulent synovial effusion is an essential aspect of treatment of septic arthritis. Optimal method of drainage varies.[7,8,22] Open surgical drainage or arthroscopic drainage is generally recommended as the initial drainage procedure of choice in hip infections particularly in children, any joint that anatomically is difficult to drain or to assess the adequacy of drainage, such as shoulders or sacroiliac joints, and coexistent osteomyelitis requiring surgical intervention.

Closed needle aspiration should be the initial treatment of choice in all cases of gonococcal arthritis and in adults with nongonococcal arthritis of the knee, although arthroscopy may be more effective in some situations like wrist, ankle and small joints.

Supportive Treatment

Treatment of an infected joint also includes meticulous attention to joint position, exercise and rehabilitation. During the acute, suppurative phase, the patient often maintains the joint in a position of slight to moderate flexion, which can lead to flexion deformities. Easily removable supporting slings, splints, or casts should be used to maintain the joint in optimal position. Even in this acute stage, muscle-tightening exercises should be initiated. Quadriceps sets are especially important in knee infections to help prevent muscle atrophy. Continuous passive motion may add protective effects by virtue of preventing adhesions, improving cartilage nutrition through enhanced synovial fluid diffusion, enhanced clearance of purulent exudates, and increased stimulation of chondrocytes to synthesize destroyed matrix.

Some patients make an uneventful recovery but usually when beginning to ambulate develop a recurrent inflammatory but sterile effusion, so-called postinfectious arthritis. Such effusions probably represent the sequelae of a marked synovitis with the added insult of active weight-bearing. This situation must be distinguished from an incompletely treated infection. The joint must again be aspirated and any remaining fluid sent for culture. After the synovial effusion is found to be sterile, nonsteroidal anti-inflammatory agents may be used for symptomatic treatment. Addition of anti-inflammatory drugs to antibiotics improves outcome.[23] Immunocompromised state like HIV infection needs to be attended.

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