CASE REPORTS

HEPARIN INDUCED THROMBOCYTOPENIA IN THE SETTING OF URGENT CARDIAC SURGERY: CAN BIVALIRUDIN BE A SAFE OPTION? – A CASE REPORT

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Abstract

Unfractionated heparin is the main anticoagulant employed in the context of cardiovascular surgery. When a patient with heparin induced thrombocytopenia (HIT) is proposed for cardiac surgery, the anticoagulation management is challenging. Bivalirudin is an alternative to heparin in the perioperative setting. We present a rare case of a patient with HIT and cardiogenic shock that required bivalirudin use in the perioperative period of an urgent reoperation of recurrent mitral valve dysfunction. Although infrequent, the use of bivalirudin can be safe in high risk patients if adequate measures follow institutional protocols, as reported in this case.

Keywords: *bivalirudin, heparin, thrombocytopenia, cardiac surgical procedure*

INTRODUCTION

Heparin induced thrombocytopenia (HIT) is an immune-mediated disorder characterized by the development of antibodies against heparin-platelet factor 4 complex. This complication emerges in 1-2% of patients undergoing cardiac surgery, mandating a cautious approach to heparin administration.[1,2] In such circumstances, the use of direct thrombin inhibitors (DTI), such as bivalirudin, emerge as first line alternatives to heparin for perioperative anticoagulation.[1,3]

We report a clinical case of a patient with history of HIT, requiring the use of bivalirudin during an urgent cardiac surgery.

CLINICAL CASE

A 64 year old female was proposed for urgent right anterior minithoracotomy due to acute prosthetic mitral valve dysfunction.

Her medical history included chronic obstructive pulmonary disease, atrial fibrillation, single vessel ischemic heart disease priorly revascularized (and still patent) and rheumatic mitral valve disease, replaced with a bioprosthetic valve two years before (Epic #31 + PT Physio #32), complicated with the development of HIT (positive test for heparin-PF4 antibodies – HIT Type II). The patient was on therapeutic warfarin, stopped the day before surgery.

Five days before the procedure, the patient was

hospitalized with the diagnosis of right-side pneumonia and pleural effusion. Subsequently, complications arose, including cardiogenic shock with rapid ventricular response atrial fibrillation and concomitant valvular dysfunction. An echocardiogram diagnosed severe obstruction of the prosthetic mitral valve by thrombus (figure 1). The therapeutic plan included a successful chemical cardioversion and urgent reoperation of the mitral valve. Pre-operatively blood analysis included Hb 14,4 g/dl, Platelets 436 000 and normal renal function.

Due to the previous HIT with maintenance of heparin-PF4 antibodies, a thorough literature review was made by a multidisciplinary team (cardiothoracic surgeons, anaesthesiologists, perfusionists, nurses) to explore available anticoagulation options. We decided to use bivalirudin as anticoagulant during cardiopulmonary bypass (CPB). As our cardiothoracic center had never used bivalirudin before, the team asked the Hospital Administration and the Pharmacy Department for drug approval and availability, and created a Protocol for bivalirudin use.

Before patient's arrival to the Operating Room (OR), the entire team met and discussed the critical stages of this rare clinical case. On arrival, the patient was conscious, receiving non-invasive ventilation and hemodynamically unstable requiring noradrenaline infusion. After induction of general anesthesia, endotracheal intubation was achieved with a left double lumen tube (37Fr). Difficult ventilation was managed and subsequent improvement in ventilatory parameters allowed for the surgery to proceed. Blood gas analysis (BGA) revealed type 2 respiratory insufficiency and baseline Activated Clotting Time (ACT) was 143 seconds. An anterior minithoracotomy was the approach of surgeons's preference and was only performed after achieving good ventilation conditions.

