



## Simultaneously Occurred Two Rare Complications Under Anticoagulant Prophylaxis After Surgery; Deep Vein Thrombosis and Skin Necrosis with Heparin Induced Thrombocytopenia Syndrome

### Busra Seker Atas\*

Department of Gynecology and Obstetrics, Sultangazi Haseki Training and Research Hospital, University of Health Sciences, Istanbul, Turkey

**\*Corresponding Author:** Busra Seker Atas, Department of Gynecology and Obstetrics, Sultangazi Haseki Training and Research Hospital, University of Health Sciences, Istanbul, Turkey.

**Received:** March 29, 2022

**Published:** June 13, 2022

© All rights are reserved by **Busra Seker Atas**.

### Abstract

**Purpose:** Review of the frequency, clinical and biological features and treatment of Heparin induced thrombocytopenia.

**Methods:** Case report and literature review.

**Results:** A 65 years old women received as antithrombotic prophylaxis low molecular weight heparin (LMWH) after gynecology surgery. Day 10, the patient had suffered from enduring, swelling and pain her arm. After physical examinations, injection site wound found in her arm looks like skin necrosis. We assumed the wound a skin necrosis with dependent on LMWH, then stopped the LMWH treatment. Her laboratory test revealed that her platelet levels were low ( $65 \times 10^3/\text{ul}$ ). While recovery is expected, day 11 her complaint were worse, her left arm was swelling and getting purple color and getting colder. Doppler ultrasound was performed on this arm, reported deep vein thrombosis (DVT). Although there was a conflict the therapy of anticoagulant, after a literature search Rivaroxaban started as medication. Meanwhile, the suspicion of heparin induces thrombocytopenia was confirmed by specific tests, ADAMTs13 activity test. Day 30, after changed for rivaroxaban as medication, her arms and platelet count return to normal after heparin discontinuation.

**Discussion:** Heparin Induced Thrombocytopenia (HIT) is an rare adverse effect of heparin therapy. Also, DVT is an condition with possibly devastating consequences. We present a case of simultaneously occurred two rare complications under anticoagulant prophylaxis after surgery; deep vein thrombosis and skin necrosis with heparin induced thrombocytopenia syndrome. Especially oncology patients have huge risk for DVT. While prevention of DVT, we should be aware of complications even there are rare conditions.

**Conclusion:** HIT and DVT are rare but life-threatening and need to be treated conditions. Full body examination and the platelet count check-up during heparin therapy.

**Keywords:** Heparin Induced Thrombocytopenia; Anticoagulation; HIT; Rivaroxaban

### Introduction

Heparin Induced Thrombocytopenia (HIT) is defined a rare complication of heparin therapy. HIT is characterized by decreasing

in platelet count after heparin initiation. Unless HIT could recognize and stop the heparin treatment, the consequences would be devastating. Therefore, when heparin is given for anticoagulant prophylaxis, should be aware of complications of heparin. In daily

practice, patients who performed surgery with any reasons, they are assessed with 'Caprini Score for DVT Risk Calculator'. The Caprini Score is based on the Venous Thromboembolism Risk Factor Assessment that predicts risk and probability of DVT. It stratifies risk for venous thromboembolism and deep vein thrombosis after surgery, based on several factors. After this assessment high scored patients undergo prevention of DVT, generally Low Molecular Weight Heparin (LMWH) is used for it. Heparin should be injected the subcutaneous tissue where commonly used areas, abdomen, the outer thigh, the outer upper arm.

**Case History**

A 65 years old woman was recently performed total abdominal hysterectomy bilaterally salpingo-oophorectomy and lymph node dissection, following diagnosed endometrial adenocarcinoma FIGO grade 2 confirmed by biopsy results. The Caprini Score is calculated as a high risk patient, then decided to start LMWH as a prevention of DVT. She had multiple risk factors for DVT such as atrial fibrillation, morbid obesity, malignancy, age. The patient presented on day 10 with complaints of about the swelling, turning blue and pain on her arms. Physical examination of the patient revealed an obese woman in mild distress. Her blood pressure was 123/81 mmHg with a pulse 100 beats per minute. She was breathing 18 times/minute with an oxygen saturation of 100%. She was afebrile. On head and neck examinations, her pupils were equal, round, reactive to light and accommodation. Her sclera was anicteric. On extremity examinations, necrotic skin tissue was detected, which is described sharply demarcating plaques and painful bullous on wounds, occurred with the measures 5\*6\*6 cm over bilateral arms which are injection site areas (Figure 1). When the wound determined which thought a skin necrosis of injection areas, immediately ordered to stop the LMWH therapy.



