Clinical and epidemiological differences between septic arthritis of the knee and hip caused by oxacillin-sensitive and -resistant *s. aureus*

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OBJECTIVE: To establish the risk factors for joint infection by oxacillin-resistant *Staphylococcus aureus* (MRSA) using clinical and epidemiological data.

METHODS: All septic arthritis cases of the knee and hip diagnosed and treated in our institution from 2006 to 2012 were evaluated retrospectively. Only patients with cultures identified as microbial agents were included in the study. The clinical and epidemiological characteristics of the patients were analyzed, seeking the differences between populations affected by MRSA and oxacillin-sensitive *Staphylococcus aureus* (MSSA).

RESULTS: *S. aureus* was isolated in thirty-five patients (46.0%) in our total sample, 25 in the knee and 10 in the hip. Of these 35 patients, 22 presented with MSSA and 13 presented with MRSA. Provenance from a health service-related environment, as described by the Centers for Disease Control and Prevention, was the only variable associated with oxacillin-resistant strains of this bacterium ($p = 0.001$).

CONCLUSION: Provenance from a health service-related environment was associated with a higher incidence of MRSA-related septic arthritis, suggesting that this agent should be considered in the initial choice of antibiotic treatment. Previous surgeries of the knee or affected limb and the absence of leukocytes might also be related to infection with this agent.

KEYWORDS: Knee Infection; Hip Infection; Septic Arthritis; MRSA.

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INTRODUCTION

Septic arthritis is an orthopedic disease that is difficult to characterize epidemiologically (1,2). In adults, the lower limbs are more often affected, with the knees being the site of highest incidence, followed by the hips (3-5). In recent years, the prevalence of this infection has increased due to the greater number of invasive orthopedic procedures, the aging population and the increased use of immunosuppressant drugs (6,7).

The most common microbial agent in septic arthritis is *Staphylococcus aureus*, with a prevalence of approximately 50% (8,9). This bacterium is the most commonly found in all age groups, with the exception of children younger than two years of age. Over the last few years, particularly since 2000, there has been an increasing incidence of oxacillin-resistant strains of this bacterium (MRSA) (8-11).

Infections by MRSA are increasing, particularly among the elderly, intravenous drug users and patients who have undergone orthopedic procedures. This increase has become a public health care issue in many parts of the world (6,12-14).

According to previously conducted studies, MRSA infections cause more suppurative complications, prolonged fevers and longer hospitalizations (15,16).

This situation may be related to a failure to consider the causative agent in the initial empirical antibiotic therapy. Weston et al. showed that a delay in starting treatment, which can occur in cases in which the agent is not considered in the initial antibiotic therapy, led to a worse prognosis for the disease (17).

The objective of this research was to establish the risk factors for joint infections due to MRSA, through a study of

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clinical and epidemiological data. The results of this research could lead to the consideration of this etiological agent in the first line of empirical antibiotic therapy for affected patients.

METHODS

All of the cases of septic arthritis of the knee and hip diagnosed and treated in our institution from 2006 to 2012 were evaluated retrospectively. All of the records of patients with IDC-10 diagnoses of septic arthritis were located and the epidemiological, clinical and laboratory data were collected through a detailed chart review, with the information recorded on a standard form. Patients diagnosed with infections for less than a year following a surgical procedure on the affected limb were excluded because these cases were considered to be possible infections of the surgical site. Patients with infections associated with joint prostheses were also excluded.

Only patients with a culture identifying a microbial agent in the initial diagnostic puncture or from surgical drainage were included. All of the cultures were obtained in appropriate surgical environments using rigorous aseptic techniques and the materials were deposited in thioglycate tubes. All of the analyses and procedures were performed according to the standards established by the Clinical and Laboratory Standards Institute (CLSI) (18). Among the selected patients, those with a positive culture for *S. aureus* were divided into two groups: strains sensitive to oxacillin (MSSA) and strains resistant to this antibiotic (MRSA).

The following parameters were analyzed for all of the patients: sex; age; cause of infection; the provenance of the patient to categorize the infection as community- or health services-related, as described by the guidelines of the Centers for Disease Control and Prevention (19); leukocyte count, C-reactive protein (CRP) and erithrocytes sedimentation rate (ESR) values from the initial blood analysis; the presence of clinical signs, such as fever, pain, or swelling in the knee or hip; the number of surgical drainages performed; clinical comorbidities (high blood pressures and diabetes); prior orthopedic surgeries of the limb or joint affected; immunosuppression (HIV, inflammatory arthritis, cancer); the time from onset of symptoms to drainage; previous joint pain; systemic and articular complications; and hospitalization time. Gram staining and synovial fluid culture results were also analyzed.

