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CORRESPONDENCE

Four Limb Ischemia: A Severe Case of Heparin Induced Thrombocytopenia

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Dear Editor,

Heparin-induced thrombocytopenia (HIT) is an immune-mediated complication secondary to exposure to heparin due to the formation of antibodies against complexes of platelet factor 4 (PF4) and heparin [1]. This antibody activates platelets causing venous or arterial thrombosis in nearly half of the cases with HIT [2]. Risk of HIT is 10 times higher after exposure to unfractionated heparin (UF) compared to low molecular weight heparin (LMWH) [3]. Herein, we present a case of a patient developing four limb ischemia secondary to HIT.

A 48 year-old-old previously healthy female presented with nausea and abdominal pain. Imaging reveled a large retroperitoneal mass invading the inferior vena cava (IVC) and extending cranially through the IVC to the right atrium. Endovascular biopsy of IVC mass showed features suspicious for sarcoma. Post procedure she developed bilateral lower extremity deep venous thrombosis for which she was started on therapeutic (full-dose) dose of UF titrated to anti-Xa activity. She underwent excision of intra-cardiac and vena caval sarcoma along with right atrial repair and IVC graft placement. Final pathology reveled leiomyosarcoma, grade 3 with 50% necrosis. Post-surgery she developed cardiogenic shock and required multiple inotropes including epinephrine, norepinephrine and vasopressin. Physical exam showed necrosis of tip of fingers and toes. Post heparin exposure Day 7, the platelet count decreased from 298,000/μl to 19,000/μl. Other labs showed creatinine at 0.7 mg/dl (within-normal range), prothrombin time at 17.7 s (mild elevation), activated partial thromboplastin time at 33.4 s (within-normal range), fibrinogen at 232 mg/dl (within-normal range) and elevated d-dimer at > 20 μg/ml. Peripheral smear exam was unrevealing except for marked thrombocytopenia. Imaging revealed new arterial thrombosis involving bilateral radial arteries, left ulnar artery, bilateral distal posterior tibial arteries, bilateral anterior tibial arteries and bilateral peroneal arteries. The 4Ts score was high at 7, which indicated a high pre-test probability for HIT. Heparin PF4 antibody immunoassay resulted with a markedly elevated optical density of 3.6, confirming the diagnosis of HIT. The patient was subsequently started on the direct thrombin inhibitor bivalirudin. Despite therapeutic anticoagulation, necrosis progressed to limb gangrene affecting all four limbs (Fig. 1). After platelet count recovery and several weeks in the hospital, the patient was started and discharged on the oral anti-factor Xa anticoagulant, apixaban. After clear demarcation of the gangrene, the patient underwent amputation of all four limbs.

The risk of HIT is highest after orthopedic (up to 5%) and cardiovascular surgeries (0.5–2%) and lowest for obstetric patients [3]. The 4Ts score is helpful in estimating the likelihood of HIT. The score takes in account several clinical markers: (1) degree of thrombocytopenia, (2) timing of platelet drop in relation to heparin exposure, (3) presence of thrombosis, and (4) other causes of thrombocytopenia. 4Ts score of 0–3 is low probability of HIT, 4–5 is intermediate probability of HIT, and 6–8 is associated with high probability of HIT [4]. For intermediate to high probability cases, immunoassay for heparin PF4 antibody

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Fig. 1 **a** Gangrene of all four limbs in a patient with heparin induced thrombocytopenia. **b** Right foot gangrene in close up

should be ordered. Serotonin release assay is used for serological confirmation of the diagnosis, although may not needed if the diagnosis is clear on basis of clinical probability (4Ts) and high titer immunoassay (OD > 2.0). If the likelihood of HIT is low based on 4Ts score, no further testing is recommended [5]. Treatment of HIT includes stopping heparin and starting alternative anticoagulation, most commonly a direct thrombin inhibitor. Increasingly, oral and subcutaneous anti-factor Xa inhibitors are being used in the treatment of HIT. The incidence of HIT can be reduced if LMWH is used instead of UH. A tertiary care hospital was able to decrease the incidence of HIT by 80% by replacing UH for LMWH for all prophylactic and therapeutic indications except heart surgery and dialysis [6]. Unfortunately, our patient developed a negative outcome that may have been prevented or lessened with earlier initiation of alternative anticoagulation had HIT been recognized prior to waiting for the heparin PF4 immunoassay. In conclusion, HIT remains a life threatening complication needing prompt awareness, diagnosis and management.

Compliance with Ethical Standards

Conflict of interest Both authors declare that they have no conflicts of interest.

References

1. Arepally GM (2017) Heparin-induced thrombocytopenia. Blood 129(21):2864–2872. https://doi.org/10.1182/blood-2016-11-709873
2. Linkins LA, Dans AL, Moores LK, Bona R, Davidson BL, Schulman S et al (2012) 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 141(2 Suppl):e495S–e530S. https://doi.org/10.1378/chest.11-2303
3. Rice L (2017) HITs and misses in 100 years of heparin. Hematology Am Soc Hematol Educ Program 2017(1):667–673. https://doi.org/10.1182/asheducation-2017.1.667
4. Lo GK, Juhl D, Warkentin TE, Sigouin CS, Eichler P, Greinacher A (2006) Evaluation of pretest clinical score (4 T's) for the diagnosis of heparin-induced thrombocytopenia in two clinical settings. J Thromb Haemost 4(4):759–765. https://doi.org/10.1111/j.1538-7836.2006.01787.x
5. Hicks LK, Bering H, Carson KR, Haynes AE, Kleinerman J, Kukreti V et al (2014) Five hematologic tests and treatments to question. Hematology Am Soc Hematol Educ Program 2014(1):599–603. https://doi.org/10.1182/asheducation-2014.1.599
6. McGowan KE, Makari J, Diamantouros A, Bucci C, Rempel P, Selby R et al (2016) Reducing the hospital burden of heparin-induced thrombocytopenia: impact of an avoid-heparin program. Blood 127(16):1954–1959. https://doi.org/10.1182/blood-2015-07-660001