Septic arthritis following joint injections: a 17 years retrospective study in an Academic General Hospital

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Abstract. Background: Septic arthritis following intra-articular infiltrations is an uncommon devastating complication correlated to high costs for the health service and often to poor outcomes. The purpose of this study is to assess a 17-years experience in a single academic multispecialist hospital managing this uncommon complication in Orthopaedic practice. Methods: Patients with diagnosis of septic arthritis following joint injections treated in our hospital from January 2002 to December 2019 were included in the study. Clinical and demographic data, pathogens, injected agent, conservative/surgical treatments were reviewed. Patient were classified according to the ore operative Charlson Comorbidity Index (CCI) and the Cierny-Mader Classification(CMC). Furthermore follow-up outcome and time occurred to infection eradication were registered. *Results:* We included in the study 11 patients with a median age of 74 years old (IQR = 61.5 - 79). The median CCI was 3 (IQR = 2 - 5) and the majority of patients belong to CMC = B class. Septic arthritis occurred mainly following corticosteroids injections and more frequently involving knees. The pathogen more often isolated was Staphylococcus aureus. Five (45%) patients referred an history of multiple intra-articular injections. 7 patients (64%) had a complete resolution following an arthroscopic debridement, 4 (36%) patients underwent to a 2-stage replacement and one of them hesitated in an arthrodesis because of a recurrent periprosthetic joint infection and extensor apparatus insufficiency. Conclusion: The authors observed a potential increased risk of septic arthritis following joint injection in patients with history of multiple injections and poor health/immunological conditions. They recommend an early arthroscopic debridement as the treatment of choice especially in septic knees performed in a multispecialist dedicated center. (www.actabiomedica.it)

Key words: Septic arthritis, Treatment, Arthritis, Joint Injection, Intra-articular injection, osteoarthritis

Background

Therapeutic joint injections are considered a viable treatment in the conservative management of osteoarthritis according to international guidelines (1-4). However, several authors have recently pointed out potential complications ranging from pain and swelling at the site of injection (20% of the cases) to even fatal sepsis described in one case (5-9). Iatrogenic septic arthritis (SA) has been reported in patients following hyaluronic acid, steroids injections and even ozone (8-10). The risk iatrogenic SA has been estimated at 0.005% and 0.0002% for joint injections (9).

Abram et al in a recent longitudinal cohort study of septic arthritis with heterogeneous causes reported a mortality as high as 10–15%, osteomyelitis incidence of 8%, and a subjective poor outcome in 20–30% of patients with an annual rate of arthroplasty in patients with a history of septic arthritis 6 times greater than that of the general population without this history and consequent significant impact upon the health system sustainability (11).

Risk factors include pre-existing joint diseases such as rheumatoid arthritis, alcoholism, diabetes, cutaneous ulcers, intravenous drug abuse and immunosuppression all associable to a poor intra-articular injection technique with Staphylococcus Aureus (S. aureus) as the most frequent etiological agent (12-14). Acute poor articular functionality, local erythema and swelling, all associated to laboratory abnormalities with elevated ESR and CRP, are the most common acute clinical aspects (15). Although potentially any joint after injection is prone to develop an infection, the most affected joint is represented by the knee in about 50% of cases and less frequently by the hip, shoulder and elbow. (9-16). Among the various complications described in the literature in septic arthritis following joint injections, mortality appears to be approximately 11% in monoarticular septic arthritis and a permanent loss of joint function nearly 40% (13-16). In the literature different treatment options in managing acute septic arthritis have been proposed ranging from oral/e.v. antibiotic therapy, arthroscopic/open articular washing/debridement, antibiotic cemented spacers, joint replacements/arthrodesis to amputations with obvious costs for the health system and often poor patients outcomes (17, 18).

Aim of this study is to retrospectively review a selected consecutive homogeneous series of septic arthritis following joint infiltrations treated in a single academic multispecialist hospital, equipped with an infective disease department, over a period of 17 years.

