Hong Kong College of Physicians
Case Report for Interim Assessment
Specialty Board of Advanced Internal Medicine (AIM)

For AIM Training, case reports should be submitted in the prescribed format together with the application form for Interim Assessment at least TWELVE Weeks before the date of Interim Assessment

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Date(s) and place (hospital) of patient encounter: September 2022, PWH
Date of report submission: 2nd March, 2026

Case report

Note: Failure to follow the prescribed format (including the number of words) results in a FAILURE mark (score between 0 and 4) for the Case Report.

Title: A Clotting Chaos

Case history:

A 50-year-old Pakistani gentleman attended the emergency department for chest discomfort and palpitations. He was admitted to the medical ward for further workup. He required 2 liters of oxygen on admission. Blood pressure was normal, but persistent sinus tachycardia was noted. Electrocardiogram shows new S1Q3T3 changes. CT pulmonary angiogram confirmed extensive pulmonary embolism. Echocardiogram showed evidence of right heart strain. A thrombus in transit from right to left atrium is also noted, with suspicion of underlying patent foramen ovale.

Cardiothoracic surgeons were consulted. Patient was transferred to tertiary referral hospital for pulmonary embolectomy and removal of intracardiac thrombus with cardiopulmonary bypass. Surgical closure of patent foramen ovale was done in the same operation. Patient was started on heparin infusion postoperatively with an activated partial thromboplastin time (aPTT) in the controlled range of 70 - 80. There was a transient platelet drop from a normal baseline at 168 (163 - 358 x 10^9/L) to a nadir of 73 x 10^9/L, then recovered to normal by post operation day 5. Due to hypotension with increasing vasopressor requirement, patient required 5 days of extracorporeal membrane oxygenation (ECMO) support. He was then discharged from the intensive care unit.

On post operation day 8, patient started to have a slight drop in platelet counts again to 157 x 10^9/L. The platelet counts further dropped to 38 x 10^9/L on post operation day 10. The patient

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was not in active sepsis, and the International Normalized Ratio (INR) was normal, therefore the thrombocytopenia was unlikely accountable by disseminated intravascular coagulation (DIC). Since the platelet drop occurred well beyond post operation day 4, it was also unlikely due to platelet consumption or hemodilution related to cardiopulmonary bypass [1]. There were no newly initiated medications that were known to cause thrombocytopenia. Hematology team was consulted for the possibility of heparin induced thrombocytopenia (HIT). The 4Ts score was 4 with an intermediate probability of HIT. Testing for anti-heparin/platelet factor (PF)-4 antibodies was ordered. Hematologists advised to switch from heparin to direct oral anticoagulants (DOAC) if deemed fit by surgical team. Patient was switched to Apixaban on the next day, and heparin infusion was discontinued.

However, patient was noted to have recurrence of sinus tachycardia on the same day of heparin discontinuation. Bedside echocardiogram reveals recurrent right atrial clot that prolapsed into the right ventricle. Urgent CT pulmonary angiogram confirmed de novo thrombus in the right atrium and inferior vena cava, also persistent pulmonary emboli in bilateral lobar and segmental arteries. Concurrently anti-heparin/PF-4 antibody came back positive on the very same day. The diagnosis of HIT was made. Hematology team was consulted again, and patient was started on intravenous Agatroban infusion for 5 days. Warfarin was started with overlap of Agatroban therapy. Platelet counts nadired at 38 x 10^9/L and gradually recovered to normal by post operation day 15. Repeated echocardiogram on post operation day 22 shows significantly reduction in size of right atrial clot. Patient was discharged on day 30 of operation.

Thrombophilia screening for this patient yielded positive lupus anticoagulant (LA), but it carried uncertain accountability as the test was done during heparinization. LA was not repeated subsequently due to high thrombotic risk with interruption of anticoagulation. Patient was advised for lifelong anticoagulation since the index thrombotic event was life threating. Patient tolerated warfarin well, maintained an optimal INR in subsequent follow up, and there has been no further recurrence of thrombotic events.

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Discussion and literature review

Heparin induced thrombocytopenia (HIT) is a rare immune reaction due to heparin exposure. It causes thrombocytopenia and thrombotic tendency which can lead to life threatening complications. The prevalence of HIT is 0.1% to 5.0% in all patients receiving heparin [2]. In patients who underwent cardiac surgery, just as our case, an observational study reviewed 11820 patients and found the HIT prevalence is 1.1% [3].

