



HYPERFIBRINOLYSIS; A SERIOUS and MORTAL COMPLICATION AFTER CARDIOPULMONARY BYPASSES: CASE REPORT

HİPERFİBRİNOLİZİS; KARDİOPULMONER BYPASS SONRASI GELİŞEN CİDDİ ve MORTAL BİR KOMPLİKASYON: OLGU SUNUMU

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Abstract

Hemorrhage is one of the major complications of cardiac surgery when using cardiopulmonary bypass (CPB). Despite all kinds of medical and surgical treatment, post bypass bleeding is still a serious problem. Hypothermia, acidosis, hypovolemia, and hypoperfusion lead to disruption of the coagulation process in severe trauma as well as in CPB. Hyperfibrinolysis (HF) is a life-threatening bleeding disorder in major trauma patients. The incidence of HF has been estimated in the range of 15% to 20%. The gold standard for the detection of HF is thrombelastography or thromboelastometry. Blood products and tranexamic acid are used in the treatment of hyperfibrinolysis. The agents that can be used as an alternative to tranexamic acid in HF treatment are aprotinin and epsilon aminocaproic acid.

Early diagnosis and treatment of HF are life-saving. For this purpose, we wanted to share this rare pathology.

Keywords: *Hyperfibrinolysis, cardiopulmonary bypass, hemorrhage.*

Öz

Kanama, kardiyopulmoner bypass (CPB) kullanılarak yapılan kalp cerrahisinin en önemli komplikasyonlarından biridir. Her türlü tıbbi ve cerrahi tedaviye rağmen baypas sonrası kanama hala ciddi bir problemdir. Ağır travmada olduğu gibi hipotermi, asidoz, hipovolemi, hipoperfüzyon nedeni ile CPB da pıhtılaşma sürecinin bozulmasına neden olur. Majör travma ve majör cerrahi sonrasında gelişebilen Hiperfibrinoliz (HF), yaşamı tehdit eden ciddi kanama bozukluğuna sebep olabilir. Kalp cerrahisi sonrası HF görülme sıklığı % 15 ile % 20 arasında tahmin edilmektedir. HF tanısında altın standart trombelastografi veya tromboelastometridir. Hiperfibrinoliz tedavisinde kan ürünleri ve traneksemik asit kullanılır. HFtedavisinde traneksemik aside alternatif olarak kullanılabilen ajanlar aprotinin ve epsilon aminokaproik asittir. Kalp cerrahisi sonrası gelişen kanama problemlerinde HF tanısı gözden kaçabilir. Bu nedenle erken teşhis ve tedavinin hayat kurtarıcı olduğu bu nadirpatolojiyi paylaşmak istedik.

Anahtar Kelimeler: *Hiperfibrinoliz, kardiopulmoner bypas, kanama.*

Introduction

Hemorrhage is one of the significant complications of cardiac surgery when using cardiopulmonary bypass (CPB). Despite all kinds of medical and surgical treatment, post bypass bleeding is still a severe problem.¹ Hypothermia, acidosis, hypovolemia, and hypoperfusion disrupt the coagulation process in severe trauma, and CPB.² Hyperfibrinolysis (HF) is a life-threatening bleeding disorder in major trauma patients.³ The incidence of HF has been estimated in the range of 15% to 20%.⁴ The gold standard for the detection of HF is thrombelastography or thromboelastometry.⁵⁻⁶ Blood products and tranexamic acid are used in the treatment of hyperfibrinolysis. The agents that can be used as an alternative to tranexamic acid in HF treatment are aprotinin and epsilon aminocaproic acid (EACA).⁷ Early diagnosis and treatment are life-saving.¹ For this purpose, we wanted to share this rare pathology.

Case Report

A 67-year-old male patient was hospitalized for heart valve surgery due to advanced aortic insufficiency and stenosis with progressive mitral regurgitation. The routine blood tests and coagulation tests performed during the preoperative preparation period were regular (Table1).

