Management of intrapulmonary hemorrhage in patients undergoing pulmonary thrombo-endarterectomy

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ABSTRACT
Massive pulmonary hemorrhage during pulmonary thromboendarterectomy (PTE) can be managed by a conservative approach with mechanical ventilatory support, positive end-expiratory pressure, lung isolation, reversal of heparin, and correct of coagulopathy. We present three challenging cases that developed intrapulmonary hemorrhage during/after PTE and managed successfully. The first patient had bleeding from the bronchial artery and right internal mammary collaterals, which was managed by coil-embolization. The second patient had a breach in the blood airway barrier in the right upper lobar segment of the lung, and the repair was done using a surgical absorbable hemostat. The third patient developed reperfusion injury, he was instituted on veno-venous extracorporeal membranous oxygenation, a week later, the patient recovered completely. An algorithm was adopted and modified to our requirements; all the 3 challenging intrapulmonary hemorrhage cases were successfully managed. This algorithm can be used for satisfactory outcomes in patients who suffer intrapulmonary hemorrhage during PTE.

Keywords: Chronic thromboembolic pulmonary hypertension, CTEPH, pulmonary hemorrhage, pulmonary thromboendarterectomy, PTE

INTRODUCTION
Chronic thromboembolic pulmonary hypertension (CTEPH) is an often-undiagnosed serious illness. The World Health Organization (WHO) has classified this disease as class 4 in the categorization of pulmonary hypertension (PH).[1] Pulmonary hypertension is defined as pulmonary vascular resistance (PVR) ≥3 Wood units in pre-capillary PH associated with a mean pulmonary artery pressure (mPAP) >20 mmHg, and pulmonary artery wedge pressure (PAWP) <15 mmHg by the 6th World symposium on pulmonary hypertension (WSPH) task force.[1] Pulmonary hypertension in chronic pulmonary thromboembolic disease occurs as a result of partial or complete occlusion of the pulmonary vascular bed due to recurrent or residual thrombi. Vascular remodeling in the distal pulmonary arteries contributes to increased PVR, leading to right ventricular dysfunction. Pulmonary endarterectomy (PTE) is the only surgical treatment which is curative for patients who are suffering from CTEPH.[2] The observed survival at 3 years was 89% for operated CTEPH compared to 70% for the non-operated group (P < 0.001).[3] The surgical procedure is technically
challenging, requiring a multidisciplinary approach involving careful patient selection, detailed preoperative, intraoperative, and postoperative care plans along with surgical expertise. According to recent report of Madani et al., the in-hospital mortality with the most experienced center has reduced from 4.4% to 2.2%. Significant pulmonary hemorrhage occurs in 1% of PTE cases and is associated with a mortality of nearly 70%. Manecke et al. reported three cases out of 600 procedures (0.5%) and suggested the friability of pulmonary vasculature, advanced age, and presence of residual pulmonary hypertension is likely to result in bleeding.

In this case report, we illustrate three challenging cases who developed pulmonary bleeding during or after PTE at a tertiary care large-volume cardiac center.

CASE REPORT

Case 1: Systemic to pulmonary arterial collateral bleed managed with coil embolization [Figure 1a]

A 38-year-old female was diagnosed to suffer from CTEPH. Her transthoracic echocardiogram (TTE) showed a dilated right atrium (RA), right ventricle (RV) and main pulmonary artery (MPA), moderate tricuspid regurgitation (TR), increased pulmonary artery pressure (PAP), and reduced biventricular function. A right heart catheterization revealed a PAP of 150/40 mmHg, with an mPAP of 80 mmHg and a PVR of 16.4 Wood units. Systemic to pulmonary arterial collaterals from right internal mammary artery to right middle and upper lobe, left internal mammary artery to left middle lobe, and from the thoracic aorta to right middle and lower lobes were identified on computerized tomography of pulmonary artery (CTPA) [Figure 1b]. PTE was performed under cardiopulmonary bypass (CPB) and deep hypothermic circulatory arrest (DHCA). During rewarming on CPB, when the heart could eject, bleeding from the endotracheal tube (ETT) was noticed and fiberoptic bronchoscopy revealed bleeding from the right intermedius bronchus.

The single lumen ETT was exchanged for a left-sided double-lumen endotracheal tube (DLT) to isolate the right lung and to prevent the soiling of the left lung. In view of severe intrapulmonary hemorrhage, failure of ventilation, and hemodynamic instability, central veno-arterial extracorporeal membrane oxygenation (VA-ECMO) was instituted with a vent in the pulmonary artery. Anesthesia was maintained with inhalation of isoflurane in 50% oxygen, fentanyl, and atracurium infusion. Anticoagulation with heparin was partially reversed with titrated doses of protamine sulfate so as to maintain the activated coagulation time (ACT) between 160 and 180 seconds. Emergency pulmonary angiography revealed the source of bleeding to be the bronchial artery and right internal mammary collaterals, which were successfully coil-embolized in the cardiac catheterization laboratory [Figure 1c]. On the 2nd postoperative day (POD), central VA-ECMO was converted to central veno-venous ECMO (VV-ECMO) in view improvement in cardiac function. Fiberoptic bronchoscopy was performed to retrieve clots from the airway on the 4th POD [Figure 1d]. With control of bleeding and improvement in oxygenation and radiography, the patient was weaned off ECMO on the 8th POD. The patient made an uneventful recovery thereafter. At the time of hospital discharge, the PAP to be 32/16 mmHg, with an mPAP of 23 mmHg and a PVR of 3 Wood units.

