MINI-FOCUS ISSUE: CONGENITAL HEART DISEASE

INTERMEDIATE

CASE REPORT: CLINICAL CASE

To Be or Not to Be Eisenmenger

The Different Shades of Blue

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ABSTRACT

Eisenmenger syndrome refers to any untreated congenital cardiac defect with an intracardiac communication that leads to pulmonary arterial hypertension, reversal of intracardiac shunting, and cyanosis. We describe a 40-year-old cyanotic patient with congenital heart disease with presumed Eisenmenger syndrome who was considered inoperable. Testing revealed a partial atrioventricular septal defect with no evidence of pulmonary arterial hypertension, and the patient underwent successful cardiac repair. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:230–5) Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

A 40-year-old man from Bangladesh with chronic cyanosis presented with atypical, left-sided, nonexertional chest pain and palpitations with reduced exercise tolerance. Family history was unremarkable. Physical examination revealed a cyanotic man with a repaired cleft lip. His blood pressure was 119/76 mm Hg, his respiratory rate was 20 breaths/min, and the systemic oxygen saturation was 82% on room air. The jugular venous pressure was measured at 4 cm above the sternal angle. The pulmonic component of the second heart sound was prominent. A 3/6 high-pitched holosystolic murmur and a 2/6 diastolic murmur were heard at the left sternal border. Both lung fields were clear to auscultation. Grade 5 digital clubbing (**Figure 1**) was noted on all extremities. Supplemental oxygen did not change his oxygen saturation levels. As a child, he was deemed inoperable.

LEARNING OBJECTIVES

- To understand the presence of atrial level shunting in the presence of normal intracardiac and pulmonary pressures.
- To understand the hemodynamics of intracardiac shunts in patients with congenital heart disease.

MEDICAL HISTORY

The patient's medical history included hyperlipidemia.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included Eisenmenger syndrome (ES) and cyanotic congenital heart disease.

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FIGURE 1 Upper Extremity Grade 5 Digital Clubbing
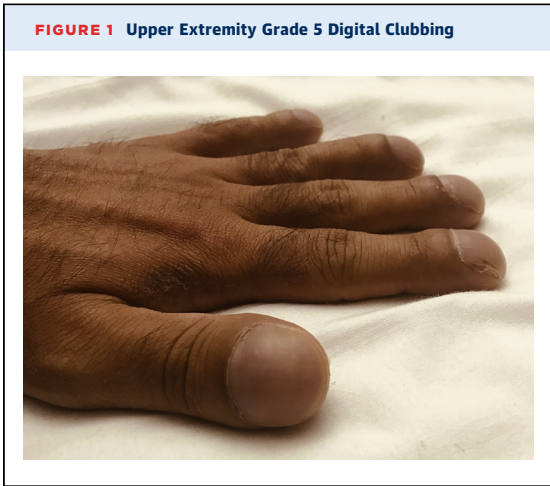
INVESTIGATIONS

Initial laboratory work revealed polycythemia and hyperkalemia (**Table 1**), consistent with mild hemolysis. An electrocardiogram (**Figure 2**) showed sinus rhythm with first degree atrioventricular block, right bundle branch block, and biatrial enlargement with biventricular hypertrophy. A chest x-ray film (**Figure 3**) showed cardiomegaly with a flask-shaped cardiac silhouette. A transthoracic echocardiogram (**Figures 4A and 4B**, Videos 1 to 4) showed normal segmental anatomy. He had a partial atrioventricular septal defect, unbalanced to the left (inflow into the systemic left ventricle [LV]). The right ventricle (RV)

