CASE REPORT

Does 'heparin-induced thrombocytopenia' hit our minds?

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Abstract

Unfractionated heparin is a widely used drug to prevent deep vein thrombosis and pulmonary emboli in patients at risk. With the advent of newer anticoagulants having lesser side effects, its use has diminished but not out of service. Here, we report a case of deep venous thrombosis, in a patient on prophylactic dose of heparin, which was later found to be a manifestation of heparin-induced thrombocytopenia (HIT). Thrombosis in the presence of heparin prophylaxis should be considered as HIT rather than a failure of anticoagulation.

Key words: Deep venous thrombosis, fondaparinux, heparin-induced thrombocytopenia, unfractionated heparin

INTRODUCTION

Heparin is a potent prophylactic and therapeutic antithrombotic drug because of its rapid onset and short duration of action. Heparin-induced thrombocytopenia (HIT) is a well-documented complication of unfractionated heparin (UFH). Thrombosis is one of the most common manifestations of HIT, in spite of that HIT *per se* as aetiology of deep vein thrombosis (DVT) is considered less common.

CASE REPORT

A 54-year-old male intubated patient was admitted to the Intensive Care Unit (ICU) following decompression hemi-craniectomy with stable haemodynamics and a Glasgow Coma Scale (GCS) of E1VtM5. The surgery lasted for 2 h; blood loss was around 500 ml, and no transfusion was required. As per our ICU protocol, the patient was put on heparin 5000 IU subcutaneous twice daily dose for DVT prophylaxis on the 2nd post-operative day.

On the 6th post-operative day, the patient developed tense swelling in the right leg extending from knee to ankle. Compression ultrasound (USG) showed the lack of compressibility and echogenic content in the lumen of right superficial femoral vein and right popliteal vein suggestive of DVT. This was subsequently confirmed with positive D-dimer and a Wells score of 4 for DVT. Initially considering it as a failure of prophylaxis, therapeutic heparin therapy was started to prevent further thrombosis formation and risk of pulmonary embolism. On the 2nd day, after giving weight-based therapeutic heparin infusion, the platelet count was found to be 44,000/μL. Retrospectively tracing back the trends of platelet count showed that the baseline platelet count was 162,000/μL, which reduced to 98,000/μL on day 5 post-operatively (5 days after starting prophylactic heparin dose, a day before the onset of DVT) [Figure 1]. The pre-test probability of HIT was 7. No other apparent

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cause for thrombocytopenia was found. Immediately heparin infusion was stopped. Haematology consultation sought and injection fondaparinux subcutaneous 7.5 mg a day was started. Platelet count showed improving trend on subsequent days.

After 5 days of fondaparinux therapy, oral warfarin was bridged till INR of 2–3 was achieved. Fondaparinux was stopped. Over this time, patient GCS improved to E4V4M6 and leg swelling reduced significantly. Repeat USG leg revealed recanalisation in the thrombosed veins. The patient got shifted back to the ward with the advice to continue anticoagulation for 3 months.

DISCUSSION

DVT of the lower extremity, especially of the proximal veins is clinically important because of the risk of pulmonary embolism. The incidence for first time venous thromboembolism (VTE) was found to be 1.92/1000 person-years.[1] VTE are associated with conditions such as cancer, hospitalisation, surgery and major trauma.

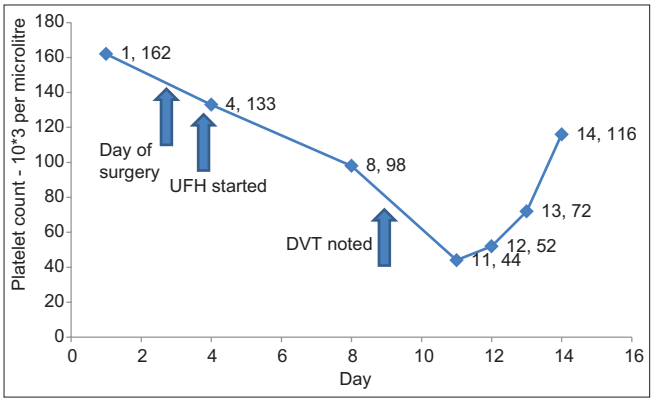

Figure 1: Platelet count over a period of 15 days

Classic symptoms of DVT include swelling, pain and erythema of the involved extremity. Physical examination may reveal a palpable cord (reflecting a thrombosed vein), calf or thigh pain, unilateral oedema or swelling with a difference in calf diameters, warmth, tenderness, erythema and superficial venous dilation. Of this, the presence of calf swelling and difference in the calf diameter of both limbs has more value in the diagnosis.[2] On the basis of Wells, score [Table 1] with a low pre-test probability of DVT, the diagnosis of DVT is low and further testing (e.g., ultrasonography) may not be needed unless the D-dimer is positive or unavailable. Ultrasound evaluation is recommended for patients with intermediate to high pretest probability of DVT. Repeat ultrasound or venography may be required for those with suspected calf vein DVT and a negative initial ultrasound investigation.[3]

