



A Case Report on Heparin Induced Thrombocytopenia in A Covid 19 Patient

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Abstract

Heparin induced thrombocytopenia (HIT) is a life-threatening complication of heparin therapy that can occur between 4-14 days after starting heparin. It is associated with significant morbidity or mortality if unrecognized. Studies indicate that the prevalence of HIT ranges from 0.1% to 5.0% in patients receiving heparin with about 25% to 50% of these patients developing HIT. Unlike other drug-induced thrombocytopenia, HIT does not usually cause bleeding, but instead causes thrombosis. Thrombosis in HIT can lead to death. Herein we present a case of a 65-year-old male patient admitted with symptoms related to COVID 19 infection category B who was a known case of atrial fibrillation, cardiac failure, Systemic Hypertension, Type 2 Diabetes mellitus, Obstructive sleep apnoea -COPD and bilateral chronic lower limb cellulitis treated according to covid 19 protocol and was put on non-invasive ventilation. Heparin was given for atrial fibrillation (AF) which resulted in heparin induced thrombocytopenia.

Keywords:Heparin induced thrombocytopenia (HIT).

INTRODUCTION

Heparin is a drug widely used for thromboprophylaxis or treatment in many clinical situations, including cardiovascular surgery and invasive procedures, acute coronary syndromes, venous thromboembolism, peripheral occlusive disease, dialysis and during extracorporeal circulation. However, it can cause serious adverse effects, including heparin-induced thrombocytopenia (HIT) which is a common, serious and potentially life-threatening condition. Unfortunately, because thrombocytopenia is common in hospitalized patients and can be caused by a variety of factors, HIT often remains unrecognized. Heparin-induced thrombocytopenia is defined as a decrease in platelet count during or shortly following exposure to heparin. The mechanism underlying heparin-induced thrombocytopenia is an immune response. The principal antigen is a complex of heparin and platelet

factor 4 (PF4). Platelet factor 4 is a small positively charged molecule of uncertain biological function normally found in α granules of platelets. When platelets are activated, PF4 is released into the circulation and some of it binds to the platelet surface. Because of opposite charges, heparin and other glycosaminoglycans bind to the PF4 molecules, exposing neoepitopes that act as immunogens leading to antibody production. In fact, patients who develop HIT produce an IgG antibody against the heparin-PF4 complex, which binds to the complex on platelet surface through the Fab region. The Fc portion of the HIT antibody can then bind to the platelet Fc receptor and this interaction triggers activation and aggregation of the platelets. Activated platelets release PF4, thus perpetuating the cycle of heparin-induced platelet activation. In addition, platelet activation leads to the

production of pro thrombotic platelet microparticles which promote coagulation. Finally, as a result of the presence of heparin like molecules on the surface of endothelial cells, the HIT antibody-PF4-heparan sulfate complexes formed on the endothelial surface may induce tissue factor expression with further activation of the coagulation cascade and thrombin generation. Thrombocytopenia in HIT is largely due to the clearance of activated platelets and antibody-coated platelets by the reticulo-endothelial system. [1-6]

CASE REPORT

A 65-year-old male patient was admitted on 6-2-2021 to our hospital with symptoms related to COVID 19 infection category B moderate severity with intermittent low-grade fever of 2 days. He was a known case of atrial fibrillation, cardiac failure, Systemic Hypertension, Type 2 Diabetes mellitus, Obstructive sleep apnoea -COPD and bilateral chronic lower limb cellulitis. On examination he was tachypneic. ABG showed hypoxia and chest x-ray showed bilateral patchy opacities. Hence, he was started on oxygen support via facemask. The HRCT chest showed multifocal confluent patches of ground glass opacities and consolidation predominantly in peripheral lower zones. He was treated according to covid 19 protocol and was put on non-invasive ventilation. Patient was noted to have persistent AF with fast ventricular response. Echo showed diastolic dysfunction. Heparin and amiodarone were initiated for AF with fast ventricular function on 8-2-21. At the time of admission his platelet count was 1.5lakh/cu mm. His condition gradually improved but he was noted to have decreasing platelet count. On 28-2-21 he developed hemoptysis and then heparin was stopped for 12 hours. Repeat chest x-rays showed clearing but ABG showed low P/F ratio and hypoxia. However, the same evening he had a sudden onset of right lower limb pain associated with loss of sensation. On examination he had cold lower limb extremities and absent peripheral pulses. The arterial Doppler study revealed femoral artery thrombosis and heparin infusion was restarted. An emergency femoral artery thrombectomy was done under femoral block and he was continued on heparin infusion which was titrated according to aPTT levels. The Next day (3-3-21) the patient was noted to have a platelet count of 20000/cumm. So heparin induced thrombocytopenia was considered and started on dabigatran 75 mg BD.