Methods

Data were collected from hospital medical records using an electronic search based on the International Classification of Diseases and Current Procedural Terminology (CPT) 711.90 code (unspecified infectious arthritis). Inclusion criteria were: presence of a complete diagnostic and imaging path for acute septic arthritis according to the protocols of our institute (Table 1), history of joint infiltrative therapy performed in the same joint within 2 weeks of the onset of symptoms, absence of any other suspicious infection source, no recent history of intravenous drugs abuse and normal findings in X-ray chest.

Exclusion criteria were: diagnosis and/or tests firstly performed in other structures and subsequently referred to our hospital and patients with an uncertain diagnosis because of missing microbiological or clinical criteria, incomplete clinical documentation and presence of other suspicious source of infection.

Adopted criteria needed to have a diagnosis of septic arthritis that had been confirmed by at least one of the criteria defined by Newman as follows (19):

- positive culture from synovial fluid;
- positive blood culture with negative synovial fluid culture;
- patients with negative blood or synovial fluid cultures but with histological and/or radiological evidence of infection and/or associated to a clear purulent fluid aspirated from joint.

Demographic characteristics (age and gender), past medical history and health/immunological status on admission, original diagnosis (osteoarthritis or rheumatoid arthritis) requiring intra-articular injection, a previous history of intra-articular injection, joint involved, bacterial pathogen, injected agent, consequent surgical treatment, time between diagnosis and surgical procedure were assessed.

Table 1. Diagnostic protoco	ol for acute septic arth	iritis
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Diagnostic protocol for acute septic arthritis		
• history and a clinical evaluation suspicious for septic arthritis,		
• blood inflammatory indices (ESR and PCR),		
• blood culture (if hyperpyrexia $>$ 38 °C),		
 culture and white blood cell count in synovial fluid (positive specimens: white blood count>50000/mm3 with a percentage of neutrophils >85%) 		
• Complete imaging: chest x-ray, joint x-ray, joint MRI		
Presence at least one of Newman Criteria fo septic arthritis		

Patient were classified according to the Charlson commorbidity Index (CCI) and the Cierny-Mader Classification(CMC) for immunological status (19, 20). The CCI is a method of categorizing comorbidities of patients based on the International Classification of Diseases (ICD) diagnosis codes found in administrative data (19). The CMC is commonly used in staging bone involvement and histologic features of osteomyelitis, a second part of this classification used to assess the immunological status of the patient into 3 categories: A, B or C. In Group A, patients had neither systemic pathologies nor compromising local factors. Group B included patients with 1 or more compromising factors, considering local (L), systemic (S) or both in association (L, S) factors. Group C included severely compromised patients often discouraging any radical surgical treatment because of an unacceptable complication risk (20).

Preoperative and postoperative pain for each patient was assed using numeric rating scale (NRS: ranged from 1 to 10) and according to the joint involved with dedicated orthopaedics scores, namely Harris Hip score (HHS), Knee Society Score (KSS) and Constant score (CS) (20-23). Pre-operative data were collected from our database. Post-operative data were gathered for clinical assessment by recalling patients for an outpatient evaluation by the authors uninvolved in the original procedures. All the conservative and surgical procedures were registered assessing the period of antibiotic therapy administration and the surgical procedure type. Furthermore, we considered the surgical procedures as acute or delayed whether performed respectively within 6 hours or over 6 hours from the diagnosis.

Finally, we used as healing criteria both the absence of clinical signs suspicious for infection and negative PCR and ESR parameters repeated over time for 2 consecutive months following the end of every treatment.

Results

From January 2002 and December 2019, we registered 383 patients treated in our hospital with a general diagnosis of septic arthritis. A total of 11 patients were identified as suitable for the study because a direct correlation with an intra-articular injection. All the demographic including sex, age, involved joint, patient diagnosis (osteoarthritis or rheumatoid arthritis), Cerny-Mader classification and Charlson comorbidity index were collected in Table 2.

