Pulmonary Thromboendarterectomy: The case of supra-systemic pulmonary artery pressures

Problem Based Learning Discussion
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OBJECTIVES
At the completion of this PBLD, the participant will be able to
1) Describe the pathophysiology, classification and incidence of chronic thromboembolic pulmonary hypertension (CTEPH)
2) Identify the indications for pulmonary thromboendarterectomy
3) Discuss the preoperative evaluation and hemodynamic considerations for CTEPH
4) Summarize the intraoperative anesthetic management and monitoring considerations for patients with severe pulmonary hypertension

CASE PRESENTATION
43 y/o woman with a history of chronic thromboembolic pulmonary hypertension is admitted in preparation for pulmonary thromboendarterectomy. Pt suffered a deep vein thrombosis (DVT) and subsequent massive pulmonary embolism (PE) several years prior while undergoing chemotherapy for uterine cancer. At the time of the PE she developed acute cardiac and respiratory failure and required mechanical ventilation. She was placed on thrombolytic therapy followed by heparin and then warfarin. Subsequently, a Greenfield filter was placed.

QUESTIONS
What are the most common hypercoaguable disorders? Differentiate between those that are inherited and those that are not.

Do the pulmonary artery pressures return to normal after an initial PE following prompt and complete initial anticoagulation therapy?
What is the pathophysiology of pulmonary hypertension in these patients?

How many patients go on to develop Chronic Thromboembolic Pulmonary Hypertension (CTEPH)?

Why do some patients develop CTEPH and others do not?

CASE CONTINUATION

Over the past year, pt noted progressive exertional dyspnea - unable to walk one block (NYHA class III). She also noted increasing lower extremity edema. More recently, walking across the room has triggered worsening SOB.

PMH: Hx of uterine cancer - otherwise unremarkable

Medications: Sildenafil 50 mg po TID, Lasix 40 mg po BID, warfarin 2.5 mg po daily

Vitals: BP 105/58 HR 105 RR 19 SpO2 89% 10 L O2 by face mask

Physical Examination:
Height: 5'4 f, Weight: 155 lb, BMI: 26
Morbidly obese, dusky in color, lips cyanotic
Sitting upright – 3 to 5-pillow orthopnea - receiving O₂ 10L/face mask
Airway: Class II, full ROM of mandible and cervical spine
Lungs: Distant breath sounds, but clear bilaterally
Heart: regular, II/VI systolic murmur noted between scapulae
Abdomen: large, hepatomegaly
Extremities: bilateral lower extremity edema

Labs: Electrolytes WNL, Hct 49.2
Platelets -230
Hepatic enzymes moderately elevated

EKG -sinus at 114, right axis deviation, incomplete RBBB, inferior strain pattern

CXR -Clear lung fields (diminished vascular markings bilaterally)

Echo -EF 70%, mild left ventricular diastolic dysfunction
RV markedly enlarged and hypertrophic - mildly depressed function
RA markedly enlarged - moderate TR
TR envelop 5 m/s, PAP 100 mm Hg + CVP

What are the causes of cyanosis?
What do you think of the hematocrit?
What do you think about the Echo findings?
**Right heart cath** - RAP 18 RV 105/15, PAP 107/55 (74)
CO 3.1, CI 1.0
PVR 1738 dyne/sec/cm$^5$
**Left heart cath** - no significant CAD

What are the most important data from the right heart cath?
Is an RVEDP of 15 significant?
PVR > SVR what does that mean? Is the blood flowing backward? Wedge pressure of 6mmHg – What are your thoughts? Is this expected?

**V/Q scan** - moderate-to-large ventilation perfusion mismatches
**Pulmonary angiogram** - suggestive of CTEPH

What is the RV response to increased volume and pressure?
What conditions will exacerbate the baseline pulmonary hypertension?
What is the typical preparation for a patient prior to PTE?
What are your hemodynamic goals in terms of rate, rhythm, preload, afterload and contractility?
What monitoring will you plan to use in this case?
If you plan to use a PA catheter, what are the pros and cons to placing awake prior to induction vs. following induction?
If a V-fib arrest should occur, how effective are external chest compressions in patients with this degree of increased pulmonary vascular resistance?
What is your plan for induction?
Which rescue drugs would you like to have available?
**CASE CONTINUATION**

**Induction**
Pt brought to OR with 18G PIV and right radial A-line in addition to standard monitors
Preoxygenated for 10 minutes to SpO2 89%.

