Catastrophic Intracardiac Thrombosis During Emergency Repair of an Expanding Aortic Pseudoaneurysm: A Case Report

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Catastrophic thrombosis is a rare but frequently fatal event following complex cardiac surgery. It is most often encountered following separation from cardiopulmonary bypass (CPB) and reversal of heparin anticoagulation, and somewhat paradoxically, at the time when bleeding from post-CPB coagulopathy is being treated. We report the case of a 41-year-old female taken to the operating room for repair of an expanding ascending aortic pseudoaneurysm. Following a prolonged operation, she developed intracardiac thrombus during transfusion of hemostatic blood products and procoagulant agents. Potential contributing factors are discussed. (A&A Practice. 2019;13:342–5.)

GLOSSARY

ACT = activated clotting time; **AT** = antithrombin; **CABG** = coronary artery bypass grafting; **CPB** = cardiopulmonary bypass; **CS** = cell saver; **DHCA** = deep hypothermic circulatory arrest; **FDA** = Food and Drug Administration; **FFP** = fresh frozen plasma; **Fib** = fibrinogen; **HIPAA** = Health Insurance Portability and Accountability Act of 1996; **IABP** = intra-aortic balloon pump; **INR** = international normalized ratio; **IV** = intravenous; **LV** = left ventricle; **OR** = operating room; **PCC** = prothrombin complex concentrate; **Plt** = platelet; **prBC** = packed red blood cell; **ST** = ST segment; **TEE** = transesophageal echocardiography; **TXA** = tranexamic acid; **UFH** = unfractionated heparin; **VKAs** = vitamin K antagonists; **WBC** = white blood cell

Cardiopulmonary bypass (CPB) results in significant insults to the hemostatic system, with almost 10% of patients experiencing severe or massive bleeding.¹ Hemodilution and consumption of coagulation factors are the primary reasons for development of coagulopathy.² Hemostatic blood products consisting of fresh frozen plasma (FFP), platelets, cryoprecipitate, and procoagulant pharmacologic agents are the mainstay of treatment.

Anticoagulant proteins are also reduced following CPB. Antithrombin (AT), for example, typically falls by 50%–60% of normal activity after CABG,³ and can reach levels in the 30%–40% range and take much longer to recover during cases requiring circulatory arrest.⁴ Focused efforts on restoring procoagulant factors can lead to a relative deficit of proteins that prevent systemic thrombosis. As we illustrate in this case, this imbalance can have devastating consequences.

Written Health Insurance Portability and Accountability Act of 1996 (HIPAA) authorization was obtained.

CASE REPORT

A 92-kg, 41-year-old woman presented with a pulsatile mass protruding from her chest wall. History was significant for hypertension and repair of type A dissection 8 months earlier. Repair was complicated by pseudoaneurysm formation, which required repeat sternotomy and replacement of the dehiscent graft with a mechanical valved conduit 2 months earlier. Her surgical wound from this repeat operation had poor healing, and she had undergone several operations for debridement and bilateral pectoralis major muscle flap chest closure.

She was febrile on arrival and empirically started on broad-spectrum antibiotics. Imaging revealed an aortic root pseudoaneurysm and partial sternal dehiscence. Transthoracic echocardiography showed an aortic root graft with a grossly normal mechanical aortic valve and a fluid collection surrounding the graft.

The patient was chronically anticoagulated with warfarin, and her international normalized ratio (INR) was 2.6 on presentation. Warfarin was held, and heparin infusion was started in anticipation of surgery within the next few days. Over the course of the next 24 hours, the pulsatile mass visibly expanded, and she developed acute kidney injury with an estimated glomerular filtration rate of 23 mL/min/1.73 m². She was taken emergently to the operating room (OR) given her worsening clinical status. Laboratory results before entering the OR: white blood cells (WBC), 11.8×10^3 μ L; hemoglobin, 9.1 g/dL; platelets, 224×10^3 μ L; INR, 2.4; and heparin level, 0.4 u/mL by anti-Xa level (institutional therapeutic range for unfractionated heparin is 0.3–0.7 u/mL).

Following placement of a left radial arterial line and peripheral intravenous (IV) lines, anesthesia was induced

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uneventfully. Right internal jugular pulmonary artery catheter and transesophageal echocardiography (TEE) probe were placed. Intraoperative TEE examination showed normal biventricular systolic function and a bileaflet mechanical aortic valve with pseudoaneurysm formation around the aortic root (Supplemental Digital Content, Video, <http://links.lww.com/AACR/A282>). Aortic-mitral curtain appeared disrupted, with continuous flow from the pseudoaneurysm into the left ventricle.