Patients with DVT or pulmonary embolism should be treated acutely with low molecular weight heparin (LMWH), intravenous or subcutaneous UFH. For patients receiving UFH, American College of Chest Physicians (ACCP) guidelines suggest that platelet counts should be regularly obtained to monitor for the development of thrombocytopenia [Table 2].[4,5]

Heparin-induced thrombocytopenia

HIT is a life-threatening, immune-mediated complication of exposure to heparin.[6] HIT is caused by autoantibodies to platelet factor 4 complexed with heparin. These antibodies cause thrombocytopenia and thrombosis by peripheral platelet activation and consumption.

Table 1: Deep vein thrombosis Wells score[3]

	Points
Clinical feature	
Active cancer (treatment on going, within 6 months or palliative)	1
Paralysis, paresis or recent plaster immobilisation of the lower extremities	1
Recently bedridden >3 days or major surgery within 12 weeks requiring general or regional anaesthesia	1
Localised tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
Calf swelling 3 cm larger than asymptomatic side	1
Pitting oedema confined to the symptomatic leg	1
Collateral superficial veins (non-varicose)	1
Previously documented DVT	1
Alternative diagnosis at least as likely as DVT	-2
Clinical probability simplified score	
DVT 'likely'	≥2
DVT 'unlikely'	≤1

DVT=Deep vein thrombosis

Table 2: Platelet monitoring[4,5]

Heparin use in post-operative cases	Monitoring of platelet count
Prophylactic dose UFH/LMWH	Every 2-3 day between day 4 and 14/until UFH stopped
Therapeutic dose UFH	Every other day between day 4 and 14/until UFH stopped
History of heparin use in past 100 days, treated with UFH or LMWH	Baseline platelet count and repeat count within 24 h

UFH=Unfractionated heparin, LMWH=Low molecular weight heparin

Table 3: Pre-test probability of heparin-induced thrombocytopenia[9]

Feature	2 points	1 point	0 points
Thrombocytopenia	>50% fall and platelet nadir 20-100×10^9/L	30-50% fall or platelet nadir 10-19×10^9/L	>30% fall or platelet nadir <10×10^9/L
Timing of platelet count fall	Clear onset on day 5-10, or≤1 day if heparin exposure within past 30 days	Consistent with day 5-10 fall, but not clear (e.g., missing platelet counts); onset after day 10; or fall≤1 day if heparin exposure 30-100 days ago	Platelet count fall<4 days without recent heparin exposure
Thrombosis or other sequelae	New thrombosis (confirmed); skin necrosis; acute systemic reaction after IV UHF bolus	Progressive or recurrent thrombosis; erythematous skin lesions; thrombosis suspected but not proven	None
Other causes of thrombocytopenia	None apparent	Possible	Definite

IV=Intravenous, UFH=Unfractionated heparin

Risk factors for HIT include the use of unfractionated rather than LMWH in surgical patients, higher heparin doses, female sex and surgery.[7]

The most common and often the first manifestation of HIT is thrombocytopenia occurring in up to 90% of those affected. Thrombosis occurs in up to 50% with venous being more common than arterial.[8]

We consider both clinical and laboratory evidence in evaluating patients for HIT. However, definitive laboratory data may not be available for several days, and it may be necessary to make a presumptive diagnosis of HIT while awaiting these data. The 4 T's score [Table 3] is used to estimate the likelihood of HIT based on readily available clinical data including the degree of thrombocytopenia, timing of platelet count drop, the presence of thrombosis and absence of other causes of thrombocytopenia.[9]

Patients with a presumptive diagnosis of HIT should have immediate discontinuation of all sources of heparin and administration of a non-heparin anticoagulant (fondaparinux, bivalirudin, argatroban, danaparoid and lepirudin) unless there is bleeding or a high risk of bleeding.

CONCLUSION

Thrombosis in the presence of heparin prophylaxis should create the suspicion of HIT rather than a failure of anticoagulation. Monitoring platelets according to the ACCP guidelines, aids in early diagnosis and treatment of HIT.

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Conflicts of interest
There are no conflicts of interest.

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