Table 1. Preoperative hemogram and coagulation tests

Parameters	Value	Unit	Reference range
Hgb	16.1	g/dL	12.5-16.3
Htc	47.4	%	36.7-47.1
PLT	206	X10 ³ /mL	152-348
PTT	15.3	sec	11.5-15.5
PTT (activation)	83	%	70-100
APTT	31.7		
INR	1.13	sec	26.5-40

Hgb: Hemoglobin, **Htc:** Hematocrit, **PLT:** Platelet, **PTT:** Prothrombin Time, **APTT:** Activated Partial Thromboplastin Time, **INR:** International normalized ratio

Aortic valve replacement (AVR) and mitral valve replacement (MVR) operation was performed using routine median sternotomy and CPB with prosthetic valves. After the procedure, the patient was followed up in the cardiovascular surgery intensive care unit (ICU). During the ICU follow-up, there was approximately 150-200 cc of hemorrhagic drainage per hour from the thorax and mediastinal drains. Therefore, the patient was treated with a total of 2 IU of erythrocyte suspension, 1IU of fresh frozen plasma, and 1 IU of platelet suspension. Protamine treatment was started when the Activated Clotting Time (ACT) was 166 sec., and 500 mg of tranexamic acid was added. At the end of the 6-hours follow-up, the patient was re-operated for bleeding revision; the total drainage was 1100 cc despite replacement and treatment. It was observed that there was no active surgical bleeding focus in the revision operation. Upon this, the patient was adequately closed and taken to the ICU stably under four-inotropic therapy. On the first night of postop, the patient underwent a total of 2 IU ES(erythrocyte suspension), 2 IU FFP (fresh frozen plasma), and 1 IU PS (platelet suspension) replacement. The drainage amount was measured as 850 mL (approximately 12 hours) until the morning of the

postoperative first day after revision. Since there was no active surgical bleeding, we decided to consult with the hematology clinic. The examinations required as a result of the consultation are as follows. The D-dimer test result was typical (Table 2).

Table 2. Postoperative first day morning test results

Parameters	Value	Unit	Reference range
PTT	26.6	sec	11.5-15.5
PTT (activation)	40	%	70-100
APTT	37.8		
INR	2.01	sec	26.5-40
Fibrinogen	1.38	g/dL	2-4

PTT: Prothrombin Time, **APTT:** Activated Partial Thromboplastin Time, **INR:** international normalized ratio, **Fibrinogen:** Fibrinogen

Upon this, the patient was considered to have hyperfibrinolysis (HF) with the hematology department. A total of 3IU ES, 3IU FFP, and 1IU PS replacement were applied to the patient with 1000 mg of tranexamic acid treatment. Along with a 2-gram Fibrinogen, the supplement was made. Under these treatments, the patient was extubated. The 24-hour drainage amount was measured as 1300 mL on the first postoperative day. Fibrinogen tests returned to normal in the control tests performed after treatment (Table3).

Table 3. Postoperative first day evening fibrinogen and D-dimer levels

Parameters	Value	Unit	Reference range
Fibrinogen	2.08	g/L	2-4
D-Dimer	0.47	mJg/mL	0-0.5

There was no problem other than a decrease in hemogram level, low platelet values, and PT elevation in coagulation tests on the second postoperative day (Table 4).

Table 4. Postoperative second-day results

Parameters	Value	Unit	Reference range
Hgb	8.0	g/dL	12.5-16.3
Htc	24.7	%	36.7-47.1
PLT	94	X10 ³ /mL	152-348
PTT	19.6	sec	11.5-15.5
PTT (activation)	59	%	70-100
APTT	32.2		
INR	1.46	sec	26.5-40
Fibrinogen	3.64	g/L	2-4
D-Dimer	0.49	mJg/mL	0-0.5

Hgb: Hemoglobin, **Htc:** Hematocrit, **PTT:** Prothrombin Time, **APTT:** Activated Partial Thromboplastin Time, **INR:** international normalized ratio

On the second postoperative day, the patient's treatment was planned as 1IU ES and 2IU FFP replacements and Tranexamic acid 500 mg treatment. Fibrinogen therapy was not performed, as the fibrinogen levels returned to normal. As the patient did not need it during the day, all inotropic

supportive treatments except Dopamine were gradually decreased and discontinued. On the second postoperative day, the total amount of drainage fell to 800 mL.

On the third postoperative day, we used only 2IU ES replacement in the treatment of the patient. No additional treatment was required. 24-hour drainage of the patient decreased to 300 mL. The patient was taken to the cardiovascular surgery service on the 4th postoperative day and was discharged without any problem on the 10th postoperative day.

