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Heparin-Induced Thrombocytopenia (HIT) in Postoperative Cardiac Surgery: Case Report

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Abstract **Case Report**

Heparin-induced thrombocytopenia (HIT) is a life- and limb-threatening complication of heparin exposure. Unfractionated heparin (UFH) and low molecular weight heparins (LMWHs) are drugs that are widely used in patients undergoing cardiac surgery and that have made it possible to avoid and treat countless venous and arterial thrombotic problems. However, its use is also associated with a paradoxical reaction that leads to a potentially very serious prothrombotic state, which annually causes numerous amputations or fatal outcomes. Although the number of amputations per HIT is not known, recent studies describe an incidence of approximately 3-4%. Therefore, below, we present a woman undergoing cardiac surgery that begins in the post-surgical period with thrombocytopenia associated with arterial thrombosis, complicated by limb amputation due to HIT.

Keywords: Thrombocytopenia, Heparin, Thrombosis, Cardiac surgery.

INTRODUCTION

HIT is a serious complication of treatment with UFH and, less commonly, after LMWH. It is caused by anti-heparin/PF4 antibodies (platelet factor 4) and is characterized by a decrease in platelets and a severe prothrombotic state 5-10 days after exposure, which facilitates the development of venous or arterial thrombosis [1]. Approximately 90% of patients with HIT after cardiac surgery appear to develop this complication due to immunization triggered by cardiac surgery; however, in approximately 10% of patients, early presentation during the first four postoperative or intraoperative days may be explained by recent immunizing exposure to heparin. Because compared to many other patient populations who develop HIT, they have high frequency of heparin exposure prior to cardiac surgery, either many months or years before (remote exposure), or in the recent preoperative period, or both. This raises the possibility that in some patients the onset of HIT may be related to preoperative heparin exposure, rather than intraoperative or postoperative heparin administration [2]. Therefore, clinical diagnosis may be particularly difficult due to the need to distinguish the common platelet count drop associated with surgery from the much less common platelet count drop associated with HIT [3]. In fact, when HIT occurs after CV (cardiovascular) surgery, it is associated with excess morbidity and mortality. In a matched study with propensity score of 11,820 patients with CV surgery, 29.1% of patients who developed HIT after cardiac surgery had a thromboembolic event and postoperative mortality was 21.8%. Fortunately, in this study, as in others, HIT was uncommon, occurring in 1.1% of patients with CV surgery [4]. Therefore, in the cardiac intensive care unit or in CV surgery patients, caution is required when calculating the 4Ts score. First, most patients will have a drop in platelet count after intravascular device placement, cardiopulmonary bypass (CPB), or extracorporeal membrane oxygenation that can mimic the degree of drop typical of HIT (≥30%-50% of baseline) [5]. However, a "biphasic drop," in which the platelet count recovers after the drop 48 to 72 hours after cardiac surgery [6]. Therefore, the 4Q index is recommended to establish the clinical probability. This must be confirmed by immunological assays, determining antibodies against the heparin/PF4 complex, or functional. A negative result of the former usually rules out the diagnosis, while the positivity of the latter usually confirms the suspicion. Therefore, treatment is aimed at reducing the intense thrombin generation that accompanies the disease [7]. However, even with the use

of alternative anticoagulants, thrombosis contributes to fatal outcomes in 6% to 26% of HIT patients [8]. In some individuals, ULICs (circulating ultra-large immune complexes) elicit uncontrolled cellular procoagulant responses that culminate in thrombosis. Numerous studies have examined the biological and clinical risk factors that predispose people to thrombotic complications in HIT. So far, there is no evidence to support a role for conventional thrombophilic abnormalities, such as factor V Leiden or antithrombin, protein C, or protein S deficiencies. Polymorphic variation in the extracellular domain of the FcγIIA receptor and its functional regulation by tyrosine phosphatases, CD148, and TULA-2 (ubiquitin ligand of T-cells), have been identified as possible genetic causes influencing predisposition to thrombosis in HIT [9]. Despite maximal anticoagulation, some patients with HIT develop refractory disease, characterized by severe and persistent thrombocytopenia, new and/or progressive thrombosis. Some of these patients respond to additional therapies targeting the immune response through treatment with intravenous immunoglobulin or therapeutic plasma exchange [10]. However, new therapeutic approaches that interfere with the cellular activation effects of HIT antibodies are required.