When agreed by the team that CPB should proceed, a loading dose of 1mg/kg of intravenous bivalirudin (C= 5mg/ml) was administered during 5 minutes, followed by an infusion of 2.5mg/kg/h. CPB was performed using femoral cannulation without cardioplegia. After five minutes, ACT was 439 seconds, considered adequate to begin CPB and continue the surgery. Additionally, 50mg of bivalirudin was added to the priming solution directly in the extracorporeal circuit by the Cardiovascular perfusionist. ACT analysis was performed every 15 to 30 minutes with bivalirudin infusion adjustments accordingly. Blood stasis was avoided in the hardshell reservoir, in the blood cardioplegia set and in the cell reservoirs; whenever possible, recirculation lines were kept open.

The surgical team initial plan was a conventional surgery to explant the prothesis and place another one. However, confronted with fibrous tissue within the mitral valve's bioprosthesis, limited mobility and the risk of avulsion of the AV groove if continuing with the first option, they opted for a transcatheter valve-in-valve implantation using a Sapiens valve #29, resulting in a favorable outcome.

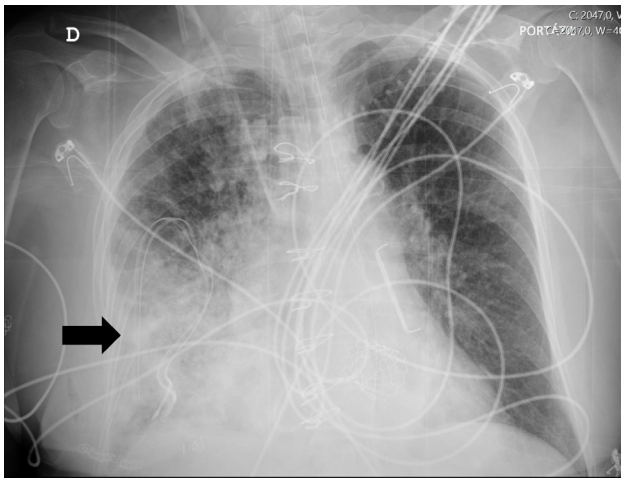

Figure 1 *Transesophageal echocardiogram showing valvular dysfunction previously to surgery; (B) Transesophageal echocardiogram showing obstruction of the prosthetic mitral valve by thrombus (white arrow).*

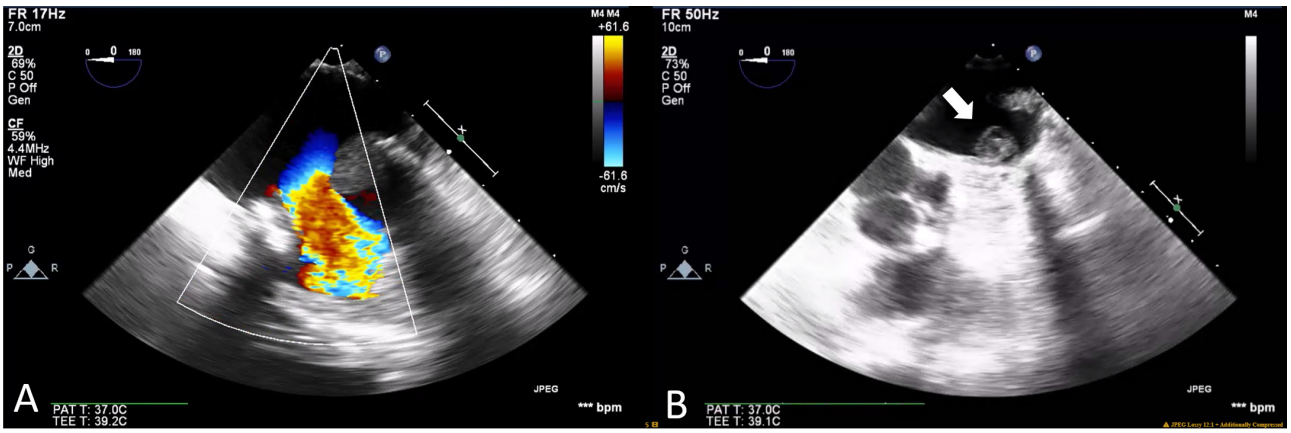

Figure 2 *Thromboelastometry (ROTEM®).*

During CPB, the Bilavirudin infusion was reduced 0.25mg/kg/h five times due to ACT values exceeding 3.5 times the baseline value, a dose adjustment based on clinical cases reported in the literature. Bivalirudin infusion ceased 10 minutes before the end of CPB, which lasted 226 minutes. During this time, the median urine flow rate was 1,53 ml/kg/h. Hemofiltration was performed at the end of CBP to mitigate the bivalirudin effect.

