Massive intracardiac thrombosis during coronary artery bypass grafting surgery

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ABSTRACT

Thrombosis is a potential life-threatening complication in patients undergoing cardiac surgery. Various clinical and heritable conditions, like cancer, trauma, immobilization, the presence of factor V Leiden or prothrombin 20210A, deficiency of or resistance to the inhibitor proteins C, S, or antithrombin, elevated levels of coagulation proteins, antiphospholipid antibody syndrome, pregnancy, and the use of exogenous hormones, may contribute to catastrophic thrombosis. Massive thrombi with cerebrovascular and cardiovascular events develop in patients with polycythemia vera (PV). However, thrombus formation in the cardiac chambers is extremely rare. We report a case of massive intracardiac thrombosis in a patient undergoing coronary artery bypass grafting.

Key Words: Heart, intracardiac thrombosis, myeloproliferative disorders, polycythemia vera

INTRODUCTION

Thrombogenic complications are potentially lethal in patients undergoing cardiac surgery. Concomitant diseases may contribute to catastrophic thrombosis in the setting of cardiopulmonary bypass (CPB). We report the anesthetic management of acute intracardiac thrombosis prior to systemic heparinization in a patient with polycythemia vera (PV) undergoing coronary artery bypass graft (CABG) surgery.

CASE REPORT

A 78-year-old, 173 cm, 100 kg man with a history of coronary artery disease and non-ST segment elevation myocardial infarction (NSTEMI) was admitted for CABG surgery. Coexisting medical conditions included hypertension, atrial fibrillation, congestive heart failure, chronic obstructive pulmonary disease, diabetes type 2, gastroesophageal reflux disease, dyslipidemia, carcinoma of prostate, and PV. He had undergone phlebotomies secondary to PV and was cleared for surgery from a hematologic standpoint. His preoperative hemoglobin level was 13.2 g/dL, white cell count 15.36 k/μL, and platelet count 769 k/μL. PT/INR were normal. Activated partial thromboplastin time was 123 s. He was on heparin infusion for 7 days prior to CABG surgery. Heparin infusion was stopped prior to line placement. Baseline activated clotting time was 159 s. ε-aminocaproic acid was administered as a 50 mg/kg load followed by a 25 mg/kg/h infusion. During graft harvest, the patient developed a sudden drop in arterial blood pressure from 84/55 to 37/30 concomitant with an increase in pulmonary artery pressure from 48/34 to 57/44 and in central venous pressure from 24 to 27. The end-tidal carbon dioxide level fell from 28 to 17 and bispectral index fell to zero. Transesophageal echocardiography (TEE) revealed clot in all four cardiac chambers [Figures 1 and 2], but the bifurcation of the main pulmonary artery could not be assessed by TEE. Heparin was administered (400 units per kg) and CPB implemented emergently. The infusion of ε-aminocaproic acid was stopped. CABG and left ventricular thrombectomy were performed utilizing deep hypothermic circulatory arrest and retrograde cerebral perfusion in an attempt to back flush any thrombus in the proximal cerebral circulation. Consultation was obtained from specialists in hematology and vascular medicine. A stat complete blood count (CBC) while on pump revealed a marked change in platelet count from 769 k/μL to 93 k/μL, while the rest of the CBC values demonstrated dilution (hemoglobin level 8.2 g/dL, white cell count 7.28 k/μL). The differential diagnosis included heparin-induced thrombocytopenia (HIT) and antiphospholipid antibody syndrome. Bivalirudin was started, but because separation from bypass was imminent the dose used was 0.75 mg/kg, followed by an infusion of 0.1 mg/kg/h. The heparin-bonded pulmonary
artery catheter was removed, and all heparin removed from the transducer flush solution. After rewarming and unclamping the aorta, TEE examination revealed ongoing clot formation in the left atrium and epiaortic ultrasound scan showed pulmonary artery thrombus. This was not addressed surgically, because the coagulation process appeared to be ongoing. Separation from bypass was accomplished with epinephrine and intraaortic balloon pump support. Protamine was given to reverse the effects of heparin.

A specimen of the thrombus was sent for pathologic analysis and read as platelet-rich thrombus. Coagulation function studies obtained immediately after surgery revealed a fibrin clot level of 94 mg/dL (normal: 200-400 mg/dL) and d-Dimer level > 20000 ng/mL (normal level <500 ng/mL).

Laboratory analysis for antiplatelet factor 4 antibody was negative on a specimen obtained intraoperatively and remained so on subsequent repeat testing. A serotonin release assay performed later was negative, as was testing for prothrombin 20210A and anticardiolipin antibodies. Levels of protein S and antithrombin normalized, but protein C function testing remained indeterminate. The patient remained neurologically intact, but the postoperative course was complicated by disseminated intravascular coagulation, multiple reoperations for chest washout, sepsis, bilateral lower extremity deep vein thrombosis, and respiratory failure requiring tracheotomy. Subsequently patient was transferred to a long-term acute care facility.