Five patients (45%, 4 knees and 1 shoulder) reported a previous history of intra-articular injections for a similar clinical condition. High serum PCR and ESR values with both an elevated white blood cell count (>50000/mm3) and percentage of neutrophilis >85% in synovial fluid were found in all patients. The most common drugs used for infiltration were corticosteroids in 7 cases (63%), hyaluronic acid in 3 cases (27%) and platelet-rich plasma (PRP) in 1 case (9%).

All the isolated bacterial species were included in Table 3 mentioning that we could not identify any bacteria in three patients and the diagnosis of septic arthritis was performed considering Newman's criteria.

Sex			
	Number (n)	Percentile (%)	
Male	7	63	
Female	4	36	
Age			
Mean (yy)	Range	Standard deviation	
70.2	54-83	10.74	
Joint involved			
	Number (n)	Percentile (%)	
Knee	8	72	
Shoulder	2	18	
Hip	1	9	
Charlson comorbidity	y index		
Mean (yy)	Range	Standard deviation	
3.8	1-10	1.21	
Cerny Mader classific	ation		
	Number (n)	Percentile (%)	
А	2	18	
B-Local	1	9	
B-Sistemic	3	27	
B-Local + Sistemic	3	27	
С	2	18	

Table 2. Demographic and clinical data

Bacterial species	Number (n) Percentile (%	
S. Aureus MRSA	5	45
S. Aureus MSSA	2	18
P. Aeruginosa	1	9
None	3	27

Table 3. Isolated bacterial species

Table 4. Pre and Post operative clinical outcome

	Mean	Range
Knee Society Score (KSS)		
Pre	18,7	8-36
Post	78.67	42-89
Constant score (CS)		
Pre	16	14-18
Post	30	28-32
HHS		
Pre	18,7	/
Post	78.67	/
NRS		
Pre	6,1	5-9
Post	2,4	0-5

All the preoperative and the post-operative (median of follow-up 36 months; IQR = 14 - 78) clinical scores including NRS, the KKS for the infected knees, the Constant score for the infected shoulders and the HHS score for the infected hip were included in Table 4. All the patients in our study underwent surgical treatment associated with systemic antibiotic therapy for at least 8 weeks. In 6 patients (55%), surgical treatment started within 6 hours from diagnosis of septic arthritis, while the remaining 5 patients (45%) received a delayed treatment ranging from 24 hours to 96 hours. Nonetheless, we did not observe any difference in terms of final infection resolution related to the time occurred between diagnosis and surgical treatment.

An arthroscopic debridement was performed in 10 patients (91%) (8 knees and 2 shoulders) achieving a complete infection resolution in 7 cases (64%), all involving knees.

In the unique case involving the hip, occurring in an obese woman, we performed as first choice a two-stage hip replacement because of a retarded diagnosis caused by associated comorbidities and clear signs of bone septic involving at the magnetic resonance imaging (MRI).

Even the two cases of glenohumeral joint infections underwent a two-stages joints replacements using a reverse shoulder replacement following an unsuccessful arthroscopic debridement.

Likewise, a HIV positive patient with knee infection underwent multiple procedures and finally ended with a knee arthrodesis because of a massive bone loss associated to an extensor apparatus insufficiency.

Discussion

Despite no major evidence in the literature about long lasting clinical advantages, intra-articular infiltrations are a common practice in conservative osteoarthritis management [1-7]. Different authors reported local complications more commonly with corticosteroids such as post injection flare, facial flushing and skin or fat atrophy at the injection site (24). Septic arthritis following intra-articular injection represents the most dangerous complication despite of a low reported incidence ranging between 0.001 to 0.072%, more frequently using corticosteroids (10). In a USA survey of 191 orthopedic surgeons, rheumatologists and general practitioners, only 12.6% of the practitioners had ever encountered septic arthritis after corticosteroid injection of the knee, and even fewer (3%) had encountered it more than once (25). Furthermore, improved antiseptic techniques and availability of preparations in refilled syringes may have lowered the incidence even more (26). Likewise, several authors considered septic arthritis following joint injections as an orthopedic emergency because of the possibility of dissemination with poor outcomes leading in exceptional cases even to death, recommending a prompt recognition and treatment as a critical issue for a successful outcome.