Repeat platelet done showed an improving trend and the platelet count became normal within 4-5 days. Later CTPA was done as the patient continued to have hypoxia and hemoptysis and it showed features of thromboembolism in right pulmonary artery peripheral branches. Patient's condition worsened due to hospital acquired pneumonia and sepsis and he expired.

DISCUSSION

HIT is one of the most serious complications related to heparin use, with a mortality rate that can reach up to 20%. At the admission time our patient's platelet count was normal. It started falling after 2-3 days which was attributed to COVID infection /secondary bacterial infection. However, when the platelet count became very low after femoral artery thrombosis and heparin infusion the possibility of HIT was considered. The fact that the platelet count improved after stopping heparin confirms the diagnosis of HIT. Normally heparin induced thrombocytopenia occurs 10-14 days after heparin therapy. But in this patient thrombocytopenia was noted soon after the start of heparin. This could be because this patient might have received heparin in the past for his AF and cardiac failure which could have triggered antibody formation in the body in such patient's thrombocytopenia can occur acutely on re-exposure to heparin. In critically ill patients with multiple comorbidities, thrombocytopenia can occur due to many other factors including gram negative sepsis, DIC, drug induced thrombocytopenia and folate deficiency. However a high index of suspicion of HIT should be kept in mind in any patient who starts having thrombocytopenia after starting heparin before a thrombotic event occurs. In such patients heparin should be stopped and anticoagulation should be continued using direct thrombin inhibitors. Diagnosis of HIT can be confirmed by functional tests and immunoassays. Functional tests include heparin induced platelet aggregation (HIPA) and serotonin release assay (SRA) and flow cytometric assay. The immunoassays utilize enzyme linked immunosorbent assay (ELISA) to detect HIT antibodies. But these immunoassays are not available in all the laboratory settings and also they are very expensive. Hence low platelet count (drop in platelet count by 30-50%) from the patient's baseline platelet count is considered as a diagnostic tool by most of the physicians for HIT. The incidence is up to 10 times higher among patients receiving

unfractionated heparin compared to those receiving low-molecular-weight heparin. HIT occurs more frequently among patients who have had a major surgery than among those who have had minor surgery. The risk of heparin induced thrombocytopenia is variable and is influenced by the heparin formulation and the clinical condition in which heparin is administered. [7-10]

CONCLUSION

HIT is a rare complication seen in patients receiving anticoagulation therapy with heparin. Because of the high morbidity and mortality of this condition, it is important that all physicians managing these patients are aware that thrombocytopenia can be an early warning sign mandating further workup to exclude HIT as a possible etiology. With vigilance and a high index of suspicion, the diagnosis can be confirmed while still in the early phase of the condition, and appropriate alternative anticoagulation can be started, resulting in reduction of morbidity and mortality.

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ABBREVIATIONS

ABG: Arterial Blood Gas

AF: Atrial Fibrillation

COPD: Chronic Obstructive Pulmonary Disease

COVID 19: Coronavirus Disease 2019

CTPA: CT Pulmonary Angiogram

DIC: Disseminated Intravascular Coagulation

ELISA: Enzyme Linked Immunosorbent Assay

HIPA: Heparin Induced Platelet Aggregation

HIT: Heparin induced thrombocytopenia

HRCT: High Resolution Computerized Tomography

PF4: Platelet Factor 4

SRA: Serotonin Release Assay

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