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Literature Review

Principles Treatment Of Septic Arthritis Of The Knee: A Brief Review

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Abstract

Septic arthritis is an emergency condition in which infection occurs in the synovial joints, resulting in the formation of pus in the synovial spaces. The incidence of septic arthritis increases in patients with an increased risk such as rheumatoid arthritis. The etiology of septic arthritis is mainly bacterial. Risk factors include iatrogenic procedures (surgery, implant placement, joint puncture) and systemic conditions (diabetes mellitus, rheumatoid arthritis receiving immunosuppressants, etc). Pathophysiology of septic arthritis is due to blood flow stasis in metaphyseal areas especially in children and intraarticular minimal blood circulation. Clinical pictures include sudden onset of fever, malaise, localized pain in the infected joint, joint swelling, and reduced range of motion. Examination for septic arthritis is a physical examination carried out are inspection (see), palpation (touch), and movement. supporting examinations include blotestsest, PCR, radiological and joint fluid tests. Treatments include non-pharmacological such as rest and physical therapy, pharmacological the form of antibiotics, and surgical therapy such as drainage incision. This study is a brief review of the current Principles Treatment Of Septic Arthritis Of The Knee. The reference to this review was taken from the latest journal up to 5 years and the latest book up to 10 years.

Background

Septic arthritis (also known as pyogenic arthritis or suppurative arthritis) is an emergency condition in which infection occurs in the synovial joints, resulting in the formation of pus in the synovial spaces.[1] The etiology of septic arthritis is mainly bacterial, other etiologies are fungi and viruses. Septic arthritis due to bacterial infection is a serious disease that rapidly destroys the articular hyaline cartilage and irreversible loss of joint function. Early diagnosis followed by appropriate therapy can prevent joint damage and joint deformity.[1]

The incidence of septic arthritis in the general population varies from 2-10 cases per 100,000 people per year.[2] This incidence increases in patients with an increased risk such as rheumatoid arthritis 28-38 cases per 100,000 per year, patients with joint prostheses 40-68 cases/100,000/year (30-70%). The peak incidence in the age group was children aged less than 5 years (5 per 100,000/year) and adults aged more than 64 years (8.4 cases/100,000 population/year). Most septic arthritis occurs in a single joint, whereas polyarticular involvement occurs in 10-15% of cases. The knee joint is the most commonly affected joint at 48-56%, followed by the hip joint at 16-21%, and the ankle at 8%.[1]

Patients with acute septic arthritis are characterized by severe joint pain, joint swelling, stiffness, and impaired function, in addition to various other systemic symptoms such as fever and general weakness The knee joint is subject to frequent and usually indolent monoarthritis (**See Figure 1)**. Several risk factors include; knee and hip prosthesis with skin infection, skin infection without prosthesis, hip and

Figure 1. The Difference Between a Healthy Knee Joint And a Septic Arthritis Knee Joint

knee prosthesis without knee and skin infection, age more than 80 years, diabetes mellitus, rheumatoid arthritis receiving immunosuppressive treatment, and joint surgery.[3] In the Philippines it was reported that Systemic Lupus Erythematosus (SLE) patients were the fifth-order risk factor for septic arthritis.[4]

Septic arthritis is closely related to systemic infection because it is difficult for germs to enter directly intra-articularly if not through the spread of hematogenous bacteria or direct inoculation due to intra-articular injection. Systemic infections originate from wounds around the joints or infections in other organs. Most AS is caused by a bacterial infection. The main sources of infection are infections of the tissues around the joints, and bacteremia originating from infections of the respiratory, gastrointestinal, and urinary tracts. Germs that are often found are; Staphylococcus aureus and Streptococci. In all age groups, 80% of cases are caused by aerobic Gram-positives (60% Staphylococcus aureus, 15% β-hemolytic Streptococci, 5% Streptococcus Pneumonia), and approximately 20% of cases are caused by Gram-negative anaerobes.[2]

Types of Septic Arthritis

Several joint disorders that need to be considered as a differential diagnosis of septic arthritis such as infection in previously affected joints, crystal-induced arthritis, reactive arthritis, traumatic arthritis, and viral arthritis.[5]

