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Outcomes of Septic Joint Arthritis of the Hand: A Dual-Center Study

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Abstract

Purpose: The optimal duration of targeted systemic antibiotic therapy after lavage for native septic hand arthritis is unknown. Significant variation in daily clinical practice has been described across different centers.

Methods: We assessed variables associated with remission in septic hand and wrist arthritis by means of a retrospective cohort study of adult patients hospitalized for septic native joint arthritis of the hand and wrist between March 2007 and March 2013 at 2 university hospitals in Switzerland. The data review was principally focused on antibiotic regimens and surgical procedures.

Results: We included 80 consecutive cases of hand arthritis (median age, 56 years; 26 women and 54 men; 16 immunocompromised individuals). All patients underwent median of a 1 surgical irrigation and received concomitant systemic antibiotic therapy for a median duration of 28 days including 5 days of intravenous therapy. Remission was achieved in 74 cases (93%); however, there were 26 episodes (33%) of non-infectious sequelae such as osteoarthritis or persistent pain. No variables were associated with remission or sequelae in the multivariate logistic regression analysis. Moreover, outcomes were identical for <5 days versus ≥ 5 days of intravenous therapy and for <2 weeks versus >4 weeks of total antibiotic treatment.

Conclusions: The rate of post-surgical remission for adult native joint hand septic arthritis is high and independent of immune suppression, number of surgical debridement procedures, and modality/duration of antibiotic therapy.

Type of study/Level of evidence: III, retrospective study.

Keywords: Antibiotic; Hand arthritis; Septic joint arthritis; Joint infection; Joint irrigation

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Introduction

Few studies have evaluated the infectious recurrence of native joint hand and wrist septic arthritis in adults. Accordingly, the optimal or minimal concomitant antibiotic treatment regimen remains controversial [1]. For this reason, surgeons and physicians often treat hand arthritis in analogy to hip and knee joint infection. Several different regimens have been recommended such as 2 weeks of intravenous therapy for streptococci, 3 to 4 weeks of intravenous for staphylococci and Gram-negative bacteria and 4 weeks of therapy for immunosuppressed patients or those with joint pathology such as severe osteoarthritis [2,3]. Other physicians only prescribe intravenous and subsequently oral antibiotics for a total of 2 weeks after surgical debridement and drainage or for longer periods of time without additional justification [1,4,5]. Assuming adequate surgical drainage, septic arthritis of the hand and wrist is theoretically treatable with a short course of oral antibiotics that have good oral bioavailability and synovial penetration [1]. The aim of this study was to compare clinical parameters associated with remission in native joint hand and wrist arthritis, placing an emphasis on surgical and antibiotic-related treatment modalities in order to inform the optimal treatment approach.

Table 1: Comparison of adult patients with hand and wrist native joint septic arthritis from 2 university hospitals in Switzerland.

n=80	Center 1 n=39	*p*-value*	Center 2 n=41
Female/male	10 (26%)/29 (74%)	0.201	16 (39%)/25 (61%)
Median age	59 years	0.227	53 years
Wrist arthritis	18 (46%)	0.001	2 (5%)
Immune suppression+	11 (28%)	0.074	5 (12%)
Intravenous drug abuse	4 (10%)	0.642	3 (7%)
Median serum C-reactive protein level	83 mg /L	0.035	39 mg/L
Bacteremia	4 (10%)	0.149	1 (2%)
Median no. of surgical interventions	1	0.105	1
Second look	11 (28%)	0.074	5 (12%)
Median duration of antibiotic treatment	28 days	0.847	25 days
≤ 14 days	10 (26%)	0.114	5 (12%)
>14 to 28 days	11 (28%)	0.114	20 (49%)
>28 days	18 (46%)	0.114	16 (39%)
Median duration of intravenous treatment	8 days	0.001	2 days
≤ 5 days	11 (28%)	0.001	36 (88%)
>5 days	28 (72%)	0.001	5 (12%)
Median delay from onset to surgery	2 days	0.028	3 days
Duration of delay >7 days	16 (41%)	0.066	9 (22%)
Remission	35 (90%)	0.361	39 (95%)
Median length of hospital stay	8 days	0.002	4 days

*Statistically significant results are italicized and bolded.
+Immunosuppression was defined as diabetes mellitus, steroids, HIV disease, pregnancy, or active cancer.