HIT is induced by immunoglobulin G (IgG) antibodies that bind to heparin/platelet factor (PF)-4 complexes. PF-4 are released from platelets, and when exposed to heparin, they bind to form immunogenic complexes. Anti-heparin/PF-4 antibody binds to the complexes then bind onto platelet and causes platelet activation and aggregation. This leads to intravascular platelet consumption and accelerates thrombin generation [4].

The most common clinical manifestation of HIT is thrombocytopenia. Typically, the fall in platelet count occur between day 5 to 10 after initiation of heparin [4]. It is atypical for the count to fall below 20 x 10^9/L, and bleeding symptoms are uncommon [5]. Alternative causes for thrombocytopenia such as sepsis or disseminated intravascular coagulation (DIC) should always be ruled out. If HIT is not timely identified and treated, paradoxical thrombotic events might follow. 10 to 20% of patients have skin necrosis localized to the heparin injection sites. Both arterial or venous thromboembolic complications including pulmonary embolism, stroke, and limb ischemia could occur [2].

The diagnosis of HIT is made by clinical and laboratory evidence. The 4Ts score is the most used score for risk stratification. It contains 4 components including: amplitude of platelet counts fall, onset of the fall, any new thrombosis, and any alternate cause of thrombocytopenia [4, table 1]. A total score of more than 6 indicates high probability of HIT, while a score of less than 3 suggests low probability. The 4T score has a high negative predictive value but a low positive predictive value [4].

Clinicians should only proceed to anti-heparin/PF-4 antibody testing if 4T score suggest at least intermediate risk of HIT [7]. This is because the antibody has high sensitivity but limited specificity [6]. Among heparin treated patients who had anti-heparin/PF-4 antibody positive, a systemic sero-surveillance study suggests that only 2 to 15% has clinically evident HIT [4]. Functional assay could be considered to further confirm the diagnosis. The gold standard functional assay is serotonin release assay, which measures the amount of serotonin released by activated platelets [6]; it is, however, not readily available in our locality.

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Of note, anti-heparin/PF-4 antibody are detectable in 20-50% of patients had undergone cardiopulmonary bypass, but the incidence of HIT after bypass is approximately at 0.5% to 2% only [6]. It is suggested that patient with genuine HIT after bypass typically demonstrate a "biphasic" pattern of platelet fall, where the count drop initially due to surgery, rebounds and fall again due to HIT [6], which is exactly compatible to the platelet trajectory in our case.

The key management of HIT is the discontinuation of heparin and switching to an alternate anticoagulation. The American Society of Hematology (ASH) guideline suggests that patient with an intermediate to high 4T score should be managed as HIT empirically, even before the result of anti-heparin/PF-4 antibody [7]. They should be started on full dose anticoagulation regardless of whether there had been any thrombotic events. This is because the immune reaction mediated by anti-heparin/PF-4 antibody generates massive thrombin, and a prophylactic dose anticoagulation would be inadequate [4].

One major consideration when choosing which non-heparin anticoagulation to use is whether there is presence of any life-threatening thrombosis [7]. In our case, patient developed recurrent right atrial clot, and there is risk of progression into massive pulmonary embolism. Direct thrombin inhibitors (DTI), given intravenously, would be more appropriate in this potentially life-threatening thrombotic event. Also, should an urgent procedure be needed in case of deterioration, DTI are preferred given their shorter half-life [7]. Argatroban, as used in our case, is an FDA approved synthetic reversible DTI. It can reach steady state in 1-3 hours, and its half-life is 40 to 50 minutes in patients without hepatic impairment [2]. Bivalirudin is another DTI recommended for use by the ASH guideline [7], but FDA approval is currently limited only to use during percutaneous coronary interventions (PCI) for patient with HIT [2]. Both DTI requires close monitoring and fine titrate to targeted aPTT, which could be a challenge in practical use.

Indirect factor Xa inhibitors can also be used as anticoagulation in HIT. Fondaparinux is given subcutaneously, while Danaparoid can be given intravenously or subcutaneously [4]. Therapeutic monitoring can be done by measuring anti-factor Xa levels, but is not routinely required [2,8], providing an advantage over DTI. However, there has been infrequent reports of exacerbation of HIT with the use of indirect factor Xa inhibitor, and small percentage of cross reactivity with anti-heparin/PF-4 antibody [4].

Oral anticoagulation could be considered in patient without life threatening thrombosis. However, warfarin, the vitamin K antagonist, must not be used during acute HIT because initial administration of warfarin results in decline of factor C which paradoxically induces prothrombotic state. Adding up to the thrombotic tendency during acute HIT, it could further increase the risk of thrombotic sequalae [6]. It must only be used when a steady state of anticoagulation is achieved by an alternate

non-heparin agent, and an overlap for at least 5 days is suggested to avoid complications [2]. Direct oral anticoagulants (DOAC), in the contrary, carries immediate anticoagulant effects. ASH guidelines suggest that they could be considered as an initial treatment for patients with HIT [7]. However, there has not been studies comparing the outcomes between DOAC and non-heparin anticoagulants yet [9]. An observational cohort study comparing 79 patients with HIT that are treated with DOAC or warfarin found no statistical difference in thrombotic or bleeding outcomes between the 2 groups. However, there is clinically significant increase in thrombotic and bleeding outcomes in the DOAC cohort [9]. More studies with larger sample size are needed to validate the findings.

In conclusion, our case illustrated a typical presentation of the uncommonly encountered event of HIT. Early suspicion and recognition are of great importance to prevent disastrous thrombotic complications.

Tables and figures (where applicable) (no more than two figures)

Table 1. 4T Scoring System for Evaluating the Pretest Probability of Heparin-Induced Thrombocytopenia.*

Variable	Score		
	2	1	0
Acute thrombocytopenia	Platelet count decrease of >50% and nadir ≥20,000/mm^3	Platelet count decrease of 30–50% or nadir 10,000–19,000/mm^3	Platelet count decrease of <30% or nadir ≤10,000/mm^3
Timing of onset	Day 5–10, or day 1 if recent heparin exposure	>Day 10 or unclear exposure	≤Day 4 with no recent heparin exposure
Thrombosis	New thrombosis or anaphylactoid reaction after heparin bolus	Progressive or recurrent thrombosis	None
Other cause of thrombocytopenia	None	Possible	Definite
Total score	6–8, indicating high score	4 or 5, indicating intermediate score	0–3, indicating low score

* Adapted from Lo et al.[31] A low 4T score (0 to 3 points) has a high negative predictive value. The day that heparin was started is considered as day 0. The onset of heparin-induced thrombocytopenia (HIT) is defined as the day that the platelet count begins to decrease. Patients in whom the score is difficult to apply, owing to missing platelet count values or coexisting conditions causing thrombocytopenia, and those with an intermediate or high score require further evaluation. This score can be included on ordering forms for HIT laboratory testing (e.g., www2.medizin.uni-greifswald.de/transfus/fileadmin/user_upload/doku_thrombo_gerinnung/platelet_lab_request_form.pdf).

Greinacher A. Heparin-Induced Thrombocytopenia. N Engl J Med. 2015 Nov 5;373(19):1883-4.

Reference (not more than 10)

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6. May J, Cuker A. Practical guide to the diagnosis and management of heparin-induced thrombocytopenia. Hematology Am Soc Hematol Educ Program. 2024 Dec 6;2024(1):388-395.
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9. Hassan K, Kinan R, Casey A, Dermady M, Mizuki B, Stanilova K, Savage H, Yuan H, Hillis E, Bertaut C, Guillory T, Coons E. Direct Oral Anticoagulants Versus Warfarin in Patients With Isolated Heparin-Induced Thrombocytopenia or Heparin-Induced Thrombocytopenia With Thrombosis. Eur J Haematol. 2025 Mar;114(3):429-435.

No of words in Case History and Discussion (excluding references):__1583___.

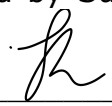
(should be between 1000-2000)

Declaration

I hereby declare that the case report submitted represents my own work and adheres to the prescribed format. I have been in clinical contact with the case selected. The case report has not been submitted to any assessment board or publication and it is NOT related to my second specialty(ies), if any. My consent is hereby given to the College to keep a copy of my case report, in written and/or electronic, at the College Secretariat and allow the public to have free access to the work for reference.

(signature of Trainee)

Endorsed by Supervisor *



(signature of Supervisor)

* Supervisors must go over the Case Report with the Trainees, advise Trainees whether further amendments are necessary, review the Originality/ Similarity Report prepared by Trainees, adherence to the required format, sign on the report and remind Trainees on issues related to copyright and plagiarism.