Univariate statistical analysis was performed using the chi-square or Fisher's exact test, or likelihood ratio tests when the frequency of the event was very low.

The tests were conducted with a level of significance of 5%.

The study was conducted following approval from the science and research ethics committee of our institution.

RESULTS

Between 2006 and 2012, 76 cases of septic knee and hip arthritis were drained and presented positive cultures. *S. aureus* was isolated in 35 (46.0%) of these patients, in the knee in 25 cases and in the hip in the remaining 10 cases.

Twenty-two of these patients presented with MSSA and 13 presented with MRSA. The average age of the patients with MRSA was 40.5+/-24.9 years old (ranging from 3 to 74 years) and the average age of those with MSSA was 39.2+/-20.9 years old (ranging from 7 to 76 years).

All of the studied data are summarized in Table 1.

Following univariate statistical analysis, provenance of the patient from a health service-related environment was the only variable associated with the presence of oxacillin-resistant bacterial strains ($p = 0.001$). Both prior surgery of the limb or joint affected and the absence of a change in the leukocyte count suggested a higher frequency of MRSA isolation but without statistical significance (Table 2).

DISCUSSION

Septic arthritis is an infection that has a significant impact on our environment. Our case series presented an average of approximately 11 cases per year, with approximately 5 cases in which *S. aureus* was identified among the cultures. Eder et al., in a 17-year analysis from Israel, found only 110 confirmed cases, while in Switzerland, Clerc et al. encountered 83 cases in 10 years, considering only knees and hips (20,21).

S. aureus is the most common agent identified in cases worldwide, with higher prevalence rates reported in Europe, Asia, the Middle East, Africa, the United States and South America (14,21-26). Some studies, such as those conducted by Frazee et al. in the United States and by Yamagishi in Japan (14,27), have shown a higher proportion of MRSA relative to MSSA. In our case series, MSSA strains remained the majority.

In cases of MRSA, patients might not receive appropriate initial empirical antibiotic treatment because the resistance profile can only be identified from the results of cultures collected from the initial puncture or from surgical drainage. Thus, it is critical to attempt to identify risk factors for the presence of MRSA, with the aim of improving the efficacy of the initial antibiotic therapy. In their series, Yamagishi et al., Clerc et al., and Helito et al. found it necessary to broaden the antibiotic therapy spectrum after analyzing definitive cultures with an antibiogram (20,25,27).

Among the variables analyzed in this study, the only one with a confirmed statistical correlation for the presence of MRSA was the provenance of the patient. Patients with a close relationship with health care services, according to the definition of the Centers for Disease Control and Prevention (19), had a greater likelihood of presenting cultures positive for MRSA. The higher prevalence of infections in hospital services and in asymptomatic carriers of this bacterium has been described previously (14,21).

Among the variables that suggested a relationship with MRSA, we believe that surgery performed previously on the limb or affected joint might have high significance. Causative agents of musculoskeletal infections are often present in an inactive state, manifesting themselves later. Courvoisier et al. described two cases of osteomyelitis of the tibia that manifested twenty years after a surgical procedure of the leg (28). These situations could warrant special attention and broadening of the spectrum of antibiotics used for the initial presentation.

Unlike the situation with limb surgeries, we did not find a plausible explanation for the absence of leukocytes in cases affected by MRSA. According to the studies of Arnold et al. and Martinez-Aguilar et al., MRSA infections evolve with more fevers and suppurative complications, conditions that are usually associated with an increased leukocyte count; however, this was not the finding in our case series (15,16).

Table 1 - Clinical and epidemiological summary of study results and statistical analysis.

	MRSA group	MSSA group	*p*
Sex			0.708
Male	8 (61.5%)	16 (72.7%)	
Female	5 (38.5%)	6 (27.3%)	
Average age (years old)	40.5	39.2	0.871
Diagnostics			
Leukocytosis	5 (38.5%)	15 (68.1%)	**0.086**
Leukocyte count (average)	10853	12915	0.325
CRP increase (number of patients)	12 (92.3%)	22 (95.6%)	
CRP value (average)	150	166	0.749
ESR increase (number of patients)	12 (92.3%)	22 (95.6%)	
ESR value (average)	69	58	0.394
Fever	5 (38.5%)	9 (40.9%)	0.886
Pain	10 (76.9%)	15 (68.1%)	0.709
Joint effusion	10 (76.9%)	17 (77.2%)	>0.999
Time to diagnosis (days)	11.4	16.6	0.585
Gram staining	7 (53.8%)	14 (63.6%)	0.568
Etiology			0.586
Hematogenic	12 (92.3%)	20 (91.0%)	
Direct inoculation	0	1 (4.5%)	
Contiguity	1 (7.7%)	1 (4.5%)	
Patient provenance			**0.001**
Community	2 (15.3%)	16 (72.7%)	
Health Services	11 (84.7%)	6 (27.3%)	
Previous articular disease	5 (38.5%)	8 (36.3%)	>0.999
Comorbidities	10 (76.9%)	10 (45.4%)	0.282
Number of comorbidities (average)	1.6	0.8	0.09
Immunosuppression	5 (38.5%)	5 (22.7%)	0.444
Previous joint surgery	4 (30.7%)	1 (4.5%)	**0.052**
Previous limb surgery	5 (38.5%)	2 (9.0%)	**0.075**
Treatment			
Number of procedures per patients (average)	2.3	1.6	0.154
Hospitalization days per patient (average)	32.8	21.5	0.109
Systemic complications	3 (23.0%)	2 (9.0%)	0.337
Articular complications	3 (23.0%)	4 (18.1%)	>0.999