Etomidate 10 mg, fentanyl 250 mcg, midazolam 5 mg, rocuronium 100 mg, dopamine infusion at 5 mcg/kg/min

Easy mask ventilation and intubation
ETT secured and mechanically ventilated with 0.5 MAC Isoflurane
Pt SpO2 drops to low 80's
BP drops from 100/60 to 70/40.

How would you treat the drop in SpO2 and BP?

Dopamine increased to 10 mcg/kg/min and epinephrine infusion started at 0.3 mcg/kg/min.

Would you use phenylephrine? Why or why not?

Surgeons notified and rushed to OR, rapid surgical prep and surgery started
SpO2 continues to decline to 69% while cardiopulmonary bypass (CPB) established
SBP continues to progressively decline to 60's after initial response to epinephrine and dopamine to 90's
TEE performed, CPB established

What would you expect to see on TEE examination?

**CASE CONTINUATION**
Surgery proceeded without complication. A right pulmonary embolectomy was performed, followed by right and left pulmonary endarterectomy under profound hypothermia and circulatory arrest.

Upon separation from cardiopulmonary bypass large amounts of dark blood emanate from the endotracheal tube. What is the most likely cause for this, and how will you proceed?
DISCUSSION

Introduction
Annually, in the United States alone, approximately 900,000 people develop blood clots in the lungs or major veins: 400,000 cases of non-fatal DVT, 200,000 cases of non-fatal PE and 300,000 cases of fatal venous thromboembolism (VTE). Chronic thromboembolic pulmonary hypertension (CTEPH) is obstruction of the major pulmonary arteries resulting in pulmonary hypertension. The incidence of CTEPH is likely under-diagnosed and as a result is an under-treated phenomenon.

Currently, approximately 10% of patients who suffer PE die within one hour due to cardiovascular collapse or respiratory failure. Approximately 3.8% of patients suffering a PE will develop CTEPH. The vast majority of patients do not develop the disease. Unfortunately, many patients with CTEPH have no clear history of an acute thromboembolic event. According to the World Health Organization, CTEPH is classified as type-4 pulmonary hypertension (pHTN).

After a clear thromboembolic event, patients often enter into an asymptomatic “honeymoon phase,” with progressive remodeling of unobstructed vasculature. It is important to remember that CTEPH can develop in the absence of documented recurrent thromboemboli.

The most common causes of hypercoaguabale disorders include the following:

A. Inherited hypercoaguabale conditions

Factor V Leiden (the most common)
Prothrombin gene mutation
Elevated levels of fibrinogen
Deficiencies of natural proteins that prevent clotting (anticoagulant proteins)
Antithrombin
Protein C and protein S
“Sticky” platelets
Abnormal fibrinolytic system

B. Acquired hypercoaguabale conditions

Cancer
Recent trauma or surgery
Pregnancy and exogenous estrogen use
Hormone replacement therapy
Immobility for any reason (i.e. illness, surgery, prolonged airplane travel)
Heparin-induced thrombocytopenia
Antiphospholipid antibody syndrome
Previous deep vein thrombosis or pulmonary embolism
Myeloproliferative disorders such as polycythemia vera or essential thrombocytosis
CTEPH Symptoms and Signs
PTE patients usually present with progressive dyspnea on exertion, particularly in young individuals. Frequently, there is a history of documented pulmonary embolism (PE) but, as mentioned earlier, there may be no obvious event. Risk factors for DVT are common. Findings on physical examination are consistent with right heart failure, including peripheral edema, hepatomegaly and jugular venous distention. Precordial examination often reveals right ventricular heave and a systolic murmur. This murmur results from turbulent flow moving through partially obstructed pulmonary vessels. Patients with atrial septal defects may present with cyanosis. Hepatomegaly and ascites develop late in the disease. LFTs may be abnormal reflecting hepatic congestion secondary to right heart failure.

EKG findings show evidence of right ventricular hypertrophy with strain. CXR often reveal clear lung fields with prominent hilar regions. Enlarged right atrium and right ventricle are commonly noted.

Arterial blood gas may reveal increased A-a gradient which may worsen with exercise. V/Q scan findings are consistent with moderate-to-large ventilation perfusion mismatches. Interestingly, signs of pulmonary hypertension and right ventricular failure on echocardiography often represent the first major clues in the diagnosis of CTEPH.

