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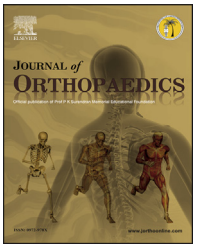

Original Article

Clinical and microbiological characteristics of patients with septic arthritis: A hospital-based study

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ABSTRACT

Background: To determine the clinical and epidemiological characteristics, etiology, underlying conditions, and outcomes of patients with primary septic arthritis and no prosthetic joints at a university hospital.

Methods: A retrospective study was performed between 2005 and 2012. Records from the Microbiology Department were reviewed, and patients with a positive culture of synovial fluid or biopsy were selected for the study. Clinical charts were reviewed using a designed protocol.

Results: 41 patients were diagnosed with septic arthritis with a positive culture. Most were diagnosed with monoarticular (85.37%) and monomicrobial (92.68%) arthritis. The most commonly involved joint was the knee (34.15%). The most frequent underlying conditions were hypertension and diabetes mellitus. *Staphylococcus aureus* was the most common pathogen (58.54%). Two cases of chronic arthritis, both caused by *Mycobacterium tuberculosis* were detected. The most frequently used antibiotic combinations were cloxacillin + ciprofloxacin and vancomycin + ciprofloxacin. Surgical treatment included needle aspiration, open joint debridement, or arthroscopic techniques.

Twelve cases had a poor outcome (destructive articular disease), and 3 patients died from staphylococcal sepsis.

Conclusions: In our hospital, septic arthritis is primarily acute, monoarticular, and monomicrobial; affects higher joints, is caused by *S. aureus*, and occurs in adult patients with underlying diseases. Outcome is good in most patients, although more than 25% of cases had articular sequels.

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1. Introduction

Septic arthritis is a medical emergency requiring prompt treatment and diagnosis.[1] This disease has a higher incidence with increased age, and many of the etiologies involved are associated with a significant disability or even death.[2] Cartilage destruction can occur within 1–2 days of the onset of symptoms[3] and is associated with a considerable mortality rate (up to 11%).[4]

Joint infection may occur by hematogenous dissemination, spread from a contiguous infection, direct inoculation of the infectious agent or postoperative contamination.[5] Diagnosis is based on microorganism identification by joint aspiration and/or blood cultures, and microbiological samples should always be taken prior to antibiotic administration.[6]

Staphylococcus aureus is a widely recognized cause of septic arthritis, and is responsible for 50–60% of infections. The second-most common cause of septic arthritis is streptococci, which accounts for up to 20% of cases, while gram-negative bacilli account for only 5–10%.[7]

A rapid and accurate diagnosis is essential in order to discriminating true infections from other pathologies that could present similar symptoms (e.g., rheumatoid arthritis, gout, chondrocalcinosis, fracture) that require different therapeutic approaches.[8] Moreover, targeted therapy is necessary for recovery and can substantially reduce morbidity and mortality.[9] In this sense, elevated results of certain laboratory examinations—such as white cell count, erythrocyte sedimentation rate, or C-reactive protein—may suggest the presence of an infection, although their specificity is low.[10]

Risks for septic arthritis are immunodeficiency, advanced age, coexisting infections, rheumatic disease, diabetes mellitus, and alcohol or intravenous drug abusers.[7,11,12] However, septic arthritis can also occur in otherwise healthy people.[13] This retrospective review evaluates the epidemiological characteristics and prognostic of patients with acute and chronic bacterial arthritis and no prosthetic joints diagnosed microbiologically at a university hospital in Madrid (Spain).

2. Materials and methods

We retrospectively reviewed the records of the microbiology department from 2005 through 2012 in search of patients with positive bacterial cultures of synovial fluid or synovial biopsies. During this period, the protocol for processing these samples remained unchanged. First, a gram stain was performed, after which the samples were inoculated onto chocolate agar, tryptic soy 5% sheep blood agar and Schaedler 5% blood agar (bioMérieux, Marcy l'Etoile, France). Some samples were also inoculated in blood culture bottles (BacT/ALERT, bioMérieux, Marcy l'Etoile, France). Identification of the isolates was performed using commonly recommended biochemical tests and commercially available identification systems (API strips, bioMérieux, Marcy L'Etoile, France). Susceptibility testing was performed using the disc diffusion test. Synovial fluids obtained from patients with chronic arthritis in addition to all synovial biopsies were processed for mycobacterial cultures as recommended, including both liquid medium (MGIT system (BD USA) between 2005 and 2009, and Versatrek system (bioMérieux, Marcy L'Etoile, France) between 2009 and 2012) and solid media (Lowenstein Jensen and Coletsos, bioMérieux, Marcy L'Etoile, France). Identification of mycobacterial isolates was performed with the GenoType MTB system (Hain, Germany).