Cannulation for CPB consisted of right femoral venous cannula, which was advanced into the right atrium and superior vena cava, and right axillary arterial cannulation. Left ventricle was vented via the right upper pulmonary vein. Heparin bolus of 400 units/kg was given, which raised baseline activated clotting time (ACT) of 175 seconds to >1000 seconds. Tranexamic acid (TXA) bolus of 15 mg/kg was given after heparinization, and infusion was started at 7.5 mg/kg/h, which was continued throughout the case. CPB was initiated, and the patient was cooled to a core temperature of 24°C before skin incision. Entry into the chest and dissection of the infected material was extremely difficult. Circulatory arrest with antegrade cerebral perfusion was initiated for distal aortic hemiarch replacement. Valved conduit was excised, and neo-annulus was created using bovine pericardium, followed by aortic valve, root, and proximal ascending aorta replacement. This required 357 minutes on CPB, including 34 minutes of circulatory arrest. Eight units of packed red blood cells (RBCs) and 15 cell-saver units were transfused to maintain hemoglobin >7.0 g/dL. ACTs were >1000 seconds during CPB, with the exception of the final ACT before separation, which was 691 seconds (Figure). It is notable that no additional heparin was administered during CPB. Laboratory results sent after the end of circulatory arrest showed a platelet count of $31 \times 10^3/\mu\text{L}$ and a fibrinogen level of 197 mg/dL.

Separation from CPB was difficult, requiring high doses of inotropes and vasopressors (0.2 $\mu\text{g/kg/min}$ of norepinephrine, 0.1 units/min of vasopressin, and 0.3 $\mu\text{g/kg/min}$ of epinephrine), as well as intra-aortic balloon pump. TEE

examination during weaning from CPB showed moderate biventricular systolic dysfunction. Methylene blue (2 mg/kg) was given for treatment of vasoplegia. After 15 minutes of hemodynamic stability, the patient was decannulated, and heparin was neutralized with 260 mg of protamine (equivalent to 0.5 mg of protamine/100 units of initial heparin bolus and CPB prime). Approximately 5 minutes after protamine, 1074 units (~12.5 units/kg, representing one half of the full reversal dose) of 4-factor prothrombin complex concentrate (PCC; Kcentra, CSL Behring, GmbH, Germany) was given to correct the baseline INR. Five units of cryoprecipitate was transfused to correct hypofibrinogenemia and coagulopathic bleeding. Sudden profound hypotension and pulseless electrical activity developed, and TEE examination revealed extensive clotting within the right atrium and throughout the heart. This was felt to be unsalvageable, and the patient expired in the OR.

DISCUSSION

Catastrophic intracardiac thrombosis following complex cardiac surgery is a rare and typically fatal event for which incidence is unknown. A recent systematic review on this topic by Tanaka and colleagues,⁵ which included cases of pulmonary embolism, compiled only 46 cases reported in the literature between 1990 and 2016.⁵ Including 2 of their own institutional cases, they reported a 30-day mortality rate of 85.4%, with most patients expiring within 72 hours. Certain commonalities can be found among these cases, which Tanaka and colleagues⁵ grouped into 3 themes based on Virchow's triad. Our case is notable for exhibiting characteristics in all these areas (Table).

The role of blood stagnation is well appreciated in thrombus formation, yet the exact mechanisms are poorly understood. In experimental fluid dynamic models, blood velocity and shear rates can be used to predict the formation of thrombus.⁶ Clinically, the incidence of left ventricular thrombus formation during ST-elevation myocardial infarction can be as high as 15%, with cardiac arrest being the primary independent predictor.⁷ This patient's poor

Figure. The timeline represents the 357-min course of cardiopulmonary bypass. The blue line and right axis represent the ACTs obtained (s), and the red line and left axis represent the patient's hemoglobin (g/dL). The red circles are the number of RBC units transfused. Platelet count is $\times 10^3/\mu\text{L}$, and fibrinogen level is mg/dL. ACT indicates activated clotting time; CPB, cardiopulmonary bypass; DHCA, deep hypothermic circulatory arrest (34 min); Fib, fibrinogen; Plt, platelet; RBC, red blood cell; UFH, unfractionated heparin.

