Pulmonary Endarterectomy Under Hypothermic Circulatory Arrest in a Patient With Heparin-Induced Thrombocytopenia

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PULMONARY ENDARTERECTOMY (PEA) is the most appropriate treatment for chronic thromboembolic pulmonary hypertension (CTEPH) and is a potential cure for the pulmonary hypertension associated with this disease.[1] The gold standard for anticoagulation during cardiopulmonary bypass (CPB) and deep hypothermic circulatory arrest (DHCA) is unfractionated heparin.[2] Rarely, the use of heparin is complicated by heparin platelet factor 4 antibodies, which is associated with heparin-induced thrombocytopenia (HIT), platelet activation, and subsequent thromboembolism, all of which make achieving adequate anticoagulation challenging.[2,3] An alternative non-heparin-based anticoagulant, bivalirudin (a direct thrombin inhibitor), has been reported to appropriately achieve anticoagulation during CPB and DHCA.[2–4] Although many alternative strategies have been utilized in this subset of patients, there is no consensus regarding the optimal strategy, and most strategies are complicated by massive bleeding complications.[2–6] The authors report a case of a patient with CTEPH and acute HIT requiring pulmonary endarterectomy and patent foramen ovale closure. The procedure was performed with CPB and DHCA using bivalirudin anticoagulation therapy with high-volume, zero-balance ultrafiltration (HVZBUF) and homologous transfusion.

CASE REPORT

A 22-year-old, 120-kg, 158-cm female was transferred from another hospital with progressively worsening dyspnea and cough complicated by hemoptysis and hypoxia (oxygen saturations of 60% to 70% on room air). Her past medical history was significant for morbid obesity (BMI 50), chronic dyspnea secondary to newly diagnosed CTEPH, and 7 pack-year smoker. Past surgical history was noncontributory. Family history was negative for thromboembolic disease. She was transferred to the authors' institution for definitive surgical treatment.

PEA workup was expedited given the lack of decreased clot burden on repeat CT scan, despite warfarin anticoagulation, and continued hypoxia despite supplemental oxygen. During the periprocedural period of her right heart catheterization, she was restarted on a heparin infusion per cardiology recommendations. Subsequently, a new thrombocytopenia (50% decrease in platelet count) was noted. HIT was confirmed by enzyme-linked immunosorbent assay for the presence of antibodies and by serotonin release assay for its thrombotic potential. She was started on argatroban for anticoagulation and heparin was discontinued. She subsequently was scheduled for urgent PEA. The use of plasmapheresis briefly was discussed. However, given the patient's worsening clinical condition, the authors felt delaying surgery for serial therapeutic plasma exchanges to achieve negative heparin-dependent, platelet-activating antibodies would place the patient at greater risk. Thus, a joint decision among the surgeon, anesthesiologist, and perfusionist was made to use bivalirudin for anticoagulation during CPB.

The day of surgery, preoperative vital signs included blood pressure of 118/72 mmHg, heart rate of 92 beats/min, and oxygen saturation of 94% on 8 L/min nasal cannula. She received a peripheral intravenous and radial arterial catheters prior to induction of general anesthesia. Anesthesia was induced with midazolam (5 mg), fentanyl (500 μg), rocuronium (150 mg), and dopamine infusion (5 μg/kg/min). Shortly after intubation, a transesophageal echocardiography probe (TEE) was placed, and internal jugular venous access was obtained. Initial, brief TEE examination revealed dilated, hypertrophied right ventricle with moderate-severe dysfunction (RV FAC 19%, minimal RV free wall motion, TAPSE 15 mm) and moderate tricuspid regurgitation (Fig 1). A heparin-free pulmonary artery catheter subsequently was inserted, which revealed worsening pulmonary hypertension with suprasystemic pulmonary artery pressure of 118/41 mmHg (systemic blood pressure of 114/65 mmHg). Although preoperative pulmonary reversibility studies were not done during her preoperative evaluation, inhaled nitric oxide was not utilized given its limited efficacy in CTEPH patients.[1] Inodilators were not used given the increased potential for right ventricle ischemia.[1]

