A 19-Year-Old Pregnant Woman With Pulmonary Hypertension With Progressive Dyspnea

Burcak Kilickiran Avci, MD; Ozge Ozden Tok, MD; Afksendiyos Kalangos, MD; Tijen Alkan Bozkaya, MD; and Zeki Ongen, MD

CASE PRESENTATION: A 19-year-old pregnant woman at week 32 of gestation was referred to our clinic with progressive shortness of breath for the further evaluation and treatment of high-risk pregnancy. Her complaints had been existing since her childhood. Two years prior to her admission, she had been diagnosed with heart failure with preserved ejection fraction due to cardiomyopathy and associated pulmonary hypertension. The patient had no family history of any cardiac disease. She had never smoked or drunk alcohol. Her clinical condition had deteriorated progressively with the pregnancy. CHEST 2021; 159(6):e371-e375

Physical Examination Findings

On admission, the patient was afebrile with a heart rate of 96 beats/min, BP 100/60 mm Hg, respiratory rate 18 breaths/min, and saturation 94% on room air. She had a World Health Organization (WHO) functional class IV (FC IV) dyspnea. Physical examination showed distended jugular veins, regular cardiac rate and rhythm with a 2/6 holosystolic murmur on the tricuspid area, minimal crackle at the basal lung areas, mild edema, and no clubbing or cyanosis.

Diagnostic Studies

Results of a complete blood count revealed a mild iron deficiency anemia (hemoglobin level, 10.3 g/dL). Renal, hepatic, and thyroid functions were normal; proBNP levels were elevated (508 pg/mL). ECG showed a normal sinus rhythm with left atrial enlargement.

Transthoracic echocardiography (TTE) revealed preserved left ventricle (LV) ejection fraction (60%), grade-3 diastolic dysfunction, and increased right ventricular systolic pressure (RVSP) of 90 mm Hg with enlarged right heart chambers, left atrium, and hypertrophied right ventricle free wall. Only mild mitral regurgitation was appreciated. Venous Doppler ultrasound scans of the bilateral legs were normal. A bedside right heart catheterization (RHC) demonstrated a combined pre-post-capillary PH; right atrial pressure was 11 mm Hg; pulmonary artery (PA) pressure was 100/50 mm Hg with a mean PA pressure of 70 mm Hg; PA wedge pressure was 33 mm Hg; cardiac index was 2.6 L/min/m^2, and a calculated pulmonary vascular resistance was 5.4 Wood units. Step-up of oxygen saturation from 62% at the right ventricle (RV) to 70% at the main PA in the absence of a significant shunt ratio (pulmonary to systemic flow ratio: 1.2) was detected. Because of the safety concern during pregnancy, further evaluation with an invasive or CT angiogram was postponed to the postpartum period.

She was started on metoprolol (50 mg) and IV furosemide (20 mg). Whenever the dose of diuretic up-

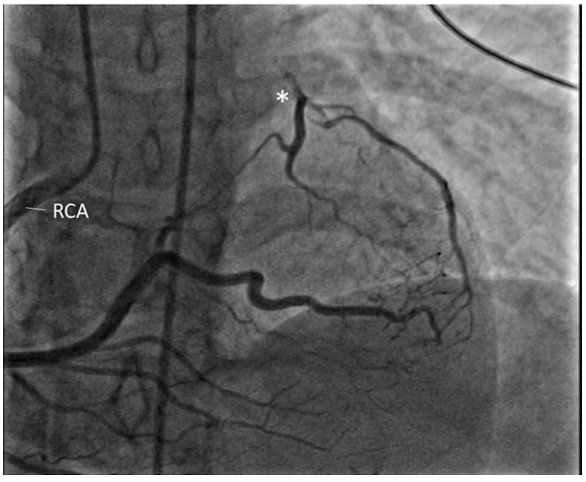


Figure 1 – *Coronary angiography reveals a normal origin of right coronary artery from the aorta and collateral circulation to the left coronary (*). RCA = right coronary artery.*

titrated, chest pain and sometimes hypotension occurred, and her condition deteriorated. She received followed up under low-dose diuretic (maximum, 40 mg) therapy until birth, which resulted in a limited reduction of RVSP from 90 to 70 mm Hg by TTE.

Delivery by cesarean-section was uneventful. She was experiencing angina with a gradually increasing frequency at postpartum period with no troponin increase. A mild decrease in left ventricular ejection fraction (LVEF) (48%) was detected on control TTE. No additional findings were detected on transesophageal echocardiography. $\dot{V}/\dot{Q}$ lung scan was normal.