In agreement with the literature, our study confirmed a prevalence of male patients, a higher incidence in the knee, a more common involvement of Staphylococcus aureus, and occasionally of coagulase-negative staphylococci and anaerobe as bacterial responsable (26-28). In relation of the type of substance injected, the most frequently infiltrated was corticosteroid compared to hyaluronic acid and PRP injection with almost the half of patients with history of previous joint injections.

We could not find any similar previous report in the literature dealing with septic arthritis following similar "biological" injections despite the potential technical complexity in preparing PRP with a possible increased risk of contamination and whose possibility should be taken in account in the future (29-31).

In our study, an history of previous intra-articular injection and the immunological/health status seems to play a key role in the surgical treatment outcome with a lower incidence of more invasive procedures in the more healthy patients. According to Cierny-Mader classification, we identified only two patients (18%) classified in class A showing an uncomplicated immunological status. Similarly, Charlson Comorbidity Index identified 4 (36%) patients with a score lower than 3 and not compromised by multiple comorbidities. Likewise, the 4 (36%) patients undergoing to multiple and more invasive surgical procedures, including 2 stages replacement/arthrodesis, were all included both in the worst Cierny-Mader class with the higher Charlson Comorbidity Index because of the associated multiple comorbidities including HIV.

In our series, all the treated patients achieved a complete infection eradication despite early or retarded surgical procedures, surgical procedure type and length of antibiotic therapies with clear improvements in the clinical parameters (NRS and orthopaedic outcomes). However the number of surgical procedures and the surgical invasivity seem to play a role in the final score achieved with worst outcome scores in patients treated with multiple and complicated procedures.

In eight knee septic arthritis, the arthroscopic debridement achieved an earlier infection resolution in the great majority of the joints (7 patients) regardless if performed within or over 6 hours from the diagnosis. The only arthroscopic knee debridement failure performed acutely, appeared more related to both poor patient immunological/health status and drug abuse confirmed by both the worst CM classes and CMI. In the 2 shoulder septic arthritis, the delayed arthroscopic debridement were not effective and both the patients underwent consequently a 2 stages replacement with

longer antibiotic therapy cycles. Poorer immunological/health status, retarded surgical procedures and more resistent isolated germs (MRSA) might be the explanations of the arthroscopic failures.

The only septic hip included in the study underwent straight a delayed 2-stage hip replacement without any previous less invasive procedure because of clear signs at the MRI of bone septic involvement and associated comorbities.

This study presents some limitations: it is a retrospective study without any control group and dealing with a relative small sample size. However, we could not find any similar study in the literature. Despite the sample size, it is one of the biggest study in the literature performed in a single multispecialist center assessing septic arthritis following joint injections using strict inclusion criteria over a period of time of 17 years and evaluating both patients immunological and health status. Furthermore, all the last follow-up procedures were carried out by authors not involved in the original patient management.

The authors underline the importance, before planning intra-articular joint injections, to assess carefully both patient medical history and immunological/health status to identify potential higher risks to develop a septic arthritis and consequently to either discourage any injection or to adopt any further procedure to low down the risk of infection as, for an example, an antibiotic prophylaxis.

An early arthroscopic debridement performed within 6 hours from the diagnosis according to the authors experience seems to offer better choice in earlier infection eradication at least in knee infections. On this purpose, considering the importance of an multidisciplinary approach including possibility of prompt microbiological exams, infectivologist assistance and orthopaedic facilities, the authors believe that patients affected by septic arthritis even following joint injection should be addressed to dedicated multispecialist centers.

Highlights:

• Septic arthritis following intra-articular injection could be a rare but devastating complication • In patients with poor immunological conditions we recommend early arthroscopic debridement as treatment of choice

Conflict of interest: The authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article

Statement: This statement is to certify that all Authors have seen and approved the manuscript being submitted. We warrant that the article is the Authors' original work. We warrant that the article has not received prior publication and is not under consideration for publication elsewhere. On behalf of all Co-Authors, the corresponding Author shall bear full responsibility for the submission.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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