Multiple re-exploration due to excessive bleeding due to coagulopathy after aortic valve replacement in patients with chronic asymptomatic hepatitis B infection: A case report

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ABSTRACT

Background: Postoperative bleeding following cardiac surgery represents a recognized and significant complication, particularly in patients with asymptomatic hepatitis B infection who have undergone open-heart procedures with a cardiopulmonary bypass machine (CPB). Patients requiring re-exploration due to bleeding face elevated mortality risks due to detrimental factors associated with the procedure, such as bleeding, transfusions, hypoperfusion resulting from cardiac tamponade or blood loss, multiple organ ischemia, and organ failure. The aim of this article is to discuss perioperative preparations specific to cases of patients with chronic hepatitis B undergoing open-heart surgery.

Case Presentation: This case study revolves around a 53-year-old Asian male who had been slated for aortic valve replacement. Transthoracic echocardiography (TTE) uncovered severe aortic regurgitation with vegetation at the non-coronary cusp (NCC) and right coronary cusp (RCC), accompanied by chamber dilatation. The patient was under Tenofovir therapy for his chronic yet asymptomatic hepatitis B infection. The surgical procedure utilized a cardiopulmonary bypass machine (CPB), but multiple re-explorations were necessitated due to excessive bleeding attributed to post-surgery coagulopathy.

Conclusion: Postoperative bleeding following cardiac surgery represents a widely recognized and serious complication, particularly in patients with asymptomatic hepatitis B infection who have undergone open-heart procedures with CPB. CPB has been extensively documented to stimulate the generation and release of various vasoactive substances and cytotoxic mediators, disrupting “rebalanced hemostasis” and leading to coagulopathy.

Keywords: Open heart surgery, CPB, asymptomatic hepatitis B patient, re-exploration, impaired coagulation function.


INTRODUCTION

Postoperative bleeding is a widely acknowledged and significant complication in cardiac surgery, contributing to elevated rates of re-exploration, increased need for blood transfusions, prolonged hospital stays, and higher costs. Its detrimental effects extend to heightened morbidity and mortality. Re-exploration due to bleeding is linked to prolonged hospitalization and heightened complications, including sternal wound infection (SWI), renal impairment, and postoperative arrhythmias.1

There is a significant rise in morbidity and mortality rates following cardiac operations involving a cardiopulmonary bypass machine (CPB) in patients with asymptomatic hepatitis B infection who undergo open-heart surgery. This heightened frequency of post-operative complications, notably bleeding and wound infections, is observed. Bleeding, indicated by increased hemorrhagic chest tube output, encompasses various forms such as gastrointestinal bleeding, cardiac tamponade, and mediastinal bleeding, all stemming from coagulopathy.2

In cases of chronic liver diseases, the coagulopathy pattern extends beyond mere anticoagulation. Instead, this set of disorders, arising from liver cirrhosis, involves both procoagulant and anticoagulant tendencies.3

CASE PRESENTATION

A 53-year-old Asian male, who had experienced dyspnea on exertion for four months leading up to hospital admission due to heart failure, was scheduled for aortic valve replacement. The physical examination and laboratory findings were normal, with parameters such as PT, aPTT, SGOT, and SGPT all within the normal range. A chest X-ray revealed cardiomegaly without indications of infection or pulmonary edema. Transthoracic echocardiography (TTE) uncovered severe aortic regurgitation with vegetation at the non-coronary cusp (NCC) and right coronary cusp (RCC), along with chamber dilatation. Coronary
angiography indicated non-significant coronary artery disease. The patient is under Tenofovir therapy for chronic yet asymptomatic hepatitis B infection and has a history of cerebrovascular accident bleeding without subsequent complications.

The patient was transported to the operating room, where radial and femoral arterial, as well as venous access, was established under sedation using midazolam (1 mg) and fentanyl (50 mcg). Lidocaine, serving as a local anesthetic, was injected at the puncture site. Anesthesia induction included fentanyl (2 mcg/kg BW), midazolam (1 mg), rocuronium (1 mg/kg BW), and co-induction with insufflation of 1-2 volume % sevoflurane in a 50% oxygen-air mixture. Intubation was conducted using an 8.0 nonkink, cuffed endotracheal tube. Anesthesia was maintained with 1-2 volume% sevoflurane in a 2 L flow of a 40%-50% oxygen-air mixture, while morphine in a continuous pump (20 mcg/kg BW/minute) served as an analgesic agent from the start of the surgery. Hemodynamics were effectively controlled throughout the 3 hours and 45 minutes of the aortic valve replacement procedure. The cardiopulmonary bypass minute was 136 minutes, and the cross-clamp time was 92 minutes.