A second RHC at the postpartum period was consistent with the prepartum period, except without oxygen step-up in the PA. Coronary angiogram showed a dominant right coronary artery (RCA) supplying left coronary system with collateral circulation (Fig 1). Left main coronary artery (LMCA) could not be visualized in the aortic root.

What is the diagnosis?

Answer: Anomalous origin of the left coronary artery from the PA (ALCAPA)–Bland-White-Garland syndrome related group 2-PH

Discussion

Left heart disease is the most common cause of PH. These patients are classified under group-2 according to WHO-PH classification. Group 2 is further subclassified into those associated with heart failure with reduced ejection fraction (HFrEF), HFpEF, valvular heart disease, and congenital post-capillary obstructive lesions. Multiple underlying causes may result in HFrEF or HFpEF. Systematic and meticulous evaluation and imaging are needed to find the exact cause and pathophysiologic mechanisms.

Having said that, routine coronary or CT angiography is included in neither current PH nor heart failure guidelines diagnostic algorithms, especially in young patients without atherosclerotic risk factors. However, this can lead to overlook of some congenital coronary anomalies such as ALCAPA that can lead to heart failure and associated PH. This challenge may be overcome by routine stepwise assessment of oxygen saturation for the possible shunt detection during RHC for the diagnosis of PH. Nevertheless, congenital coronary anomalies have not been defined separately or underlined in WHO-PH classification scheme. Clinical suspicion and detailed history can change these patients' outcomes remarkably.

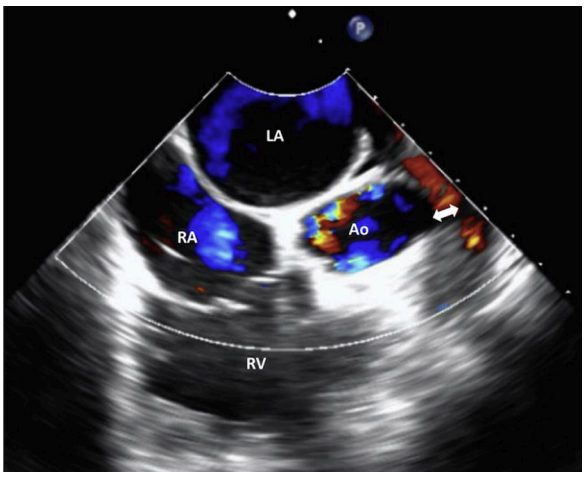


Figure 2 – *Short axis of the aortic root by color Doppler transesophageal echocardiography shows the illusion of a normal left main coronary artery origin (double-sided arrow). Ao = aorta; LA = left atrium; RA = right atrium; RV = right ventricle.*

ALCAPA is a rare congenital condition that generally presents in infancy. The presence or absence of intercoronary collateral circulation from the RCA to the left coronary system distinguishes between the two clinical types of ALCAPA: infancy and adulthood. Most of the infants present with dilated cardiomyopathy secondary to ischemia within a few months after birth. Regrettably, without early surgical correction, it is fatal commonly in the first years of life. Patients with an adequate collateral circulation can remain asymptomatic until adulthood or may present with angina, dyspnea, or palpitation. Various clinical presentations, such as HFpEF or HFrEF, mitral regurgitation, sudden cardiac death, and ventricular arrhythmia, and rarely PH could be seen.

Chronic myocardial ischemia is the main problem in patients with ALCAPA. In addition, retrograde flow from the high-pressure coronary system to the low-pressure pulmonary system causes loss of perfusion pressure in coronary arteries and results in extensive ischemia, so-called "coronary steal syndrome." Ischemia results in impaired LV diastolic function, reduced LVEF, LV dilatation, and mitral regurgitation, all of which can consequently lead to PH. Unlike the LV, RV myocardium is possibly less prone to ischemic injury as coronary perfusion continues throughout the entire cardiac cycle in the RCA, and RV has a lower oxygen demand. However, with the development of PH, an increase in RV pressure overload and RV mass cause a reduction in RCA flow in systole and a greater oxygen requirement; therefore, RV may become more susceptible to ischemia.

Diagnosis of ALCAPA could be challenging. Color-flow Doppler echocardiography can demonstrate the anomalous origin and retrograde flow in the LMCA. However, without clinical suspicion and optimal imaging quality, it could be overlooked easily. Also, it is well-recognized that echocardiography can suggest a normal origin of left coronary artery from the aortic root in ALCAPA (Fig 2). CT and/or invasive angiography are the other methods of choice that could show the anomaly and collaterals directly.