CASE REPORT

Case report of a 71-year-old woman with a history of systemic arterial hypertension, persistent atrial fibrillation and inactive rheumatic heart disease and mitral insufficiency of 4 years of evolution, begins with deterioration of functional class NYHA II, ECOTT (echocardiogram) is performed where double mitral lesion is detected for which she is subjected to a surgical medical session being accepted for the day 08.26.24, her admission to the internal medicine service is requested where during her stay they initiate thrombo prophylaxis with LMWH 6 days prior to the surgical procedure. She was transferred to surgery where mitral valve replacement was performed with placement of a 27 mm SJ mechanical prosthesis (Saint Jude) with a cardiopulmonary bypass time of 110 minutes. The patient is admitted to the post-surgical intensive care unit unstable, with vasopressor and inotropic support and invasive mechanical ventilation. During her admission, she was treated with LMWH at a prophylactic dose and an echocardiogram was performed with a 42% LVEF, grade II diastolic dysfunction, and right ventricular systolic dysfunction. During her stay, a progressive decrease in platelet count was observed. Initially, thrombocytopenia associated with cardiac surgery was considered, however, an isobiphasic wave was observed in the platelet count since admission, with a recovery in the platelet count 72 hours after surgery (Table 1). Peripheral blood smears and platelet count are requested with different anticoagulants such as EDTA and sodium citrate, without observing significant changes in serum platelet levels (Table 2). Rheumatological profile is performed without abnormalities. Anti-heparin /PF4 positive antibodies are requested. Management with LMWH is discontinued and rivaroxaban therapy is initiated for heparin-induced thrombocytopenia. Despite thrombo prophylaxis, progressive peripheral vascular involvement is observed with changes in coloration and hypothermia in the distal region of the 4 limbs. It is evaluated by the angiology service and is not a candidate for open revascularization therapy or endovascular therapy due to the characteristics of the lesions (Figure 1, 2, 3, 4). It is assessed by the general surgery service for distal necrosis of the four limbs. Next, the patient underwent surgery for supracondylar amputation of the left pelvic limb, amputation of the second finger of the right pelvic limb, transmetacarpal amputation of the right hand and amputation at the level of the distal radius ulnar joint in the left upper extremity.

Table 1:

Evolution of platelet count during in-hospital stay			
Study	08/20/2024	08/26/2024	08/29/2024
Platelets (ul)	277.0	11.0	116.0
By: the authors Source: Medical history			

Table 2:

Platelet count results measured using different anticoagulants	
Anticoagulant	Platelet count
EDTA	65 /ul
Sodium Citrate	64/ ul
By: the authors Source: Medical history	

Figure 1:

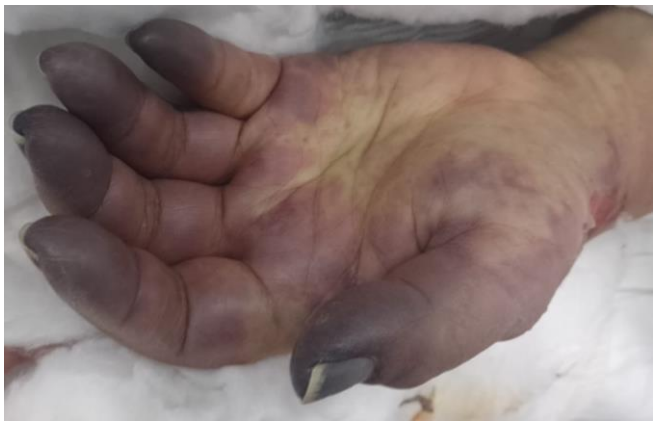


Figure 2:

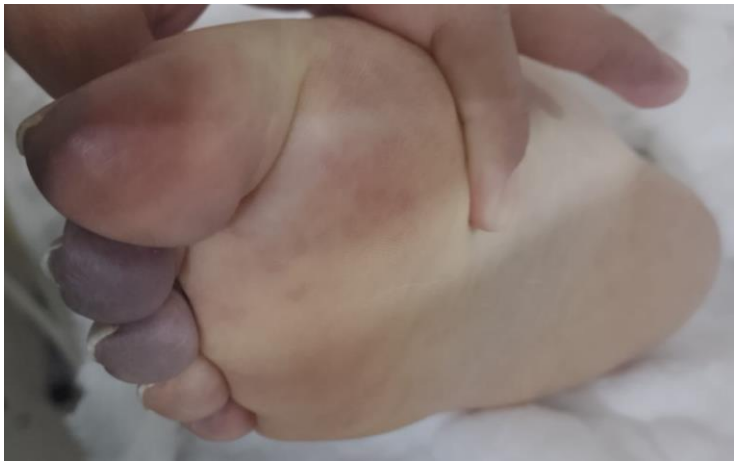


Figure 3:

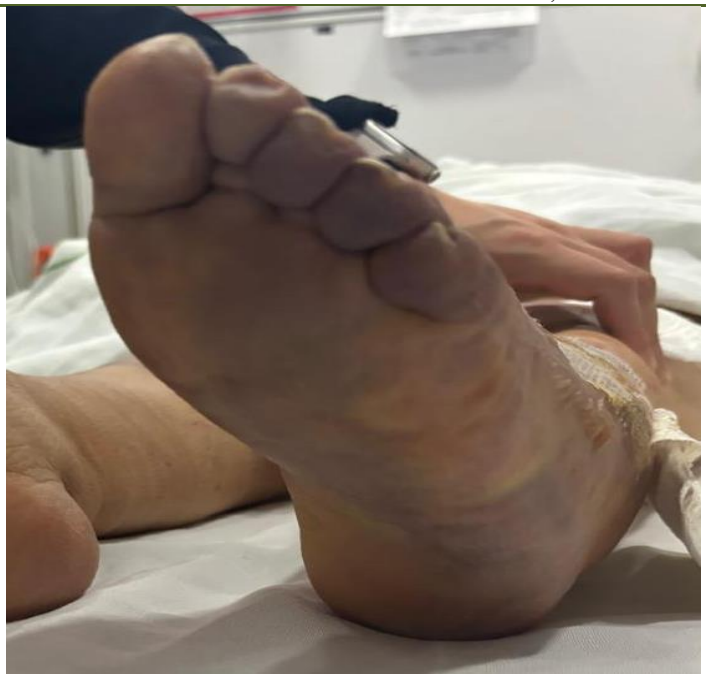
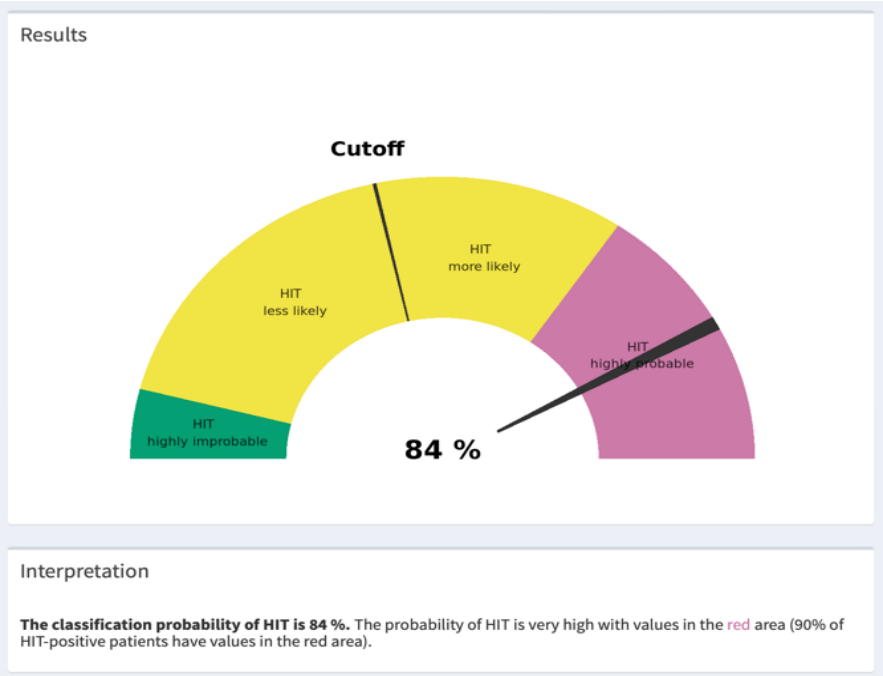


