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Pulmonary thromboendarterectomy in patients with chronic thromboembolic pulmonary hypertension and hemoglobinopathies

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TO THE EDITOR:

We report two cases of patients with sickle cell disease (SCD) and chronic thromboembolic pulmonary hypertension (CTEPH) who underwent pulmonary thromboendarterectomy (PTE), highlighting the scarcity of such cases in Brazil and the special care required during the perioperative period.

Patient 1 was a 38-year-old man with a diagnosis of CTEPH and SCD (homozygous hemoglobin SS) who had a history of recurrent vaso-occlusive crises and was being followed at the Pulmonary Circulation Outpatient Clinic of the Federal University of Minas Gerais *Hospital das Clínicas*, located in the city of Belo Horizonte, Brazil. The patient had been referred to *Hospital Madre Teresa*, located in the same city, with a complaint of progressive dyspnea—World Health Organization Functional Class (WHO-FC) IV—having been receiving anticoagulation with warfarin for 1 year and having been taking tadalafil for 1 month; he had previously been evaluated at that facility with a view to undergoing PTE. On admission, the patient was pale and had increased jugular venous pressure, peripheral cyanosis, mild leg edema, and tachypnea. Physical examination revealed the following: HR = 75 bpm; blood pressure (BP) = 103/60 mmHg; RR = 28 breaths/min; and room-air SpO_2 = 90%. Lung auscultation revealed fine infrascapular crackles. Cardiac auscultation revealed a regular cardiac rhythm with normal heart sounds, accentuation of the second heart sound in its pulmonic component, and no murmurs. His abdomen was painless, and he had hepatomegaly without ascites. After cardiac dysfunction was stabilized, he was reevaluated with a view to undergoing PTE. Previous CT angiography of the chest had shown an extensive filling defect in the lobar, segmental, and subsegmental branches of the right lower lobe, as well as intraluminal filling defects in the anterior segment of the right upper lobe and in the apical posterior segment of the left upper lobe. Ventilation-perfusion lung scintigraphy revealed multiple, bilaterally distributed areas of segmental hypoperfusion, a bilateral parenchymal lung process (probably a sequela of tuberculosis), and an increased cardiac silhouette. An echocardiogram showed that the left ventricle dimensions and contractile function were preserved; the right ventricle dimensions were markedly increased, the ventricle measuring 50 mm in its maximum diastolic diameter, with signs of myocardial hypertrophy and reduced contractility throughout the ventricular wall; the right and left atria were moderately and mildly increased, respectively; tricuspid regurgitation was moderate, with a tricuspid regurgitant jet velocity of 4.87 m/s; and the estimated pulmonary artery systolic pressure was 115 mmHg. Right heart catheterization (RHC) revealed the following: mean pulmonary artery pressure (mPAP) = 42 mmHg; pulmonary artery wedge pressure (PAWP) = 6 mmHg; pulmonary vascular resistance (PVR) = 456.0 dyn/s/cm^{-5}; and cardiac index (CI) = 3.32 L/min/m^2. Pulmonary angiography revealed hypoperfusion of the upper, middle, and lower lobes of the right lung, together with occlusion of a right lower lobe segmental artery. As preoperative preparation, the patient received six exchange transfusions, and his hemoglobin S (HbS) level reached 36% (vs. 68.1% at baseline). The intraoperative period was uneventful. In the postoperative period, the patient had an undefined focus of infection, the size of which was reduced with the use of antibiotics. He was discharged on day 21, without the need for oxygen supplementation. Three months after PTE, the patient was asymptomatic (WHO-FC I). An RHC revealed the following: mPAP = 24 mmHg; PVR = 269.6 dyn/s/cm^{-5}; and CI = 3.22 L/min/m^2 (Table 1). In addition, the six-minute walk distance (6MWD) was 500 m, the SpO_2 decreased from 91% to 85%, and the HR increased from 82 bpm to 128 bpm.

Patient 2 was a 53-year-old woman with SCD (heterozygous hemoglobin SC) and a self-reported one-month history of progressively worsening dyspnea (WHO-FC II) who was diagnosed with acute pulmonary thromboembolism. Having been receiving anticoagulation with warfarin for 5 months, the patient experienced worsening of dyspnea (WHO-FC IV) and had episodes of syncope. On admission to the Pulmonary Circulation Outpatient Clinic of *Hospital Júlia Kubistchek*, located in Belo Horizonte, for evaluation of her condition, she was WHO-FC IV, was acyanotic, had ankle edema, and was intolerant of the supine position. Her vital signs were as follows: HR = 98 bpm; BP = 100/60 mmHg; RR = 26 breaths/min; and room-air SpO_2 = 89%. Her breath sounds were normal, and there was an accentuated second heart sound. An echocardiogram showed that the left ventricle dimensions and systolic function were preserved; the right ventricle measured 37 mm in its maximum diastolic diameter, with normal contraction; tricuspid

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Table 1. Patient hemodynamic results before and after pulmonary thromboendarterectomy.