**Figure 1:** Injection site wound in day 10 postoperatively.

Her blood chemistry panel revealed serum glucose level, electrolytes, liver, kidney functional test with in normal range. Her blood count levels are with in normal range but platelet count was  $65 \times 10^3/\text{ul}$  which is low level. On hospital day 11, the patient reported improvement of symptoms. Vital signs were within normal limits. She complained of changing the color of her arm and went worse the vision of her wound, getting colder of her arm. On extremity examinations, cold and purple arm was detected like avascular. The clinical condition was monitored by a multidisciplinary team, consulted with the hematology, cardiovascular surgery, dermatology and orthopedy department quickly. After the hemotologic evaluations, in blood smear shows normochromic-normocytic anemia, (not seen erythrocyte fragmentation), normal number/morphology of leukocytes and thrombocytopenia (the real number of platelets was  $50-60 \times 10^3/\text{ul}$ ). According to her complains and clinical signs directed us to prompt HIT (heparin induced thrombocytopenia syndrome). '4Ts HIT Probability Testing' is used to confirm diagnosis HIT (Figure 2). Thus, 4T score was calculated to be 6 which is considered as high probability. Then measurement of ADAMTS13 activity was revealed with in normal range, HIT diagnosis became definitive. The consultant doctor recommended discontinuation of LMWH and to start oral anticoagulant therapy. She had bilateral upper extremity venous duplex that was reported as DVT on right axillary venous simultaneously. DVT condition is consulted with Cardiovascular surgeon, he recommended to continue anticoagulant therapy in subcutaneous or peroral.

4Ts HIT Probability Testing (Pretest)	Score
<b>Thrombocytopenia</b>	
- 50% decrease in platelets AND nadir $\geq 20,000$ AND no surgery within preceding 3 days	2
- > 50% decrease BUT surgery within preceding 3 days OR any combination of platelet decrease and nadir that does not fit the criteria for Score 2 or Score 0	1
- < 30% decrease OR platelet nadir < 10,000	0
<b>Timing (from first day of most recent heparin/LMWH exposure)</b>	
- Platelet drop day 5-10 after start of heparin OR within 1 day if previous exposure within the last 5-30 days	2
- Consistent with fall between days 5-10 but not clear OR within 1 day of start with exposure in past 31-100 days OR onset of thrombocytopenia after day 10	1
- Platelet fall is within 4 days of start without recent heparin exposure in the last 100 days	0
<b>Thrombosis</b>	
- New thrombosis, skin necrosis at injection sites, post-heparin acute systemic reaction, adrenal hemorrhage	2
- Progressive or recurrent thrombosis on therapeutic anticoagulant, suspected thrombosis not yet proven, OR erythematous skin lesions at heparin injection sites	1
- Thrombosis not suspected	0
<b>Other Causes for Thrombocytopenia</b>	
- No other cause for platelet count fall is evident	2
- Possible other cause is evident (e.g. sepsis without proven source, thrombocytopenia associated with initiation of ventilator, other)	1
- Probable other cause is present (e.g. within 72 hours of surgery, confirmed bacteremia/fungemia, chemotherapy/radiation within 20 days, DIC, post-transfusion purpura, nadir < 20 AND with other potential drug cause, non-necrotizing skin lesions at injection sites, other)	0
<b>Pretest Probability Score:</b> 6-8 = high 4-5 = intermediate 0-3 = low	<b>Total =</b> _____ <b>(8 maximum)</b>

**Assessment and Action:**  
 Score  $\leq 2$  – no presence of HIT or need to test for antibody  
 Score of 3-4 – warrants additional consideration and potential need to request an antibody assay  
 Score  $\geq 5$  – request antibody assay and consider initiating an alternative anticoagulant

**References:**  
 Linkins LA, Dans AL, Moores LK, et al. Treatment and prevention of heparin-induced thrombocytopenia: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e495S-530S.  
 Warkeintin TE. Heparin-induced thrombocytopenia: pathogenesis and management. British Journal of Haematology 2003; 121:535-55.