was moderately hypoplastic with normal systolic function. The atrioventricular valves had attachments to the crest of the ventricular septum. A small ventricular septal defect was visualized but not well defined. The left atrioventricular valve was hypoplastic with an annulus dimension of 1.88 cm (z-score of –2.9). He had a large ostium primum atrial septal defect (ASD) with a near common atrium. There was a cleft mitral valve with mild to moderate left atrioventricular valve regurgitation. The LV ejection fraction was estimated at 45%. The LV outflow tract was elongated and unobstructed. There was mild tricuspid valve regurgitation. The pulmonary valve was anterior to the aortic valve without stenosis or regurgitation, and the aortic root was dilated. The right superior vena cava (SVC) drained into the right atrium (RA). A left SVC was seen draining into an unroofed coronary sinus. The inferior vena cava (IVC) was dilated and entering normally into the RA. The pulmonary veins were not well defined.
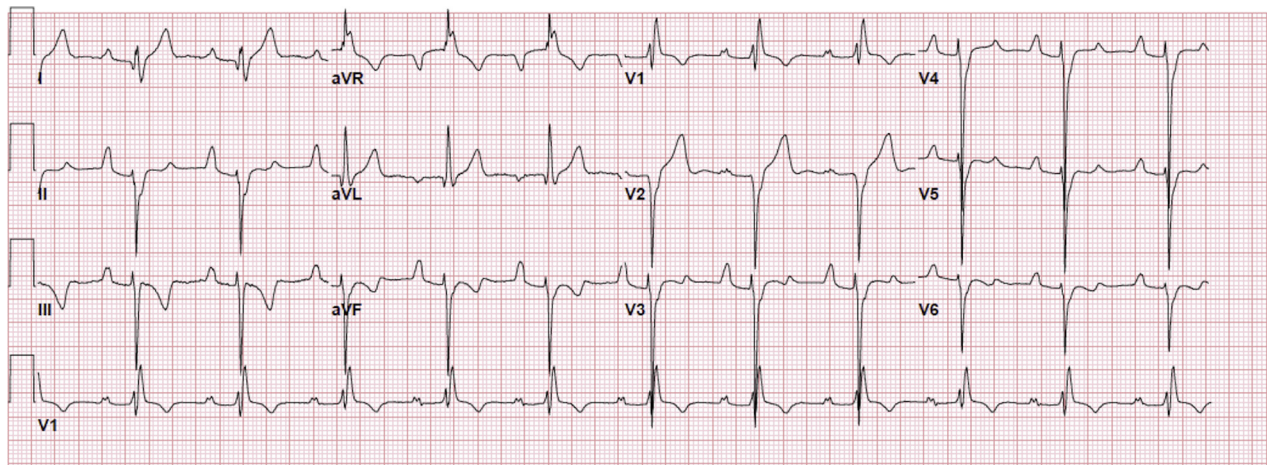
Cardiac magnetic resonance (**Figure 5**) showed a partial atrioventricular septal defect with a large ostium primum ASD and atrioventricular valves on the same plane. The left atrioventricular valve was committed to the inflow of the LV and attached to the crest of the ventricular septum. A small membranous ventricular septal defect could not be excluded. The RV was hypoplastic with preserved systolic function (RV end-diastolic volume index: 56 ml/m²; right ventricular ejection fraction: 48%). The anterior leaflet of the left atrioventricular valve had a cleft with partial prolapse and mild regurgitation. The RA was severely enlarged. There was a functionally bicuspid aortic valve with fusion of the right coronary and noncoronary cusps. Mild aortic regurgitation was noted. The ascending thoracic aorta was enlarged, measuring 4.6 cm at the level of the main pulmonary artery. The aortic root was dilated at the level of the sinuses of Valsalva, measuring 4.3 cm. The right SVC drained into the right-sided common atrium. The left SVC drained into an unroofed coronary sinus.

MANAGEMENT

The right heart catheterization (**Table 2**) performed revealed normal pulmonary pressures with normal pulmonary vascular resistance (PVR), negating the possibility of Eisenmenger syndrome. Bilateral aortopulmonary collaterals were embolized. The patient underwent successful surgery, involving multiple intraoperative steps, leading to 2-ventricular repair (**Figure 6**, Video 5). The presence of bilateral SVC with

ABBREVIATIONS AND ACRONYMS

ASD = atrial septal defect

ES = Eisenmenger syndrome

LA = left atrium

LV = left ventricle

PA = pulmonary artery

PVR = pulmonary vascular resistance

RA = right atrium

RV = right ventricle

SVC = superior vena cava

TABLE 1 Initial Laboratory Test Values

Laboratory Test	Result	Reference Range
Hemoglobin, g/dl	19.8	13.9-16.3
Hematocrit, %	62.1	429-52
BNP, pg/ml	<10	<100
INR	1.0	0.89-1.20
Troponin I, ng/ml	<0.01	0.009-0.030
Sodium, mEq/l	136	1,359-145
Potassium, mEq/l	5.5	3.59-5.20
Chloride, mEq/l	105	969-108
CO₂, mEq/l	19.7	22.09-30.00
Urea nitrogen, mg/dl	8	69-23
Creatinine, mg/dl	0.52	0.709-1.300
AST, U/l	38	19-35
ALT, U/l	28	19-45
ALK phosphatase, U/l	81	389-126
Bilirubin total, mg/dl	1.5	0.19-1.20
Bilirubin direct, mg/dl	0.4	0.09-0.80

ALK = alkaline; ALT = alanine transaminase; AST = aspartate aminotransferase; BNP = brain natriuretic peptide; CO₂ = carbon dioxide; INR = international normalized ratio.