Case 2: Breach in blood airway barrier

A 36-year-old male with a history of deep vein thrombosis (DVT) in both lower extremities, presented with increasing shortness of breath on exertion and recurrent hemoptysis for 2 years. TTE showed dilated RV, RA, and pulmonary artery (PA) with severe TR, thrombus in MPA, and significantly reduced RV systolic function. Pre-operative PAP was 100/50 mmHg, with an mPAP of 65 mmHg and a PVR of 17.5 Wood units. CTPA revealed central hypodense filling defects in the MPA, right pulmonary artery (RPA), and left pulmonary artery (LPA) with multiple foci of calcification. The patient underwent PTE surgery on CPB with DHCA. Intraoperative findings revealed an MPA thrombus, UCSD level I disease in RPA, and UCSD level II disease in LPA [Figure 2]. The surgeon suspected a breach in the blood airway barrier in the right upper lobar segment of the lung, hence repair…
was performed using a surgical absorbable hemostat (Surgicel®, Ethicon, Johnson & Johnson, US).[7] Lung isolation was performed by exchanging ETT to a left-sided DLT and conservative management of bleeding was instituted. After the administration of protamine, bleeding via ETT abated. Post-operative PAP was 50/20 mmHg, with an mPAP of 35 mmHg and a PVR of 8 Wood units. The patient had an uneventful recovery and was discharged in a stable condition on the 12th POD.

**Case 3: Reperfusion pulmonary edema (RPE) [Figure 3]**

A 24-year-old female complained of dyspnea on exertion and was investigated to confirm a diagnosis of CTEPH. She gave a recent history of hemoptysis when she presented for surgery. Pre-operatively, she had PAP of 124/50 mmHg, with an mPAP of 74 mmHg, at an aortic pressure of 140/80 (mean; 100) mmHg and a PVR of 20 Wood units. The TTE showed dilated RA, RV, PA, moderate TR, increased PAP, and borderline left ventricular function. After PTE, the patient exhibited impaired oxygenation and a decreased partial pressure of oxygen (PaO₂)/inspired oxygen (FiO₂) ratio despite chest X-ray being normal. Inhaled nitric oxide at 60 parts per million was initiated because of persistent pulmonary hypertension. The patient continued to be hypoxic despite adequate ventilation with FiO₂ of >0.6. On the 2nd POD, she developed pink frothy secretions from ETT, reduced compliance of lung and radiological features of pulmonary edema. Reperfusion injury was diagnosed after excluding other causes of this clinical picture. A central VV-ECMO (RA to PA) was instituted to maintain oxygenation. Patient was sedated with fentanyl and midazolam infusion. Heparin was administered to achieve anticoagulation to maintain the ACT between 160 and 180 s and activated thromboplastin time of 1.5 times the normal. After one week of ECMO, she made a complete recovery, and her PAP before hospital discharge was 34/18 mmHg, with an mPAP of 24 mmHg and a PVR of 4 Wood units.

**DISCUSSION**

PTE is a technically very demanding procedure that needs skill, precision, and expertise. An expert center should perform ≥20 PTE operations per year with a <10% mortality rate. Patients with University of California San Diego (UCSD) level IV disease previously considered inoperable now are undergoing surgery in expert centers. Three different causes of intrapulmonary hemorrhage have been highlighted in this report. (i) Bleeding due to rupture of fragile bronchopulmonary collateral: a considerable number of patients suffering from CTEPH present with hemoptysis; such patients may undergo pulmonary angiogram to identify specific collaterals for coil embolization; this can be done either in the immediate preoperative period or after surgery if the patient bleeds from the ETT. Gan et al., showed us that preoperative transcatheter occlusion of the bronchopulmonary collateral artery can reduce the incidence of reperfusion pulmonary edema and reduce ECMO usage.[8] Reesink et al., reported that 5 of 79 patients with CTEPH (6%) had moderate to severe hemoptysis due to systemic to pulmonary arterial collateral bleed, requiring medical intervention.[9] (ii) Damage to blood-airway barrier: If the surgeon suspects violation of the blood-airway barrier during endarterectomy, the surgeon attempts to locate the breach and pack it with a surgical absorbable hemostat as is described.[10] (iii) Reperfusion pulmonary edema: RPE occurs in 10 – 14% of patients following hyper-perfusion of areas of the lung that have undergone endarterectomy. RPE is a hypoxic state associated with a PaO2/FiO2 ratio <300, opacity on chest radiograph, and no alternative
explanation such as pneumonia or atelectasis. Management of RPE is supportive including the use of ECMO as a bridge to recovery.\textsuperscript{[10,11]}

There are several other techniques that have been described in the literature techniques to help control pulmonary bleeding after endarterectomy; these use of positive end-expiratory pressure (PEEP), topical vasoconstrictors,\textsuperscript{[6]} temporary overnight clamping of the culprit PA beyond the lobar branch,\textsuperscript{[12]} bronchial occlusion with a Fogarty balloon catheter while on peripheral VA-ECMO.\textsuperscript{[13]} With refractory bleeding, using VV and VA ECMO is lifesaving.\textsuperscript{[11,14]} The algorithm for these complications has been published in the textbook of cardiac anesthesia edited by Kaplan.\textsuperscript{[15]} We have adapted and changed this algorithm to suit our requirements with satisfactory outcomes in patients who suffer intrapulmonary hemorrhage during PTE [Figure 4].

Acknowledgments
The authors would like to acknowledge Dr. V. M. Annapandian (academic consultant), Narayana Hrudayalaya Foundations, for his help in editing this manuscript.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial(s) will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Ethical statement
This study was approved by the institutional review board and ethics committee.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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