Research Open

Endocrinology, Diabetes and Metabolism Journal

Volume 3 Issue 2

Case Report

Dalteparin Induced Skin Necrosis in a Patient Following Pelvic Floor Repair Surgery

Sabeeh Shams[1], Aysha Basir[1] and Najeeb Shah[2]*

[1]Blackpool Victoria Hospital, Blackpool, England
[2]Diabetes and Ensocrine Registrar, Hull Royal Infirmary, Hull, England

Corresponding Author: Najeeb Shah, Diabetes and Endocrine Registrar, Hull Royal Infirmary, Hull, England; **Email:** najeeb_shah01@hotmail.com

Received: January 27, 2019; **Accepted:** January 31, 2019; **Published:** February 09, 2019;

Abstract

Low Molecular Weight Heparin (LMWH) is commonly used as prophylaxis in the post-op surgical patients but very few adverse effects have been reported. Skin Necrosis is a rare side-effect of Dalteparin therapy and makes up 0.28% [1] of all the reported side effects from its use. This paper focuses on the conservative management of such a case.

Introduction

Dalteparin is commonly used because of its once daily dose for venous thromboembolism prophylaxis with no adjustment required for the weight of the patient. It mainly acts by interacting with the factor Xa and IIa [2]. Skin necrosis has rarely been reported and most cases present within one month[1] of its use and lesions can heal very quickly once the drug has been stopped [3].

The precise mechanism still remains unclear but multiple mechanisms of hypersensitivity have been proposed which include [4]

1. Cell mediated hypersensitivity to heparins evidenced by formation of plaques
2. Immediate hypersensitivity to heparins appear as palmoplantar pruritis after subcutaneous injections
3. Eosinophilia
4. Formation of antibodies (Heparin Platelet Factor 4 antibodies) has been linked mostly to the heparin induced thrombocytopenia and cause skin necrosis similar to coumarins.

Skin and provocation tests are contraindicated in patients who have developed skin necrosis or heparin induced thrombocytopenia [4].

Case Report

71 year old patient with a background history of Deep Vein Thrombosis, Pulmonary Embolism and previous Hystrectomy was admitted for a routine Anterior Colporraphy and Posterior Colpo-perineorraphy. As per NICE recommendation she was started on Dalteparin injection for venous thromboembolism prophylaxis 6 hours after surgery. On post-op day three, patient developed painful skin discoloration on both dalteparin injection sites and examination revealed lesions measuring 1.5x2cm and 2x2.5cm on either side of the umbilicus respectively. They were warm to touch with surrounding erythema however patient was apyrexial and systemically well. See Figure 1.

Figure 1a

Figure 1b

Blood work revealed a platelet count of 679/l thus ruling out LMWH induced thrombocytopenia and other relevant blood tests revealed; Haemoglobin 155g/l, White cell count 9.7 × 10^9/l, International Normalized Ratio 1.0 with completely normal electrolytes. Patient was not taking any antiplatelet or any other anticoagulant at the time. Patient was treated with Loratidine 10mg OD and Ibuprofen 400mg TDS. On post-op day 4, the necrotic area started to develop a blister but the skin on the top remained intact. Patient was advised to keep them covered with sterile gauze pieces so as to prevent the rupture of the blister.

On post-op day 13, patient was reviewed again and examination showed that the lesions were settling down, the one on the right side of the umbilicus had started to reduce in size without any scarring whereas the one on the left was still dark blackish in colour but the surrounding erythema and bruising had settled. Throughout the recovery process patient remained afebrile and only needed paracetamol and ibuprofen for pain control. See Figure 2.

Figure 2a

Figure 2b

Discussion

According to the 2018 NICE guidelines any patient undergoing abdominal surgery should receive low molecular weight heparin for a minimum of 7 days if the venous thromboembolism (VTE) risk outweighs the risk of bleeding[3] in conjunction with anti-embolism stockings which produce a pressure of 15-20mmHg at calf until they no longer have reduced mobility [5]. The ACOG and ACCP guidelines state that in case of moderate risk of thromboembolism chemical prophylaxis should be given until the day of discharge [6]. In case of our patient the reduction in mobility was only for the time they remained inpatient for the above mentioned elective procedure and therefore was discharged without a prescription for further LMWH therapy however was advised to keep the anti-embolism stockings on for a period of four weeks. There have been sporadically reported cases of LMWH induced skin necrosis however a life-threatening association of LMWH is Heparin Induced Thrombocytopenia (HIT) which in our case was ruled out by checking the platelet count as soon as the skin lesions were reported on post-op day three and then re-checked on day 8. The following chart was used to assess the risk of HIT (guidance from British Haematology) [7]

