

# Septic Arthritis of the Knee Following Intraarticular Injections in Elderly Patients: Report of Six Patients

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**ABSTRACT:** **Background:** Intraarticular injections for the local treatment of osteoarthritis are widely used in the office or hospital setting. Septic arthritis is a potential catastrophic complication of intraarticular injection, as bacterial arthritis of any cause is associated with up to 15% mortality and residual impairment of joint function in up to 50% of survivors. There is lack of evidence regarding the precautions that should be taken to avoid such a complication, as well as how often it is encountered.

**Objectives:** To report our experience with the clinical presentation, diagnosis and treatment of knee septic arthritis following intraarticular injections.

**Methods:** We followed six patients who were admitted to the hospital and underwent surgery for the treatment of pyogenic arthritis following injection to the knee joint in outpatient clinics.

**Results:** All but one patient were over 70 years old with comorbidities. Three patients were injected with steroid preparations and three with hyaluronic acid several days before admission. In all six patients the infection was treated surgically and three of them had undergone more than one operation during their hospitalization. Four of the six patients were treated by means of an open arthrotomy and synovectomy, and the other two were treated successfully with arthroscopic lavage and synovectomy. One patient underwent an above-knee amputation due to septic shock and died after several days.

**Conclusions:** Despite the rarity of this complication, surgeons must be aware of the possibility of pyogenic arthritis when administering injections, especially in elderly patients with serious underlying medical conditions.

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**KEY WORDS:** septic arthritis, knee, injection, corticosteroids, hyaluronic acid, elderly

corticosteroid injections are postinjection flare, facial flushing, and skin or fat atrophy of the injection site [5-7].

The overall incidence of side effects of hyaluronic acid injections, also referred to as viscosupplementation, has been reported to be around 1% to 3% per injection. The most common adverse event is an injection-site inflammatory reaction of the treated knee (i.e., pain, warmth, swelling) that lasts from 1 to 2 days [8,9]. Of the less common side effects, pyogenic arthritis is one of the greatest concerns, with reported incidences ranging from 1 in 3000 to 1 in 50,000 following corticosteroid injection [6]. Improved antiseptic techniques and availability of corticosteroid preparations in prefilled syringes may have even lowered the incidence. In a survey of 191 orthopedic surgeons, rheumatologists and general practitioners, only 12.6% had ever encountered septic arthritis after corticosteroid injection of the knee, and only 3% had encountered it more than once [4].

Septic arthritis following hyaluronic acid injections seems rare, but has been described [10-12]. A deep infection following an intraarticular injection may develop due to direct inoculation of bacteria by the injection, to hematogenous seeding of the percutaneous injection tract, or to activation of quiescent infection by an injected steroid [4]. The most common organism encountered is *Staphylococcus aureus*, with occasional involvement of other organisms, including coagulase-negative staphylococci and anaerobes [13].

Prompt recognition and treatment of the infected joint is critical for a successful outcome. The cornerstones of treatment include early diagnosis, pathogen identification by synovial fluid cultures, surgical debridement and tailored antibiotic therapy. Irrigation and debridement of the knee joint may be accomplished by either a formal arthrotomy or the arthroscopic technique. In addition to proper debridement of the infected joint, it is important to obtain cultures during surgery. Beginning immediate treatment with antibiotics even before culture results are obtained is of paramount importance.

## PATIENTS AND METHODS

This study is a case series where all the clinical, laboratory and intraoperative findings were collected retrospectively.

Intraarticular injections of corticosteroids and hyaluronic acid to the knee are widely practiced as a conservative treatment modality for osteoarthritis [1-4]. However, there are certain side effects related to intraarticular injections, most commonly with corticosteroids. The most common side effects of

**Table 1.** Patient demographics and comorbidities, the injected preparation and presenting symptoms

Patient	Gender	Age (yrs)	Comorbidities	Preparation injected	Time from injection to symptoms (days)	Presenting symptoms and physical exam
1	F	87	IHD, hyperlipidemia	Corticosteroid	2	No fever, pain, swelling
2	M	86	CAF, COPD, HTN, IHD, CHF, CRF	Corticosteroid	1	No fever, chills, pain, swelling
3	F	71	DM, hyperlipidemia	Corticosteroid	3	No fever, pain, swelling, difficulty walking
4	M	70	Hyperlipidemia	Hyaluronic acid	2	Subfebrile fever, pain, swelling
5	F	75	Asthma, IHD, hyperlipidemia	Hyaluronic acid	2	No fever, pain, swelling
6	F	64	HTN, pulmonary hypertension, MVR	Hyaluronic acid	5	No fever, pain, swelling

IHD = ischemic heart disease, CAF = chronic atrial fibrillation, COPD = chronic obstructive pulmonary disease, HTN = hypertension, CHF = congestive heart failure, CRF = chronic renal failure, DM = diabetes mellitus, MVR = mitral valve replacement

