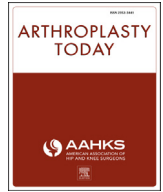




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Case report

Late hemorrhagic pseudoseptic arthritis encountered during total knee arthroplasty due to hyaluronic acid viscosupplementation

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ABSTRACT

Osteoarthritis (OA) is the most common form of arthritis and affects approximately one-third of people in the United States aged 65 years and older. Since 2013, the American Academy of Orthopaedic Surgeons has not been able to recommend using hyaluronic acid for patients with symptomatic OA of the knee. Subsequent publications have also cautioned against the use of viscosupplementation based on lack of efficacy and the potential for harm. We present a case of late hemorrhagic pseudoseptic arthritis encountered during TKA due to hyaluronic acid viscosupplementation. Our triad of findings includes (1) acute and chronic inflammatory cells on frozen section, (2) synovitis with hemosiderin deposition, and (3) blackened cartilage with iron deposition on permanent histopathology. Our case is unique in that it shows a previously undescribed late complication of viscosupplementation.

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Introduction

Osteoarthritis (OA) is the most common form of arthritis and affects approximately one-third of people in the United States aged 65 years and older [1]. OA involves the progressive loss of hyaline cartilage with underlying bony changes. Patients with OA suffer from pain, joint effusions, and stiffness. Disease in weight bearing joints (eg, hips and knees) has greater impact. The majority of those affected report movement limitations, and approximately 25% have difficulty with activities of daily living [2]. OA is independently associated with excess mortality, morbidity, as well as high socioeconomic costs [3–5]. Treatment of knee OA is based on many factors including age, severity, and functional status with total knee arthroplasty (TKA) being the most invasive but definitive option.

In 2013, the American Academy of Orthopaedic Surgeons published recommendations for the nonarthroplasty treatment of knee OA [6]. Nonarthroplasty treatment options included conservative measures such as weight loss, pharmacologic treatment with nonsteroidal anti-inflammatory drugs, and procedural treatments including intraarticular injections and arthroscopy. Intraarticular hyaluronic acid (HA) injections, a relatively new modality, aimed to restore the viscoelastic properties of joint fluid in patients with OA. At that time, the authors could not recommend using HA, with a strong strength of evidence, for patients with symptomatic OA of the knee. Where previous guidelines found inconclusive evidence, the 2013 guidelines reviewed 14 studies and found no clinically significant treatment effects for pain, function, or stiffness. Their meta-analysis showed a low likelihood that an appreciable number of patients achieved clinically important benefits.

Subsequent publications have also cautioned against the use of viscosupplementation. A industry-sponsored, multicenter, randomized, double-blind trial of nearly 200 patients with mild to moderate OA found no statistical difference on outcomes measures at 1, 3, and 6 months between intraarticular injection of HA vs placebo [7]. In addition, a systematic review of 19 trials found double-blind, placebo-controlled trials had much smaller treatment effects than open-label trials. Based on assessment of the best evidence, these authors concluded that HA injections offer no

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clinically important improvements in pain, function, or stiffness compared to placebo [8]. However, despite this clear lack of efficacy, viscosupplementation remains common especially in areas where there is a higher density of physicians [9].

Recent studies and case reports have revealed a potential harm from viscosupplementation. Both minor and severe inflammatory reactions have been documented and raise safety concerns. The most commonly reported adverse reaction is mild pain or swelling at the site of the injection, which occurs in 1%-20% of patients. This inflammatory response typically begins within 1-72 hours [10-12]. The likelihood of these reactions increases up to 8-fold in those who pursue multiple treatment sessions [12]. Studies have found a varying antibody response to different sources of hyaluronan with Synvisc (Sanofi-Aventis, Bridgewater, NJ) eliciting the greatest immunogenic response in limited animal models [13,14]. However, other products have also been described to cause similar reactions of varying severity [10]. Recently, more long-term risks have also been described. At the 2015 Annual Meeting of the American Association of Hip and Knee Surgeons, one paper showed a significantly higher incidence of postoperative infection and infection requiring reoperation in patients who had received therapeutic injection within 7 months before TKA [15].

Our case is unique in that it shows a previously undescribed complication of viscosupplementation. We present a case of late hemorrhagic pseudoseptic arthritis encountered during TKA. Our triad of findings includes (1) acute and chronic inflammatory cells on frozen section, (2) synovitis with hemosiderin deposition, and (3) blackened cartilage with iron deposition on permanent histopathology.