Methods

Setting: The Geneva and Vaud University Hospitals are 2 tertiary centers in Western Switzerland (Hôpitaux Universitaires Genève [HUG] and Centre Hospitalier Universitaire Vaudois [CHUV]). Each center is equipped with a Hand Surgery Unit and 2 teams of surgeons and infectiologists. Open debridement, drainage, and irrigation for arthritis were usually performed as an emergency. During the first 2 days after surgery, the joint was immobilized with a cast. Associated pain was managed with the maximum recommended doses of paracetamol and ibuprofen and the addition of morphine as necessary. Steroid use is generally avoided for adult septic hand arthritis [6]. Revision surgery was performed at the discretion of the attending surgeon. Selection of the antibiotic regimen was performed by infectiologists. Surgeons (C. T. M., T. R., N. L., M. G., and E. G.) and an infectious diseases expert (I. U.) retrospectively recorded demographic, therapy, and outcome variables in an Excel® spreadsheet in 2 independent groups. Any disagreements between the groups were resolved by consensus. Database assembly was concluded on June 30, 2016.

Study design, definitions and criteria: We performed a retrospective dual-center cohort study of all adult patients hospitalized for acute native joint infectious arthritis of hand and wrist between March 2007 and March 2013. Eligible cases had a minimum follow-up period of 2 months at the same Hand Surgical Unit. We applied several exclusion criteria. Since arthritis can be caused by various bacterial and viral pathogens, we only included infections with purulent synovial fluid and confirmed bacterial growth on intraoperative specimens. To enhance specificity, we only considered samples with positive cultures on agar plates and significant growth. Cases with growth in liquid enrichment culture only were excluded. Other exclusion criteria included episodes of recurrent arthritis; patients who did not undergo surgical drainage; rheumatoid polyarthritis; the presence of an implant; adjacent osteomyelitis; neoplasms; adjacent bone trauma; amputation as the primary therapeutic approach; viral, fungal, mycobacterial, mycoplasmal, gonococcal, brucellar, parasitic, and nocardial arthritis; and pediatric cases [7-9]. We defined remission as complete clinical and laboratory resolution of the infection for a minimal active follow-up period of 2 months after the completion of antibiotic treatment. Recurrence was evidenced by new signs of infection with the same microorganism at least 2 weeks after the completion of treatment for the initial episode. Sequelae were non-infections handicaps persisting at 2 months follow-up. The study protocol was approved by the ethics committees of both participating hospitals (No. 08-017R, No. 15-014, and Protocol 258/15).

Statistical analyses: We compared patient groups using Pearson χ^2 or Wilcoxon rank-sum tests. Separate unmatched logistic regression analyses were used to determine associations with the outcomes "remission" and "sequelae." Independent variables with $p \leq 0.2$ in the univariate analysis were introduced stepwise into a multivariate analysis unless variables were related to surgical interventions, antibiotic treatment, or the care facility, in which case they were automatically included in the final model [10]. Using these criteria, the final variables were age, number of surgical interventions, duration of intravenous antibiotic treatment, duration of total antibiotic treatment, immune suppression, and the tertiary center. Incubation times and antibiotic durations were assessed as both categorical and continuous variables. For analysis as a categorical variable, the total duration of antibiotic therapy was divided into 0 to 14 days, 15 to

Table 2: Comparison of adult patients with recurrent hand and wrist native joint septic arthritis and remission.

n=80	Recurrence n=6	*p*-value*	Remission n=74
Female/male	1 (17%)/5 (83%)	0.389	25 (34%)/49 (66%)
Median age	58 years	0.277	55 years
Immune suppression+	3 (50%)	0.056	13 (18%)
Intravenous drug abuse	0 (0%)	0.43	7 (9%)
Median serum leukocyte count	8.4 g/L	0.058	10.6 G/L
Bacteremia	0 (0%)	0.511	5 (7%)
Second surgical look	3 (50%)	0.056	13 (18%)
Antibiotic treatment ≤ 14 days	1 (17%)	0.423	14 (19%)
Antibiotic treatment 14 to 28 days	1 (17%)	0.423	30 (41%)
Antibiotic treatment >28 days	4 (67%)	0.423	30 (41%)
Median delay from onset to surgery	0 day	0.476	2 days
Duration of delay >7 days	4 (67%)	0.052	21 (28%)
Non-infectious sequelae	4 (67%)	0.063	22 (30%)

*Statistically significant results are italicized and bolded.
+Immunosuppression was defined as diabetes mellitus, steroids, HIV disease, pregnancy, or active cancer.

