

# Pseudo-septic arthritis developed after hyaluronic acid injection: A case report

## Hylarunoik asid enjeksiyonu sonrası gelişen psödo-septik artrit: Olgu sunumu

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### Abstract

One of the most frequent causes of knee pain is knee osteoarthritis. Intra-articular hyaluronic acid (HA) injection is one of the preferred treatment methods. Although, systemic side effects are not seen, rarely local side effects as pain and swelling can be seen. Following HA injection, some cases with pseudo-septic manifestations unrelated to crystal formation have been reported. In this case report, a patient with knee pain which aggravated with medial tibio-femoral osteoarthritis refractory to conservative treatment methods including administration of non-steroidal anti-inflammatory drugs and others is presented. After intra-articular HA injection, her preexisting knee pain worsened, and swelling, and increase in local temperature were added to the clinical picture. Based on clinical, and laboratory examinations, and analysis of synovial fluid, diagnosis of pseudo-septic arthritis which mimicked manifestations of septic arthritis was made. Clinical, and laboratory improvement was achieved with early treatment. If following intra-articular HA injection, knee pain of the patient aggravates suddenly with local swelling and heat, then the possibility of pseudo-septic arthritis of the affected knee should be always kept in mind.

**Keywords:** Knee, Pseudo-septic arthritis, Hyaluronic acid, Knee osteoarthritis

### Öz

Diz ağrısının en sık nedenlerinden biri diz osteoartritidir. İntraartiküler hyaluronik asit (HA) enjeksiyonları sık tercih edilen tedavi yöntemlerinden biridir. HA enjeksiyonlarından sonra sistemik yan etkiler neredeyse hiç görülmemekle birlikte, seyrek olarak ağrı ve şişlik gibi lokal yan etkiler görülebilmektedir. HA enjeksiyonu sonrası, kristal oluşumuna bağlı olmayan psödoseptik artrit tablosu literatürde çok az sayıda olguda bildirilmiştir. Bu olguda medial tibia-femoral osteoartrite bağlı yürümekle şiddetlenen, nonsteroidal antiinflatuar ve diğer konservatif tedavi yöntemlerine yansız diz ağrısı olan ve intraartiküler HA enjeksiyonu uygulandıktan sonra dizinde mevcut olan ağrının artması, şişlik ve ısı artışı eklenmesi nedeniyle yapılan klinik muayene, laboratuvar tetkikleri ve sinoviyal sıvı analizi sonucu hastaya septik artrit tablosunu taklit eden psödoseptik artrit tanısı kondu. Erken tedavi ile klinik ve laboratuvar iyileşme sağlandı. Dize intraartiküler HA enjeksiyonu sonrası bir hastada aniden diz ağrısında artma, şişlik ve ısı artışı olursa, etkilenen eklemde psödoseptik artrit olasılığı her zaman akılda tutulmalıdır.

**Anahtar kelimeler:** Diz, Psödoseptik artrit, Hyaluronik asit, Diz osteoartrit

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## Introduction

Nowadays, in knee pains associated with osteoarthritis (OA) intraarticular hyaluronic acid (HA) injection is one of the preferred treatment methods. As its mechanism of action improvement of viscoelastic properties of the synovial fluid, and its anti-inflammatory, and anti-nociceptive characteristics have been proposed [1]. The guideline for the treatment of knee OA formulated by TIAR indicated its potential usefulness in mild, and moderate knee OA unresponsive to pharmacological, and non-pharmacological treatment modalities [2]. Development of pseudo-septic arthritis is rarely seen following HA injection, and very few relevant case reports have been indicated in the literature [3-5]. In this paper, a rarely seen case with acute monoarticular pseudo-septic arthritis developed 2 days after intra-articular HA injection in a patient with knee osteoarthritis has been presented.

## Case presentation

A 67-year-old female patient consulted to our outpatient clinic with knee pain related to medial tibio-femoral osteoarthritis which worsened while walking, and did not respond to nonsteroidal anti-inflammatory drugs, and other conservative treatment methods. A single intra-articular dose of HA (Monovisc®) was applied. Before injection the region to be intervened was firstly wiped with iodine-based antiseptic solution, and then left to dry. The procedure was performed with extreme care paid to sterility. Two days after the procedure, the patient reapplied to our output clinic with swollen and severely painful knee.