Case History

A 70-year-old female presented to us with a chief complaint of right knee pain. She had previously been treated by an outside

orthopaedist for knee OA with a series of 3 weekly Orthovisc (DePuy Synthes, Warsaw, IN) injections 2 months prior. There was no effusion or acute inflammatory reaction after these initial HA injections. She reports having tried acetaminophen, various nonsteroidal anti-inflammatory drugs, narcotics, and topical medications over the past 8 months. All failed to provide any relief. She relates constant, debilitating pain when walking, kneeling, and going up or down the stairs that has acutely worsened.

Her past medical history includes asthma and hyperlipidemia. Her only medication is simvastatin. She has no known medical allergies. Her social history includes infrequent alcohol use, and she is a nonsmoker.

Physical examination revealed an overweight female with a body mass index of 29 kg/m². She had an antalgic gait. The dermis overlying her right knee was intact without erythema or warmth. Her knee examination revealed a moderate effusion, diffuse tenderness to palpation, and palpable crepitation during passive range of motion. Goniometer assessment exhibited a 20° flexion contracture, and maximal flexion was limited to 90°. Strength testing limited by pain but discernibly intact for age. Mechanical alignment showed a valgus deformity. Weight bearing radiographs were obtained, which showed severe tricompartmental arthritis (Fig. 1).

Taking into consideration her history of knee injections and the severity of her symptoms, inflammatory markers were obtained to rule out infectious or other inflammatory etiology. Her white blood cell (WBC) count and C-reactive protein (CRP) were within normal limits at 5.9×10^9 per liter and <0.5 mg/dL, respectively. Her erythrocyte sedimentation rate (ESR) was found to be slightly elevated at 38 mm/h. The decision was made to proceed with TKA.

In the operating room, the knee was prepped and draped in the usual sterile fashion. Preoperative antibiotics consisting of 2 grams cefazolin were administered before skin incision. A 12-cm longitudinal incision was made through the skin centered over

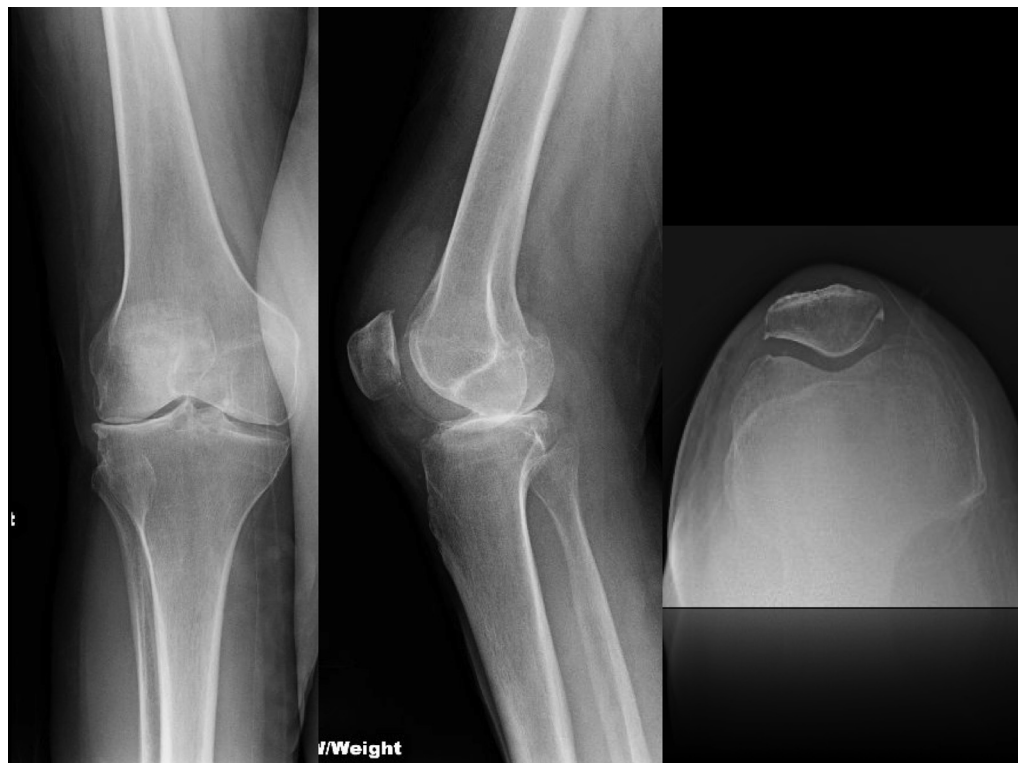


Figure 1. Preoperative radiographs. Preoperative anteroposterior (AP), lateral, and merchant weight bearing views of the right knee showing severe tricompartmental arthritis.

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