28 days, and >28 days, corresponding to local prescription practices. Intravenous antibiotic therapy was similarly stratified as 0 to 5 days and >5 days. Incubation time prior to surgical drainage was arbitrarily stratified at ≤ 7 days and >7 days. Furthermore, we graphically plotted remission rate against the duration of antibiotic administration to detect potential thresholds of minimal antibiotic duration. A *p*-value ≤ 0.05 (2-tailed) was statistically significant.

Results

Patients: We screened 90 consecutive cases of native septic hand and wrist arthritis; of these, 3 patients met multiple exclusion criteria and 7 were addicted to intravenous drugs and thereby excluded from the study. Thus, 80 cases (26 women and 54 men) with a median age of 56 years (range, 18 to 94 years) were included in the analysis. Twenty patients (25%) were immunocompromised as a result of diabetes mellitus (9 patients), chronic steroid medication (3 patients), untreated human immunodeficiency virus (2 patients), severe alcoholism (3 patients), or oncological treatment for an active cancer (3 patients). Detailed patient data stratified by center are summarized in Table 1. CHUV had significantly more cases of wrist arthritis, longer durations of intravenous antibiotic use, and longer hospital stays than HUG (p<0.05).

Origin of infection and pathogens: The origin of infection was not reported in 20 cases (25%). The remaining 60 causes were domestic animal bites and other trauma (n=38), surgical site infections (n=6), intravenous drug abuse (n=6), and locoregional arthritis following an adjacent soft tissue infection (n=10). The median serum level of C-reactive protein at admission was 53 mg/L (range, 2mg/L to 410 mg/L) and 5 patients had bacteremia. Among 28 different microbiologic combinations, the predominant pathogen was *Staphylococcus aureus* in 26 cases (33%), of which 2 were methicillin-resistant. Twenty episodes (25%) were due to streptococci *S. pyogenes* (n=7) and *S. dysgalactiae* (n=4). The most frequent Gram-negative bacteria were *Pasteurella multocida* (n=4) and *Pseudomonas aeruginosa* (n=4).

Treatment: Patients underwent surgical treatment with a median delay of 2 days after infection onset (range, 0 to 48 days). Surgical re-intervention was performed a median of 3 days after the first operation. All patients received systemic antibiotic therapy. Irrigation was performed with 0.9% saline without local antibiotics or antiseptics. Wound dressings were changed once per day during the first 2 post-operative days. We identified 24 different intravenous antibiotic regimens and 18 different oral antibiotic regimens. Amoxicillin/clavulanate was the most frequently prescribed drug (65 episodes; 81%). Quinolones were used in 18 cases (23%), clindamycin in 19 cases (24%), and co-trimoxazole in 4 cases (5%). There was no specific reason for choosing non-beta-lactam treatment, but this selection was often related to an anamnestic penicillin allergy. In 5 cases of staphylococcal infection (6%), rifampicin was used in combination therapy despite the absence of foreign material. The median duration of total antibiotic therapy was 28 days (range, 1 to 132 days): therapy was ≤ 14 days in 15 cases (19%), 15 to 28 days in 31 cases (39%), and >28 days in 34 cases (43%). The median duration of intravenous therapy was 5 days (range, 0 to 47 days): the duration was <5 days in 47 cases (59%) and >5 days in 33 cases (41%). Immunocompromised patients tended to have longer treatment durations (median values, 32 days vs. 24 days in immunocompetent patients), but this difference was not statistically significant (p =0.12).

Outcomes: Seventy-four patients (93%) were still in remission after a median active follow-up period of 6.5 months (range, 3 to 63 months). In the crude comparison, there were no significant associations between any variables and remission (Table 2). Twenty-seven patients (33%) experienced sequelae including osteoarthritis (15 patients), deformation (2 patients), digital flexion deformity (2 patients), hypoesthesia (3 patients), and persistent pain (5 patients).

We performed unmatched logistic regression analyses with the outcomes "remission" (Table 3) and "sequelae" (Table 4). There were no significant associations between any variables and remission (Table 3). Intravenous therapy <5 days had the same outcome of >5 days (Odds Ratio [OR]: 0.2; 95% Confidence Interval [CI]: 0.1-3.9) and <2 weeks of total antibiotic treatment yielded the same outcome as >4 weeks (OR: 1.0; 95% CI: 0.1-20). Female sex was the only variable associated with sequelae (OR: 4.0; 95% CI: 1.1-15.2; Table 4). We were unable to detect a threshold antibiotic duration for recurrence or sequelae (data not shown). All final models were statistically adequate in terms of goodness-of-fit, with area under the

Table 3: Variables associated with remission after native joint septic hand and wrist arthritis (logistic regression).

	Univariate analysis	Multivariate analysis
n = 80	Odds ratio (95% confidence interval)	Odds ratio (95% confidence interval)
Age (continuous variable)	1.0 (0.9-1.0)	1.0 (0.9-1.1)
Hospitalization at Center 1 vs. Center 2	0.8 (0.2-9.8)	0.6 (0.1-9.0)
Immune suppression[+]	0.2 (0.1-1.2)	0.3 (0.1-1.6)
Serum C-reactive protein level at admission	1.0 (1.0-1.1)	-
Serum leukocyte count at admission	1.4 (0.9-2.1)	-
Delay from onset to surgery	0.9 (0.9-1.0)	-
Duration of delay >7 days	0.2 (0.1-1.2)	0.2 (0.1-1.4)
Number of surgical interventions	0.4 (0.2-0.9)	0.6 (0.3-1.4)
Second look	0.2 (0.4-1.2)	0.2 (0.1-2.0)
Duration of antibiotic treatment	0.9 (0.9-1.0)	0.9 (0.9-1.1)
>28 days vs. ≤ 14 days	0.7 (0.3-1.4)	1.0 (0.1-20.0)
Duration of intravenous treatment	1.0 (0.9-1.0)	1.0 (0.9-1.1)
>5 days vs. ≤ 5 days	0.1 (0.1-1.1)	0.2 (0.1-3.9)

*Statistically significant results are italicized and bolded.
[+] Immunosuppression was defined as diabetes mellitus, steroids, HIV disease, pregnancy, or active cancer.

Table 4: Variables associated with non-infectious sequelae after native joint septic hand and wrist arthritis (logistic regression).

	Univariate analysis	Multivariate analysis
n = 80	Odds ratio (95% confidence interval)	Odds ratio (95% confidence interval)
Female	4.1 (1.5-11.1)	4.0 (1.1-15.2)
Age (continuous variable)	1.0 (1.0-1.0)	1.0 (0.9-1.1)
Immunosuppression[+]	1.3 (0.4-4.1)	-
Serum C-reactive protein level at admission	1.0 (1.0-1.0)	-
Serum leukocyte count at admission	1.4 (0.9-1.1)	-
Delay from onset to surgery	1.1 (0.9-1.1)	1.0 (0.9-1.1)
Duration of delay >7 days	0.7 (0.3-2.1)	-
Number of surgical interventions	1.4 (0.8-2.4)	2.9 (0.9-1.1)
Second look	1.8 (0.6-5.7)	0.2 (0.1-2.0)
Duration of antibiotic treatment	1.0 (0.9-1.1)	0.9 (0.9-1.1)
>28 days vs. ≤ 14 days	1.0 (0.3-3.5)	1.3 (0.3-7.2)
Duration of intravenous treatment	0.9 (0.8-1.0)	0.8 (0.6-1.0)
>5 days vs. ≤ 5 days	0.3 (0.1-0.9)	-

*Statistically significant results are italicized and bolded.
[+]Immunosuppression was defined as diabetes mellitus, steroids, HIV disease, pregnancy, or active cancer.

curve values of 0.86 (95% CI: 0.62-1.00) and 0.81 (95% CI: 0.70-0.92), respectively.

Discussion

We report our experience treating 80 patients with septic native joint hand and wrist arthritis hospitalized in 2 different university hospitals in Western Switzerland. There were no significant associations between surgical parameters and remission. Likewise, we were unable to determine a threshold antibiotic duration for recurrence or sequelae. The odds ratios of antibiotic-related parameters and associated variability were often close to a value of 1, indicating equality. Specifically, outcomes did not vary when the duration of intravenous therapy was less than or greater than 5 days or when the total antibiotic duration was less than 2 weeks or more than 4 weeks. These observations were also valid for a subgroup of immunocompromised patients.

Few reports have addressed the appropriate or optimal antibiotic regimen for hand septic arthritis [1,4,11]. Angly et al. [11] investigated 31 adult patients who were operated for digital arthritis and reported zero recurrence of infection after surgery with an antibiotic regimen comprised of a median of 2 days intravenous therapy and 17 days oral therapy. Sendi et al. [4] retrospectively analyzed 101 cases of surgery for hand and wrist arthritis in adults and described a median of 2 days intravenous antibiotic therapy and 14 days of oral antibiotic therapy for acute cases. In this study, the corresponding duration for chronic infections was 28 days and cure of infection was noted in all episodes, with a good functional outcome in 79% of patients. To date, several studies have acknowledged the utility of short antibiotic durations for infectious arthritis, especially in children. Kim et al. [12] compared short and long durations of antibiotic treatment among 20 children

and found that intravenous therapy <10 days was sufficient after surgical drainage for hip arthritis. The results of a randomized clinical trial conducted by Peltola et al. [13] favored a 10-day rather than 30-day course of antimicrobial treatment for childhood septic arthritis. Jagodzinki et al. [14] prospectively demonstrated the efficacy of 3 days of intravenous therapy followed by 3 weeks of oral antibiotic therapy in a cohort of 70 children with septic arthritis in joints of the upper extremities. Consistent with our findings, another report indicated that early conversion from parenteral to oral antibiotics after a median of 7 days was equally effective to later conversion for the treatment of pediatric arthritis in a cohort of 186 children [15]. A cut-off of 7 days for conversion from intravenous to oral antibiotic therapy was similarly confirmed in a trial comparing 7 and 14 days of parenteral antibiotic therapy in 130 pediatric cases of acute hematogenous bone and joint infection [16].

In the present study, we observed sequelae in 33% of cases, consistent with the findings of Ross et al. [17] (sequelae in 26% of cases) and Vispo-Seara et al. [5] (sequelae in 20% of cases) in various contexts of septic arthritis. Our regression analysis did not reveal significant associations between any variables and sequelae except for female sex, suggesting that treatment modality is secondary to patient baseline characteristics when predicting the likelihood of recurrence and sequelae.

Our study had some limitations. First, the generalizability of our findings is limited given the nature of the study as a retrospective, dual-center investigation in a resource-rich setting. Second, we were unable to control for some important variables such as intraoperative severity scores, suction drain duration, or radiologic scores. Third, our analysis may have overlooked long-term sequelae in patients who underwent treatment elsewhere after the initial surgery; however, we believe that this scenario is unlikely as our facilities are the only tertiary centers for infections of the hand and wrist in the geographic area. Fourth, we did not investigate alternative treatments such as repetitive arthrocentesis or continuous irrigation [1,9]. Additionally, we cannot exclude bias in terms of confounding by indication; e.g., patients who were assumed to have a favorable outcome may have been preferentially prescribed short antibiotic courses. Finally, the current sample size was too small to allow for stratification by pathogen and antibiotic resistance pattern. S. aureus was the predominant pathogen in less than a third of patients and resistant pathogens were encountered in less than 10% of all episodes. As a general rule, therapeutic recommendations do not take into account the pathogen itself and rely on clinical presentation. Moreover, we demonstrated similar outcomes in previous studies comparing S. aureus and S. pyogenes in hand arthritis and flexor tenosynovitis [18,19]. For these reasons, we did not incorporate additional pathogen-related variables into our final models.

Conclusion

The results of the present retrospective dual-center study suggest that a total of 2 weeks of post-surgical antibiotic administration (5 days intravenous therapy followed by 10 day of oral therapy) is sufficient for septic joint arthritis of the hand and produces similar outcomes to 4-week antibiotic therapy. A future randomized controlled trial is necessary to confirm these findings for clinical application.

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