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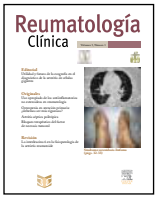

Original Article

Polyarticular Septic Arthritis: Analysis of 19 Cases

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ABSTRACT

Objective: Polyarticular septic arthritis accounts for 15% of all septic arthritis, but there are few references in the literature. We describe characteristics of patients with polyarticular septic arthritis in a rheumatology service.
Patients and method: Retrospective analysis of patients with septic arthritis involving more than one joint. Only patients with positive culture of synovial fluid were included. Clinical, analytical, and radiological variables are reviewed.
Results: Nineteen patients (14 male) had a polyarticular infection. Mean age was 55 years. Mean time from onset to diagnosis was 6 days. The knee was the most commonly involved joint, followed by ankle. The mean number of joints involved per patient was 3. Risk factors included diabetes, chronic renal, or hepatic disease, gout, and rheumatoid arthritis. Most commonly isolated agents were *S aureus* (47%) and *S agalactiae* (21%). Blood cultures were positive in 52.6% and 15.8% had septic shock. Scintygraphic bone scan showed a polyarticular uptake. Mean duration of antibiotic therapy was 46 (27) days. Clinical outcome was good in 52.6%, complicated in 26%, and mortality rate was 15.8% (3 cases). Joint debridement was performed in 21%.
Conclusions: Multiple joint involvement does not exclude the diagnosis of septic arthritis. Inflammatory arthritis is an important risk factor. *S aureus* in the main infectious agent. The morbidity and mortality of this condition are important, so we need to maintain a high index of suspicion for the condition.

Artritis séptica politópica: análisis de 19 casos

Palabras clave:
Poliartritis séptica
Infección poliarticular
Embolia séptica

RESUMEN

Objetivo: El 15% de las artritis sépticas corresponde a formas poliarticulares, si bien son escasas las series publicadas. Evaluamos las características de los enfermos con artritis séptica poliarticular recogidos en un servicio de reumatología.
Material y método: Análisis retrospectivo de las artritis piógenas con afección oligoarticular o poliarticular. Se incluye únicamente a los enfermos con aislamiento del germen en el líquido articular. Se analizan las variables clínicas, analíticas y radiológicas de la serie.
Resultados: Se registraron 19 casos (14 varones y 5 mujeres) con una media de edad de 55 años. La media del tiempo hasta el diagnóstico fue 6 días. La articulación afectada con mayor frecuencia fue la rodilla, seguida del tobillo. La media de focos infecciosos por paciente fue 3 (intervalo, 2-6). Los factores de riesgo más frecuentes fueron la diabetes mellitus, la insuficiencia renal crónica, la hepatopatía crónica, la gota y la artritis reumatoide. Los gérmenes aislados fueron *Staphylococcus aureus* (47%), *S. agalactiae* (21%) y bacilos gramnegativos. Los hemocultivos fueron positivos en el 52,6%, y el 15,8% presentó shock séptico. La gammagrafía con 99Tc mostró la afección politópica cuando fue realizada. La duración media del tratamiento antibiótico fue 46 ± 27 días. La evolución fue satisfactoria en el 52,6% y tórpida en el 26%, con mortalidad del 15,8% (3 casos). Se realizó artrotomía en el 21%.
Conclusiones: La presencia de oligoartritis o poliartritis no excluye el diagnóstico de artritis infecciosa. Entre los factores de riesgo destacan las artropatías inflamatorias previas. *S. aureus* es el microorganismo causal

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más frecuente. La morbilidad y la mortalidad de esta forma de infección articular son importantes, por lo que debe mantenerse un alto índice de sospecha y realizar una exploración sistemática de todas las articulaciones.