FIGURE 2   Electrocardiogram

the left SVC draining to the unroofed coronary sinus added complexity to the atrial baffle repair. The key to creating an adequate baffle was for atrial septation to allow for unobstructed pulmonary vein flow into the new left atrium (LA) and for the left SVC coronary sinus complex to drain into the new RA (**Figure 7**, Video 6). Ligation and division of the left SVC allowed for moving the baffle higher to include the coronary sinus complex to drain into the LA (a small but obligatory right-to-left shunt). In the absence of a

**FIGURE 3   Chest Radiograph (Posteroanterior Image)**

bridging vein, it was redirected to the RA, which required a Gore-Tex graft (W.L. Gore and Associates, Newark, Delaware). The adequacy of the tricuspid valve and the RV were the most vulnerable aspects of the surgery in this patient. With a marginal tricuspid valve and hypoplastic RV, a small ASD (right-to-left shunt) was left to provide LV preload and adequate cardiac output if clinically needed. Performing a bidirectional Glenn is an alternative, but the pulmonary artery (PA) pressures need to be low (mean pulmonary artery pressure of <15 mm Hg) for this physiology to be successful. A modified biatrial cryomaze operation was performed along with left atrial appendage exclusion. The post-operative course was complicated by a short period of hemodynamic instability requiring vasopressor support and atrial fibrillation, which was treated with amiodarone and anticoagulation. The patient was discharged in stable condition, with oxygen saturations of 96% on room air.

DISCUSSION

Patients may rarely present with chronic unexplained hypoxemia. The common causes of hypoxemia are shunts (intracardiac and extracardiac) and ventilation-perfusion mismatch within the lung (1). Less common causes include hypoventilation, low inspired oxygen concentration, impaired pulmonary oxygen diffusion, and inadequate replenishment of a systemic oxygen debt, leading to low mixed venous saturation and subsequent arterial hypoxemia (1). In the absence of pulmonary hypertension, the typical shunting in ASDs is overwhelmingly left to right. Shunting is usually distinguished from ventilation-

FIGURE 4 Pre-Operative Transthoracic Echocardiogram
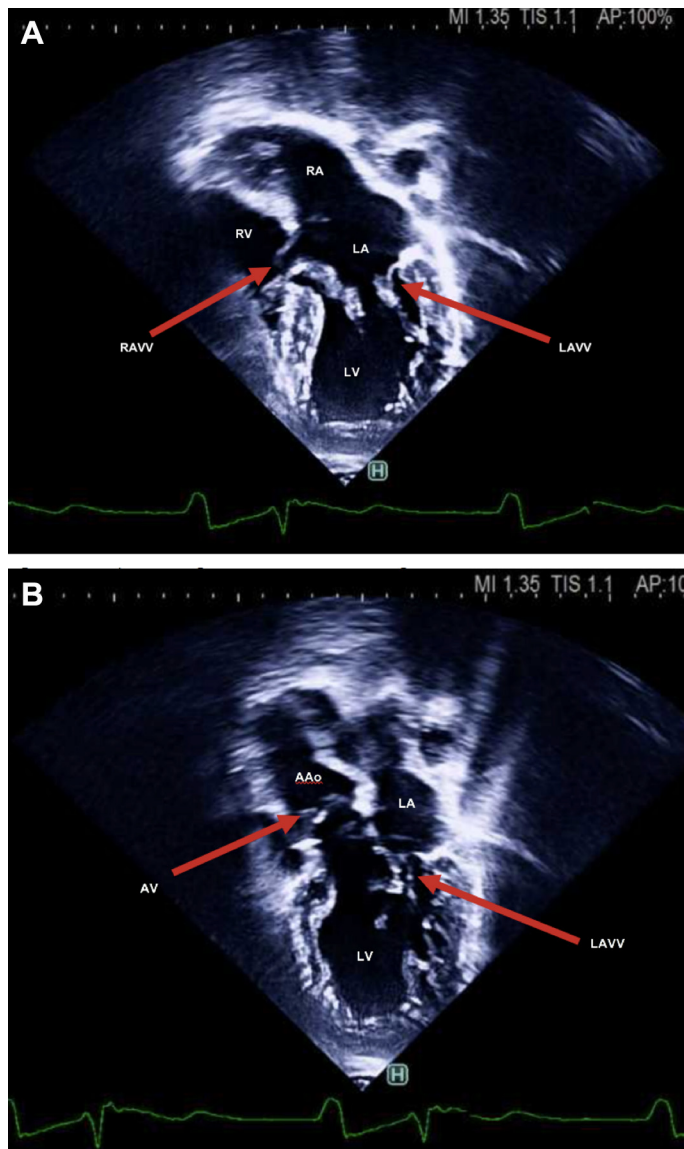
(A) Pre-operative transthoracic echocardiogram: 4-chamber apical view. **(B)** Pre-operative transthoracic echocardiogram: 3-chamber left ventricle (LV) outflow tract view. AAo = ascending aorta; AV = aortic valve abbreviations; LA = left atrium; LAVV = left atrioventricular valve; RA = right atrium; RAVV = right atrioventricular valve; RV = right ventricle.