**Figure 2:** Outline for calculating 4T scores.

As a result, there was a conflict. Whereas HIT syndrome's therapy is to stop the LMWH, but also she could be cured with anticoagulant because diagnosed with DVT simultaneously. Development of HIT syndrome restricted us to continue an anticoagulant therapy on this patient. On the other hand, unless we treat the DVT, the severe complications would develop. As a result of past research, only Fondaparinux is recommended in these situations which is an oral anticoagulant such as dabigatran, apixaban or rivaroxaban. After this research, we switched the therapy to Rivaroxaban from LMWH.

### Discussion and Conclusion

All around the world, Venous thromboembolism remains the most preventable cause of death in hospitalized patients and is known to cause significant morbidity with associated health-care expenditure.

In 2008, the eighth edition of the American College of Chest Physicians (AT8) guidelines for the prevention of VTE endorsed the need for an "active, formal strategy" to prevent hospital-induced VTE. VTE prophylaxis measures to reduce VTE and promote appropriate prophylaxis to at-risk patients in the hospital setting.

Over the past 5 years, individual thrombosis risk assessment has become an accepted practice in most surgical specialties [1]. Caprini Risk Assessment Tool for VTE is one of the risk score scales. In our case we use the Caprini risk assessment tool to utilize the risk. According to many studies, when compared to unfractionated heparin, LMWH has a lower incidence of HIT, reduced risk of bleeding, and thromboembolic complications. Given these prevention information, LMWH use is widespread. Our case report features the two rare complications, skin necrosis depending on HIT and development of DVT under VTE prophylaxis in a patient at the same time.

Heparin-induced thrombocytopenia (HIT) is a rare complication of heparin therapy. Its pathogenesis includes thrombotic events such as DVT as in our case. Upper limb thrombosis, involving the axillary or subclavian vein, is a less common phenomenon [1]. This condition is subject to the same risk factors and therapy as the formation of lower limb DVT [2]. Cancer is a major risk factor for secondary DVT similar to our case. Approximately, between 30% and 40% of all upper limb DVTs are cancer-related [3]. In our case, Venous duplex ultrasound of her left arm demonstrated

compressible radial, ulnar, and brachial veins with decreased compressibility in the right axillary vein and confirmed the presence of thrombosis extending throughout the length of the vessel.

HIT requires immediate discontinuation of all heparin products and initiation of anticoagulation with different agents in efforts to prevent further progression [4]. An alternative form of anticoagulation in patients with HIT stops the progression of the disease and further antibody formation, and resolves further thrombosis due to platelet activation. Alternatives usually include direct thrombin inhibitors such as argatroban or bivalirudin, fondaparinux, danaparoid, or direct oral anticoagulants (DOACs) such as apixaban or rivaroxaban. There are previous reports of using DOACs successfully in the initial management of HIT [5]. Based on this information, we chose the fondaparinux therapy which she had already used for AF. Xeralto (oral antithrombotic) started to begin cure, patient felt better and the view of swollen, uncirculated and cold arms is gone in hours. Discontinuation of the heparin injections promptly leads to recovery in weeks (Figure 3).



Figure 3: Injection site wound at 1 months postoperatively.

### Bibliography

1. Gordon H Guyatt, et al. "Antithrombotic Therapy and Prevention of Thrombosis". 9<sup>th</sup> ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines.

2. Joffe H V. "Upper-extremity deep vein thrombosis: a prospective registry of 592 patients". *Circulation* 110 (2004): 1605-1611.
3. Abdullah BJ., *et al.* "Incidence of upper limb venous thrombosis associated with peripherally inserted central catheters (PICC)". *British Journal of Radiology* 78 (2005): 596-600.
4. Mahmoud Fath. "Heparin-induced thrombocytopenia (HIT): Identification and treatment pathways". *Global Cardiology Science and Practice* 2 (2018): 15.
5. Warkentin TE., *et al.* "Direct oral anticoagulants for treatment of HIT: update of Hamilton experience and literature review". *Blood* 130.9 (2017): 1104-1113.