Tissue Necrosis After Use of Enoxaparin in Total Knee Arthroplasty: A Case Report

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Abstract

Tissue necrosis at the injection site of enoxaparin is a rare adverse effect. Most of the reported clinical course of this necrosis is uneventful. Here we review a case of tissue necrosis that developed after use of enoxaparin and required debridement followed by reconstructive surgery. Until now, such a case has not been reported in the English-language literature. As enoxaparin is being used more often for prevention of deep vein thrombosis in patients who undergo arthroplasty surgery, awareness and recognition of this adverse event and careful supervision of all patients who receive this medication are essential.

Enoxaparin, a low-molecular-weight heparin (LMWH) used to prevent and treat deep vein thrombosis, has been evaluated in several clinical trials.[1,2] Skin necrosis caused by LMWH is a rare but probably underreported complication.[3,4] Most published reports suggest that the skin reactions are benign.[4,5] The English-language literature includes only 1 case in which reconstructive surgery was required to manage this complication, which developed after use of a different LMWH.[5,6]

In this article, we report a case of skin and subcutaneous fat necrosis that developed after use of enoxaparin as venous thromboprophylaxis in primary total knee arthroplasty (TKA). Necrosis management required debridement and a soft-tissue reconstruction procedure. The patient provided written informed consent for print and electronic publication of this case report.

Case Report

A 51-year-old woman underwent elective TKA for advanced seropositive rheumatoid arthritis of the right knee—which up until then was being managed with methotrexate and prednisolone. The patient's body mass index was 25. She had no history of concomitant medical illness and was not taking any broad-spectrum antibiotics. Thromboprophylaxis began on day of surgery with LMWH 40 mg (Clexane; Sanofi-Aventis, Paris, France) every 24 hours administered subcutaneously to the lower abdomen. There was no prior heparin exposure. The next day, erythema and a rash (no itching) developed at the injection site. Subsequently, subcutaneous LMWH was given in the thigh. The reaction was similar, however, with intense pain, overlying erythema, pruritis, and swelling at the injection site. The injection was discontinued. Platelet count and clotting profile, including protein C, protein S, and antithrombin III, were within normal limits. We discussed the case with a hematologist, discontinued LMWH, and started the patient on aspirin for further thromboprophylaxis.

As the pain and swelling persisted and the local skin showed necrosis (Figure 1), the wound was debrided. An incision was made at the margin of the skin area, which was blackened so we could avoid devitalizing already compromised tissue. A small amount of hematoma was evacuated, and the underlying muscles were decompressed. The vascularity of the skin and subcutaneous tissue was significantly compromised. The wound was left open and was dressed regularly until the area of necrosis was more clearly demarcated. The wound was debrided further; once it was granulated, the plastic surgeon performed split-thickness skin grafting (Figure 2). The patient eventually made a full recovery both at the graft and the donor site. Skin and fat necrosis was confirmed on histology with inflammation of blood vessels and without any evidence of primary vasculitis.

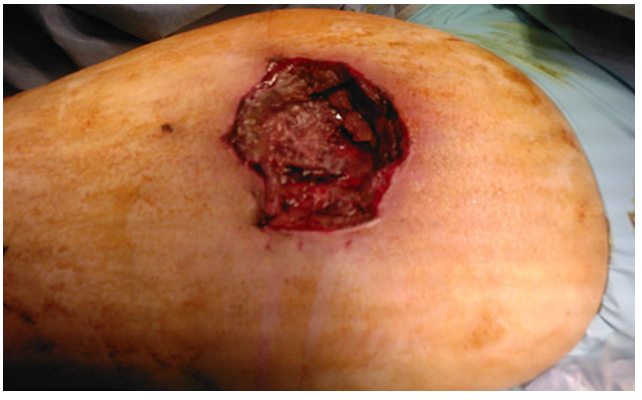

Figure 1. After debridement for skin necrosis.

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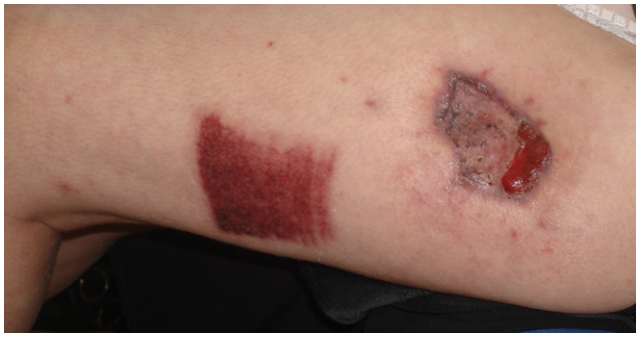

Figure 2. Healed wound with split-thickness skin graft.

Discussion

The popularity of LMWH has increased over the past few years.[7] Since the National Institute for Health and Clinical Excellence (NICE) published its 2007 guideline on prevention of thromboembolism in patients undergoing arthroplasty surgeries,[8] LMWH use has gone up exponentially. As this medication is being used more often, its adverse effects, which include skin reactions, will be seen more often as well.[9,10]

There have been case reports of reactions occurring both local to and distant from injection sites.[11] The published reports suggest that diabetes, obesity, concomitant use of broad-spectrum antibiotics, and female sex are predisposing factors for heparin-induced skin necrosis.[12] The etiology of LMWH-induced skin necrosis is unclear. According to Handschin and colleagues,[5] there are 3 mechanisms: heparin-induced thrombocytopenia, type III hypersensitivity reaction to LMWH, and skin necrosis secondary to repeated local trauma at the injection site and local hemorrhage.

The anticoagulant-related complications experienced by our patient, who came in for TKA, resulted in a significant increase in morbidity. She was in the hospital for more than 3 weeks and required 3 additional surgical procedures. She was started on aspirin for thromboprophylaxis, as Phillips and colleagues[10] confirmed that a patient with a reaction to a preparation of subcutaneous heparin may develop the same reaction with other LMWH preparations.

Our patient's case highlights 2 facts: (1) all skin reaction/erythema cases secondary to use of LMWH are not benign and (2) greater vigilance is warranted. Awareness, recognition of the complication, discontinuation of all heparin treatments, and careful supervision of all patients who receive this medication are essential. With publication of the NICE guideline, and subsequent widespread use of LMWH, this complication is becoming increasingly common. Therefore, the most important part of managing this condition is to discontinue LMWH immediately on recognizing a skin reaction.

Authors' Disclosure Statement

The authors report no actual or potential conflict of interest in relation to this article.

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