	Points (0, 1, or 2 for each of 4 categories: maximum possible score = 8)		
	2	**1**	**0**
Thrombocytopenia	>50% fall and platelet nadir ≥20 × 10^9/l	30–50% fall or platelet nadir 10–19 × 10^9/l	Fall <30% or platelet nadir <10 × 10^9/l
Timing_* of platelet count fall or other sequelae	Clear onset between days 5 and 10; or ≤1 d (if heparin exposure within past 30 d)	Consistent with immunization but not clear (e.g. missing platelet counts) or onset of thrombocytopenia after day 10; or fall ≤1d (if heparin exposure 30–100 d ago)	Platelet count fall ≤4 d (without recent heparin exposure)
Thrombosis or other sequelae (e.g. skin lesions)	New thrombosis; skin necrosis; post-heparin bolus acute systemic reaction	Progressive or recurrent thrombosis; erythematous skin lesions; suspected thrombosis not yet proven	None
Other cause for thrombocytopenia not evident	No other cause for platelet count fall is evident	Possible other cause is evident	Definite other cause is present

The diagnosis of skin necrosis was made on clinical grounds however to confirm the findings, skin biopsy/histology is recommended [4]. In our case we did not do a biopsy nor tested for antibodies as the patient was systemically well and did not develop thrombocytopenia. The option to involve Plastic surgeons in view of possible worsening of necrosis and skin breakdown which might have required skin graft was considered. The safe alternatives to Low Molecular Weight Heparin (such as enoxaparin and dalteparin) are fondaparinux and unfractionated heparin [8] which is an ultra-LMWH and its cross-reactivity to dalteparin is rare [4].

It should be noted that our patient has had deep vein thrombosis and pulmonary embolism following a coronary angiogram in year 2000 for which she received warfarin for one year and had hysterectomy in 2012 for which she did have dalteparin injections for 10 weeks and developed similar lesions and didn't seek any medical attention at that time as not all the injection sites developed the reaction and these were not as large and painful as the current ones. This suggests that she might have developed sensitivity to LMWH and had an exaggerated response to re-exposure.

Conclusion

Skin necrosis has an association with Heparin Induced Thrombocytopenia and should be investigated as it can be life threatening. Fondaparinux and Unfractionated Heparin can be considered for chemical thromboprophylaxis as safe alternate options in high risk cases. Prompt treatment with Non-steroidal anti-inflammatory agents together with anti-allergics and simple analgesia should be instituted. Early involvement of Dermatologists and Plastic Surgeons should be considered if tissue damage is extensive. In cases of previous skin reactions to LMWH therapy subsequent therapy with a similar agent should be avoided as the spectrum of subsequent reaction may be worse as demonstrated with our case. We do not recommend the use of Antibiotics unless there is clear clinical and biochemical evidence of superadded soft tissue infection.

References

1. Fragmin and Skin necrosis - from FDA reports. April 2018.
2. Nutescu EA, Burnett A, Fanikos J, Spinler S, Wittkowsky A (2016) Pharmacology of anticoagulants used in the treatment of venous thromboembolism. *J Thromb Thrombolysis* 41: 15–31. [Crossref]
3. Katsourakis A, Noussios G, Kapoutsis G, Chatzitheoklitos E (2011) Low Molecular Weight Heparin-Induced Skin Necrosis: A Case Report. *Case Reports in Medicine* 2011: 857391
4. Bircher AJ, Harr T, Hohenstein L, Tsakiris DA (2006) Hypersensitivity reactions to anticoagulant drugs: diagnosis and management options. *Allergy* 61: 12
5. Venous thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism. March 2018.
6. Shaw HA, Shaw JA. Thromboembolism in Gynecologic Surgery. March 2016.
7. Watson H, Davidson S, Keeling D. Guidelines on the diagnosis and management of heparin-induced thrombocytopenia: second edition. October 2012.
8. Coelho J, Izadi D, Gujral S (2016) Enoxaparin Induced Skin Necrosis. *Eplasty* 16: 40

Citation:
Sabeeh Shams, Aysha Basir and Najeeb Shah (2019) Dalteparin Induced Skin Necrosis in a Patient Following Pelvic Floor Repair Surgery. *Endocrinol Diabetes Metab J* Volume 3(2): 1–3.