At RHC, a step-up in oxygen saturation of ≥5% at the main PA compared with the RV indicate a shunt at the great vessel level. Because shunt presence depends on the pressure difference between the pulmonary and coronary arteries, an increase in pulmonary pressures is

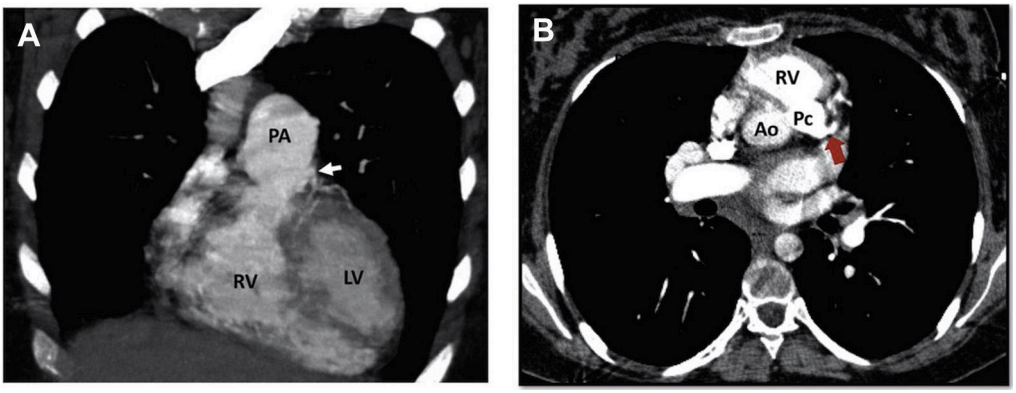


Figure 3 – *A-B, Multislice CT shows the origin of the left main coronary artery from main pulmonary artery (white and red arrows, respectively). Ao = aorta; LV, left ventricle; PA = pulmonary artery; Pc = pulmonary conus; RV = right ventricle.*

associated with antegrade LMCA flow, which can mask the coronary steal. Still, significant changes in hemodynamic conditions, such as pregnancy, may lead to retrograde flow to PA. Especially in the third trimester of pregnancy, both increased volume load and cardiac mass lead to increased myocardial wall stress that may increase coronary vascular resistance markedly and cause shunting to the PA, even in the presence of severe PH.

The treatment in adults is surgical reimplantation of the LMCA into the aorta or placement of a coronary bypass graft and ligation of the origin of the LMCA. To improve the symptoms of the patient and to prepare the patient for surgery, treatment strategy may include anticongestive therapy. However, this treatment should be given extremely cautiously in patients with severe PH. Because lowering the pressure in the PA may switch the antegrade flow in LMCA in the opposite direction, it will lead to coronary steal and typical angina.

Reimplantation/revascularization of the anomalous artery provides a reliable oxygenated flow to the myocardium. However, various case reports in the literature have demonstrated that, despite significant symptomatic and hemodynamic improvements after surgery, some patients may experience arrhythmia, persistent mitral regurgitation, LV dysfunction, or sudden death on the long-term follow up. Persistent perfusion defects could also be detected.

Clinical Course

A CT angiogram revealed an anomalous LMCA that originated from the posterior aspect of the dilated main PA (Fig 3). Surgical coronary artery root reimplantation was performed by experienced cardiovascular surgeons. After surgery, angina resolved dramatically. Furosemide dose could be titrated up to 320 mg/d, and spironolactone 50 mg/d was added to the treatment with no concomitant hypotension and angina. The exercise capacity of the patient increased gradually during the following long-term period. Seven months after the surgery, she was WHO-FC II and the 6-minute walk distance was 420 m. The left atrium and right heart chamber dimensions and RVSP (38 mm Hg) were decreased, and LVEF increased to 52% on TTE. A small ischemic area in the distal left anterior descending territory (anteroapical segment) was detected on follow-up single photon emission CT images. Ten months after surgery, catheterization was performed; a marked decrease in right atrial pressure (4 mm Hg), mean PA

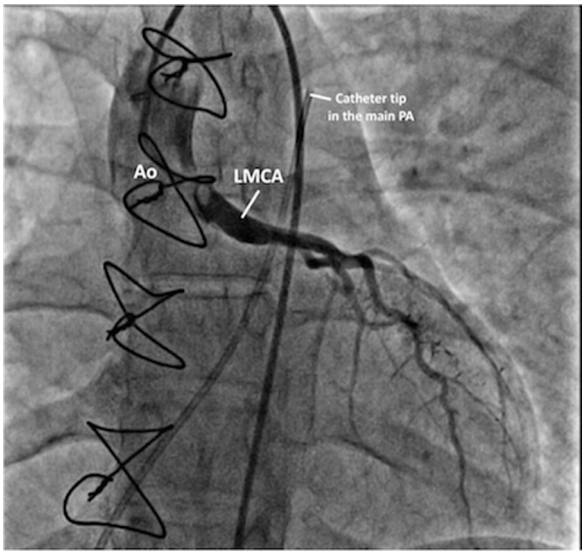


Figure 4 – *Postoperative coronary angiography shows the origin of the left main coronary artery from the aorta. Ao = aorta; LMCA = left main coronary artery; PA = pulmonary artery.*

