

Unfractionated heparin induced thrombocytopenia: A case review

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Received - 03 February 2019

Initial Review - 26 February 2019

Accepted - 04 April 2019

ABSTRACT

Heparin-Induced Thrombocytopenia (HIT) is a disastrous, potentially devastating immune-mediated adverse drug reaction resulted in the formation of antibodies which activate platelets in the presence of heparin. Here, we presented an exemplifying case of a 45-year-old male patient, a known case of Deep Venous Thrombosis admitted in Emergency Department with complaints of left groin pain along with passing bloody clot in urine for past 5 days. The patient was diagnosed as Renal Artery Thrombosis with the help of radiological findings and was treated with Inj. Heparin. Thrombocytopenia developed on the first day of therapy and confirmed with Heparin PF4 IgG ELISA Immunoassay. The patient switched to inj. Argatroban and later changed to oral anticoagulant therapy. Platelet count gradually came to normal upon stoppage of Inj. Heparin. To avoid a catastrophic outcome, heparin should be stopped before initiating proper management.

Keywords: Immunoassay, Thrombocytopenia, Thromboprophylaxis, Thrombosis.

Heparin is widely used for thromboprophylaxis or treatment in many clinical situations, including acute coronary syndromes, venous thromboembolism, atrial fibrillation, peripheral occlusive disease, dialysis, and during extracorporeal circulation. Approximately, one-third of the hospitalized patients in the USA, or about 12 million patients per year receive heparin [1].

Heparin-Induced Thrombocytopenia (HIT) is a dangerous, potentially lethal, immunologically mediated adverse drug reaction to unfractionated heparin (UFH) or less commonly with low molecular weight heparin (LMWH). The prevalence of HIT ranges from 0.1%-5.0% of the patients receiving heparin, with 35-50% of the patients developing thrombosis [2]. Approximately, 10% to 20% of patients will develop transient mild thrombocytopenia after 1 to 4 days of heparin therapy. The platelet count rarely goes below 100,000/ml, often becomes normal despite further heparin administration and is generally without clinical sequelae [3].

CASE REPORT

A 42-year-old male patient was admitted in the emergency with the complaints of radiating left groin pain along with passing bloody clot in urine for the past 5 days. On exploration of the patient history, it was found that he had a past history of Deep Venous Thrombosis and was admitted for pulmonary embolism 8 months back.

On the time of admission, the vitals were stable and the patient physical parameters were found to be normal except mild

abdominal swelling with distension. Laboratory finding shows that haemoglobin: 7.4g/dl, total count: 13,720ccmm, Platelet count: 90,000, erythrocyte sedimentation rate (ESR): 103mm/Hr, plasma Fibrinogen: 675mg% and Lactate Dehydrogenase: 1106U/L.

The ultrasound examination reveals non-excreting right kidney with perinephric fat stranding, wedge-shaped arterial perfusion with a hypodense filling defect in the renal vein suggestive of venous infarctions and acute renal vein thrombosis. Sub-acute thrombosis of the infra-hepatic abdominal inferior vena cava involving the whole length for about 13cm with chronic deep venous thromboses of bilateral common iliac, external and internal vein with pelvic venous collaterals, sub-acute to chronic thrombus with recanalization of the both visualized portion of the common femoral vein.

To remove the thrombus, thromboaspiration along with renal vein balloon angioplasty was done with the help of Ultrasound guidance. A 10mg Alteplase bolus was given to the internal jugular vein over 20minutes, the only 20ml of clot removed and repeated with 5mg bolus but it went unsuccessful. So, low dose Heparin protocol was started with a loading dose of 4000 unit followed by maintenance dose of 800unit/hr, which is calculated based on the patient weight of 65kg, on regular monitoring of activated Partial Thromboplastin Time (aPTT).

The patient was treated for 4 days with regular monitoring of aPTT, platelet, International Normalised Ratio (INR) and prothrombin time (Table 1). The patient platelet counted started declining which reached the lowest level of 15,000Cell/mm³ [3] (Figure 1). So heparin was stopped and to access HIT, we used 4 T's pre-test scoring

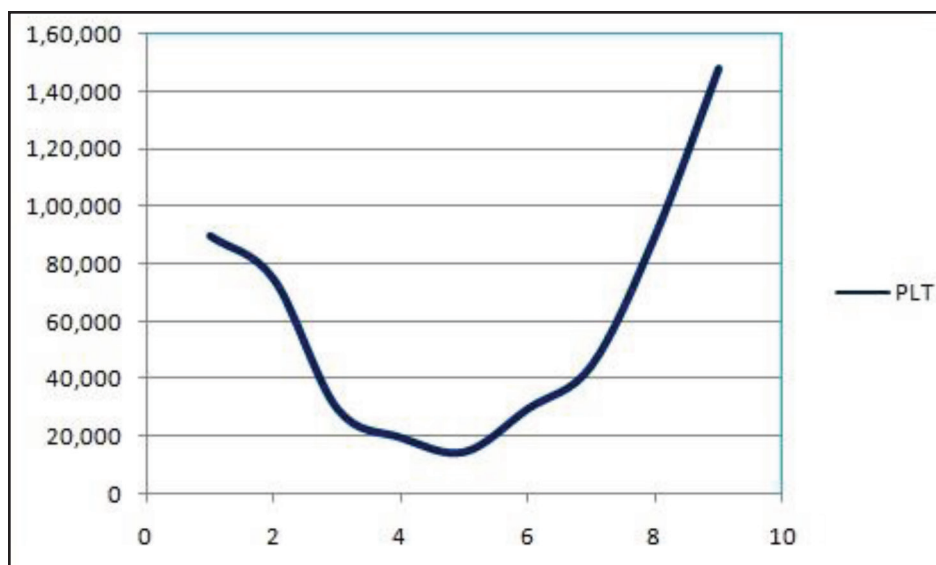


Figure 1: Change in the Platelet count of the patient from day 1 of heparin therapy.

system and HIT expert probability score (HEP) (Table 2 and 3). Heparin-Induced Thrombocytopenia can be assessed using the pre-test probability score and confirmed using HIT laboratory assays (Table 4).