1. Crystal-induced arthritis

Gout and pseudogout mimic the signs and symptoms of septic arthritis. So that the joint fluid must be examined using a polarized light microscope for the presence of negative birefringent crystals (uric acid) or positive birefringence (calcium pyrophosphate dihydrate) to rule out crystal disease in the joints.However, it should be remembered that there have been reports of concomitant arthritis with crystal-induced joint disease.[2]

2. Reactive arthritis

The existence of a joint inflammatory response to the presence of a bacterial infection process outside the joint is known as reactive arthritis. Often the patient has a history of infections in the distal parts such as the gastrointestinal tract (eg Shigella spp., Salmonellaspp., Campilobacterspp., or Yersiniaspp.), genitourinary tract (eg chlamydia and mycoplasma), and respiratory tract (eg Streptococcus pyogenes). The joint is inflamed but sterile. The PCR examination detected microbial antigens in the joints. The presence of these microbial antigens reflects the natural filtering response of the synovium and increasing numbers of these bacterial antigens will stimulate inflammation. Patients also often experience enteropathies or uveitis, skin lesions, or mucous membranes.[2]

Pre-existing joint infection. Patients with underlying chronic joint diseases such as rheumatoid arthritis, osteoarthritis, and other connective tissue diseases experience flares and give a picture resembling septic arthritis or have an infection that gives a poor prognosis because there is often a delay in the diagnosis of septic arthritis. Often the patient has no fever and an indolent clinical picture. Thus the diagnosis of septic arthritis should always be considered if there is a sudden inflammation of one or both joints in this patient.[2]

3. Traumatic arthritis

Traumatic arthritis is arthritis caused by trauma either blunt trauma, penetration, or repeated trauma or trauma from inappropriate movement of the joints which in turn causes avascular necrosis. Avascular necrosis occurs due to the cessation of blood flow to the femoral head and then the bones become brittle. The surrounding cartilage becomes damaged and causes complaints and symptoms in the form of swelling, pain, joint instability, and internal bleeding. The joint fluid analysis found a lot of red blood cells.[2]

4. Viral arthritis

Patients with viral arthritis are usually manifested by polyarthritis generally involving symmetrical small joints, fever, lymphadenopathy, and a characteristic rash. On examination of the joint fluid, there were many mononuclear cells and normal glucose levels.[2]

Pathogenesis

The pathogenesis of septic arthritis is multifactorial and depends on the interaction of the bacterial pathogen and the host immune response. The processes that occur in natural joints can be divided into three stages: bacterial colonization, infection, and induction of a host inflammatory response.[6]

1) Bacterial colonization

The tissue tropism of bacteria is very important for the occurrence of joint infection. S. aureus has a variety of receptors (adhesins) that mediate effective adhesion to a variety of joint tissues. These adhesins are tightly regulated by genetic factors, including accessory gene regulators (agr), staphylococcal accessory regulators (SAR), and sortase A.[9]

2) Bacterial virulence factor

Apart from adhesin, other materials of the bacterial cell wall are peptidoglycan and polysaccharide microcapsules which play a role in regulating the virulence of S. aureus through their influence on opsonization and phagocytosis. Microcapsules (thin capsules) are important at the start of bacterial colonization in the joint space which allows staphylococcal adhesin factors to bind to host proteins and further capsule production will be increased to form thicker capsules that are more resistant to host immune clearance. So the role of microcapsules here is resistance to phagocytosis and opsonization and allows bacteria to survive intracellularly.[6]

3) Host immune response

Once colonized in the joint space, bacteria rapidly proliferate and activate an acute inflammatory response. Synovial cells initially release pro-inflammatory cytokines including interleukin-1β (IL-1β), and IL6. These cytokines activate the release of acute-phase proteins from the liver and also activate the complement system.[7]

In septic arthritis organisms could enter joints through *direct inoculation*, via deployment from network periarticular or through Genre blood which is the route infection most common Normal joints have component protective to prevent the process of infection, namely: cells synovial own ability to phagocytize and fluid synovial own ability bactericidal.[8]