Anesthesia was maintained with fentanyl, isoflurane, and rocuronium. During surgical preparation and completion of the TEE examination, the patient became acutely hypoxic to a nadir of SpO_2 of 55% on F_IO_2 of 1, with concomitant increases in pulmonary artery pressures and systemic hypotension. Recruitment maneuvers, escalation of PEEP, multiple boluses of phenylephrine, vasopressin, and epinephrine provided no relief. Simultaneous TEE examination revealed a large PFO (not diagnosed on previous studies) with right-to-left flow. A brief trial of zero PEEP offered no improvement in hemodynamics. During this period of hemodynamic instability, The cardiac surgeons proceeded with plans for emergent CPB.

The CPB circuit was primed with 50 mg of bivalirudin and an intravenous loading dose of 1 mg/kg followed by an infusion at 2.5 mg/kg/h (based on actual weight) were given approximately 10 minutes before cannulation. Post-bivalirudin activated clotting time (ACT) was 379 seconds (baseline 133). Given the severe hypoxemia, CPB was instituted, and a repeat bolus of 1 mg/kg of bivalirudin was administered simultaneously to achieve goal ACT >480 seconds. Despite the increase in ACT $>2.5\times$ above baseline with initial bivalirudin

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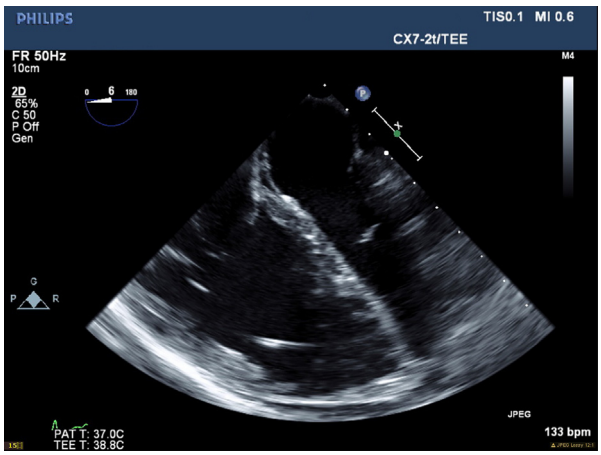

Fig 1. Intraoperative pre-CPB TEE image revealing dilated, hypertrophied RV with flattening of interventricular septum.

loading dose, the decision was made to administer a second loading dose given the authors' institution's previous experience with CPB thrombosis in the setting of bivalirudin usage and lower ACTs. After the second loading dose of bivalirudin, repeat ACT was 544 seconds.

Through cannulation of the high ascending aorta and the superior vena cava, partial flow bypass was instituted to improve hemodynamics. Bicaval cannulation then was used to achieve full-flow CPB. A left ventricular vent was placed via the right superior pulmonary vein, and a retrograde cardioplegia catheter was placed in the coronary sinus. An antegrade cardioplegia catheter and aortic root vent were placed in the mid-ascending aorta. Systemic cooling to a core temperature of 18°C was performed, and her head was packed with ice. During the cooling and prior to initiation of DHCA, a 0.2-mg/kg bolus of bivalirudin was administered at the surgeon's request, with no change in the infusion rate, to maintain ACT >480 seconds. When the bladder temperature reached 18°C, antegrade and retrograde cardioplegia were infused followed by initiation of DHCA. After dosing cardioplegic solution, the line was flushed with Plasma-Lyte® to remove residual blood. The DHCA arrest periods were limited to approximately 20 minutes. The right PEA required 2 DHCA periods, 20 and 5 minutes, respectively, and the left PEA required one 22-minute period (Fig 2). During periods of DHCA, the arterial and venous lines were clamped, and the CPB circuit was recirculated distal to the arterial filter, via a bridge, back to the venous reservoir. In between periods of DHCA arrest, CPB was reinstituted, and cardioplegia was redosed. After adequate bilateral PEA, the patient was rewarmed to 37°C, and the newly diagnosed PFO was closed.