Right heart catheterization demonstrates the severity of pulmonary hypertension. Typically patients have PVR > 300 dyne/sec/cm$^5$ with mean PA pressures > 25 mmHg. Dilated right ventricle (RV), global RV dysfunction and RV compression of left ventricle (LV) with bowing of the interventricular septum toward LV during systole are common findings on echocardiography. Tricuspid regurgitation is a common finding while thrombus may be seen in the main PA and/or right PA.

Pulmonary angiography may show
1. irregular arterial contours with abrupt cut-off or narrowing of vessels
2. pulmonary artery webs and bands, which are organizations of the thromboembolic material in the vessel lumen with subsequent scar formation
3. pouch defects
4. obstruction of lobar or segmental arteries at their point of origin

Role of Medical Therapy
Standard medical therapy includes chronic anticoagulation with warfarin to a target goal INR 2-3. Although the utility of pulmonary vasodilators before PTE has been investigated, there is limited evidence regarding outcome benefits. Pulmonary vasodilators include: bosentan (endothelin antagonist); sildenafil (phosphodiesterase inhibitor); epoprostenol (prostaglandin). Recent AHA guidelines on CTEPH strongly suggest that the lack of pulmonary vasodilator therapy should never delay PTE.
**Pulmonary Thromboendarterectomy**: PTE is the treatment of choice for patients with chronic, thromboembolic pulmonary hypertension. Organized thrombi along with a thin lining of intima are removed while leaving the media intact. It is performed through a median sternotomy on cardiopulmonary bypass. Deep hypothermic circulatory arrest is commonly employed during the endarterectomy to prevent bleeding from the bronchial collaterals. The surgery often provides immediate (and sometimes permanent) relief of the pHTN, but residual pulmonary hypertension is relatively common and may be managed by oral vasodilator therapy.

**Predictors of Outcomes**
Of note, outcomes are better at institutions with significant experience. To date, the University of San Diego has the largest PTE experience worldwide. Since 1970, the perioperative mortality for PTE at the University of San Diego has been quoted at 6.4%; however, it has fallen to 2.5% within the last 3 years due to refinements in perioperative techniques. According to the international CTEPH registry, in-hospital mortality for PTE is 4.7% and 1-year mortality is 7%. Perioperative complications include neurologic issues (11.2%), bleeding (10.2%), pericardial effusion (8.3%), residual pulmonary hypertension (16.7%), pulmonary reperfusion edema (9.6%), the need for extracorporeal membrane oxygenation (3.1%) and infection (18.8%). Neurologic complications increased if DHCA was used and increased significantly if DHCA >60 minutes.

The Jamieson Classification is an intraoperative classification system that categorizes patients according to surgical specimen based on pattern of pulmonary occlusion.
- Type 1 (25%): Fresh thrombus in main and/or lobar arteries
- Type 2 (40%): Chronic intimal thickening proximal to the segmental arteries
- Type 3 (30%): Intimal disease limited to the segmental arteries; technically the most difficult
- Type 4 (<5%): Distal arteriolar vasculopathy without visible thromboembolic disease. (Associated with the highest surgical mortality rate; In fact, PTE does not benefit these patients. It is important to identify these patients preoperatively as they quality for medical therapy and not surgical therapy.)

Postoperative outcome in patients by classification
- Type 1 mean decrease in PAS $35.5 \pm 16.3$ mmHg
- Type 2 mean decrease in PAS $36.3 \pm 18.2$ mmHg
- Type 3 mean decrease in PAS $18.5 \pm 19.4$ mmHg
- Type 4 mean decrease in PAS $0 \pm 15.6$ mmHg
The degree of pHTN and right ventricular dysfunction are not contraindications to PTE. Patients with operable disease may derive significant benefit from reduction in pHTN leading to improved right ventricular function and resolved or improved tricuspid regurgitation. Thistlewaite et al., noted that patients with distal thromboembolic disease (Type 3-4) had higher perioperative mortality, required longer inotropic support and had longer hospital stays compared with patients with type 1-2 thromboembolic disease.

**PTE Indications**
This is a complex surgical procedure that carries significant risk. Surgical candidates must be chosen carefully. There must be functional cardiac impairment (typically NYHA class III or IV) and hemodynamically significant pulmonary vascular obstruction. Typically PVR > 300 dynes/sec/cm^5^ and PA pressure > 25 mm Hg. It is not uncommon to encounter values > 1000 dynes/sec/cm^5^ and suprasystemic pulmonary artery pressures. The patients should not have any concurrent illness that is an immediate threat to life and they must desire surgery based on poor cardiorespiratory function and understand the significant risks.