In rheumatoid arthritis and SLE disease occur decline function immune the Bacteria could enter the room joints through several method that is, entering through the operating process are joint , through action aspirations joints, injections corticosteroids, or other traumas. Successful bacteria enter the cavity joints in a few hours raising reaction inflammation of the membranes synovial form hyperplasia and proliferation and occur release factors inflammation as *cytokines* and *proteases* that cause degradation from cartilage joints (**See Figure 2**).[6]

In Rheumatoid arthritis has happened to damage joints, this makes it easy to happen something infection membrane synovial, in joints, this happens neovascularization and occur enhancement factor appearance later adhesion causing happening bacteremia and continued Becomes infection of joints. The consequence of infection joints is damage to

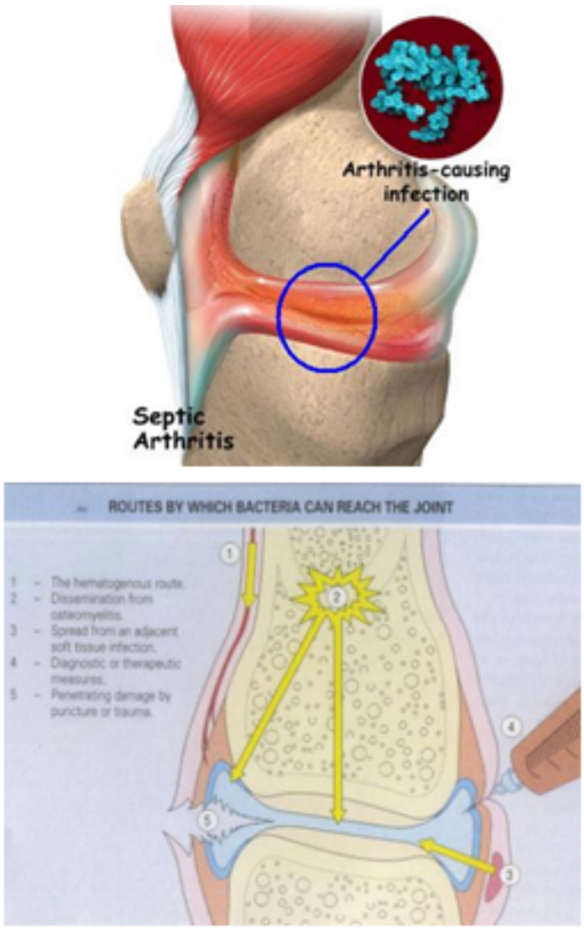

Figure 2. Pathogenesis of Septic Arthritis of The Knee

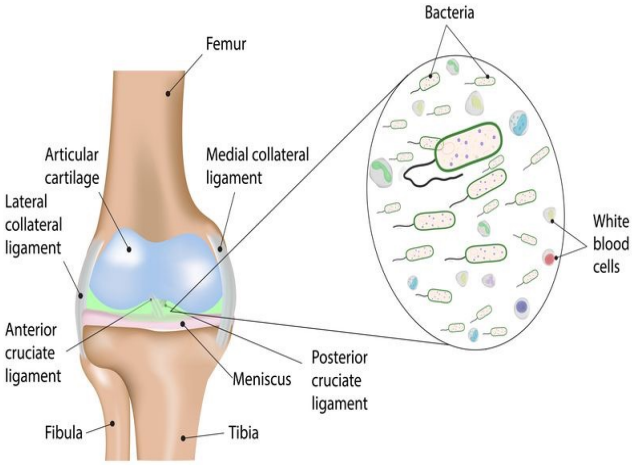

Figure 3. Septic Arthritis of The Knee

articular cartilage. On *S aureus chondrocyte proteases* germs that could react with later host polymorphonuclear *leukocytes* activate synthesis cytokines and various product inflammation other causes hydrolysis from collagen and proteoglycans.[9]