Discussion

Hemorrhage is one of the major complications after cardiac surgery with cardiopulmonary bypass (CPB). Despite all kinds of medical and surgical treatment, postoperative bleeding after cardiac surgery is still severe. Hyperfibrinolysis (HF) can be one of the reasons for nonsurgical bleeding after CPB.¹ Hyperfibrinolysis is a pathology with uncontrolled increased fibrinolytic activity to fibrin formation and is associated with excessive bleeding.⁷ The incidence of HF has been estimated at 15% to 20%.⁴ Scanned our last five years of data, although there were operations with CPB in our clinic for many years, HF-related bleeding was not observed. Therefore, we wanted to share this rare complication.

The gold standard for diagnosing HF is thrombelastography or thrombelastometry.⁵ Levrat *et al.* explained that thrombelastography remains a complex and time-consuming procedure. For the same reasons, the other techniques used to diagnose hyperfibrinolysis (plasmin-antiplasmin complex, plasminogen activator inhibitor-1, thrombin activatable fibrinolytic inhibitor, D-dimers/plasmin-antiplasmin) are also not relevant in the context of hemorrhagic shock. Furthermore, we cannot do these tests routinely for logistic and economic reasons.⁸ Since there is no possibility of thrombelastography in our clinic, we used routine blood tests and coagulation tests while diagnosing the patient's HF. Disseminated intravascular coagulation (DIC) is an important problem in the differential diagnosis. While DIC has schistocytes in the peripheral smear, platelet counts are low. Prothrombin time (PTT) and activated partial thromboplastin time (APTT) are prolonged, and D-dimer levels are above average. Fibrinogen values are typical.⁹

Due to the absence of schistocytes in the peripheral smear of the patient, standard D-Dimer test, low fibrinogen values, and prolonged PTT, HF was considered for diagnosis. The only condition that did not comply with HF was a decrease in the patient's platelet levels. However, because thrombocytopenia was not profound and progressive, DIC was not considered. Thrombocytopenia was thought to be due to excessive bleeding.

Blood products (such as ES, FFP, PS) and tranexamic acid are used to treat hyperfibrinolysis. The agents that can be used as an alternative to tranexamic acid in HF treatment are aprotinin and epsilon aminocaproic acid.⁷ Patients who received empiric dosing of tranexamic acid (TXA) had lower overall mortality and a lower risk of death due to bleeding in The Clinical Randomization of an Antifibrinolytic in Significant Haemorrhage (CRASH)-2 trial.¹⁰ It is used routinely in elective cardiac surgery or some severe surgeries. It has been shown to reduce blood loss and the need for blood transfusion without increased thromboembolic events and is easily accessible and helpful.¹¹ TXA was administered as a 1 g bolus over 10 minutes followed by a second 1 g infusion

over eight hours.⁷ Compared with TXA, the synthetic lysine analog EACA (epsilon aminocaproic acid) is ten times less potent and is not associated with reduced transfusion requirements in elective surgery. Aprotinin was withdrawn from the market after it was associated with increased mortality in a randomized trial of patients undergoing cardiac surgery.¹²

For our patient, we used a total of 10 IU ES, 8 IU FFP, 3 IU PS replacements after the operation day when HF developed as a blood product with the replacement, and Tranexamic acid treatment was started as 2 g per day. Since the fibrinogen level was low on the first postoperative day, we added 2 g of fibrinogen therapy. We continued the tranexamic acid treatment until the third day after the operation. On the third postoperative day, the amount of drainage dropped to normal levels, and the drainage turned normal. The patient was discontinued on the 4th day by stopping tranexamic acid treatment and was discharged on the 10th day without any problem.

Conclusion

HF is a significant problem that can cause cardiac surgery, severe mortal bleeding. It should be considered in bleeding that started in the early period after cardiac surgery, and the cause of which cannot be explained. The diagnosis is supported by the absence of schistocytes in the peripheral smear, normal D-dimer levels, and average platelet counts, with prolonged PTT and APTT in patients with bleeding in the early period after cardiopulmonary bypass. Early diagnosis and treatment are life-saving. For this purpose, we wanted to share this rare pathology.

Author Contributions

ZT, MK: Design; MK: Project development; ZT, BK: Data collection; ZT: Analysis; ZT: Literature search; ZT, TÇ, ÖM: Manuscript writing; ZT, MK: Critical review

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