Introduction

Bacterial arthritis is considered a medical emergency with an important morbidity and mortality, particularly in when there are several affected joints at the same moment, both due to the severity of infection as well as the diagnostic delay. Approximately 15% of cases of septic arthritis reported in the literature series correspond to polyarticular forms,[1,2] even when specific references are scarce for this clinical presentation. Half of them are produced in patients with rheumatoid arthritis (RA) and the rest in subjects with chronic diseases or immune response alterations. Polyarticular infection is infrequent in the healthy adult, with the exception of the oligoarticular or polyarticular affection of gonococcal disease. Although *Staphylococcus aureus* is the most common infectious agent found, baseline disease in the patient can lead to the predominance of other germs such as streptococci and gram negative bacteria.

The objective of the present work is to evaluate the characteristics of patients with septic arthritis of several joints that were seen at our hospital, with particular attention to the form of presentation and the prognosis. There is no data in the Spanish literature on polyarticular septic arthritis, a fact that justifies the present study.

Patients and Method

A retrospective analysis of peripheral septic arthritis was carried out in the registry of the section of rheumatology of a university hospital, which attends to a reference population of approximately 700 000 inhabitants. A study of all of the coded septic arthritis was performed (code IV A1 of the ACR classification)[3] in the department's registry from 1985 to 2007 (database with diagnostic codes). For study purposes, cases with affection of more than one peripheral joint were selected, something we defined as a polytopic septic arthritis, both in the case of oligoarthritis as in polyarthritis. Patients with simultaneous affection of peripheral and axial joints were also included, but we excluded those with an exclusively axial skeleton affection. The microbiologic criterion for inclusion was the isolation of the germ in synovial fluid. Cases due to mycobacterias, brucella, and fungi were excluded.

Variables registered included: age, gender, risk factors for infection, osteoarticular infection localization, port of entry, fever (axillary temperature >37°C), time to diagnosis (days), bacterial infection clinical signs, Gram stain and joint fluid cultures, blood cultures, presence of other septic foci (such as endocarditis), antibiotic treatment undertaken (administration route, dose, duration) arthrotomy, progression, complications in joint movement, and concurrent complications.

Diagnostic x-rays or radiological reports were examined in those cases in which it was possible. In the cases in which they were available, bone scans, and magnetic resonance findings were analyzed.

The method was descriptive and results were compared with the main references from the medical literature. In addition, a comparison between means was performed in subgroups of patients with and without previous rheumatic disease, as well as in patients with and without known risk factors for joint infection (Student *t* test).

Results

Between 1985 and December 2007, at the Section of Rheumatology of the Hospital Universitari Germans Trias i Pujol of Badalona, there were 19 patients registered as having an osteoarticular infection with the affection of 2 or more foci. Gender distribution was 14 men and 5 women, with a mean (standard deviation) (interval) age of 55 (19) (17-89) years. Mean time of diagnostic lag between the start of symptoms and the diagnosis was 6.3 (4.6) (1-15) days. The most frequently affected joint was the knee, followed by the ankle (Table 1). The mean number of affected joints per patient was 3.1 (1) (2-6). The general characteristics of the series are reflected in Table 2.

The most frequent risk factors were: diabetes mellitus (6 cases), chronic renal failure (3), chronic liver disease (3), gout (3), alcoholism (2), rheumatoid arthritis (2), acquired immunodeficiency syndrome (2), and addiction to intravenous drugs (2). Some patients presented more than 1 risk factors while in 6 cases (31.6%) there were none recognized. As a possible port of entry, the skin was identified in 6 cases (2 diabetic feet with ulcerations), puncture, or intravenous catheter in 2, and previous arthrocenthesis (without infiltration) in 1 case. In 6 cases there was no evidence of a port of entry.

The isolated germs (Table 3) were: *S aureus* (9 cases; 47%), 1 of them resistant to methylcillin; *S agalactiae* (4 cases; 21%); *S epidermidis, S pneumoniae, S dysgalactiae, Neisseria gonorhroeae, Escherichia coli,* and *Salmonella* in 1 case each; 1 patient (case 15) had a joint infection by more than 1 infectious agent (*S aureus* in knee, *Klebsiella* in an elbow, and *Citrobacter freundii* in the other elbow).