Figure 4:

DISCUSSION

Diagnosis of heparin-induced thrombocytopenia (HIT) at the bedside remains a challenge, exposing a significant number of patients at risk of late diagnosis or overtreatment [11]. In a rigorously executed prospective cohort study involving 1393 patients with suspected HIT at 10 study centers, they developed, validated, and implemented an easy-to-use machine learning algorithm for HIT diagnosis. The TORADI-HIT algorithm integrates clinical features, which are commonly available, and laboratory tests are routinely used. Tested on the validation data set, the performance of the model was high compared to the currently recommended diagnostic algorithm with the 4T score and immunoassay test results [12]. It is possible to observe compliance with the clinical score 4 T in this clinical case, in addition to which we have positive anti-heparin/PF4 antibodies, with which we calculate the clinical probability through the TORADI-HIT algorithm, which yields a probability of 84%, which translates into a high probability of HIT (Graph 1).



Graph 1:

Because heparin-induced thrombocytopenia (HIT) is a prothrombotic disorder mediated by ultra-large immune complexes (ULIC) containing immunoglobulin G (IgG) antibodies to a multivalent antigen composed of platelet factor 4 and heparin. The limitations of current antithrombotic therapy in HIT support the need to identify additional pathways that may be targets for therapy. Activation of FcγRIIA by HIT ULIC initiates various procoagulant cellular effector functions. A potentially significant role for complement in the regulation of FcγRIIA-mediated effector functions in HIT, complement 1 and 3 are identified as potential therapeutic targets. The importance of complement for the pathogenesis of these immunothrombotic disorders will require further validation in preclinical models [13]. Therefore, further studies focusing on less characterized aspects of the disease, such as complement activation, structural studies of antigenic complexes, and characterization of pathogenic and nonpathogenic antibodies, are needed [14]. since intravenous immunoglobulin has been shown to disrupt platelet activation by HIT antibodies by interfering with FcγRIIA -dependent platelet activation and is effective for the treatment of thrombosis and refractory disease and could be a therapeutic target in this clinical case [15], likewise therapeutic plasma exchange is another modality often used as adjunctive therapy for the treatment of acute or subacute THI, particularly for the management of emergent cardiac surgery or as salvage therapy for refractory disease. The efficiency of therapeutic plasma exchange in HIT is presumed to be secondary to anti-PF4 clearance, but drawbacks include only transient effects on antibody clearance and limited availability in the community setting. Emerging therapies in the preclinical stage include bacterial proteases to cleave IgG [16]. Despite the fact that the past 2 decades have witnessed significant progress in our understanding of the clinical manifestations and biological mechanisms underlying thrombotic complications in THI. Treatment outcomes in HIT remain suboptimal, as current therapies do not interfere with the cell activation effects of HIT antibodies, however, we must consider the possible emerging therapeutic banks trying to avoid the dreaded complications of this pathology such as thrombosis with limb amputation, as can be seen in this case five.

CONCLUSION

HIT remains a challenging diagnosis that requires interdisciplinary collaboration to recognize, manage and treat effectively. Although current approaches have substantial limitations, there have been significant advances in improving outcomes for patients with this condition. Rapid advances in automation, as well as new diagnostic tools such as the TORADI-HIT algorithm improve diagnostic performance as they have demonstrated a satisfactory correlation with the clinic, thus offering a hopeful future for timely diagnosis, rapid and effective treatment of HIT and avoidance of fatal complications such as amputation-associated thrombosis.

Ethical Responsibilities

Data confidentiality: The authors declare that they have followed their workplace's protocols regarding the publication of patient data.

Right to privacy and informed consent: The authors have obtained informed consent from the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.

Use of artificial intelligence to generate texts: The authors declare that they have not used any type of generative artificial intelligence in the writing of this manuscript or for the creation of figures, graphs, tables or their corresponding captions or legends.

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