Septic Arthritis vs. Reactive Arthritis — Diagnostic Workup and Treatment

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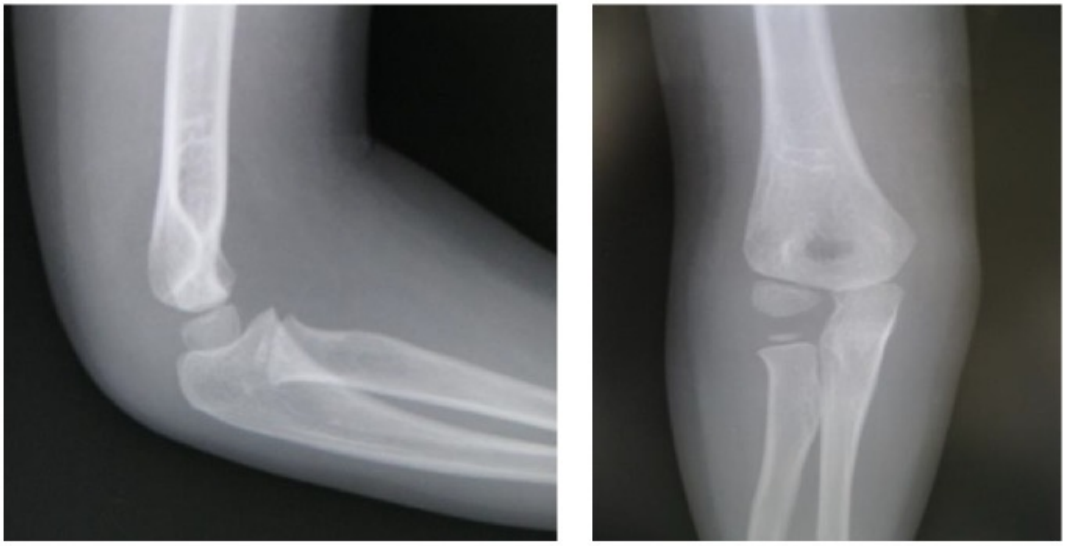
Septic arthritis is characterized by joint infection. Infections of the bones and joints are uncommon and can be fatal. Therefore, septic arthritis is a medical emergency. Because of the high fatality rate in septic arthritis, any case of arthritis should be considered septic until proven otherwise. The key to the successful treatment of septic arthritis is early diagnosis and treatment.



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Definition of Septic Arthritis

Septic arthritis/infectious arthritis refers to the invasion of the joint space by microorganisms such as bacteria, viruses, and fungi.

Epidemiology of Septic Arthritis

The estimated annual incidence of septic arthritis in developed countries is approximately 2 cases per 100,000 persons per year. The incidence of septic arthritis in Western Europe is higher and is estimated to range from 4 to 10 cases per 100,000 persons per year.

The incidence of septic arthritis in populations with low socioeconomic status, such as the aboriginal people of Australia, can be as high as 29 cases per 100,000 persons per year. The incidence of septic arthritis in children ranges from 5 to 12 cases per 100,000 persons per year.

In the United States, the incidence is approximately 7.8 cases per 100,000 persons per

year. The mortality rate in hospitalized patients with septic arthritis in the United States is approximately 10%. Because of the high mortality rate, epidemiologic studies were performed to understand why the risk of septic arthritis has been increasing in the last few years.

Gonococcal arthritis represents up to 75% of the cases of septic arthritis, especially among sexually active teens. Other common organisms include *Staphylococcus* species.

The main explanations for the observed increase in the incidence of septic arthritis in developed countries are as follows:

- Increased incidence of infections related to orthopedic procedures. This has to lead to an increase in prosthetic joint arthritis, which now accounts for 6%–10% of total arthritis cases.
- Aging
- Use of immunosuppressive therapy

Etiology of Septic Arthritis

The most commonly involved organism in septic arthritis is *Staphylococcus aureus*, which is responsible for up to 56% of cases. Recently, methicillin-resistant *S. aureus* has emerged as a cause of septic arthritis. *S. aureus* septic arthritis is more commonly seen in patients having orthopedic procedures.

Streptococcal septic arthritis is also common in adults, with *Streptococcus pyogenes* being the most commonly isolated microorganism of the *Streptococcus* genus. Streptococcal septic arthritis is usually associated with a history of chronic diseases, autoimmune disorders, skin infections, and trauma, and it is more frequently seen in the elderly. Pneumococci and gram-positive bacilli have also been reported as possible causes of septic arthritis; however, they are not common.

Gram-negative cocci are responsible for 20% of septic arthritis cases, with *Neisseria gonorrhoeae* and *Neisseria meningitidis* the most common causative organisms of this family.

Pathogenesis of Septic Arthritis

Microorganisms gain access to the synovium by 3 main mechanisms:

- Direct inoculation by medical procedures or trauma
- Contiguous-focus infections
- Hematogenous spread, which is the most common route

The synovium is highly vascularized, and there is no blood barrier to prevent bacteria and other organisms from accessing the joint space. Moreover, joint fluid is an excellent environment for bacterial growth once bacteria gain access. Joints that have undergone some destruction, such as after rheumatoid arthritis, are more susceptible to infections due to increased adhesion and neovascularization of the joint.

If the host is immunocompetent, a protective immune response is initiated to eliminate the causative bacteria. In most cases, however, the infection cannot be halted, and the patient eventually develops sepsis. This leads to the destruction of articular cartilage, inflammation of the joint space, and resulting pannus formation. Large effusions may form, impairing blood supply to the region, and, thus, causing necrosis and death of bone

tissue.

Clinical Presentation of Septic Arthritis

Patients often present with a 2-week history of fatigue, erythema, tenderness, and decreased range of motion affecting a single joint. Fever is a common finding in septic arthritis; however, it is usually mild. One-third of the patients develop a fever with a temperature greater than 39°C.

Predisposing factors such as rheumatoid arthritis, history of orthopedic procedure, or other autoimmune diseases should be explored in patients presenting with septic arthritis. Although **septic arthritis is usually monoarticular**, polyarticular septic arthritis has been reported in immunocompromised patients. Finally, any patient presenting with acute joint disease should be considered to have septic arthritis until it can be proven otherwise.

Diagnostic Workup for Septic Arthritis

The definitive diagnosis of septic arthritis is made by the direct demonstration of bacteria in the synovial fluid or after culture of the pathogen. In most cases, however, **clinical diagnosis with supporting laboratory testing is all that is needed.**

Laboratory tests show an elevated erythrocyte sedimentation rate, high C-reactive protein level, and leukocytosis. White blood cell counts higher than 50,000/m3 in the synovial fluid are highly suggestive of septic arthritis.

A patient can be confidently diagnosed with septic arthritis if

- The erythrocyte sedimentation rate is greater than 20 mm/h
- White blood cell count greater than 11,000/m3
- Joint white blood cell count greater than 50,000/m3

Blood culture results might be positive in up to 70% of cases; therefore, they should be requested in all patients suspected of having septic arthritis.

Aspiration of the synovial fluid in any patient presenting with a swollen joint is a mandatory step in the diagnostic workup of septic arthritis. In addition to obtaining the count of white blood cells in the synovial fluid, it is also recommended that joint fluid glucose and lactate levels be measured. An elevated joint lactate level and a joint fluid glucose level of less than 40 mg/dL support the diagnosis of septic arthritis.

The first imaging modality requested in septic arthritis is plain radiography. Osteopenia is commonly seen. If the infection is severe, diffuse joint space narrowing might be seen. Ultrasonography is helpful for detecting joint effusions. A computed tomography scan of the joint is helpful for visualizing the local edema, bone erosions, and sclerotic changes of the joint. The most accurate imaging modality in septic arthritis is magnetic resonance imaging.

It is important to remember that the definitive diagnosis of septic arthritis is made by the direct demonstration of bacteria in the aspirated synovial fluid.

Treatment of Septic Arthritis

The mainstay treatment of septic arthritis is debridement and **removal of the purulent material and the initiation of antibiotics** as early as possible. The usual course of therapy for nongonococcal arthritis is 2 weeks for streptococci and gram-negative cocci, 3 weeks for staphylococci, and 4 weeks for pneumococci and gram-negative bacilli.

It is recommended that treatment **begin with a broad-spectrum antibiotic** that covers all of these microorganisms, and then a narrow-spectrum antibiotic can be used once the causal microorganism has been identified.

An Overview about Reactive Arthritis

Reactive arthritis is a common cause of lower limb oligoarthritis and is seen in young adults. It is characterized by a distinct distribution of the affected joints and a high prevalence of extra-articular manifestations.

Reactive arthritis is precipitated by an infection at a distant site with genetic susceptibility in the host due to the presence of the HLA-B27 gene. The exact pathogenesis of reactive arthritis is still not clear; however, autoimmunity and cross-reactivity are possible explanations for the disease.

Epidemiology of Reactive Arthritis

The incidence of reactive arthritis is estimated to be approximately 30 cases per 100,000 persons per year. The condition is most commonly seen in men ages 20 to 40 years, with a male-to-female ratio of 3 to 1. The risk of developing reactive arthritis is 50 times greater in people with the HLA-B27 gene.

The most commonly preceding infections in reactive arthritis are nongonococcal urethritis and bacterial enteric infections.

Important Definitions Related to Reactive Arthritis

	Definition
Reactive arthritis	Aseptic inflammatory arthritis triggered by infection at a distant site in a patient who is HLA-B27 positive.
Reiter’s syndrome	The presence of urethritis, conjunctivitis, and arthritis in a patient with infectious dysentery. Or Presence of peripheral arthritis for more than one month in association with urethritis or cervicitis.
Uroarthritis	Reactive arthritis that is secondary to a urinary tract infection.
Sexually acquired reactive arthritis (SARA)	Reactive arthritis in a patient with a recent history of a sexually transmitted infection.
Rheumatic fever	Systemic inflammatory illness with carditis in addition to arthritis after a history of group A streptococcal pharyngitis.

Clinical Presentation of Reactive Arthritis

Patients present with mild localized joint disease in addition to systemic manifestations. Monoarthritis and widespread polyarthritis are not commonly seen in reactive arthritis. Enthesopathy, psoriasiform mucosal lesions, cutaneous lesions, inflammatory eye

diseases such as conjunctivitis, and cardiovascular lesions are the main extra-articular manifestations of reactive arthritis.

Diagnostic Workup for Reactive Arthritis

The diagnostic workup for reactive arthritis involves 2 main steps:

- Exclusion of other causes of arthritis by laboratory investigations
- Positive test result for the HLA-B27 gene

Additional tests that may suggest the likelihood of reactive arthritis include testing urine samples for chlamydia infections.

The differential diagnosis of reactive arthritis and how to exclude other possibilities are summarized in the following table.

Diagnosis	Prompt investigations that can distinguish between the diagnosis and reactive arthritis
Rheumatoid arthritis	• Positive rheumatoid factor, anti-CCP antibodies • Bony erosions on radiography
Gout arthritis	• Presence of urate crystals on joint aspiration
Inflammatory bowel disease associated arthritis	• History of inflammatory bowel disease diagnosis that is confirmed by colonoscopy and biopsy
Septic arthritis	• **Should be excluded in any case of acute joint disease** • Presence of bacteria on synovial fluid aspiration • Positive blood culture results
Infective endocarditis associated arthritis	• Positive blood cultures • Presence of abnormalities on echocardiography
Rheumatic fever	• Positive antistreptolysin O titer • Positive DNAse B antibodies • Arthritis with a systemic illness that meets the modified Jones criteria

Treatment of Reactive Arthritis

Antibiotics are not helpful in the treatment of reactive arthritis. Nonsteroidal anti-inflammatory drugs are first-line treatments for reactive arthritis. Cyclooxygenase 2 inhibitors appear to be superior to nonsteroidal anti-inflammatory drugs.

Cases that are resistant to nonsteroidal anti-inflammatory drugs might benefit from a single intramuscular dose of 80–120 mg methylprednisolone. A dose of 10–20 mg oral prednisolone once per day, tapered down over 1week to 3months, is another approach for severe reactive arthritis.

Patients with recurrent, chronic, or erosive reactive arthritis should receive disease-modifying antirheumatic drugs (DMARDs) such as sulphasalazine. Methotrexate and leflunomide might also be helpful in reactive arthritis; however, evidence supporting their routine use in clinical practice for reactive arthritis is still lacking. **Physiotherapy** is important for improving joint mobility and function.

References

Hamdulay SS, Glynne SJ, Keat A. When is arthritis reactive? Postgraduate Medical Journal. 2006;82(969):446-453. doi:10.1136/pgmj.2005.044057.

Best practice & research:
http://www.bprclinrheum.com/article/S1521-6942(11)00025-8/fulltext

Notes