Synovial fluid had a mean cellularity of 43 500 (14 000-100 000) cells/μL and only in 5 cases was it over 50 000 cells/μL. In 5 cases the obtained sample was insufficient to perform a cell recount and priority was given to the culture. Gram's stain showed a positive result in 9 (47.4%) cases, was negative in 4 (21%) and the result was not recovered in 6 (31.6%). The synovial fluid culture allowed the identification of the microorganism in all of the cases. In 10 (52.6%), blood cultures were positive for the same germs isolated in the joint fluid; in 2 (10.5%) a concomitant endocarditis was proven; 3 (15.8%) presented septic shock, produced in the first 48 hours after being admitted to the hospital.

Of the 3 patients with gout, 2 had gouty arthritis during the episode of septic arthritis, with the observation of urate crystals under polarized light microscopy (cases 13 and 15). Both cases

Table 1
Localization of Osteoarticular Infection in 19 Patients

	Joints, No.	Patients, No.
Knee	17	12
Ankle	8	6
Shoulder	5	5
Wrist	5	4
Acromioclavicular	5	3
Elbow	4	3
Diskitis	3	3
Elbow bursitis	3	2
Metatarsal joints	2	2
Sternoclavicular	1	1

Table 2
General Description of the Series

Case	Age	Gender	Localization of Infection	Joints/Foci, No.	Risk Factors
1	30	M	Ankle, 1st MTF, elbows, knees, pubis	6	No
2	43	F	Wrist, shoulder, ankle	3	No
3	73	M	Knees, gluteal abscess, metaphiseal osteomyelitis	4	Rheumatoid arthritis, diabetes, gout
4	65	M	Knee, ankle	2	No
5	35	M	Ankles, wrist	3	No
6	49	F	Shoulder, sternoclavicular	2	No
7	60	M	Shoulder, knee, ankles	4	Alcoholism, cirrhosis
8	75	M	Wrists, elbow, diskitis	4	Chronic renal failure
9	17	F	Knees, shoulder	3	AIDS
10	72	F	Knee, osteomyelitis of the toe phalange	2	Chronic renal failure, rheumatoid arthritis
11	42	F	Knee, shoulder, diskitis	3	Drug addiction, hepatitis B and C infection
12	26	M	Knees	2	Previous drug addiction, AIDS
13	73	M	Wrist, elbow, knees	4	Chronic liver disease, spleen lymphoma, gout, diabetes, chronic renal failure
14	46	M	Elbow bursitis, myositis on the leg, ankles	3	Diabetes mellitus
15	71	M	Knee, 2 elbow bursitis	3	Diabetes, gout
16	89	M	Hip, knee	2	No
17	72	M	Acromioclavicular, diskitis C7-D2	2	Psoriasis, total hip prosthesis
18	53	M	Bilateral acromioclavicular, hip	3	Diabetes mellitus
19	53	M	Knee, bilateral acromioclavicular, hip	4	Diabetes mellitus

Table 3
Clinical, Microbiological, and Radiologic of the Series

Cases	Port of Entry	Fever	Diagnostic Lag, d	Synovial Fluid Culture	Blood Cultures	Radiograph
1	Skin	Yes	2	*S aureus*	*S aureus*	Normal
2	Unknown	Yes	4	*S agalactiae*	*S agalactiae*	Joint impingement
3	Arthrocenthesis	Yes	15	*E Epidermidis*	Negative	Erosion
4	Urinary infection	Yes	10	*S agalactiae*	Negative	Osteopenia
5	Unknown	Yes	3	*N Gonorroheae*	Negative	Joint impingement
6	Pneumonia	Yes	5	*S agalactiae*	Unknown	Joint impingement
7	Unknown	Yes	6	*E coli*	*E coli*	Unknown
8	Catheter, arteriovenous fistula	No	2	*S aureus*	*S aureus*	Unknown
9	Unknown	Yes	3	*Salmonella*	Negative	Erosion
10	Skin	Yes	15	*S aureus*	Negative	Joint impingement
11	Drug addiction	Yes	3	*S aureus*	Negative	Erosion
12	endocarditis	yes	4	*S aureus*	*S aureus*	Unknown
13	Infected wound amputation	No	7	*S aureus resistant*	*S aureus*	Previous joint disease
14	Diabetic foot, trauma	Yes	7	*S aureus*	*S aureus*	Soft tissue gas
15	Skin, diabetic foot	Yes	3	*S aureus, Klebsiella pneumoniae, Citrobacter freundii*	*S aureus*	Previous joint disease
16	Unknown	Yes	8	*S dysgalactiae*	Negative	Joint impingement
17	Skin	Yes	15	*S aureus*	*S aureus*	Unknown
18	Unknown	Yes	6	*S pneumoniae*	Unknown	Normal
19	Unknown	No	1	*S agalactiae*	*S agalactiae*	Joint impingement