Discussion of management
PV is a myeloproliferative disorder that is classified as a clonal stem cell disease that includes myelofibrosis with myeloid metaplasia and chronic myeloid leukemia.[1] It is more common in men and has a prevalence of 4-16/1,000,000 population.[2,3] While bleeding can occur in PV, the frequency of thrombosis is much greater.[4] PV is associated with venous and arterial thrombosis. Abnormalities in blood viscosity, platelets, and leukocytes have been identified even though the mechanisms involved in this hypercoagulable state are unclear. There is an increased risk of graft thrombosis as compared with the unaffected population secondary to hyperviscosity.[5] In addition to elevated hemoglobin, hematocrit and red cell mass, the diagnostic criteria for PV include platelet count >400 k/μL and white cell count >12 k/μL as was evident in our case.

Other clinical and heritable conditions associated with a thrombotic tendency include cancer, surgery, trauma, immobilization, the presence of factor V Leiden or prothrombin 20210A, deficiency of or resistance to the inhibitor proteins C, S, or antithrombin, elevated levels of coagulation proteins, antiphospholipid antibody syndrome, pregnancy, and the use of exogenous hormones. Patients on heparin, as was this man, may develop antibodies to the complex of heparin and platelet factor 4, resulting in the syndrome known as HIT. Testing for HIT was negative, but the data are lacking on the behavior of the SRA and the anti-PF4 enzyme-linked immunosorbent assay in the setting of acute, fulminant HIT as is described above.

Thrombus formation in the cardiac chambers is an extremely rare complication of PV but can happen in the presence of predisposing factors such as myocardial muscular impairment, atrial fibrillation, or chamber dilatation.[6] This patient did have atrial fibrillation and evolving NSTEMI in the setting of PV. PV can cause both bleeding and thrombosis in the same patient. There are case reports with left ventricular and right atrial thrombus formation in patients with PV.[3,5] There is also a reported case of congestive heart failure due to massive intraventricular thrombus with pulmonary valve involvement in a patient with PV.[6]

Raised hematocrit and platelet count leading to hyperviscosity are well-recognized causes of the thrombosis in PV. Therapeutic options for PV include controlling platelet count and hematocrit to reduce
thromboembolic events such as phlebotomy and aspirin. In high-risk patients, addition of cytoreductive therapy such as hydroxyurea, anagrelide, or interferon alpha may be considered. The management algorithm to prevent clotting in PV and essential thrombocythemia follows in Table 1.

During perioperative period, hypercoagulable state is magnified. The risks of thrombosis are high when the underlying myeloproliferation is poorly controlled as reflected by erythrocytosis and thrombocytosis. Goal of therapy is to maintain hematocrit <45% in males and <42% in females. The risk of bleeding complications increase at platelet count >1000 × 10⁹/L. The goal of therapy is to achieve a platelet count of 400 × 10⁹/L. Cytoreductive therapy such as hydroxyurea or anagrelide considered based on risk/benefit ratio.

Anticoagulation and antiplatelet agents are critically important in patients with PV after coronary artery surgery. Anticoagulation with heparin infusion, warfarin sodium, and clopidogrel was done in two cases postoperatively that underwent coronary artery surgery.[7]

Our practice in regard to anticoagulation in PV is to check daily platelet count, aspirin therapy, hydroxyurea, and platelet apheresis to reduce platelet count. We would consider heparin infusion, followed by warfarin sodium, clopidogrel in high-risk patients. An appropriate compromise be done between the increased risk of bleeding and thrombosis.

**CONCLUSION**

Perioperative management of patients with PV who need surgery pose a unique challenge. They need to be evaluated and optimized from a hematological standpoint, by correcting both the hematocrit and essential thrombocythemia. We encourage vigilance during CPB and its aftermath in patients with PV, or any other myeloproliferative disorder, regarding the rare, but potentially lethal occurrence of massive thrombosis.

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**Table 1: Management algorithm for prevention of thrombosis in polycythemia vera and essential thrombocythemia**

| Treatment PV | Treatment essential thrombocythemia |
|--------------|------------------------------------|
| High risk    | Phlebotomy + low dose aspirin + hydroxyurea | Hydroxyurea + low dose aspirin |
| Intermediate risk | Phlebotomy + low dose aspirin | Low dose aspirin |
| Low risk     | None of the above | Phlebotomy + low dose aspirin |

PV: Polycythemia vera