**Table 2.** Blood tests and synovial fluid analysis at the time of diagnosis

Patient	Serum laboratory values				Synovial fluid analysis		
	WBC	NEUT%	ESR	C-reactive protein	WBC k/ $\mu$ l	NEUT%	Smear
1	15.77	63.6	>100	11.84	60,000	88	–
2	7.16	82	55	–	50,000	85.7	–
3	14.69	80	15	17	105,000	91	+
4	12.2	72.4	50	16	68,030	91.8	–
5	10.37	90.6	–	17.64	28,250	96.5	+
6	12,450	77	–	33.56	82,250	93	–

WBC = white blood cells, NEUT = neutrophils, ESR = erythrocyte sedimentation rate

**Table 3.** The organism cultured, antibiotic and surgical treatment

Patient	Causative microorganism	Antibiotic treatment	Surgical treatment (days from admission)
1	<i>Streptococcus viridans</i>	IV cloxacillin	Arthrotomy (1)
2	MSSA*	IV cloxacillin	Arthrotomy (1) Arthrotomy (18) Above-knee amputation (34)
3	<i>Streptococcus oralis</i>	IV vancomycin + PO ciprofloxacin	Arthrotomy (1) Arthrotomy (3) Arthrotomy (14)
4	–	IV cefazoline	Arthroscopic lavage and synovectomy (1) Arthroscopic lavage and synovectomy (7)
5	Staphylococcus coagulase-positive	IV cloxacillin + PO rifampicin	Arthroscopic lavage and synovectomy (8)
6	Staphylococcus coagulase-negative	IV cefazoline	Arthrotomy (15)

\*MSSA = methicillin-sensitive *Staphylococcus aureus*, IV = intravenous, PO = per os

Institutional Ethics Committee approval was obtained for this study in March 2011. We included all patients diagnosed with septic arthritis of the knee following an intraarticular injection in an outpatient clinic for the treatment of osteoarthritis. Between September 2006 and January 2010 we treated six patients diagnosed with septic arthritis of the knee following intraarticular injection. Demographic patient data are presented in Table 1. All six patients were admitted within a few days of receiving an injection, and all were diagnosed with monoarticular septic arthritis of the injected knee.

## RESULTS

The mean age was 75 years (range 64–87). Most of the patients had significant comorbidities, as summarized in Table 1. Three of the patients were treated with a corticosteroid preparation, the other three with hyaluronic acid.

All patients arrived at the emergency room 1 to 5 days after the injection. One patient (# 3) was transferred to our medical center from another hospital where she was diagnosed and underwent her first operation. The main presenting complaints [Table 1] were pain, swelling of the involved limb and difficulty walking. All patients had general malaise at the time of presentation to the emergency room but none of the patients had fever. One patient had a subfebrile fever and another patient had chills.

Physical examination of all six patients revealed swelling of the involved knee, the presence of an effusion, and pain on active and passive movement. Blood test results and synovial fluid analysis on admission are shown on Table 2. Four patients had a mildly elevated white blood count. Most of the patients had elevated sedimentation rate or C-reactive protein. The synovial fluid analysis revealed a white blood cell count of above 50,000 in most of the patients, with a high percentage of neutrophils. Only two had a positive Gram stain on direct microscopy at admission.

The causative bacteria on synovial fluid culture were staphylococci or streptococci. One patient (# 4) had a sterile culture, probably due to treatment with oral antibiotics before admission, prescribed by his primary care physician. Once synovial fluid analysis and cultures were obtained, we began intravenous antibiotic treatment with cefazolin. Pathogen-specific therapy was tailored after culture results were received. The cultured microorganisms and antibiotic treatment administered to each patient are summarized in Table 3.

All patients had undergone surgical treatment. In four patients surgical intervention was performed within the first 24 hours of admission. Patient 6, a 64 year old woman, refused surgery during the first 2 weeks of hospitalization and was therefore initially treated only with intravenous antibiotics. Since her condition did not improve, she finally gave consent and underwent an arthrotomy. Patient 5, a 75 year old woman,

was diagnosed with septic arthritis during a hospitalization in the internal medicine department where she was admitted due to another medical condition. She was immediately transferred to our unit and underwent prompt surgical debridement. One patient (# 3) was transferred to our hospital after being diagnosed and treated surgically in another medical center. This patient eventually needed further surgical debridements, the first of which was performed 3 days after her admission.

The type of surgery, the number of surgical interventions and the time intervals between surgeries for each patient are summarized in Table 3. Three of the six patients had undergone more than one surgery. Four patients were treated with formal arthrotomy and two were treated successfully with arthroscopy. The intraoperative findings in all cases included congested and thickened synovium with a purulent material. We used surgically placed postoperative drains in all six patients. One patient (# 2), an 86 year old man, was admitted to the intensive care unit postoperatively after his second arthrotomy due to progressive sepsis. Later on he developed septic shock. He was taken once again to the operating room for an urgent above-knee amputation. He continued to deteriorate and eventually died in the ICU from septic shock and multiorgan failure a short time after the surgery.

Postsurgically all patients were treated in the same manner: antibiotics were given for 4 to 6 weeks after surgery, the knees were immobilized for 3 days after surgery and were then put in a continuous passive-motion physiotherapy machine, and the drains were left for several days. The mean duration of hospital stay was 22.5 days (range 9–40). Patients were discharged and continued follow-up in our hospital clinic. The infection finally resolved in five patients.