Table. Summary of Case Risk Factors for Catastrophic Thrombosis as Categorized by Tanaka et al⁵

Altered Blood Flow	Vascular/Endothelial Injury	Altered Blood Coagulability
Low cardiac output	Vessel injury	Imbalance of procoagulant and anticoagulant factors
<ul style="list-style-type: none"> • LV dysfunction on multiple inotropes 	<ul style="list-style-type: none"> • Major aortic surgery • Third-time sternotomy 	<ul style="list-style-type: none"> • Dilution • 8 units pRBCs • 15 units CS • Inadequate heparinization
Mechanical support	Extracorporeal flow	Procoagulant interventions
<ul style="list-style-type: none"> • IABP 	<ul style="list-style-type: none"> • Prolonged CPB • 357 min 	<ul style="list-style-type: none"> • Tranexamic acid • 5 units cryoprecipitate • 4-factor PCC • 1074 units

Virchow's triad consists of altered blood flow, vascular injury, and altered blood coagulability, which make up the column headings. Bolded items consist of general factors, and bulleted items specifically apply to the presented case. Abbreviations: CPB, cardiopulmonary bypass; CS, cell saver; IABP, intra-aortic balloon pump; LV, left ventricle; PCC, prothrombin complex concentrate; pRBCs, packed red blood cells.

contractility following CPB likely represents an analogous risk factor.

The endothelium plays a critical role in preventing thrombus formation through synthesis and expression of thrombomodulin, tissue factor pathway inhibitor, and endothelial protein C receptor.⁸ In addition to disrupting this thromboresistance, vessel injury—another component of Virchow's triad—causes endothelial expression of procoagulant agents such as tissue factor, as well as synthesis of von Willebrand factor. Aortic surgery in particular, with its generally longer CPB times, is associated with significantly higher thrombin generation than other types of cardiac surgery.⁹ This case was a repeat sternotomy with ascending aorta and hemiarch replacement, likely resulting in widespread endothelial injury at the macrovasculature and microvasculature levels.

Thrombotic risks imposed by altered blood flow and vessel injury are typically mitigated by anticoagulation, which is likely why thrombosis most often occurs following protamine administration. In this case, heparin management was suboptimal because only the initial bolus dose was administered. Although heparin concentration was not monitored, it is likely that heparin levels were subtherapeutic over much of the time on CPB. It is well known that elevated ACT measurements diverge from heparin concentration due to hemodilution, anemia, hypothermia, and hypofibrinogenemia during CPB.^{10,11} Taking into account the patient's increased heparin sensitivity from warfarin therapy and multiple RBC and cell-saver units transfused, ACTs of >1000 would likely not reflect adequate heparin anticoagulation.

Hemodilution also likely created other aspects of altered blood coagulability, the third aspect of Virchow's triad. The patient's platelet count had fallen to <15% of baseline values midway through CPB (Figure). Although AT levels were not measured, it is not unreasonable to assume they underwent a similar reduction. The potential for thrombin generation following prolonged CPB reaches supranormal levels in the absence of AT.¹²

Kcentra is approved by the US Food and Drug Administration (FDA) for reversal of vitamin K antagonists (VKAs) in patients who require urgent surgery. It contains procoagulant factors II, VII, IX, and X, anticoagulant proteins C and S, and small amounts of heparin and AT. The addition of these anticoagulant components may decrease the risk of thrombotic complications when compared to 3-factor PCCs, which do not contain proteins C and S.¹³ While recombinant factor VIIa will normalize INR, it does not correct underlying coagulopathy, and has risk of thrombotic complications due to its activated state and lack of anticoagulant components.¹³ When factors II, VII, IX, and X were restored with 4-factor PCC and fibrinogen was provided via cryoprecipitate, there was likely little systemic AT to control where thrombus was formed. The impaired ability to break down clots with TXA therapy should also be acknowledged, although what part antifibrinolytics play in systemic thrombosis is unclear.

In conclusion, acute thrombosis is multifactorial in origin, likely conforming to the "Swiss cheese" model in which multiple factors must line up for the pathology to occur. We agree with the call by Tanaka and colleagues⁵ for registries to better understand and prevent this devastating complication of cardiac surgery. Until then, clinicians should consider the accumulation of risk factors in the context of Virchow's triad when administering procoagulant therapy after complex cardiac surgery. ■■

DISCLOSURES

Name: Ratna Vadlamudi, MD, FASE.

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