Further studies with more patients must be conducted to confirm this result.

None of the other variables studied reflected a difference between the MRSA and MSSA groups, not even the presence and number of comorbidities or immunosuppression; therefore, distinguishing this profile of sensitivity in the initial presentation remains difficult.

Table 2 - Statistical analysis.

Variable	*p*
Joint	0.259
Sex	0.708
Inoculation type	0.586
Provenance	**0.001**
Fever	0.886
Pain	0.709
Swelling	>0.999
Grams staining	0.568
Comorbidities	0.282
Number of comorbidities	0.09
Immunosuppression	0.444
Prior joint disease	>0.999
Previous surgery of the affected joint	0.052
Previous surgery of the affected limb	0.075
Systemic complications	0.337
Articular complications	>0.999
Leukocyte count	0.325
Leukocytosis	0.086
CRP value	0.749
ESR value	0.394
Number of drainages	0.154
Time from drainage to onset of symptoms	0.585
Hospitalization time	0.109

This study had some limitations, such as the retrospective data analysis and the relatively small number of patients. However, given the lack of literature data on this subject in our country, we believe that this analysis could be very relevant.

Provenance from a health services-related environment was associated with a higher incidence of septic arthritis related to MRSA, suggesting that this agent should be considered in the initial selection of an antibiotic treatment. Prior surgeries to the affected joint or limb and the absence of leukocytes might also be related to articular infections caused by this agent.

AUTHOR CONTRIBUTIONS

Helito CP was responsible for the project development and manuscript writing. Zanon BB was responsible for bibliographic research, data collection and manuscript writing. Miyahara HS, Lima AL, Oliveira PR were responsible for the project development and analysis of the results. Vicente JR and Demange MK were responsible for the bibliographic research and manuscript review. Pecora JR and Camanho GL were responsible for the project supervision and manuscript review.

REFERENCES

1. Donatto KC. Orthopedic management of septic arthritis. Rheum Dis Clin North Am. 1998;24(2):275-86, http://dx.doi.org/10.1016/S0889-857X(05)70009-0.