**Hemodynamic consideration** for the preop, induction and the pre bypass period include

1) Several days prior to surgery, IVC filter is placed to prevent future emboli.
2) Informed consent is imperative.
3) Awake radial arterial line and large bore peripheral intravenous catheter.
   Hemodynamic assessment and decision making is centered on right ventricular function. Because of the right-sided pressures, the coronary blood supply to the right ventricle is at risk.
4) Maintenance of adequate systemic vascular resistance, adequate inotropic state, and normal sinus rhythm serve to preserve systemic hemodynamics as well as right ventricular coronary perfusion.
5) Preoperative cardiac cath data are useful in determining the induction sequence. Typically avoid sedation outside the OR due to risk of hypercarbia with hypoventilation. Induction accomplished with combination of fentanyl, midazolam, etomidate and muscle relaxation. Inotropic support may be necessary during induction to prevent worsening right ventricular dysfunction.
6) Consider induction with inotropic support if there is evidence of impending cardiovascular decompensation.
**Monitoring:** The following are recommended

1) Internal jugular cordis and pulmonary artery catheter.
2) Femoral arterial catheter is placed because of prolonged hypothermic CPB; the radial artery catheter significantly underestimates systemic pressures in the post CPB period.
3) Intraoperative TEE is valuable in monitoring and assessing cardiac function during PTE.
4) Processed encephalogram is monitored throughout the procedure. This allows confirmation of isoelectric EEG. Cerebral oximetry is also used.
5) Temperature monitoring is measured via urinary catheter and rectal probe for core temperatures estimation. Tympanic membrane probe is used for estimation of brain temperature.
6) PAC measures blood temperature, allowing quantification of thermal gradients.
7) Be prepared for DHCA (EEG monitoring, head cooling, pharmacologic interventions to decrease cerebral metabolic activity, steroids)

**Signs of impending decompensation include:**

a. RV end diastolic pressure > 14 mm Hg
b. Severe tricuspid regurgitation
c. PVR > 1000 dynes/sec/cm^5

**Surgical Approach and Initiating CPB:** After median sternotomy, CBP is established with venous bicaval cannulation (inferior and superior vena cava) and aortic cannulation. DHCA is initiated and the patient is cooled to a core temperature of 20°C and a tympanic temp of 15°C with cooling blanket around the head. Circulatory arrest is achieved and an isoelectric EEG should be achieved during endarterectomy of each pulmonary artery. Rewarming is required, and generally takes 90-120 minutes to achieve core temperature of 36.5°C. The process of separation from CPB is similar to other surgeries involving CPB. Keep in mind that end-tidal carbon dioxide is a poor measure of ventilation adequacy in these patients both before and after CPB, because dead space ventilation is an integral part of the disease.

**Post cardiopulmonary Bypass Period:** Reperfusion pulmonary edema can occur usually presenting as frothy sputum. If frothy sputum arises, the ETT should be suctioned and increasing amounts of PEEP applied. If frank blood, not frothy sputum, is returning from the endotracheal tube, surgical bleeding is the probable cause. If severe bleeding persists, fiberoptic bronchoscopy should be used to evaluate the source of bleeding. Lung isolation should be considered.
Treatment for pulmonary hypertension.
The goals of treatment for pHTN are to lower pulmonary artery pressure and normalize cardiac output as early in the disease process as possible before right ventricular failure ensues.

Anesthetic management of individuals with PAH undergoing cardiac or general surgery is challenging because perioperative increases in PVR readily occur and may provoke right-sided heart failure, resulting in death. The intolerance of the RV to these sudden increases in PVR is a major concern and should always be in the forefront of providers’ considerations.

In general, intravenous anesthetics have less effect on hypoxic pulmonary vasoconstriction, PVR, and oxygenation than do volatile agents. Nitrous oxide has been reported to increase PVR, but it is not an absolute contraindication in these patients. Isoflurane may be beneficial by decreasing PAP and has been frequently used during noncardiac procedures. Fentanyl may be given as an adjunct or a primary anesthetic agent in these patients because it causes little myocardial depression and excellent circulatory stability.
References: