Deep vein thrombosis after sodium hyaluronate injection to knee joint: a case report

Deep vein thrombosis due to sodium hyaluronate

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Abstract

Hyaluronic acid is widely used in medical procedures such as intra-articular injections. In addition to some risks of this procedure such as sepsis and injury to neighboring structures, deep vein thrombosis and pulmonary embolism should be kept in mind as rare complications. For this reason it is recommended that intra-articular injection of hyaluronic acid be performed by the ultrasound guidance (usg) method. In this report we present a 67-year-old man with lower extremity deep vein thrombosis following a sodium hyaluronate injection to the right knee joint due to lower extremity pain. The patient was treated with warfarin sodium and low molecular weight heparine and recanalized flow was achieved in common, superficial, and deep femoral veins and in the popliteal vein within the six-month follow-up period.

Keywords

Complication; Deep Vein Thrombosis; Injection; Joint Pain; Sodium Hyaluronate; Thromboembolism

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Introduction

Although intra-articular or intradermal injection of sodium hyaluronate is accepted as a safe and effective treatment for cosmetic procedures and joint pain, there is also a low risk of sepsis and injury to neighboring structures [1-2]. There are also a few cases of pulmonary embolism due to the injection of sodium hyaluronate with the infusion of larger volume than usual to the knee joints [3]. Deep venous thrombosis may develop after surgical or intervention procedures.

In this report we present the diagnosis, treatment, and follow-up period of a patient with lower extremity deep venous thrombosis after a sodium hyaluronate injection to his right knee joint.

Case Report

A 67-year-old man was admitted to our clinic with complaints of lower right extremity pain, swelling, and difficulty while walking. These complaints had started 15 days previously. The patient had a history of sodium hyaluronate injection (20 mg/2 ml) to the right knee joint due to osteoarthritic joint pain one month before. Before the injection, right lower extremity venous Doppler usg was performed for deep vein thrombosis but no thrombosis was detected.

His symptoms did not diminish despite the nonsteroidal anti-inflammatory treatment. He reported hypertension and chronic obstructive pulmonary disease as additional diseases. After informed consent, the patient was included in this study.

Physical examination of the patient's right leg revealed swelling of the whole extremity, increased heat, tenderness, and pretibial mild edema. Peripheral pulses were palpable and there were no signs of ischemia. His thigh and calf were painful during palpation and Homan's sign was positive.

Laboratory findings included complete blood count, C-reactive protein, and biochemistry results related to kidney and liver functions and these results were normal. But D-dimer was 3.9 mg/L, higher than a normal value. The thrombophilia panel results, including Factor V Leiden, FII Prothrombin, MTHFR C 677 T, and MTHFR A 1298 C, were normal. In addition, anti-cardiolipin and anti-phospho-lipid antibodies were negative; protein C, Protein S, and antithrombin were normal.

Right lower extremity venous Doppler usg indicated acute-subacute thrombus material in the common, superficial, and deep femoral veins and in the popliteal vein. There was no flow or-response to the compression.

Low molecular weight heparin (LMWH) (enoxaparin sodium) 8000 anti Xa/0.8 ml twice a day proper to his weight, upper knee compression socks, and elevation of the extremity were-started as the initial therapy. Warfarin sodium, 5 mg a day, was added to the therapy in the third day and LMWH was stopped when his International Normalised Ratio (INR) was above 2. His symptoms diminished and he was discharged from the hospital one week after admission with the suggestion of monthly INR controls.

The third month lower right extremity venous Doppler usg revealed recanalized flow in the venous structures mentioned above but there was still thrombus material on the vein walls compatible with the chronic period. His INR value was proper for his treatment (between 2-3) so warfarin sodium treatment was continued for another three months.

Sixth month venous Doppler usg revealed complete patency in the common, superficial, and deep femoral veins and in the popliteal vein and there were no thrombus materials. But irregularity on venous wall structures was reported. Warfarin sodium treatment was stopped and treatment continued with 100 mg per day of acetylsalicylic acid. After six months of this therapy there was no repetition of symptoms or thrombus, and treatment was stopped at the end of one year.

Discussion

Hyaluronic acid is used in different fields of medicine such as in cosmetic procedures for lip augmentation and correction of facial wrinkles and it is also used in orthopedics for the management of knee osteoarthritis pain [4-5]. Its effects on bone healing have also been studied in the literature [6]. Hyaluronic acid is produced by a microbiological engineering technique of non-animal origin so it is devoid of immunological reactions, but there have been some complications reported in the literature, such as inflammatory nodule, allergic reactions, blue bumps, and granulomas [7]. Venous thromboembolism, categorized as deep vein thrombosis and pulmonary embolism, may occur in isolation or as a complication of other diseases or procedures [8]. Likewise, deep vein thrombosis and the pulmonary embolisms that develop as a consequence are life-threatening complications following orthopedic surgeries and interventions [9].

Hyaluronic acid is one of the foreign materials accepted as an embolic [10]. Park et al. reported a pulmonary embolism case after a cosmetic vaginal procedure with sodium hyaluronate injection. According to this study, thromboembolism was associated with the injection of hyaluronate to an extensive venous plexus that immediately surrounded the vagina [7].

Similarly, Jang et al. reported a case of pulmonary embolism after injection of hyaluronic acid for removal of facial wrinkles [4]. Famularo et al. published a case report of a pulmonary embolism detected in a patient after the intra-articular injection of hyaluronate to hip joints [11]. Lacoste at al. reported arterial and venous thrombosis as immediate complications following hyaluronic acid injection [12]. In our case, the patient had a history of sodium hyaluronate injection to his right knee and he developed deep vein thrombosis soon after this injection.

Price et al. explained the possible mechanisms of thromboembolism, including excessive local tissue pressure induced by large-dose and high pressure, local massage by an unexperienced practitioner, migration effect, and direct intravascular injections [13]. In our study the probable cause of deep vein thrombosis was the direct injection of hyaluronic acid to the venous system. Migliore et al. declared that the ultrasound guidance technique is useful to ensure delivery of hyaluronic acid inside the target joint. The hands-free technique of intra-articular injection does not guarantee that hyaluronic acid enters the articular space [14].

To conclude, sodium hyaluronate is used in different fields of medicine with favorable therapeutic effects and a good tolerability profile but thromboembolism cases caused by hyaluronic acid injection have been rarely reported in the literature. It must be kept in mind that it is an embolic material that can lead to thromboembolism. Although ultrasound guidance is not used

widely, it is important to position the hyaluronic acid inside the joint to avoid complications.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study 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. No animal or human studies were carried out by the authors for this article.

Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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