ACT was checked approximately every 15 to 20 minutes while on CPB. As shown in Figure 3, after the first period of DHCA the ACT continued to rise, as expected, given significant hypothermia and continued infusion. However, the ACT continued to rise during rewarming, which prompted decreasing the bivalirudin infusion dose to 2.0 mg/kg/h when she was about 35°C. Shortly thereafter, the decision was made to discontinue bivalirudin infusion and begin steady-state HVZBUF in an attempt to minimize post-CPB transfusion given the persistently elevated ACT. HVZBUF was achieved using a polysulfone filter with a large pore size of 65,000 daltons (Minntech Hemocor HPH 1000TS ®, Minneapolis, MN), which has been identified as effective for the elimination of bivalirudin.[7] HVZBUF was achieved with Plasma-Lyte® infusion in a 1:1 ratio to the volume of effluent. Vacuum suction was applied to the effluent side of the membrane to achieve an estimated transmembrane pressure of approximately −400 mmHg. Additional doses of sodium bicarbonate and calcium chloride were administered to maintain a pH of 7.4 and achieve an ionized calcium concentration of 1.34 mmol/L at termination of CPB. Twenty-five percent albumin was administered to attempt to increase or at least maintain a normal serum oncotic pressure during CPB. HVZBUF, at a rate of approximately 256 mL/min, was continued while on CPB for nearly 50 minutes with continuous visual inspection for clot formation and repeated ACT measurements, achieving a total ultrafiltrate volume of 13 liters (urine output during this time was approximately 1 liter). The ACT decreased to 405 seconds, at which time CPB was terminated, and the patient was decannulated. A continuous infusion of 50 mg/h of bivalirudin was administered in the recirculating CPB circuit to avoid pump thrombosis while hemostasis in the operative site was achieved.

After separation from CPB with intravenous vasopressin (2 U/h), systemic blood pressure was 105/57 mmHg with PA pressures was 43/22 mmHg, and CI was 2.4 L/min/m^2. TEE revealed mild tricuspid regurgitation with improved right ventricle function and no flow across the intra-atrial septum. ACT continued to slowly decrease with improving coagulation status over the next 90 minutes (Fig 3). Packing and direct pressure were utilized, and the 1 unit of previously harvested autologous blood was administered. Adequate hemostasis was achieved in the operating room, and the pericardium and sternum were closed. The last ACT in the operating room remained elevated at 263 seconds.

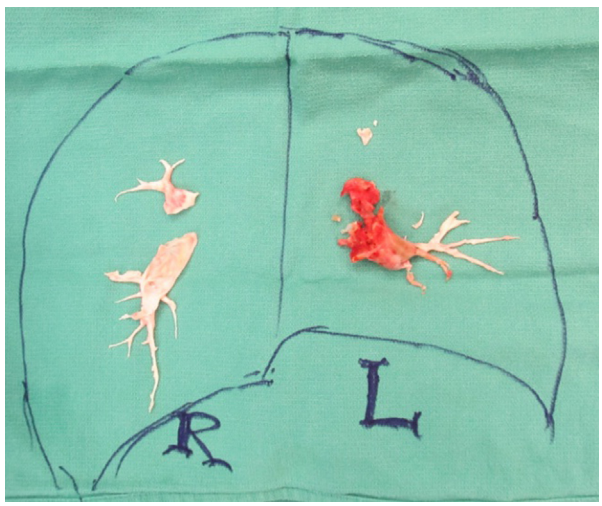

Fig 2. Bilateral endarterectomy specimen demonstrating type I disease on the left with evidence of major vessel clot and type II disease on the right with evidence of more chronic and fibrotic disease with no fresh clot.