Because of the lowering platelet level, 1 unit of Platelet was given as management to normalize the platelet level. Platelet count was gradually raised to a normal level within 6 days after the stoppage of inj. Heparin. Instead of Heparin, Inj. Argatroban 130mcg/min infusion was given to the patient with aPTT monitoring, every 3hrs and the dose was adjusted to maintain the level within 1.5-3 times the base i.e. between 70-100seconds. After 5 days, Inj. Argatroban was switched to oral therapy with starting of a minimum dose of Tab. Warfarin 1mg and the dose was adjusted with INR. The patient was fully recovered after 10 days in the critical care unit and later shifted to the ward and thereby discharged with a prescription of Tab. Warfarin 4mg with the advice of regular monitoring of INR.

DISCUSSION

Heparin-induced thrombocytopenia (HIT) is a potentially devastating immune-mediated adverse drug reaction caused

by the emergence of antibodies that activate platelets in the presence of heparin. It is the most important and most frequent drug-induced type of thrombocytopenia. If unrecognized, it is associated with significant morbidity and mortality [1]. HIT may develop in two distinct forms: type I and type II. HIT type I (also known as heparin-associated thrombocytopenia) is a non-immunologic response to heparin treatment, mediated by a direct interaction between heparin and circulating platelets causing platelet clumping or sequestration. HIT type I affects up to 10% of patients, usually occurs within the first 48–72 h after initiation of heparin treatment and is characterized by mild and transient thrombocytopenia (rarely, 100 000/mm³), often returning to normal within 4 days once the heparin is withdrawn. Whereas HIT type II is immune-mediated and associated with a risk of thrombosis [4].

In the present case, the patient had a history of renal artery thrombosis which was treated with Heparin. The treatment failure resulted in the left renal nephrectomy. Within 100 days of heparin therapy, the patient got readmitted with similar complaints and diagnosed as right-sided renal artery thrombosis and after the initiation of heparin therapy on the first day itself, the patient developed thrombocytopenia. It was assessed with the help of

Table 1: Changes in the PLT count, aPTT and INR values of the patient

Days	I	II	III	IV	V	VI	VII	X	XII
PLT	90,000	75,000	30,000	20,000	15,000	30,000	45,000	90,000	1,48,000
APTT	36	36	55	55	123	56	33	32	32

Table 2: The 4 T's Pre-test Scoring System for Heparin-Induced Thrombocytopenia [5]

Clinical Parameters	Score	Clinical description of the presentation
Thrombocytopenia	2	Platelet count fall > 50%, but lowest platelet count $\geq$ 20,000 mm ³
Timing (of platelet count fall or thrombosis)	2	Platelet fall within 1 day of the start of heparin within 5-30 days
Thrombosis	2	New thrombosis
Other cause of platelet decline	2	No alternative explanation for platelet fall is evident
Composite Score	8	High Risk

Table 3: Heparin-Induced Thrombocytopenia Expert Probability (HEP) Score [5]

Clinical Parameters	Score	Clinical factor and presentation
The magnitude of fall in platelet count	1	30 - 50%
The timing of fall in platelet count	3	Previous heparin exposure in the last 100days
Nadir platelet count	2	>20,000
Thrombosis	2	Progression of pre-existing arterial or venous thrombosis while on heparin
Skin necrosis	0	Not applicable
Acute systemic reaction	0	Not applicable
Bleeding	0	Not applicable
Other causes of thrombocytopenia	0	Not applicable
Composite Score	6	High Risk

Table 4: HIT screen (Heparin PF4 IgG ELISA Immunoassay) [5]

Optical Density	Percentage Probability of Clinical HIT	Result
1.40	53.3%	Positive

Pre-test Risk and Probability Score in which 4Ts Score and HIT Expert Probability (HEP) Score got values of 8 and 6 showed a high risk of developing Thrombocytopenia [5]. The confirmation test used here is Heparin PF4 IgG ELISA Immunoassay screen, in which the test confirmed thrombocytopenia with a percentage probability of 53.3%.

After the verification, heparin was stopped and started inj. Argatroban with an initial infusion dose of 130mcg/min (2mcg/kg/min) gradually increases up to a steady state of aPTT within 1.5- 3 times the base i.e. between 70-100seconds. After 5 days of Argatroban therapy, it was switched to oral therapy i.e. Tab. Warfarin 2mg with reducing the dose of inj. Argatroban 2mcg/kg/min with regular monitoring of INR [6] and the patient was discharged with Tab. Warfarin 4mg once daily with proper a follow-up of INR ratio.

CONCLUSION

Heparin-induced thrombocytopenia (HIT) is the most commonly facing immunological disorder in hospitalized patients over the

past 6 decades. Since the initial time of the description, studies were encountered to analyze the pathogenesis, complication and proper management of HIT, which help to tackle the disease on its initial stage I documented this case to make an impact to solidify HIT's place in the differential diagnosis of Thrombocytopenia.

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Funding: None; Conflict of Interest: None Stated.

How to cite this article: Das V, Fumilayo L. Unfractionated heparin induced thrombocytopenia: A case review. *Indian J Case Reports*. 2019;5(2):154-156.

Doi: 10.32677/IJCR.2019.v05.i02.020