progressed poorly and 1 of the patients died due to multiorganic failure.

The subgroup of patients with previous rheumatic disease (RA, gout; n=4) had a higher mean age than the rest of the group (72 [9] and 50 [19] years respectively; *P*=.001). There were no differences between both subgroups in the distribution according to gender, number of infectious foci, time of diagnostic delay, and progression of the process. No significant differences were found in the subgroups with and without risk factors (13 and 6 cases respectively) regarding age, diagnostic delay, number of joints affected, duration of treatment, and progression.

Information on the x-rays of the patients was retrieved in 15 (79%) cases: normal in 2 (10.5%), signs of previous joint disease in 2 (10.5%), joint impingement in 6 (31.6%), erosion in 3 (18.8%), isolated osteopenia 1 (6.2%), and the presence of gas in soft tissue in 1 (6.2%).

A bone scan with MDP-^{99m}Tc was carried out in 9 (47.4%) patients, evidencing a polytopic uptake (Figure) in 8 cases and was negative in 1. A gammagram with ^{67}Ga or marked leukocytes was performed also in 4 (21%) patients with the suspicion of osteitis (1 pubic symphysis, 1 cervical spondylodiskitis, 2 tibial osteitis).

Mean duration of antibiotic therapy (Table 4) was 46 (27) (15-105) days. The most commonly employed therapeutic combination in the days before the definite identification of the germ was cloxacilin (2 g intravenous every 4 h) and cephtriaxone (2 g intravenous/24 h). in the past 2 years the treatment of some of the patients has been completed in an outpatient manner, in a program of home hospitalization.

The progression of the joint infection was satisfactory in 10 (52.6%) cases and poor in 5 (26.3%); 3 (15.8%) deaths attributable to infection occurred: one of them in a patient with AIDS who died of sepsis after 5 days of treatment (case 9), a patient with a resistant staphylococcus infection who presented multiorganic failure (case 13), and a patient with mitral necrotizing endocarditis (case 8). In another patient (case 12) follow-up was lost because the patient abandoned the hospital without being discharged after 22 days of intravenous antibiotic treatment.

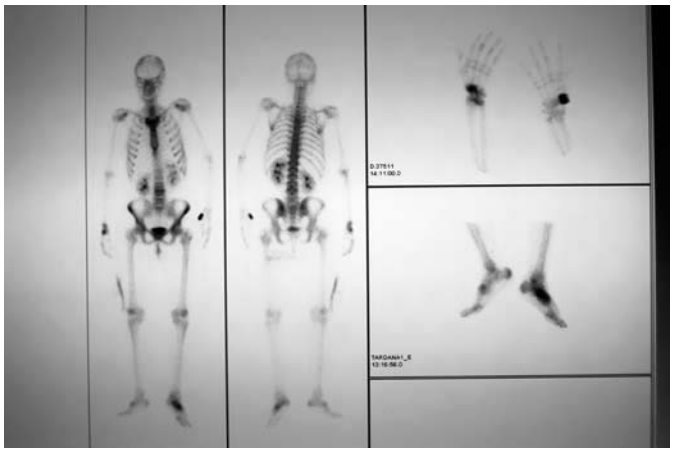

Figure. Case 2. Bone scan with MDP-^{99M}Tc. Useful in the detection of silent and multiple septic foci in their initial phases. Reinforcement of the moderate intensity activity on the left scapulohumeral joint. The right hand shows an increase in radiocarpal uptake and an increased intensity in the trapecium-trapezoidal area. The left tarsal region shows a general increase in activity.