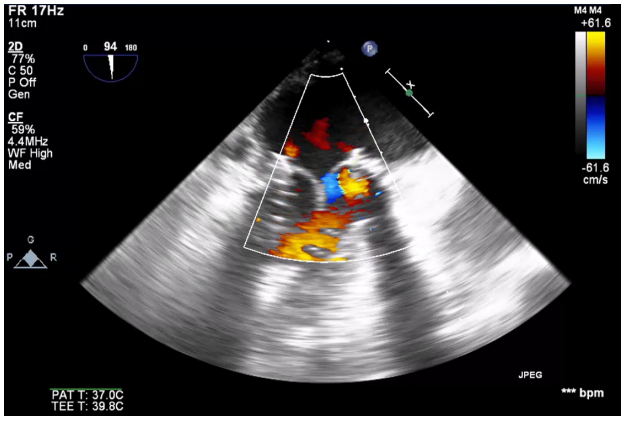

Figure 3 *?????*

Noradrenaline and nitroglycerine's perfusion was needed to adequate hemodynamic profile as CPB was ended. Immediately after exiting CPB (cardiopulmonary bypass), the patient experienced cardiac arrest with ventricular fibrillation, needing three-stacked shocks (200J) for successful resuscitation.

Thromboelastometry (ROTEM®) (Figure 2) guided the administration of blood products, including 2 units of red blood cells, 2 units of platelets, 6 units of plasma and tranexamic acid 1g, to compensate for losses, that occurred throughout surgery without any particular moment of severe bleeding, and to maintain blood volume, preventing coagulopathy.

The last intraoperative ACT was 187 seconds and no clots were found in the circuit. Hemostasis was achieved at the end of the procedure without any further actions.

Post-procedure, the patient was transferred to the intensive care unit, mechanically ventilated. After 12h, there was no major bleeding, the aPTT was within normal range and anticoagulation was started with argatroban.

DISCUSSION

Bivalirudin, a direct and reversible inhibitor of thrombin, offers unique characteristics, including intravenous administration, rapid onset of therapeutic ACT