On physical examination of the patient, marked effusion, increased local temperature, and restricted range of motion of the knee which received HA injection were detected. The patellar effusion was aspirated, and clinical sample aspirated with sterile injector was inoculated on culture media for bacteriologic culture. On microscopic examination of the synovial fluid leukocytosis (37.000 cells/mm<sup>3</sup>) (PNL, 70 %, and lymphocyte, 30 %) was detected. Any bacterial growth was not detected on cultures. Fluid sample obtained was analyzed under polarized light microscope, and any crystal formation was not encountered. Some laboratory findings were also measured. Routine hematological, and biochemical values were within normal limits. Erythrocyte sedimentation rate (ESR: 62 mm/hr), and C-reactive protein (120 mg/dL) levels were also measured. Since clinical findings mimicked those of septic arthritis, ampicillin at daily doses of (1.5 g qid) was started till culture results of the synovial fluid were obtained. Antibiotherapy was terminated after negative culture results were obtained, and suspicion of septic arthritis was discarded. The patient was followed up with nonsteroidal anti-inflammatory drugs. Complaints of the patient, and adverse laboratory test results regressed completely within nearly 15 days. In this case we use Naranjo Adverse Drug Reaction Probability Scale Worksheet and calculated +6 point. This result is considered probably drug adverse reaction and this adverse reaction also reported Monovisc® Company. The patient's consent was taken for this case report.

## Discussion

Intra-articular hyaluronan injection draws considerable attention as an alternative OA treatment in patients with osteoarthritic knee who did not benefit from other treatment options. Its mechanism of action has been suggested to relate to its anti-inflammatory, anabolic, local analgesic, and chondro protective effects [6]. The aim in OA is to improve impaired viscoelastic properties of the synovial fluid in OA. Although after intra-articular HA injections systemic side effects are almost never seen, rarely local adverse effects as local pain, and swelling can be seen. In very few cases cited in the literature, manifestations of aseptic arthritis after HA injection unrelated to crystal formation have been reported [7,8].

Pseudo-septic arthritis has been described in only 2 cases after injection of sodium hyaluronan (Ostenil®), and in all remaining cases it was described following injection of hylane GF-20 (Synvisc®) [7,9]. However, in the literature any case developed related to cross-linked sodium hyluronate (Monovisc®) injection has not been reported so far. This case we presented with this respect is the only case reported developed after cross-linked sodium hyluronate injection. Pseudo-septic arthritis is generally seen within 24-72 hours after intra-articular injection [10]. Also in our case, similarly, pseudo-septic arthritis developed within 48 hours after injection.

Synovial fluid typically has inflammatory characteristics. Symptoms, and clinical findings regress completely with non-steroidal drugs, and corticosteroids within 3-21 days [7,9,10]. Our case we have presented was followed up with nonsteroidal anti-inflammatory treatment, and within nearly 6 days nearly complete cure was achieved. Because of severity

of clinical manifestations, and their occurrence following injection, it mimics acute septic arthritis. However, nonobservance of pathogens in direct microscopy of synovial fluid, rapid onset of symptoms within a short time after injection, dramatic, and faster response to anti-inflammatory drugs, and corticosteroids discriminate pseudo-septic arthritis from septic arthritis. Blood culture should be and absolutely obtained to exclude septic arthritis which might develop due to infectious causes. Besides, synovial fluid should be obtained through arthrocentesis for direct examination, and culture, and then empirical IV treatment should be initiated.

Although the mechanism of pseudo-septic arthritis is not fully understood, the current emphasis is on the production of proinflammatory cytokines, and inflammatory process induced by HA degradation products. In addition to this hypothesis, it has been indicated that inhibition of flow of synovial fluid with inappropriate injection technique may contribute to the development of pseudo-septic arthritis [11].

In conclusion, severe joint involvement which mimics acute septic arthritis may develop following intra-articular HA injections. We, the physicians, should keep this clinical picture in mind, perform diagnostic laboratory examinations, and administer rapid, and effective treatment.

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