Arthrotomy was performed in 4 (21%) cases; in a diabetic patient with necrotizing fasciitis and myositis, making an infracondyleal amputation necessary (case 14), and in another case a soft-tissue debridement was performed. Complications were seen in the form of joint movement limitation in 9 (47.4%) patients.

Discussion

The bibliographic references regarding polyarticular septic arthritis are scarce. Dubost et al[4] published in 1993 the biggest series, with a total of 25 cases. Approximately 15% of bacterial arthritis is polyarticular. Men predominated, both in the literature as in the present series. The most common underlying disease was RA, present in half of the published cases.[5]

Immunodeficiency and other chronic diseases are other predisposing factors detected. The presence of an underlying rheumatic disease leads to even more variability in its presentation, making a synovial fluid culture of the utmost importance in all of the cases. In addition to RA, gout can also be associated to a multiple joint infection, although this is not often reflected in the literature.[6] In a series of 30 cases of coexisting septic arthritis and gout, 3 (10%) patients had an oligoarticular infection,[7] with a mortality of 6.7%. In our group, gouty arthritis was present in 3 (18.7%) patients, even more cases than RA (12.5%).

Patients with infectious polyarthritis are older and have a greater frequency of positive blood cultures than patients with monoarticular infection.[4,5] Infectious monoarthritis in RA is more common in women,[8] while septic polyarthritis is more common in males, both in the general population and in patients with RA. Frequently, these patients present concomitant extra-articular infections, especially endocarditis, lung and soft tissue infections. Septic polyarthritis must be considered even in the context of a less florid clinical picture, because up to a third of cases has little fever and an absence of leukocytosis.

Thirty to fifty percent of septic arthritis that occur in patients with RA are polyarticular. They generally appear in patients with an evolved disease, who are treated with steroids and frequently have foot ulcers. In patients with systemic lupus erythematosus (SLE) it is less frequent than in RA, although literature references have increased in the past decades.[9] In these patients, gramnegative bacilli infection, particularly *Salmonella* (60% of septic arthritis) is more common.[10] An oligoarticular presentation is frequent and the hip seems to be especially affected. It appears in young women who have undergone steroid treatment and the presence of multiple avascular necroses has been described as a risk factor for polyarticular infection,[11] with a mortality of 10%-25%.

HIV infected patients also are at risk for polyarticular infection, especially when CD4 <200/µL.[12] Two of our patients had AIDS.

In our series, apart from the already mentioned chronic joint disease, diabetes mellitus, chronic liver disease, and chronic renal failure also had a great protagonist role as risk factors. However, it must be pointed out that almost a third of the patients did not have recognizable risk factors, as has been communicated by other authors.[13]

The most commonly affected joint, as referenced in the literature, is the knee, followed by the elbows, shoulders, and hips. However, in this series second place went to the ankle. The frequent affection of the acromioclavicular joint, bilateral in 2 patients, also stands out. The mean number of infected joints in our patients was 3, something similar to what is referred in the literature.[4,5] The importance of looking for infection sites on the spine in patients with proven septic arthritis must be pointed out. Narváez et al[14] showed that 36% of patients with bacterial intervertebral arthritis presented