perfusion mismatch by the inability of supplemental oxygen to improve arterial oxygenation and lessen the alveolar-arterial oxygen gradient. Patients with shunts exhibit inadequate improvement in arterial oxygen saturation following supplemental oxygen. Our patient had right-to-left shunting in the presence of normal PA and intracardiac pressures. Several hypotheses may explain why right-to-left shunting occurs in such patients, including a "flow phenomenon," with preferential flow from the IVC directly through the ASD into the left atrial chamber. This can also occur due to a decrease in RV compliance, which may occur with RV ischemia or infarction or be due to a hypoplastic RV, as seen in this patient. Rarely, such right-to-left shunting in the absence of pulmonary hypertension can be due to the accentuation or reversal of interatrial gradients seen with the normal respiratory cycle or with Valsalva maneuvers (2,3). The orientation of the atrial septum in some patients to the horizontal axis

FIGURE 5 Pre-Operative Cardiac Magnetic Resonance: Steady-State Free Precession Axial Slice Showing Underlying Cardiac Anatomy
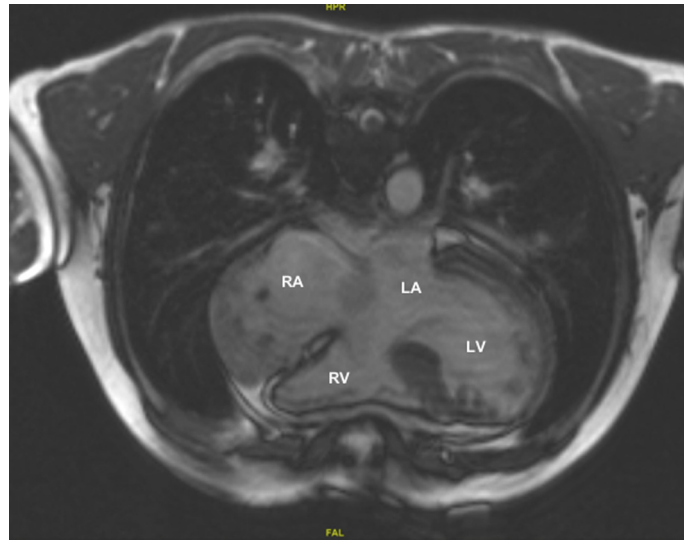
Abbreviations as in **Figure 4**.

may also result in this preferential right-to-left blood flow across the atrial septum ([4]).

ES is diagnosed in the presence of congenital heart disease with pulmonary arterial hypertension, which causes right-to-left shunting leading to cyanosis ([1],[4]). The RV hypertrophies to compensate for the pulmonary hypertension, leading to higher RV pressure than LV pressure, resulting in right-to-left shunting, decreased blood flow to the lungs, and eventually hypoxemia and cyanosis. On admission, our patient was assumed to have Eisenmenger physiology because of the large unrepaired ASD with chronic cyanosis and severe clubbing. However, his right heart catheterization revealed normal pulmonary pressures with normal PVR,

thereby ruling out ES. It was postulated that he likely had persistent hypoxemia with reversal of atrial level shunting due to a combination of a noncompliant hypoplastic RV and a "flow phenomenon" with blood flowing directly across the large primum ASD and not secondarily due to elevated PA pressures or PVR leading to a reversal of flow causing ES. It could also be postulated that the redundant atrial septum billowed outward into the RA, intercepting IVC blood and shunting it through the primum ASD into the left atrium. The right-to-left shunting in our patient was not associated with elevated right-sided pressures, with the mean RA pressure being approximately 1 mm Hg less than the mean LA pressure.