Dopamine at a rate of 3 mcg/kg BW/minute and epinephrine at 0.02 mcg/kg BW/minute were initiated following the cessation of cardiopulmonary bypass and were consistently administered during the patient’s transfer to the intensive care unit. Four hours post-surgery, the patient underwent re-exploration in the operating theater due to excessive bleeding (3010 ml/4 hours). Over the course of 95 minutes during the re-exploration surgery, 200 cc of hemorrhagic pericardial effusion and 50 cc of blood clot were evacuated. Suspecting the Substernal notch as the source of bleeding, it was tamponed with three pieces of gauze. The coagulation profile test revealed a prolonged aPTT exceeding 180 seconds (more than 5 times the normal level), while PT remained within normal limits. Thrombocyte levels decreased to 130,000, and fibrinogen levels dropped to 194.8 mg/dL. To resuscitate the patient and enhance hemostasis function, transfusions of packed red cells (PRC), fresh frozen plasma (FFP), cryoprecipitate, and platelets, amounting to 1296 cc, 625 cc, 309 cc, and 1004 cc, respectively, were administered. Following surgery, the patient was transferred back to the ICU, where his condition stabilized, and hemostatic function improved. The aPTT reduced to 34.8 seconds, PT was not examined, leukocyte count increased to 19,610, thrombocyte levels decreased to 110,000, and procalcitonin levels measured 19.6. Tranexamic acid (1 g) was administered every 8 hours, and vitamin K (10 mg) was given intravenously. The next day, another re-exploration was conducted, revealing 50 cc of blood clot outside the pericardium. No active bleeding source was found, and the old tampon was replaced with two new gauzes. Open chest management was initiated. On the second day of treatment, thrombocyte levels dropped to 56,000, leukocyte count increased to 21,420, fibrinogen levels measured 184.6, and aPTT increased to 64.9 seconds, while PT remained normal. An additional 500 cc of PRC was administered due to a hemoglobin level of 6.8 g/dL, and intravenous administration of 10 mg of vitamin K continued. Despite prolonged aPTT and low thrombocyte and fibrinogen values, there was no further active bleeding. On the third day of treatment, the patient succumbed to sepsis and refractory metabolic acidosis.

DISCUSSION

There is a significant rise in morbidity and mortality rates following cardiac operations with CPB among patients with asymptomatic hepatitis B infection who have undergone open-heart surgery, leading to an increased frequency of post-operative complications, particularly bleeding and wound infections. This bleeding, which includes gastrointestinal bleeding, cardiac tamponade, and mediastinal bleeding as indicated by heightened hemorrhagic chest tube output, stems from coagulopathy associated with chronic liver diseases. Importantly, this coagulopathy is not confined to anticoagulation but encompasses both procoagulant and anticoagulant tendencies, a group of disorders arising from liver cirrhosis. This concept is embodied in the idea of “rebalanced hemostasis.” As outlined by this framework, the alterations in hemostasis establish a fresh equilibrium among procoagulant, anticoagulant, and fibrinolytic systems due to the relative insufficiency of procoagulant and anticoagulant factors. This delicate hemostatic balance is inclined to lean towards either bleeding or thrombosis, contingent on the specific provoking circumstantial risk factors.

The decision to proceed with surgery for our patient was determined by the clinical presentation, which included exertional dyspnea, and the trans-thoracic echocardiographic results revealing severe aortic regurgitation, the presence of vegetation on the non-coronary cusp (NCC) and right coronary cusp (RCC), along with elevated left ventricle filling pressure. The viable surgical option for chronic aortic regurgitation is restricted to aortic valve replacement through the use of a cardiopulmonary bypass (CPB) machine. However, it is widely acknowledged that elective cardiac operations involving CPB are deemed inappropriate for patients with moderate to severe hepatic dysfunction due to the associated high morbidity and mortality.

Comprehensive evidence verifies that the employment of cardiopulmonary bypass (CPB) prompts the production and discharge of diverse vasoactive substances and cytotoxic mediators. These components influence coagulopathy, the immune system, vascular resistance, vascular permeability, fluid balance, and the fundamental operations of organs. Supplementary factors, such as hypothermia, hemodilution, and hypoperfusion during CPB, may similarly contribute to the morbidity and mortality observed postoperatively.

Numerous investigations have illustrated the existence of endotoxin in a patient’s bloodstream subsequent to undergoing cardiopulmonary bypass (CPB). In the plasma, endotoxin associates with LPS-binding protein, a human serum protein whose concentration rises during the acute phase reaction, giving rise to a complex identified as the endotoxin–LPS-binding protein complex. This intricate formation subsequently binds to the macrophage receptor CD14, markedly
amplifying the production of macrophage TNF-α. Endotoxin possesses the capability to induce the release of Nitric Oxide by both endothelial and smooth muscle cells, facilitated by the inducible form of the enzyme NOS (iNOS). Nitric oxide, originating from iNOS (iNO), is implicated in the pathophysiology of the inflammatory state, resulting in vasodilation and heightened vascular permeability. This mechanism stands as one of the contributors to the perturbation of rebalanced hemostasis in individuals with liver disease, potentially tilting the equilibrium towards hemorrhage.

Excessive bleeding following cardiac surgery represents a severe post-operative complication, often leading to hemorrhagic shock and occurring in up to 12% of patients. The criteria established by Kirklin and Barratt-Boyes define post-operative bleeding as excessive if it meets certain conditions: draining more than 500 ml in the first hour, more than 400 ml in each of the first two hours, more than 300 ml in each of the first three hours, exceeding 1000 ml in total during the first four hours, and surpassing 1200 ml in total during the initial five hours. Additionally, excessive bleeding includes cases where bleeding restarts (indicating a potential surgical cause) and instances of sudden massive bleeding.