The clinical charts of the selected patients were reviewed using a predefined protocol that includes data from clinical examination, underlying diseases, relevant laboratory examinations (i.e., C-reactive protein, erythrocyte sedimentation rate, cytochemical joint fluid, and polymorphonuclear cell count), radiological studies, medical and surgical treatment, and outcome. Patients with any type of orthopedic implant were excluded. The study was approved by the Clinical Trials Committee of our hospital.

3. Results

Forty-one patients (25 male and 16 female) with a mean age of 61 years (range, 2–90 years) were included in the study. Only one child was included. Diagnosis was based on identification of the microorganism isolated from synovial biopsy ($n = 6$) or synovial fluid ($n = 35$).

There were 35 patients with monoarticular infection, while 6 patients presented a polyarticular infection. The distribution of infected joints involved in monoarticular infection appears in Table 1. Two patients had chronic monoarticular arthritis due to *Mycobacterium tuberculosis*. Thirty patients had at least one comorbidity (see Table 2).

The most frequent infecting organisms were *S. aureus* and *Streptococcus* spp. The prevalence of these species was 23 (58.54%) *S. aureus* (2 of which were methylcillin-resistant *S. aureus*), 7 (21.95%) *Streptococcus* sp. (3 of which were *Streptococcus agalactiae*), 4 (12.19%) *Escherichia coli*, and 3 (7.32%) other species. Polymicrobial disease was detected in 3 (7.32%) of cases. The high number of group B streptococcus detected in the *Streptococcus* spp. isolations compared to other streptococcal species is remarkable since Group B streptococcal arthritis in adults is uncommon.[14] All these patients were women and nonpregnant adults, despite recognition and incidence of *S. agalactiae* infections among nonpregnant and elderly adults are increasing. It has been shown that this

Table 1 – Distribution of joints involved in 35 patients with septic arthritis.

Joint	*n* (%)
Knee	14 (40)
Shoulder	8 (23)
Hip	4 (11)
Ankle	3 (9)
Wrist	2 (6)
Metatarsophalangeal	2 (6)
Metacarpophalangeal	1 (3)
Sternoclavicular	1 (3)
Total	35 (100)

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Table 2 – Medical comorbidities in patients with septic arthritis.

Comorbidity	n
Rheumatoid arthritis	2
Osteoarthritis	2
Hyperuricemia	3
COPD[a]	2
HF[a]	2
HCV[a]	3
HBV[a]	2
HIV	2
Diabetes mellitus	7
Other hepatopathies	3
Hematologic disease	4
Chronic renal failure	3
Other diseases	13

[a] COPD: chronic obstructive pulmonary disease; HF: heart Failure; HCV: hepatitis C virus disease; HBV: Hepatitis B virus disease.

microorganism can cause serious invasive infections in nonpregnant adults and is now established as a well-known cause of septic arthritis, accounting for 5–10% of all cases. In our study, only one child (a 2-year-old girl) presented septic arthritis, caused by *Streptococcus pyogenes* localized in the hip joint.

In our cases, most cases of gram-negative arthritis were produced by *E. coli* (2 of which were extended-spectrum beta-lactamase-producing strains), and all of these cases were simultaneously detected by blood culture.

The mean values of laboratory parameters included C-reactive protein (CRP) 13.44 ± 12.19 mg/dl, erythrocyte sedimentation rate (ESR) 55.00 ± 31.35 mm/h, leukocytes 12,286 ± 5725 μl (mean polymorphonuclear 71.80 ± 12.76%, lymphocytes 17.16 ± 11.14%). Moreover, 11 patients had other alterations in other biochemical parameters such as glucose, urea, or creatinine. Four patients showed previous infections (2 urinary infections and 2 respiratory tract infections) unrelated to the joint infection.