TABLE 2 Cardiac Hemodynamics

|	R-SVC	L-SVC	RA	RV	PA	LV	RUPV	RLPV	LUPV
Oxygen saturations, %	58	53	73	78	78	84	96	95	98
Pressures, mm Hg			6 (M)	18/3 (S/D)	15/5/9 (S/D/M)	110/6 (S/D)			

Pulmonary vascular resistance: 0.79 WU (1.22 U × m²). Systemic vascular resistance: 27.38 WU (42.43 U × m²). Heart rate: 62 beats/min. Vo_2: 120 ml/min/m² (assumed). Hemoglobin: 20.0 g/dl. Inspired O_2: 21%. pH: 7.39. Pco_2: 40.0. Po_2: 55.0. HCO_3: 24.0.

D = diastolic; L-SVC = left superior vena cava; LUPV = left upper pulmonary vein; LV = left ventricle; M = mean; PA = pulmonary artery; R-SVC = right superior vena cava; RA = right atrium; RLPV = right lower pulmonary vein; RUPV = right upper pulmonary vein; S = systolic.

FIGURE 6 Post-Operative Transthoracic Echocardiogram: Apical 4-Chamber View
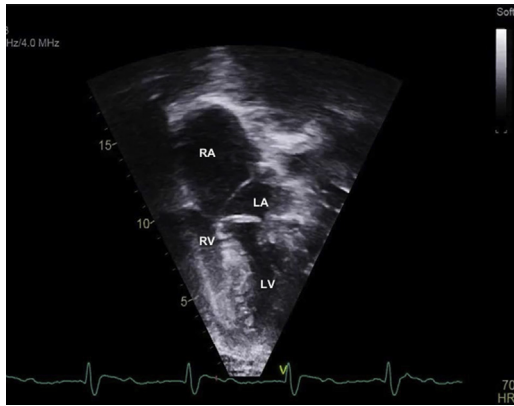
Abbreviations as in **Figure 4**.

FIGURE 7 Post-Operative Computed Tomography Angiography Reconstruction (Coronal View) Demonstrating the LSVC Anastomosed to the RAA With an Unobstructed Baffle That Courses Rightward and Anteriorly
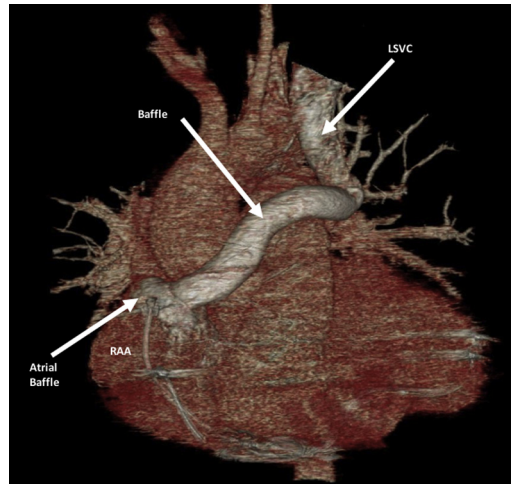
LSVC = left superior vena cava; RAA = right atrial appendage.

FOLLOW-UP

The patient felt markedly better at his 1-month follow up, reporting occasional dizziness and chest pressure, but he denied shortness of breath. Oxygen saturation on room air was 93% without signs of cyanosis.

CONCLUSIONS

Recognizing whether a patient has ES significantly affects management. It is not surprising that oxygenation did not improve in our patient, given that the interatrial shunt occurred in a setting of normal PA pressures. Our patient had refractory hypoxemia because of a right-to-left atrial shunt in the setting of normal intracardiac pressures and underwent complex cardiac repair with excellent results. The present case illustrates one of the many causes of hypoxia and highlights the importance of understanding the hemodynamics and mechanisms causing abnormal intracardiac flow and impaired oxygenation with intracardiac shunts in patients with complex congenital heart disease.

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KEY WORDS congenital heart disease, Eisenmenger syndrome, pulmonary hypertension

APPENDIX For supplemental videos, please see the online version of this paper.