CASE STUDY

Lovenox Induced Tissue Necrosis, a Case Report and Literature Review

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Abstract Lovenox is a trade name for Enoxaparin. It is a low molecular weight heparin (LMWH) and has other trade names like Clexane and Xaparin. It is an anticoagulant used to prevent and treat venous thromboembolism events (VTE) like deep vein thrombosis or pulmonary embolism, and is given as a subcutaneous injection. General speaking, the most common skin reactions as a result of enoxaparin use are: urticarial, ecchymosis, and even skin necrosis due to vasculitis. These side effects are usually located at the injection site. New studies have pointed out the side effect that could occur a distance from the site of Lovenox injection. In our case extensive skin and subcutaneous tissue necrosis developed at the abdominal wall injection site. © 2015 Elsevier Inc. All rights reserved.

Introduction

Lovenox is a trade name for Enoxaparin. It is a low molecular weight heparin (LMWH) and has other trade names like Clexane and Xaparin. It is an anticoagulant used to prevent and treat venous thromboembolism events (VTE) like deep vein thrombosis or pulmonary embolism, and is given as a subcutaneous injection. It works by targeting anti-Xa and anti-IIa factors.^{1,2} The approved enoxaparin regimens that recommended are: 1 mg/kg twice daily, 1.5 mg/kg once daily for inpatient, or 1 mg/kg for outpatient treatment of DVT.³ Enoxaparin compared to the standard unfractionated heparin is easier to monitor.^{4,5} General speaking, the most common skin reactions as a result of enoxaparin use are: urticaria, ecchymosis, and even skin necrosis due to vasculitis. These side effects are usually located at the injection site. New studies have pointed out the

side effect that could occur a distance from the site of Lovenox injection.¹ These complications are still not fully understood from the pathophysiological point of view. Another interesting case has been reported and showed that Lovenox may cause eruptive Angiokeratomas, which are vascular tumors that appeared at patient hands, legs, and oral mucosa which disappeared two weeks after cessation of Lovenox.⁶

There are other rare cases which have been reported after Lovenox injection. The first case in a patient, status post arthroscopic surgery, who received a course of Lovenox injection treatment, but unfortunately tissue necrosis developed at the injection site.⁷ Another case study revealed skin necrosis in a 69-year-old diabetic patient after using Lovenox injection, which only appeared around the area where the patient usually injected himself with insulin daily for four years.⁸

Case Report

The patient is a 63 year-old-African American-male with a history of severe peripheral vascular disease with

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failed bypass grafting status post right BKA and previous left AKA. He had wound infection and was admitted post operatively to the hospital for wound care, intravenous antibiotics therapy and rehabilitation. He was also placed on subcutaneous Lovenox injections daily to his abdomen. The patient developed redness and painful, sharply demarcated plaques at the sites of injections, which in the following 2 weeks became necrotic and involved skin and subcutaneous (Fig. 1).

Lovenox was stopped and two weeks later tissue necrosis on the abdominal wall was well demarcated. The patient was a candidate for debridement of the necrotic tissue and negative pressure wound therapy (NPWT) placement to remove a source of infection and fasten healing but he finally he decided to receive hospice level of care and palliative wound care instead.

Discussion

Lovenox (enoxaparin sodium) is a widely-used antithrombotic agent injected subcutaneously and used to prevent the risk of blood clots in case of bed-ridden patients due to their prolonged illness.² Also, it is commonly used after surgery as a prophylaxis to prevent DVT after certain types of surgery, for example, fracture neck of femur, hip and knee replacement, and abdominal surgery; however, the dose of Lovenox given depends on the type of surgery performed and the condition of the patient. It is important to calculate the dose of the Lovenox accurately before given to patient because incorrect dosing for example, over or under-anticoagulation, could make complication easy to happen.

Low BMI, old age, pregnancy, and renal insufficiency (especially when the creatinine clearance [CrCl] < 30 mL/min) all of these factors would make you very conscious and alert when you are going to prescribe Lovenox. In our case report, the skin necrosis occurred after two weeks from

the initiation of therapy. Skin necrosis induced by heparin or low molecular weight heparin is a rare complication; however, from the literature search, there were approximately more than 25 cases of tissue necrosis associated with LMWH injection.^{9–11} Lovenox is an optional treatment in cases of Heparin Induced Thrombocytopenia (HIT), the reason for that is the risk of HIT occurrence is greatly reduced with Lovenox¹⁰; however, other studies are not recommending use of enoxaparin in patients with history of heparin-induced thrombocytopenia or HIT with thrombosis due to the cross reaction to the heparin-platelet factor-4 antibody.

The diagnosis of the tissue necrosis that occurs with Lovenox treatment is usually suspected clinically; however, a skin biopsy is recommended. Then, histopathology will clearly demonstrate necrosis of skin and subcutaneous tissue, and even will show inflammation and clot formation of the small blood vessels underneath the skin. Moreover, this proves that Lovenox is the cause of this tissue necrosis. A blood investigation should be obtained from the patient to check protein C and protein S, and make sure they are within normal concentration or level.^{9,12}

From a literature search, many studies have found that the mechanisms behind LMWH-induced skin necrosis are part of an immunologically mediated response. First, when we inject the heparin through the skin, it will induce immune platelets aggregation, which likely results in Heparin-induced thrombocytopenia syndrome (HIT).^{10,13} The second rationale for tissue necrosis caused by LMWH is that it induces a type III hypersensitivity reaction, which is also known as an Arthus-type reactions due to antigen-antibody complex formation in the blood vessels at the level of cutaneous tissue of the skin.¹³ Finally, fat tissue in the subcutaneous tissue has relatively poor blood perfusion, causing the injected LMWH to linger longer resulting in local tissue damage. This would explain the elevated risk in obese patients.^{9,13}

Conclusions

This case describes an unusual clinical scenario of tissue necrosis at the injection site of Lovenox as an antithrombotic treatment. Clinicians should be vigilant to early recognition of tissue necrosis so that the Lovenox treatment can be discontinued before tissue damage becomes extensive. Any damaged tissue should be debrided as appropriate, necessary reconstructive surgery performed, and proper wound care administered.

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Figure 1 Abdominal wall necrosis at injection sites.

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