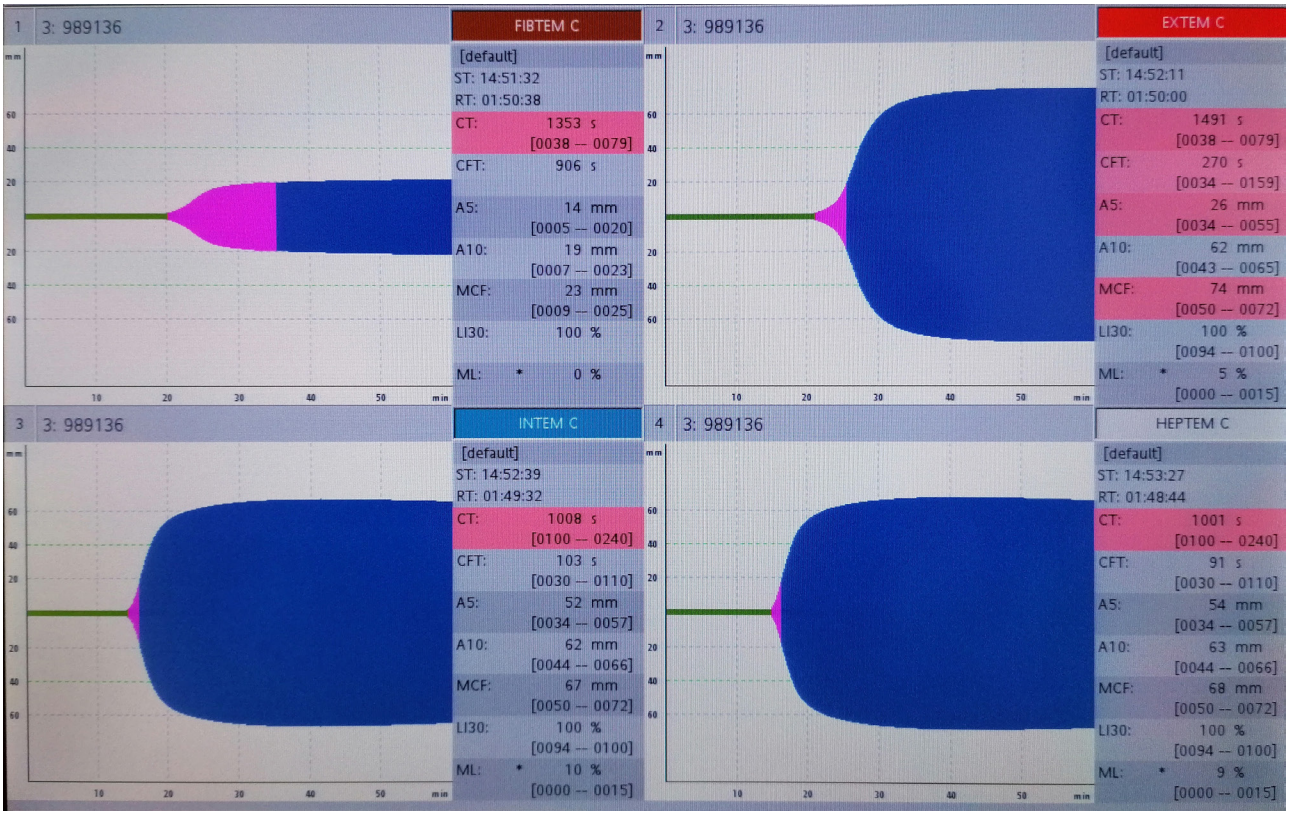

Figure 4 *?????*

values within 5 minutes, and elimination via enzymatic cleavage and renal mechanisms with an elimination half-life of 20-30 minutes in the absence of renal impairment. Unlike heparin, bivalirudin does not have a specific reversal agent.[1,3] Argatroban, another direct thrombin inhibitor, has a slower onset and a longer elimination half-life then bivalirudin and there is limited data of its use in cardiac surgery, specifically when CPB is applied.[3] These are some of the reasons why argatroban is not the first choice for anticoagulation during cardiac surgery.

Clinical Practice Guidelines support bivalirudin as a reasonable option in cases similar as the one presented (Class IIa Recomendation, Level of Evidence B)[4] and efficacy and safety of bivalirudin were also demonstrated in Coronary Artery Bypass Surgery.[5]

Point of care monitoring involves ACT, and despite its lack of specificity for bivalirudin concentrations, it shows a good correlation with bivalirudin plasma levels. The recommended target for on pump cardiac surgery is a 2.5 fold prolongation of the baseline value.[1,3] Following these recommendations, the baseline value of 143 seconds was extended to 439 after the bivalirudin bolus.

ACT values were evaluated every 20 minutes and the bivalirudin's perfusion adjusted. The perfusionist's performance was adapted to avoid any area of blood stasis in the circuit since it may lead to thrombus formation. As described in the literature, hemofiltration increases bivalirudin's elimination[3] and it was used in the case described to reduce the risk of bleeding. The final endpoint was to achieve a balance between sufficient anticoagulation and avoidance of haemorrhagic complications, a paramount concern associated with bivalirudin use, as highlighted in the literature.[1,6,7]

In the setting of cardiac surgery, limited prospective studies exist regarding the use of bivalirudin in patients with HIT and other than that the experience relies on different case reports.[1,3] Adverse events have been documented, warranting further research, mainly in patients with renal failure.[8-10]

In conclusion, the issues related to bivalirudin encompass its accessibility, price, the absence of more targeted tests for its monitoring, and the absence of a reversal agent.[11] HIT is a rare condition in patients proposed for cardiac surgery which results in its very infrequent use. This case report highlights the need for safely using this drug in high risk patients, emphasizing the importance of understanding its pharmacology and adherence to institutional protocols to prevent life-threatening complications.

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