## DISCUSSION

There is a long history of injection of steroids and hyaluronic acid derivatives into joints for the purpose of symptomatic relief and anti-inflammatory effect. However, controversy persists as to whether or not this treatment has any long-term effects and there is no evidence that injection of either corticosteroids or hyaluronic acid alters the natural history of the disease. In a metaanalysis comparing intraarticular injections of corticosteroids with placebo, corticosteroids were probably more effective but their effect was short-lived and lasted only a few weeks [1]. The Cochrane group reported 1 week as the only time point at which a statistically significant difference can be found between corticosteroids and placebo [14].

Intraarticular hyaluronic acid injections have been extensively studied in numerous clinical trials. While not all studies have shown benefit, several meta-analyses of various

trials suggested that it provides some modest improvement in patients with knee osteoarthritis [8,15-17].

In a recent multicenter, randomized, double-blind study, Jørgensen et al. [3] compared injections of hyaluronic acid to placebo and found no significant benefit for hyaluronic acid in a 1 year follow-up. Wang and researchers [17] reviewed 20 blinded, randomized, controlled trials that compared intraarticular hyaluronic acid with placebo in patients with knee osteoarthritis. They noted that patients older than 65 years of age and those with the most advanced radiographic stage of osteoarthritis (complete loss of the joint space) were less likely to benefit from intraarticular injection of hyaluronic acid.

In 2009, the American Association of Orthopedic Surgeons published clinical management guidelines for the non-arthroplasty treatment of osteoarthritis of the knee based on a systematic review of published studies [18]. The guidelines suggest that corticosteroids be used for short-term pain relief only. The board could not recommend for or against the use of hyaluronic acid.

We have retrospectively studied six patients who presented to our medical center with pyogenic monoarthritis of the knee following an injection. As we have shown, injections with either corticosteroids or hyaluronic acid may have deleterious consequences, with significant morbidity and even mortality. The six patients were all older adults, with a mean age of 75 years. In this particular age group, the treatment of osteoarthritis may be challenging. Elderly patients are usually treated with a wide array of concomitant medications, and the tolerability of current therapeutic regimens for osteoarthritis must be considered. The potential adverse effects of systemic treatments such as non-steroidal anti-inflammatory drugs in older adults may be devastating. A localized therapy such as intraarticular injections may seem safe and therefore attractive. However, the efficacy of this treatment, as mentioned before, is limited to pain relief only, and for a limited time. Moreover, the treatment of osteoarthritis with intraarticular injections in this specific age group has been shown to be less beneficial [17].

Although quite rare, septic arthritis of the knee may develop following injections to the joint. As we have shown, the treatment of such infections may be prolonged, involving recurrent operations, long-term regimen of antibiotics, and remaining disability. One of our patients, an 87 year old man, did not recover and developed septic shock for which he underwent an urgent below-knee amputation. Unfortunately, he did not survive and eventually died in the intensive care unit. Septic arthritis of the knee may therefore be both a limb-threatening and a life-threatening condition.

When treatment with an intraarticular injection is being considered, the general condition of the patient must be thoroughly assessed, including his or her comorbidities, the degree of osteoarthritis, concomitant drugs used by the patient, past injections and their effect, and history of pre-

ICU = intensive care unit

vious infections. One also should clarify if the patient is a candidate for arthroplasty in the future. If the patient is a candidate for total knee replacement, treatment with intra-articular injections of steroids could put him or her at increased risk for developing a deep infection following arthroplasty, as suggested by Papavasiliou et al. [19]. The decision to administer intraarticular injections to the knee should therefore not be made lightly.

Despite the rarity of septic arthritis following injections, patients should be informed of the risk of septic arthritis and the possible consequences. Furthermore, the increased risk for future deep infections after arthroplasty should be discussed with patients who are possible candidates for total knee replacement.

A full aseptic technique includes proper draping, use of chlorhexidine, sterile gloves, and separate needles for drawing and injecting. Studies that examined the precautions taken before intraarticular injections revealed a wide variation among physicians [4]. In an article published in the *Journal of Bone and Joint Surgery* in 1969, Bentley and Goodfellow [20] presented what they called disorganization of the knee joint after injections with hydrocortisone. They concluded: "The case against multiple injections is so strong that the practice should, in our opinion, be discarded, which implies that even a single injection requires strong justification." We totally agree with their statement. Intraarticular injection to the knee is not a harmless procedure and can be both limb-threatening and life-threatening. Furthermore, its long-term benefit is still questionable. We believe that other treatment options should be sought before offering this modality to patients. If administered, it should be done with a strict anti-septic technique.

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**“It is of interest to note that while some dolphins are reported to have learned English – up to fifty words used in correct context – no human being has been reported to have learned dolphinese”**

Carl Sagan (1934-1996), American astronomer and writer

**“Before we set our hearts too much on anything, let us examine how happy are those who already possess it”**

Francois, duc de La Rochefoucauld (1613-1680), French moralist