Our patient experienced profuse bleeding, reaching a total of 3010 cc in 4 hours in the ICU, meeting the Kirklin and Barratt-Boyes criteria, necessitating re-exploration. In the initial re-exploration, 200 cc of hemorrhagic pericardial effusion and 50 cc of blood clot were evacuated, with suspicion pointing to the substernal notch as the bleeding source. During the second re-exploration, 50 cc of blood clot outside the pericardium was discovered, with no active bleeding source identified. Consequently, the patient underwent treatment involving open chest management and delayed sternal closure. Anticipating postoperative bleeding following cardiac surgery, which could necessitate surgical re-exploration, is frequently a complex task. Urgent and intricate surgeries, particularly cardiac procedures performed under hypothermic circulatory arrest, and patients with additional health complications like hepatic or renal dysfunction are more prone to an escalated risk of postoperative bleeding and the need for re-exploration. Patients subjected to re-exploration due to bleeding are correlated with a heightened mortality rate. A recent investigation posits that the increased mortality is not solely attributed to the act of re-exploration itself but rather to the adverse factors associated with re-exploration, encompassing bleeding, transfusions, hypoperfusion from cardiac tamponade or blood loss, multiple organ ischemia, and organ failure.

In cases of extensive bleeding, transfusion becomes imperative. Massive bleeding necessitates the administration of fresh frozen plasma (FFP), platelets, cryoprecipitate, and, potentially, factor concentrates such as fibrinogen and prothrombin complex concentrates (PCCs) are employed. The objective is to replenish the circulating levels of hemostasis factors. Nevertheless, the replacement of volume following cardiac surgery with critical bleeding might involve substantial fluid volumes, frequently resulting in the occurrence of hypothermia and acidosis, thereby introducing further complexity to the bleeding scenario. In our patient’s case, to prevent additional bleeding, 625 cc of FFP, 1297 cc of packed red cells (PRC), 1000 cc of platelets, and 389 cc of cryoprecipitate were administered. Initially, this approach successfully reduced bleeding, but it resulted in subsequent acidosis.

We have gained insight into the importance of mitigating potential adverse effects on hemostasis, and in doing so, we recognize the significance of adhering to the PROPRR trial recommendation for massive transfusions. The trial suggests maintaining a high fresh frozen plasma (FFP) to platelets to packed red blood cells (RBC) ratio of 1:1:1. This ratio has been demonstrated to provide a survival benefit.

We have comprehended that adopting a more secure and enhanced approach to transfusing blood components entails directing the transfusion based on laboratory or point-of-care coagulation testing. Conventional laboratory tests are frequently time-consuming, and assessments like PT/INR and PTT, despite gauging procoagulant factors, do not account for the decline in anticoagulant factors or the complex interactions among cells and coagulation factors in whole blood. Additionally, these tests do not evaluate clot strength and stability, as their focus is on the initiation of fibrin polymerization, which occurs at exceedingly low levels of thrombin generation.

Point-of-care testing, represented by thromboelastography (TEG), has attracted attention in recent scholarly reviews. TEG boasts a quicker processing time compared to traditional coagulation tests and has demonstrated effectiveness in guiding factor replenishment, leading to decreased quantities of red blood cell and plasma infusions. TEG exhibits promising clinical potential in assessing the severity of coagulopathy and the risk of bleeding in individuals with chronic liver disease. This diagnostic tool scrutinizes all aspects of hemostasis, encompassing the dynamics of clot formation (the equilibrium between procoagulant and anticoagulant factors), clot strength (involving platelets and fibrinogen), and clot stability (encompassing fibrinolysis and FX), employing whole blood. Available data suggests that TEG provides a more precise reflection of the hemostatic equilibrium in patients with chronic liver disease beyond surgical scenarios.

**CONCLUSION**

Postoperative bleeding is a widely recognized and significant complication, particularly among patients with asymptomatic hepatitis B infection who have undergone open-heart surgery with CPB. CPB has been extensively documented to induce the production and release of various vasoactive substances and cytotoxic mediators, disturbing “rebalanced hemostasis” and leading to coagulopathy. To prevent and manage post-operative bleeding effectively, it is essential to establish collaborative efforts among cardiac surgeons, perfusionists, anesthetists, clinical pharmacists, and ICU physicians.

**CONFLICT OF INTEREST**

The author reports no conflicts of interest in this work.
ETHICAL CONSIDERATION
This study was obtained ethical clearance from the institutional review board of Faculty of Medicine, University of Indonesia - RSUP Nasional Dr. Cipto Mangunkusumo number KET-309/UN2. F1/ETIK/PPM.00.02/2023. Informed consent was obtained from every patient before the study was performed.

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AUTHORS' CONTRIBUTION
All authors contributed equally to this study’s preparation, execution, and manuscript writing.

REFERENCES