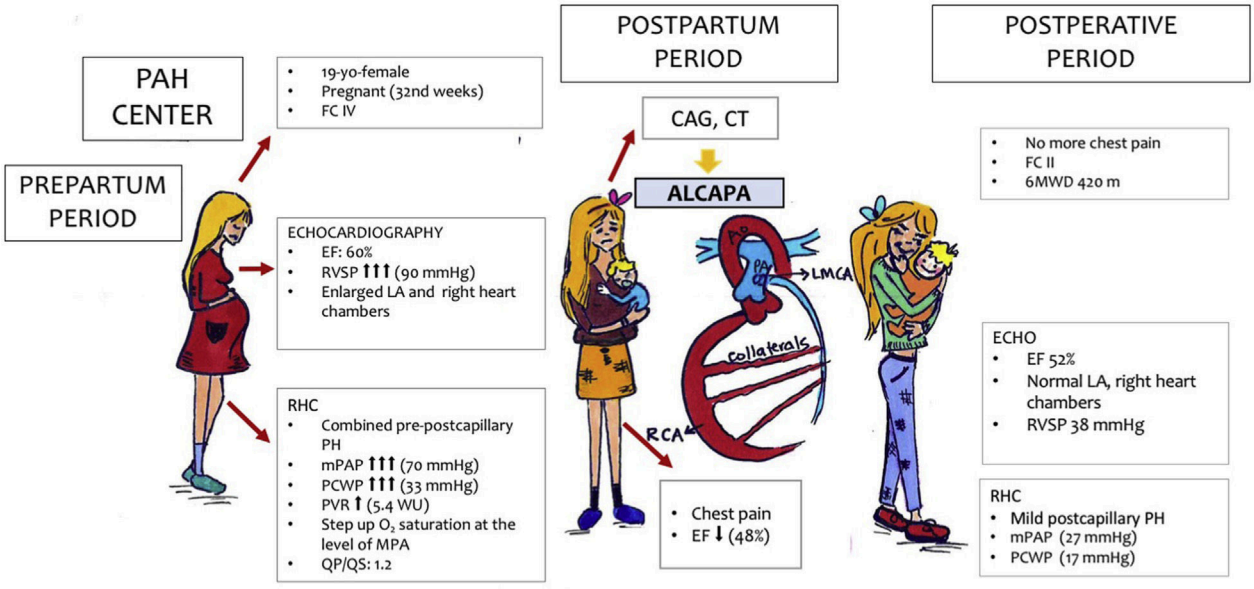


Figure 5 – *An illustrated summary of the case. 6MWD = 6-minute walk distance; ALCAPA = anomalous origin of the left coronary artery from the pulmonary artery; CAG = coronary angiography; EF = ejection fraction; FC = functional capacity; LA = left atrium; MAP = main pulmonary artery; mPAP = mean pulmonary artery pressure; O_2 = oxygen; PAH = pulmonary arterial hypertension; PCWP = pulmonary capillary wedge pressure; PH = pulmonary hypertension; PVR = pulmonary vascular resistance; QP/QS = pulmonary to systemic flow ratio; RHC = right heart catheterization; RVSP = right ventricle systolic pressure; WU = Wood unit.*

pressure (27 mm Hg), PA wedge pressure (17 mm Hg), and calculated pulmonary vascular resistance (1.9 Wood units) were found. Coronary angiography showed a normal antegrade flow from the reimplanted LMCA without any kinking or stenosis (Fig 4). An illustrated summary of the case is given in Figure 5.

Clinical Pearls

1. *PH can emerge in association with various diseases. The cornerstone of treatment of PH is to find the exact cause with detailed clinical assessment, the proper use of multimodality cardiac imaging, and heart catheterization.*
2. *In a patient with a group 2 PH, although rare, ALCAPA should also be considered in differential diagnosis.*
3. *ALCAPA could be unnoticed on echocardiography and, unless suspected, could not be detected on standard RHC as well. The definitive diagnosis is made by CT or invasive coronary angiography.*
4. *Surgery is the only definitive treatment choice in ALCAPA, regardless of the severity of PH.*
5. *Persistent abnormalities in cardiac function could still be detected after surgery. Continued long-term follow up is necessary.*

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Suggested Readings

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