In infection Due to *N. gonorrhea* there is an influx of white blood cells into the joint causing only minimal joint damage compared to *S aureus.* then cause

interference with the flow of blood vessels and cause aseptic necrosis of the bone. This breakdown process could happen 3 days early in patients who experience infected joints without treatment.[6]

Viral infection can happen through method invasion direct (rubella) or through antibody-antigen product complex for example, in hepatitis B virus infection, *parvovirus B19* and *lymphocytic choriomeningitis viruses*. In addition, septic arthritis can also occur due to local processes other, most often in the gastrointestinal, with germs most common namely: *Salmonella enteritidis*, *Salmonella typhimurium*, *Yersinia enterocolitica*, *Campylobacter jejuni*, *Clostridium difficile*, *Shigella sonnei*, *Entamoeba histolytica*, *Cryptosporidium*. The most common second infection on genitourinary is *Chlamydia trachomatis* (See Figure 3).[9]

The morbidity that can occur is in the form of joint dysfunction and the incidence of mortality depends on the causative agent, in N gonorrhea the mortality rate is low, whereas in A aureus it can reach 50%. 56% occur in men, 45% of septic arthritis occurs over the age of 65.[6]

Clinical Symptoms

The classic symptoms of septic arthritis are sudden onset of fever, malaise, localized pain in the infected joint, joint swelling, and reduced range of motion. Several patients only complain of mild fever. Fever is reported in 60-80% of cases, usually mild fever and high fever occurs in 30-40% of cases up to more than 39 0C. Pain in septic arthritis is typically severe and occurs at rest as well as with active or passive movement.[10]

In addition, a history of rheumatoid arthritis, a history of injections in the joint area, and a history of diarrhea should be explored. Are there extra-articular symptoms, a history of intravenous drug use, or a history of blood vessel catheterization? Is there a history of venereal diseases, are there other diseases that cause a decrease in the immune system such as liver disease, diabetes mellitus lymphoma, and use of immunosuppressive drugs?[4]

The clinical symptoms of septic arthritis in non-gonococcal infections are sudden onset of joint swelling, feeling warm and very painful, most commonly occurring in the knee joint (50% of cases), whereas in children it most often occurs in the hip joint, the hip joint is usually in the position of flexion and external rotation and is very painful when moved. Approximately 10-20% of polyarticular infection occurs, usually 2 or 3 joints. Polyarticular septic arthritis usually occurs in patients with rheumatoid arthritis, patients with soft tissue infections, or in patients with severe sepsis.[8]

The initial evaluation includes a detailed history taking including predisposing factors, looking for transient or persistent sources of bacteremia (skin infections, pneumonia, urinary tract infections, presence of invasive procedures, injecting drug users, etc.), identifying any systemic disease affecting the joints or the presence of joint trauma.[5]

The knee joint is the most frequently affected in both adults and children, ranging from 45%-56%, followed by the hip joint, 16-38%. Polyarticular septic arthritis, which typically involves two or three joints, occurs in 10%-20% of cases and is frequently associated with rheumatoid arthritis. If there is a fever and flare in rheumatoid arthritis, the possibility of septic arthritis needs to be considered.[9]

Examination

Physical

The physical examination carried out is inspection (see), palpation (touch), and movement. Movement ones. The first is that we look at the behavior (how it behaves (how is the position of the joint/part which is the joint/part affected), swelling, deformity, wasting of the muscles around the joint, and redness of the overlying skin. Determine the pattern of joint disease, for example, small or large joints. And also we see whether it is attacked monoarticularly or polyarticularly.[11]

After inspection (seeing) we can feel/feel heat or not and determine swelling in the form of bone (osteoarthritis), fluid (effusion, synovitis), and tissue (rheumatoid nodules). When touched, whether there is pain or not.[11]

After inspection and palpation, the patient is asked to perform movements such as flexion, extension, abduction, adduction, internal rotation, and external rotation. We see if the patient can perform the above movements or if there is pain while doing so.[11]

On physical examination of the joint, signs of erythema, swelling (90% of cases), warmth, and tenderness are found which are important signs for diagnosing infection. The effusion is usually very large and is associated with a limited range of motion of the joint, both active and passive. But this sign becomes less obvious when the infection affects the spine, hip, and shoulder joints.[10]

Support

1. **Peripheral blood examination**
   There was an increase in leukocytes with a predominance of segmental neutrophils, increased sedimentation rate, and C-reactive Protein (CRP). This test is not specific but is often used as an additional marker in the diagnosis, especially in suspected septic arthritis of the joint. Blood culture is positive in 50-70% of cases.[12]
2. **Examination of joint fluid**
   Joint fluid aspiration should be carried out immediately if septic arthritis is suspected, if it is

difficult to reach, such as in the hip and shoulder joints, use a radiological guide. Joint fluid looks cloudy, or purulent, joint fluid leukocytes more than 50,000 cells/mm3 predominantly PMN, often reaching 75% -80%. In patients with malignancy, receiving corticosteroid therapy, and frequent injecting drug users with leukocytes less than 30,000 cells/mm3. Joint fluid leukocytes of more than 50,000 cells/mm3 also occur in inflammation due to crystal buildup or other inflammations such as rheumatoid arthritis. For this reason, it is necessary to examine the joint fluid using a polarized light microscope to look for crystals. The presence of crystals in the joint fluid also does not rule out concomitant septic arthritis.[12]

Synovial fluid gram stain should be performed, and it is positive in 75% of cases of staphylococcal culture-positive arthritis and 50% of gram-negative bacilli culture-positive arthritis. This gram stain can guide initial antibiotic therapy pending culture and sensitivity test results. Joint fluid cultures are performed for aerobic, anaerobic, and if indicated for fungi and mycobacteria. Synovial fluid cultures are positive in 90% of nongonococcal septic arthritis.[2]

3. **Polymerase Chain Reaction (PCR) examination**

Bacterial polymerase chain reaction (PCR) examination can detect the presence of bacterial nucleic acid in small amounts with almost 100% sensitivity and specificity. Some of the advantages of using PCR in detecting an infection include:

- Detect bacterial quickly
- Can detect slow-growing bacteria
- Detect non-culturable bacteria
- Detecting bacteria in patients receiving therapy
- Identify new bacteria as causative

But PCR also has weaknesses, namely false positive results if the material or reagent is contaminated during the inspection process.[2]

4. **Radiological examination**

Radiological examination on the first day usually shows a normal picture or an underlying joint disorder. Initial findings include swelling of the joint capsule and affected joint soft tissue, displacement of the fat pad, and widening of the joint space. Periarticular osteoporosis occurs in the first week of septic arthritis. Within 7 to 14 days, diffuse joint space narrowing and erosion due to cartilage destruction. In advanced stages that do not receive adequate therapy, radiological features show joint destruction, osteomyelitis, ankylosis, calcification of the periarticular tissue, or loss of subchondral bone followed by reactive sclerosis.[2]

Ultrasound examination can show abnormalities both intra and extra-articular which are not visible on radiographic examination. Highly sensitive for detecting minimal joint effusion (1-2 mL), including deep joints such as the hip joint. Hyperechoic synovial fluid and joint capsule thickening are characteristic features of septic arthritis.[11]

Another examination used in septic arthritis where the joint is difficult to evaluate clinically or determine the extent of bone and tissue infection is CT, MRI, or radiology.[10]

Management

The main goals of treating septic arthritis are joint decompression, joint sterilization, and restoration of joint function. Treatment of septic arthritis includes non-pharmacological, pharmacological, and joint fluid drainage.[13]

1) Non-pharmacological therapy

The patient is advised to rest the affected joint in the acute phase. Rehabilitation is important to maintain joint function and reduce the morbidity of septic arthritis. Rehabilitation should be initiated at the onset of arthritis to reduce loss of function. In the acute, suppurative phase, the patient must maintain a slightly to moderately flexed position which tends to contracture. Splinting is sometimes necessary to maintain a position with optimal function; knee joint in extension position, hip joint in neutral extension and rotation position, elbow flexed 90°, and wrist in a neutral position until slightly extended. Even in the acute phase, isotonic exercises must be performed immediately to prevent muscle atrophy. Joint movement, both active and passive, must be carried out no later than 24 hours after the complaint improves.[8]

2) Pharmacological therapy

Once septic arthritis is suspected, samples are immediately collected for examination and appropriate antibiotic therapy is performed and joint fluid drainage is performed immediately. The choice of antibiotic should be based on several considerations including clinical condition, age, pattern and local bacterial resistance, and the results of gram staining of joint fluid.[8]

Antibiotic modification is carried out when there are culture results and bacterial sensitivity. It should be noted that vancomycin should not be continued in patients with B lactam-sensitive staphylococcal or streptococcal infections. The clinical course of the patient also needs to be taken into consideration because the correlation between in vitro and in vivo bacterial sensitivity tests is not absolute. In general, the recommendation is to administer intravenous antibiotics for at least 2 weeks, followed by oral antibiotics for 1-4 weeks. Longer administration of intravenous antibiotics is indicated for bacterial infections that are difficult to eradicate such as P aerogenosa or Enterobacter spp. In cases of S aureus bacteremia and

secondary S aureus arthritis, 4 weeks of parenteral antibiotics were given to prevent recurrent infections. Intra-articular administration of antibiotics is ineffective and can cause chemical synovitis.[12]

a) Antibiotic
   The choice of antibiotic should be based on the results of the joint fluid culture. Before the culture results are available, you can be given a choice of antibiotics such as penicillin G/clindamycin/cloxacillin if it is caused by Staphylococcus aureus. Whereas for gram-positive can be given vancomycin. For gram negatives with a decreased immune system, aminoglycosides/antipseudomonal/penicillin/3rd generation cephalosporins can be given. And for gram negatives with a good immune system, penicillin/ceftriaxone can be given. Meanwhile, in old age can be given antibiotics with a broad spectrum.[13]
b) Joint drainage
   The technique of drainage depends on the joint involved, the stage of infection, and the patient's response. Although an infected joint can be drained with satisfactory results through repeated aspiration, the hip joint and possibly other joints that are difficult to drain should be performed arthrotomy as soon as possible after identification of septic arthritis.[13]
c) Surgical action
   Considered in conditions such as coxal infection in children, joints that are difficult to drain, together with osteomyelitis, and also an infection that develops into the surrounding soft tissue.[2]

Conclusion

Septic arthritis is an emergency condition in which an infection occurs in the synovial joint resulting in the formation of pus in the synovial space. The etiologies include bacteria, fungi, and viruses. The peak incidence in the age group is children aged less than 5 years and adults aged more than 64 years. The joints affected include the knees, hips, and ankles. Risk factors for septic arthritis include knee and hip prostheses with skin infection, skin infection without prosthesis, hip and knee prosthesis without knee and skin infection, age over 80 years, diabetes mellitus, rheumatoid arthritis receiving immunosuppressive treatment, and joint surgery. Septic arthritis is closely related to systemic infection because it is difficult for germs to enter directly intra-articular if not through hematogenous bacterial spread or direct inoculation due to intra-articular injection. Several joint disorders need to be considered in the differential diagnosis of septic arthritis such as infection in previously affected joints, crystal-induced arthritis, reactive arthritis, traumatic arthritis, and viral arthritis. The pathogenesis of septic arthritis is multifactorial and depends on the interaction of the pathogenic bacteria and the host's immune response. The processes occurring in natural joints can be divided into three stages: bacterial colonization, infection, and induction of a host inflammatory response.

The clinical symptoms of septic arthritis in non-gonococcal infections are sudden joint swelling, feeling warm, and very painful, most commonly occurring in the knee joint, for those occurring in the hip joint usually in a flexion and external rotation position and are very painful when moved. The physical examination carried out is inspection (see), palpation (touch), and movement. While the supporting examinations include peripheral blood examination, joint fluid examination, polymerase chain reaction (PCR) examination, and radiological examination. Management includes non-pharmacology such as rest and physiotherapy, pharmacology in the form of antibiotics, and surgical therapy such as drainage incisions.

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