Patient	Preoperative period (RHC)				Immediate postoperative period (SG)				Late postoperative period (RHC)			
	PAP(m)	CI	PVR	CO	mPAP	CI	PVR	CO	PAP(m)	CI	PVR	CO
	mmHg	L/min/m^2	dyn/s/cm^{-5}	L/min (Fick)	mmHg	L/min/m^2	dyn/s/cm^{-5}	L/min (thermodilution)	mmHg	L/min/m^2	dyn/s/cm^{-5}	L/min (Fick)
1	70/28 (42)	3.32	456	6.32	27	4.65	145	8.28	46/13 (24)	3.22	269.6	5.94
2	100/25 (50)	2.02	1,010.4	3.33	30	3.09	301	5.49	38/15 (22)	2.05	284.0	4.51

RHC: right heart catheterization; SG: Swan-Ganz; PAP: pulmonary artery pressure; (m): mean; CI: cardiac index; PVR: pulmonary vascular resistance; CO: cardiac output; and mPAP: mean pulmonary artery pressure.

regurgitation was mild; tricuspid regurgitant jet velocity was 4.22 m/s; and the estimated pulmonary artery systolic pressure was 81 mmHg. Chest CT angiography showed that there was a thrombus in the right lower lobe artery; the main pulmonary artery measured 34 mm; there were areas of mosaic attenuation in both lungs; and bronchiectasis and bronchiolectasis were present in the basal lung segments, being accompanied by fibroatelectatic striae. Ventilation-perfusion lung scintigraphy revealed absence of right-lung perfusion in the upper lobe, middle lobe, and anterior basal segment of the lower lobe and absence of left-lung perfusion in the posterior apical portion of the upper lobe. An RHC revealed the following: mPAP = 50 mmHg; PAWP = 8 mmHg; PVR = 1,010.4 dyn/s/cm^{-5}; and CI = 2.02 L/min/m^2. Pulmonary angiography revealed moderate hypoperfusion of the right upper lobe and mild hypoperfusion of the right lower lobe. The 6MWD (with supplemental oxygen) was 278 m; the SpO_2 decreased from 98% to 92%; and the HR increased from 95 bpm to 124 bpm. After a diagnosis of CTEPH was established, the patient was started on bosentan and tadalafil. At the outpatient clinic, the patient was evaluated with a view to undergoing PTE, being referred to the *Hospital Madre Teresa* for the procedure. As preoperative preparation, the patient received four exchange transfusions, and her HbS level reached 16.6% (vs. 46.5% at baseline). The intraoperative period was uneventful. At 3 months after surgery, she was asymptomatic (WHO-FC I). Another RHC showed the following: mPAP = 22 mmHg, PVR = 284 dyn/s/cm^{-5}, and CI = 2.05 L/min/m^2 (Table 1); 6MWD = 465 m; SpO_2 increased from 94% to 97%; and HR increased from 70 bpm to 100 bpm.

As described in the literature,[1-3] CTEPH is characterized by the presence of organized thrombi in the pulmonary arteries after at least three months of full anticoagulation, accompanied by an mPAP > 20 mmHg, a PAWP ≤ 15 mmHg, and a PVR > 3 Woods Units or 240 dyn/s/cm^{-5}, with at least one perfusion defect detected by lung scintigraphy or chest CT angiography. CTEPH and SCD comorbidity has a prevalence of 6-11% and is one of the causes of death in such patients. The pathophysiology of CTEPH in SCD involves factors such as sickling, hemolysis, endothelial inflammation and dysfunction, hypercoagulability, and pulmonary artery thrombosis.[4]

Patients with SCD who are candidates for anesthetic and surgical procedures require special care, given the occurrence of hypoxia, metabolic or respiratory acidosis, hypothermia, infections, and hypovolemia, all of which are associated with surgical trauma. Increased sickling and increased vaso-occlusive crises are common. Patients with SCD can also experience acute chest syndrome, pain crises, priapism, and stroke. Therefore, appropriate preoperative preparation is crucial, and the surgical team should include a hematologist.[5-7]

Studies on the treatment of CTEPH in patients with SCD are scarce. Strategies for treating such patients include optimizing disease treatment and identifying potentially modifiable etiologies. One treatment option, for selected patients, is PTE, which can produce satisfactory outcomes if there is appropriate patient preparation to minimize the effects of cardiopulmonary bypass, hypothermia, and periods of total circulatory arrest that increase the risk of sickling.[3] It has been suggested that HbS levels be maintained between 30% and 10% through exchange transfusions.[5,7] However, there is a risk of recurrent or persistent pulmonary hypertension due to proliferative pulmonary arteriopathy secondary to chronic hemolysis. In addition, there may be *in situ* proximal pulmonary thrombosis, which is difficult to differentiate from new thromboembolic events in the differential diagnosis.[6]

Chief among the largest studies on the treatment of CTEPH in patients with hemoglobinopathies is the study carried out by Mahesh et al.[3] at Papworth Hospital in the United Kingdom. In that study, 19 patients with hemoglobinopathies/hemolytic anemia and CTEPH were retrospectively evaluated regarding treatment with PTE. In that case series, it was decided that HbS levels would be reduced to ≤ 20% through the use of partial exchange transfusions preoperatively and immediately before cardiopulmonary bypass. These measures resulted in significant improvements in PVR, as well as in recovery of FC and 6MWD in the late postoperative period.[3]

In conclusion, PTE is a feasible treatment option for patients with SCD and CTEPH. Given the complexity of the underlying disease and of the surgical treatment, procedures should be performed at facilities that are referral centers for CTEPH and have experience in PTE. Under those conditions, satisfactory outcomes can be achieved.

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