

Pyogenic arthritis of the fingers and the wrist: Can we shorten antimicrobial treatment duration?

Running Title: Arthritis of the fingers and hand

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Key points: Small joint arthritis of the finger and hand show considerable differences to septic arthritis of the larger joints. In this study, one or two surgical interventions and median antimicrobial treatment duration of 14 days showed a successful outcome.

KEYWORDS: septic arthritis; pyogenic arthritis; small joints; hand infections

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Abstract

Background: Pyogenic arthritis of the small joints (SJA) of the hand and wrist is a known but poorly described entity. The objective of this work was to characterize the clinical presentation, antimicrobial treatment and surgical interventions of native SJA treated in our tertiary centre.

Methods: According to predefined variables, medical records of adult patients with SJA treated in a Swiss university hospital between 2005 and 2013 were retrospectively analysed.

Results: The median age of 97 patients (101 joints) was 52 years (IQR 38–68 years); 52% had no comorbidity. SJA of the second and third fingers accounted for 53% of infections, with metacarpal-phalangeal and proximal interphalangeal joints most commonly involved. Of 86 (89%) episodes with an exogenous source, 63 (65%) followed a trauma. The most commonly isolated microorganism was *Staphylococcus aureus* (38%), followed by beta-haemolytic streptococci (13%) and *Pasteurella* spp. (11%). Eighty-seven episodes (89 joints) in patients with follow-up examinations were included in treatment and outcome analyses. Up to two surgical interventions were required to cure infection in 74 (83%) joints. Median antimicrobial treatment duration was 14 days (IQR 12–28 days), with amoxicillin/clavulanate administered in 74 (85%) episodes. At follow-up, cure of infection was noted in all episodes and good functional outcome in 79% of episodes.

Conclusions: SJA shows considerable differences from clinical patterns reported for larger joints. In our series, the outcome was good with no more than two surgical interventions and median treatment duration of 14 days in 79% of episodes.

Introduction

Pyogenic arthritis of the small joints of the hand and wrist is a known but poorly described entity. In previous reports, this condition accounted for less than 5% of all joint infections [1]. In recent analyses of 248 cases of septic arthritis, 37 (14.9%) involved the hand and 20 (8.1%) the wrist [2]. The management of pyogenic small joint arthritis (SJA) is less standardized than that of septic arthritis of the large joints (e.g., hip or knee joint) for both surgical treatment and antimicrobial therapy. The epidemiology of microorganisms causing SJA is not well established, as few studies have described it [3-5]. In addition, the optimal duration of antimicrobial therapy is yet to be elucidated [3, 4]. It is uncertain whether smaller and larger joints should be treated equally long. The objective of this work was to characterize the clinical presentation, the surgical interventions and antibiotic treatment duration of native SJA treated in our tertiary centre.

Methods

Subjects, setting and data set

We reviewed the medical records of adults (i.e., age \geq 18 years) with native SJA treated at the Department of Plastic and Hand Surgery, Bern University Hospital, Switzerland, from 2005 to 2013, according to extensively predefined variables. Two data sets were built after data acquisition, one for clinical presentation and one for treatment outcome analyses. For clinical presentation analyses, all episodes were reviewed. For outcome assessment, only those episodes of infection with a follow-up investigation were included.

Definitions

An episode of infection required the clinical suspicion of SJA, and at least one of the following criteria: (i) intraoperative pus surrounding the joint, (ii) evidence of leucocytes in microscopic analyses of obtained samples, and (iii) growth of microorganisms consistent with

SJA. The final diagnosis of SJA also required exclusion of an alternative diagnosis (e.g., gout).

For all analyses except surgical treatment, the total number of infection episodes was defined as the denominator. Thus, each patient could have only one episode, irrespective of the number of joints involved, unless it reoccurred after a previous episode had been classified as having been eradicated. The second episode was further categorized as relapse (i.e., infection with the same microorganism) or new infection (i.e., infection with a newly cultured microorganism). For analyses of surgical treatment, the total number of involved joints was defined as the denominator.

On the basis of the patient's history, pathogenesis was categorized as haematogenous, exogenous or inconclusive. Each episode was categorized as either acute (symptoms for <3 weeks for haematogenous or <4 weeks for exogenous pathogenesis) or chronic (symptoms for ≥ 3 weeks for haematogenous or ≥ 4 weeks for exogenous pathogenesis). These definitions were extrapolated from those used for the categorization of periprosthetic joint infections [6].

Surgical treatment was classified as a complex or non-complex procedure. The latter consisted of incision, debridement, lavage and drainage with the intention to preserve the joint. More extensive surgical procedures were categorized as complex interventions.

For outcome assessment, the latest available follow-up examination was used. Assessments included cure of infection and regain of joint function.

Statistical analyses

GraphPad Prism 5.0 was used for statistical analysis. Differences in group proportions were assessed by contingency tables and the chi-square test, or by Fisher's exact probability test if the frequency was smaller than 5. A two-tailed p-value of ≤ 0.05 was considered significant.

The local ethical committee and the Department of Research of the University Hospital of Bern, Switzerland, approved the study (KEK-BE: 2016-01756).

Results

Number of native SJA episodes

In the 9-year period included in the study, we identified 137 episodes. Twenty-seven episodes were excluded because of unfulfilled infection criteria (20 episodes), insufficient data (5 episodes), an alternative diagnosis (1 episode) or patient age < 18 years (1 episode). Thirteen episodes were infections involving an implant. Thus, 97 native SJA episodes were available for clinical presentation analyses. Each patient had only one infection episode, and no relapses or second episodes of infection were noted. Of these 97 episodes, 101 small joints were involved. Ten patients with 10 episodes that involved 12 joints were lost to follow-up. Thus, 87 SJA episodes of infection involving 89 joints were available for outcome analyses.

Clinical presentation

Demographics: The median age of patients was 52 years (interquartile range [IQR] 38–68 years), and 62% were male. Fifty (52%) of the patients had no comorbidities. Of the other 47 (48%) patients, comorbidities included chronic heart failure (11%), arterial hypertension (9%), renal insufficiency (9%) and diabetes mellitus (8%). A rheumatic disorder (Sjögren syndrome, rheumatoid arthritis, gout, crystal arthritis [e.g., calcium pyrophosphate dihydrate crystal deposition disease], connective tissue disease, psoriasis, systemic lupus erythematosus)

was described in 16 (16%) patients, and 13 (13%) individuals were taking immunosuppressive drugs (e.g., prednisolone) or had a comorbidity that impaired immunity (e.g., chronic lymphatic leukaemia).

Involved small joints and postulated pathogenesis: In 48 (49%) patients, infections occurred in the right hand and in 49 (51%) patients, in the left hand. The distribution of the involved joints is illustrated in Fig. 1. SJA of the second and third finger together accounted for more than half (n = 53 of 101, 53%) of all involved joints. Infections of the metacarpal-phalangeal and proximal interphalangeal joints of these two fingers accounted for 40% (n = 40 of 101) of all involved joints.

Categorization of pathogenesis was possible in all cases. In 86 (89%) episodes, the postulated pathogenesis was exogenous, and in 63 (65%) of these, infection followed trauma. The most common traumas were cut, stab or bruise injuries related to job or household activities (45 [46%] of 97 episodes, 71% of 63 exogenous episodes), followed by animal bites (18 [19%] of 97 episodes, 29% of 63 exogenous episodes). Of the remaining 23 episodes belonging to the exogenous group, infection evolved from adjacent infected tissue (e.g., infected gout tophus perforated into the joint, untreated skin and soft tissue infection) in 14 episodes and from a previous medical intervention (iatrogenic) in 9 episodes. In 11 (11%) episodes with a presumed haematogenous pathogenesis, the source of infection remained undetected in most cases (8 of 11 episodes). In these cases, the pathogenesis was postulated from the history of a previous sepsis or proven bacteraemia. Foci for haematogenous seeding were identified in three episodes and included aortic valve infective endocarditis, needle injection abscess in an intravenous drug user and urinary tract infection. The duration of symptoms before presentation was often short. The overall mean duration was 5.4 days, and 82 [85%] of 97 SJA episodes were categorized as acute infections.

Microbiology: The list of identified microorganisms is presented in Table 1. The most frequent isolated microorganism was *Staphylococcus aureus* (38%), followed by beta-haemolytic streptococci (13%) and *Pasteurella* spp. (11%). In seven (7%) episodes, more than one pathogen was identified (i.e., polymicrobial infection), while in the remaining 61 (63%) episodes, only one microorganism was cultivated. In 29 (30%) of 97 episodes, no organism was identified, but the definition of infection was fulfilled. In retrospect, the resistance profiles of the isolated microorganisms indicated that empiric therapy with amoxicillin/clavulanate would have been active against 84% of 83 different pathogens.

In 56 (58%) of 97 episodes, antimicrobial prophylaxis was given before we obtained biopsy samples. The most frequently administered compound was amoxicillin/clavulanate (66%). The difference in proportion of SJA with prophylaxis administered before biopsies samples were obtained that showed negative culture results (14%) and SJA in which antibiotic therapy was administered only after samples were obtained with positive culture results (27%) was not significant (chi-square with Yates' correction, two-tailed $P = 0.314$).

Treatment and outcome

Only infection episodes with at least one follow-up examination were included in these analyses (87 episodes involving 89 joints).

Surgical therapy: The number of joints (and not the number of episodes) was used as the denominator in our analysis of surgical therapy. Among non-complex cases, 63 (71%) of 89 joints required only one intervention, and 11 (12%) required two surgical interventions. Of these 74 (83%) joints, the first intervention consisted of incision, lavage and debridement, while the second intervention was considered a second look. In three (3%) additional joints, more than two interventions were required. The surgical procedure in the other 12 (13%) joints was considered complex. In four joints, arthrodesis (one temporary, three permanent)

was performed, in four joints soft tissue damage required a flap, and in four joints the extent of infection required amputation (two on the distal interphalangeal and two on the proximal interphalangeal level).

Agent and duration of antimicrobial chemotherapy: Amoxicillin/clavulanate was the most frequently administered compound in the post-operative period (74 [85%] of 87 episodes). The compound was given intravenously (IV) with a dose ranging from 1.2 to 2.2 gram every 6 to 8 hours. In 60 (81%) of these 74 episodes, empiric therapy with amoxicillin/clavulanate was continued after microbiological results were available. The oral dose ranged from 625 to 1000 mg every 8 hours, and the transition from IV to oral route occurred 3 to 5 days after definite surgery in the vast majority of the cases. Other compounds, such as clindamycin (n = 17, 20%) and ciprofloxacin (n = 9, 10%, either monotherapy or in combination with another compound) were administered less frequently. The overall median treatment duration was 14 days (IQR 12–28 days). Of the 72 episodes involving 74 joints that required only one or two non-complex surgical interventions, the median treatment duration was also 14 days (IQR 9–19 days).

Follow-up examination: The median time interval from the last surgical intervention to the follow-up investigation in our outpatient clinic was 2.3 months (IQR 1–5 months). Infection resolution was observed in all episodes. Joint function was impaired or non-existent in 12 (13%) of 89 joints (see Surgical Therapy section). In seven additional (8%) cases, painful arthrosis developed and required arthrodesis. In one case, post-infectious extensor tendon adhesion occurred and tenolysis was performed. Further follow-up was uneventful. Thus, infections were cured in 100% of our serious native SJA episodes, and joint function was not considerably impaired in 79% of episodes.

Discussion

Pyogenic SJA of the hand and wrist requires prompt treatment to avoid articular destruction with consecutive impaired function [7]. Therefore, patients with SJA should be rapidly transferred to centres in which pyogenic SJA is managed by an interdisciplinary team consisting of a hand surgeon and an infectious diseases specialist.

In this study, we were able to analyse a larger number of SJA episodes than have previously been reported [3, 4, 8-10]. We noted three considerable differences between septic arthritis of the larger joints (e.g., hip or knee joint) described in the literature and our series of pyogenic SJA.

First, the diagnosis of pyogenic SJA is less standardized than the diagnosis of septic arthritis in larger joints. While local pain, warmth, swelling and decreased range of motion in the involved joint are important clinical features for the diagnosis of SJA, synovial fluid is not obtained to determine a leucocyte count or the proportion of polymorphonuclear leucocytes, nor is it obtained to determine glucose or lactate levels. In contrast, laboratory analysis of synovial fluid contributes to the diagnosis in larger joints [11]. Nonetheless, in SJA, samples must be obtained for microbiological and crystal analyses because simultaneous crystalline and bacterial arthritis can occur. Alongside microscopic examination of Gram-stained samples, a semi-quantitative leucocyte count should be performed, although this method is imprecise. To the best of our knowledge, no criteria for the definition of SJA have been formulated. In this study, we postulated rigid criteria prior to obtaining data. However, these criteria need to be validated in a different patient population (internal validation) and in other centres (external validation) before the definition can be widely used.

Second, a considerable proportion of patients with septic arthritis of larger joints are older than 60 years or have comorbidities that are known risk factors for infection [12, 13]. In

contrast, more than half of our patients had no comorbidity and the median age was 52 years. Diabetes mellitus, a rheumatic disorder or immunosuppression were each reported in approximately 10% of our population. Thus, patients with SJA are commonly younger and healthier than those reported in the literature with septic arthritis of the larger joints.

Third, the pathogenesis of most septic arthritis cases of the larger joints is haematogenous [14]. The larger volume within these joints allow accumulation of a considerable amount of cells contributing to inflammation. Laboratory values such as white blood cell count or C-reactive protein in the serum are helpful in the diagnosis of large joint arthritis. In SJA, the majority of infections occur exogenous. The joint volume is smaller. Systemic inflammatory parameters in serum are often not markedly elevated. In our series, the vast majority of infections occurred following trauma, such as injuries related to job or household activities or animal bites. Interestingly and in contrast to other reports [15], no fight bite was noted within our cohort.

The types of injury parallel the most frequent pathogens. *S. aureus*, beta-haemolytic staphylococci and *Pasteurella* spp. accounted for 62% of all isolated microorganisms. Moreover, the observation that 84% of identified microorganisms were susceptible to amoxicillin/clavulanate treatment justifies our policy to use this agent as an empiric post-operative agent. This may not be true for other centres where the prevalence of methicillin-resistant *S. aureus* or multi-drug-resistant Gram-negative bacilli is higher than in our institution.

A high proportion of patients (58%) received antibiotics before surgical intervention. This observation can be explained by the fact that most infections were post-traumatic. According to Swiss recommendations, animal bites should be treated empirically with antibiotics [16]. In addition, in available operating theatres within a hospital, indications for surgery other than

hand infections are prioritized in cases of emergency [17]. If the waiting time for surgery is significant, patients may receive pre-emptive antibiotic therapy. This practice can alter the microbiological results of intraoperatively obtained samples [18]. Although we did not find a statistical difference in bacterial growth between patients with and without antimicrobial prophylaxis, we cannot estimate the role of antimicrobial agents in susceptible microorganisms only. In other words, the growth of pathogens resistant to antimicrobial prophylaxis may have biased the categorical variable.

Incision, lavage and debridement is very effective in SJA. In the vast majority of infection episodes (83%) in our study, only one or two interventions were necessary. This result indicates the surgical possibility of thoroughly washing out a small joint, a task that can be difficult in larger joints. It also points towards the importance of rapid referral of patients in order to preserve the joint. In 12 (13%) of 89 joints, the infection was associated with destructive development, requiring extensive surgery. This proportion is comparable to that reported in other series [3, 4].

The optimal antimicrobial treatment duration in SJA is undetermined. In larger joints, antibiotics are given for up to 6 weeks, the first 2 weeks of antibiotics administered intravenously [19]. In our patient population, the decision on treatment duration is taken on the basis of clinical examination by the interdisciplinary team. Half of our patients were treated for 14 days or less, irrespective of the isolated microorganism. In non-complex cases, 75% of patients had a treatment duration of 19 days or less. In our institution, the switch from intravenous to oral treatment is commonly performed no later than the fifth day after surgery in these cases. Since our study design did not include a comparison group, we cannot firmly conclude whether antibiotic treatment duration in SJAs can be shortened. Nonetheless, we experienced high cure rates with short treatment duration in this study.

Our study has limitations, including its retrospective nature and the use of medical records for data collection. However, all variables and definitions were determined before obtaining data. The definition of infection also requires validation. Categorization of acute and chronic infection was arbitrary. It was transferred from categorization of periprosthetic joint infection because no uniformly accepted categorization for SJA is available. However, in retrospect, duration of symptoms was short in the vast majority of cases, irrespective of categorization. We were unable to analyse the true influence of antimicrobial prophylaxis on culture negativity, but all infections were classified as cured in follow-up examinations. We did not compare surgical techniques between various surgeons, and we considered the surgical intervention in non-complex cases to be standard procedure. There is no standardized definition of cure. While an amputation cures the infection, it also leads to loss of function. In this study, we differentiated between cure of infection and regain of joint function, though successful outcome was only considered when both variables were fulfilled. Finally, there was a large variability in time of follow-up examinations among patients, three quarters of them having an examination within 5 months of surgery. Thus, our outcome results may be overestimated. Nonetheless, we expected patients with failures to have been referred to our center. As a consequence of this study, we have introduced regular and structured follow-up examinations per protocol for patients with septic SJA in our outpatient clinic.

In conclusion, our retrospective single-centre analyses showed that patients with pyogenic SJA are typically younger and healthier than those reported with septic arthritis of the larger joints. The most common pathogenesis was exogenous inoculation of the joint with *S. aureus*, beta-haemolytic streptococci or *Pasteurella* spp. following trauma. Non-complex cases were treated with no more than two surgical interventions and the median antimicrobial treatment duration was 14 days.

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Conflict of interests

None to declare.

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References

1. Dubost JJ, Soubrier M, Sauvezie B. Pyogenic arthritis in adults. *Joint Bone Spine* **2000**; 67(1): 11-21.
2. Kennedy N, Chambers ST, Nolan I, et al. Native Joint Septic Arthritis: Epidemiology, Clinical Features, and Microbiological Causes in a New Zealand Population. *J Rheumatol* **2015**; 42(12): 2392-7.
3. Kowalski TJ, Thompson LA, Gundrum JD. Antimicrobial management of septic arthritis of the hand and wrist. *Infection* **2014**; 42(2): 379-84.
4. Angly B, Steiger R, Zimmerli W. [Septic arthritis of finger joints]. *Handchir Mikrochir Plast Chir* **2007**; 39(2): 118-23.
5. Weinzweig N, Gonzalez M. Surgical infections of the hand and upper extremity: a county hospital experience. *Ann Plast Surg* **2002**; 49(6): 621-7.
6. Osmon DR, Berbari EF, Berendt AR, et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis* **2013**; 56(1): e1-e25.
7. Osterman M, Draeger R, Stern P. Acute hand infections. *J Hand Surg Am* **2014**; 39(8): 1628-35; quiz 35.
8. Sinha M, Jain S, Woods DA. Septic arthritis of the small joints of the hand. *J Hand Surg Br* **2006**; 31(6): 665-72.
9. Richard JC, Vilain R. Acute septic arthritis of the fingers. A clinical study of 87 cases. *Ann Chir Main* **1982**; 1(3): 214-20.
10. Boustred AM, Singer M, Hudson DA, Bolitho GE. Septic arthritis of the metacarpophalangeal and interphalangeal joints of the hand. *Ann Plast Surg* **1999**; 42(6): 623-8; discussion 8-9.
11. Carpenter CR, Schuur JD, Everett WW, Pines JM. Evidence-based diagnostics: adult septic arthritis. *Acad Emerg Med* **2011**; 18(8): 781-96.
12. Dubost JJ, Couderc M, Tatar Z, et al. Three-decade trends in the distribution of organisms causing septic arthritis in native joints: single-center study of 374 cases. *Joint Bone Spine* **2014**; 81(5): 438-40.
13. Geirsson AJ, Statkevicius S, Vikingsson A. Septic arthritis in Iceland 1990-2002: increasing incidence due to iatrogenic infections. *Ann Rheum Dis* **2008**; 67(5): 638-43.
14. Shirliff ME, Mader JT. Acute septic arthritis. *Clin Microbiol Rev* **2002**; 15(4): 527-44.
15. Goon PK, Mahmoud M, Rajaratnam V. Hand Trauma Pitfalls: A Retrospective Study of Fight Bites. *Eur J Trauma Emerg Surg* **2008**; 34(2): 135-40.
16. Vogt M. [Diagnosis and treatment of bites by cats, dogs and humans]. *Dtsch Med Wochenschr* **2003**; 128(19): 1059-63.

17. Juon BH, Iseli M, Kreutziger J, Constantinescu MA, Vogelin E. Treatment of open hand injuries: does timing of surgery matter? A single-centre prospective analysis. *J Plast Surg Hand Surg* **2014**; 48(5): 330-3.

18. Al-Mayahi M, Cian A, Lipsky BA, et al. Administration of antibiotic agents before intraoperative sampling in orthopedic infections alters culture results. *J Infect* **2015**; 71(5): 518-25.

19. Mathews CJ, Weston VC, Jones A, Field M, Coakley G. Bacterial septic arthritis in adults. *Lancet* **2010**; 375(9717): 846-55.

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Table 1. Microorganisms cultured from 97 patients with small joint arthritis of the hand and wrist.

Microorganisms	n (%) ^a
<i>Staphylococcus aureus</i>	37 (38)
Beta-haemolytic streptococci	13 (13)
<i>Pasteurella</i> spp.	11 (11)
Gram-negative bacilli ^b	7 (7)
<i>Streptococcus pneumoniae</i>	2 (2)
Fungi ^c	2 (2)
Anaerobes	1 (1)
Other ^d	3 (3)
Polymicrobial infection	7 (7)
Monomicrobial infection	61 (63)
No growth	29 (30)

^a The sum of percentages of microorganisms is 77% (growth in 71% of infection episodes) because of polymicrobial infections.

^b Gram-negative bacilli consisted of *Enterobacter cloacae*, *Escherichia coli*, *Pantoea agglomerans*, *Aeromonas hydrophila* and *Pseudomonas aeruginosa*.

^c Fungi consisted of *Candida albicans* and *Trichosporon asahii*.

^dOther consisted of coagulase-negative staphylococci and *Corynebacterium pseudotuberculosis*, microorganisms that were considered clinically relevant by the treating team.

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Figure 1.