2. Pioro MH, Mandell BF. Septic arthritis. Rheum Dis Clin North Am. 1997;23(2):239-58, http://dx.doi.org/10.1016/S0889-857X(05)70328-8.
3. Shetty AK, Gedalia A. Septic arthritis in children. Rheum Dis Clin North Am. 1998;24(2):287-304, http://dx.doi.org/10.1016/S0889-857X(05)70010-7.
4. Bettin D, Schul B, Schwering L. Diagnosis and treatment of joint infections in elderly patients. Acta Orthop Belg. 1998;64(2):131-5.
5. Dessì A, Crisafulli M, Accossu S, Setzu V, Fanos V. Osteo-articular infections in newborns: diagnosis and treatment. J Chemother. 2008;20(5):542-50.
6. Mathews CJ, Weston VC, Jones A, Field M, Coakley G. Bacterial septic arthritis in adults. Lancet. 2010;375(9717):846-55, http://dx.doi.org/10.1016/S0140-6736(09)61595-6.
7. Geirsson AJ, Statkevicius S, Víkingsson A. Septic arthritis in Iceland 1990-2002: increasing incidence due to iatrogenic infections. Ann Rheum Dis. 2008;67(5):638-43.
8. Gillespie WJ, Nade S. Musculokeletal infections. Melbourne: Blackwell Scientific Publications; 1987. pp 283–302.
9. Carpenter CR, Schuur JD, Everett WW, Pines JM. Evidence-based diagnostics: adult septic arthritis. Acad Emerg Med. 2011;18(8):781-96, http://dx.doi.org/10.1111/j.1553-2712.2011.01121.x.
10. Kaplan SL. Recent lessons for the management of bone and joint infections. J Infect. 2014;68 Suppl 1:S51-6.
11. Dubost JJ, Soubrier M, De Champs C, Ristori JM, Bussiére JL, Sauvezie B. No changes in the distribution of organisms responsible for septic arthritis over a 20 year period. Ann Rheum Dis. 2002;61(3):267-9, http://dx.doi.org/10.1136/ard.61.3.267.
12. García-Arias M, Balsa A, Mola EM. Septic arthritis. Best Pract Res Clin Rheumatol. 2011;25(3):407-21, http://dx.doi.org/10.1016/j.berh.2011.02.001.
13. Goldenberg DL. Septic arthritis. Lancet. 1998;351(9097):197–202, http://dx.doi.org/10.1016/S0140-6736(97)09522-6.
14. Frazee BW, Fee C, Lambert L. How common is MRSA in adult septic arthritis? Ann Emerg Med. 2009;54(5):695-700, http://dx.doi.org/10.1016/j.annemergmed.2009.06.511.
15. Arnold SR, Elias D, Buckingham SC, Thomas ED, Novais E, Arkader A, Howard C. Changing patterns of acute hematogenous osteomyelitis and septic arthritis: emergence of community-associated methicillin-resistant Staphylococcus aureus. J Pediatr Orthop. 2006;26(6):703-8, http://dx.doi.org/10.1097/01.bpo.0000242431.91489.b4.
16. Martínez-Aguilar G, Avalos-Mishaan A, Hulten K, Hammerman W, Mason EO Jr, Kaplan SL. Community-acquired, methicillin-resistant and methicillin-susceptible Staphylococcus aureus musculoskeletal infections in children. Pediatr Infect Dis J. 2004;23(8):701-6, http://dx.doi.org/10.1097/01.inf.0000133044.79130.2a.
17. Weston VC, Jones AC, Bradbury N, Fawthrop F, Doherty M. Clinical features and outcome of septic arthritis in a single UK Health District 1982-1991. Ann Rheum Dis. 1999;58(4):214-9, http://dx.doi.org/10.1136/ard.58.4.214.
18. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing – 22nd ed. CLSI document M100-S22. Wayne, PA: Clinical and Laboratory Standards Institute; 2012.
19. Centers for Disease Control and Prevention. CDC/NHSN surveillance definition of health care-associate infection and criteria for specific types of infections in the acute care setting. Am J Infect Control. 2008;36(5):309-32.
20. Eder L, Zisman D, Rozenbaum M, Rosner I. Clinical features and aetiology of septic arthritis in northern Israel. Rheumatology. 2005;44(12):1559-63, http://dx.doi.org/10.1093/rheumatology/kei092.
21. Clerc O, Prod'hom G, Greub G, Zanetti G, Senn L. Adult native septic arthritis: a review of 10 years of experience and lessons for empirical antibiotic therapy. J Antimicrob Chemother. 2011;66(5):1168-73, http://dx.doi.org/10.1093/jac/dkr047.
22. Al Arfaj AS. A prospective study of the incidence and characteristics of septic arthritis in a teaching hospital in Riyadh, Saudi Arabia. Clin Rheumatol. 2008;27(11):1403-10, http://dx.doi.org/10.1007/s10067-008-0934-9.
23. Dubost JJ, Soubrier M, Sauvezie B. Pyogenic arthritis in adults. Joint Bone Spine. 2000;67(1):11-21.
24. Razak M, Nasiruddin J. An epidemiological study of septic arthritis in Kuala Lumpur Hospital. Med J Malaysia. 1998;53 Suppl A:86-94.
25. Helito CP, Noffs GG, Pecora JR, Gobbi RG, Tirico LE, Lima AL, et al. Epidemiology of septic arthritis of the knee at Hospital das Clínicas, Universidade de São Paulo. Braz J Infect Dis. 2014;18(1):28-33.
26. de Souza Miyahara H, Helito CP, Oliva GB, Aita PC, Croci AT, Vicente JR. Clinical and epidemiological characteristics of septic arthritis of the hip, 2006 to 2012, a seven-year review. Clinics. 2014;69(7):464-8, http://dx.doi.org/10.6061/clinics/2014(07)04.
27. Yamagishi Y, Togawa M, Shiomi M. Septic arthritis and acute hematogenous osteomyelitis in childhood at a tertiary hospital in Japan. Pediatr Int. 2009;51(3):371-6, http://dx.doi.org/10.1111/j.1442-200X.2008.02740.x.
28. Courvoisier A, Grimaldi M, Rubens-Duval B, Chaussard C, Saragaglia D. Flare-up of previously quiescent chronic osteomyelitis 20 years after childhood skeletal traction: a report of two cases. Orthop Traumatol Surg Res. 2011;97(8):886-9, http://dx.doi.org/10.1016/j.otsr.2011.05.016.