Cytochemical tests of synovial fluid were performed in 14 patients, and in all of them a polymorphonuclear cell count of at least 90% was detected, with a mean cellularity of 50,451 cells/mm^3.

Ten biopsy samples were processed for histopathology, and in 6 of them inflammation signs (polymorphonuclear infiltrates) were detected. Seventeen synovial fluids were inoculated in blood culture bottles, obtaining the same bacteria as the normal cultures in all cases. Thirty-three patients were treated with surgery and antibiotic treatment, whereas 8 patients received only medical treatment. Regarding medical treatment, a combination of antibiotic therapy is recommended. In our case, the best results were noted with the combination of cloxacillin/vancomycin + quinolone (ciprofloxacin).

The mean follow-up was 1.43 ± 1.04 years (range, 0.5–5 years). Two patients were lost to follow-up. Fifteen patients had a poor outcome due to the development of osteoarthritis or pain persistence (41.67% of *S. aureus* cases), and 3 of those patients (20%) died because of staphylococcal septic shock.

4. Discussion

In our hospital, bacterial arthritis occurs mainly in elderly male patients, having a mean age of 61 years. They are predominantly produced by *S. aureus*, and most have monoarticular (85.37%) and monomicrobial (92.68%) involvement. The most commonly affected joint is the knee, followed by the shoulder, but any joint can be affected. Extra-articular features such as fever, arthritis, pain, and inflammation were the most common presentations. These features have also been documented in the literature.

According to the literature, septic arthritis is relatively uncommon in infants, is mainly monoarticular, and frequently affects the knee and hip joints, being *S. aureus* the most commonly identified microorganism in neonates and children above 2 years of age. Early diagnosis and appropriate treatment of these patients are associated with excellent outcomes.

Gram-negative bacilli arthritis is the least frequently detected form and is usually associated with invasive urinary tract infections, intravenous drug use, older age, compromised immune system, and skin infections. The two most common gram-negative organisms detected in adults are *Pseudomonas aeruginosa* and *E. coli*.

As in our series, tuberculous arthritis normally presents as chronic monoarticular arthritis and early diagnosis is difficult due to the atypical clinical manifestations and non-specific imaging findings associated with the disease. Both cases were diagnosed by synovial biopsy. Surgical debridement and strict adherence to antituberculous chemotherapy usually result in satisfactory functional outcomes.

Polyarticular septic arthritis has a low incidence but poor prognosis. As described in the literature, most polyarticular cases (66.67%) are caused by *S. aureus*, and the most frequently implicated joint is the knee followed by the ankle.[15]

It is well known that a combination of medical and surgical treatment is important for a good outcome of patients. Surgical treatments include open debridement, drainage and lavage of the joint, or arthroscopy lavage. Both are safe and effective procedures for debridement of septic arthritis and arthroscopy has been shown to be as useful as open surgery, particularly when the knee is involved. Antibiotic treatment should be started immediately after culture specimens are obtained, because cartilage damage occurs early. Choice of the most appropriate antibiotic depends on the suspected organism, local sensitivity, and resistance pattern. So far, no consensus or guidelines exist on length of antibiotic treatment for septic arthritis. However, parenteral antibiotic for 2–4 weeks followed by 4–8 weeks of oral antibiotic has been recommended.

Interestingly, 2 of our patients were infected with methicillin-resistant *S. aureus*, and 2 other patients presented extended-spectrum beta-lactamase *E. coli*. Due to frequent hospitalizations, some patients are at high risk of multiresistant organism infections.

Laboratory tests such as CRP (≥0.5 mg/dl), ESR (≥20 mm/h), polymorphonuclear cell count, or leukocytes orient the diagnosis of arthritis, as values tend to be high when an infection occurs. These markers are non-specific for diagnosing the

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infection. Fluid aspirate analysis, radiologic studies (including radiography), and pathology of the tissue sample allow for additional information leading to accurate diagnosis of septic arthritis.

Declaration of interest

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JE was member of an advisory committee for prosthetic joint infections of Pfizer.

Conflicts of interest

All authors have none to declare.

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