Table 4
Treatment and Progression of Cases

Cases	Duration of Antibiotic Treatment, d	Debridement	Evolution	Complications
1	28	No	Good	No
2	30	No	Good	Sympathetic-reflex dystrophy wrist D
3	90	Yes; knee and gluteus	Poor	Gluteal abscess, septic shock
4	18	No	Good	No
5	16	Yes; ankle D	Good	No
6	80	Soft tissue debridement	Good	No
7	54	No	Good	Ascitis, esophageal variceal bleeding
8	15	No	Death	Mitral necrotizing endocarditis
9	Death on the fifth day	No	Death	Death
10	23	No	Poor	
11	34	No	Good	No
12	22	No	Unknown	Endocarditis
13	Death on the fifth day	No	Death	Multiorganic failure
14	42	Amputation	Good	
15	56	Yes; knee and bilateral elbow bursotomy	Poor	Generalized edema, malnutrition, acute renal failure, foot ischemia, gout
16	46	No	Good	No
17	105	No	Poor	Septic shock, myopathy with tetraparesia, respiratory insufficiency
18	50	No	Good	Diabetes mellitus
19	78	Yes; posterior girdlstone	Poor	Wound infection, bleeding

simultaneously with other foci of joint or soft tissue infection. *S aureus* is the most common infectious agent, implicated in 50%-80% of cases. Group B streptococcus, pneumococcus, and *Hemophilus influenzae* also produce polyarticular infection. A third of the cases of bacterial arthritis due to *Stresptococcus agalactiae* affect more than one joint.[15] In the septic polyarthritis of a patient with RA the main agent is *S aureus,* while in other patients it is more frequent to see streptococci and gramnegative bacilli, especially *H influenzae.* Blood cultures are positive in most of the cases and there is frequently other septic, extra-skeletal sources.[4]

Six percent of the general series of septic arthritis are attributed to *S pneumoniae.* The polyarticular form (25%-36%) and bacteremia (72%) are more frequent with this germ than with other germs.[16-18] Most of the cases have an extraarticular source of pneumococcal infection.[19] On the contrary, Dubost et al[20] compared 2 series of septic arthritis induced respectively by *Streptococcus* (55 cases) and *S aureus* (166 cases), without differences regarding polyarticular presentation. Another of the germs frequently implied in the polyarticular infection is *H influenzae*. Borestein et al,[21] in a series of 29 cases of septic arthritis in adults, produced by this agent, observed a polyarticular involvement in 48% and the associated risk factors included alcoholism, RA, SLE, and diabetes mellitus.

Apart from polyarticular, sometimes the infection is polymicrobial,[22] as occurred in one of the patients in our series. Due to its severity it must also be remembered that *Neisseria meningitides* can present inflammatory arthritis and, more rarely, septic polyarticular arthritis.[23]

Mortality in septic polyarthritis reaches 30% of cases in spite of proper antibiotic treatment, versus 4% in cases of monoarticular infection. This number has remained stable during the past 40 years. In the present study 3 (15.8%) patients died in the context of a polyarticular infection, all of them with important comorbidity. Factors related to a poor prognosis were age over 50, RA, staphylococcal infection, and a late diagnosis. Mortality in septic polyarthritis in the context of RA reaches 50% of patients, versus 16% of monoarticular infections in RA.[5]

Epstein et al[9] documented 7 cases of non-gonococcal septic arthritis, 5 of whom had an underlying rheumatic disease with an immediate mortality of 57%. In the review of the literature it was seen that the mortality of the polyarticular forms was duplicated in patients with RA when compared to the rest (56% and 23%, respectively).

Age also plays a role on prognosis. Gavet et al,[24] in a series of 335 cases of septic arthritis, described a group of 42 (12.5%) patients who were older than 80, 12% of them with polyarticular affection.

Septic arthritis in patients over 80 years of age has a mortality rate of 9.5%, very superior to that of patients under 60 (0.7%). In our group, only 1 patient was older than 80 and the ages of the patients that died were 73, 75, and 17 years.

Some authors have pointed out that surgical debridement is frequent in all of the patients with polyarticular infection,[4,5] and in our series 4 (21%) patients underwent an arthrotomy.

As a conclusion it must be stated that the presence of oligo or polyarthritis does not exclude the diagnosis of infectious arthritis. The existence of risk factors is important, including precious inflammatory joint disease. *S aureus* continues to be the most frequent causal micro-organism. Morbidity and mortality (15%-50%) in this for of joint infection is important, making it necessary to have a high level of suspicion and perform a systematic examination of all of the joints.

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