Asking Bubbles for Direction: Assessment of a Classic Glenn Shunt Using Agitated Saline Contrast Echocardiography

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INTRODUCTION

Superior cavopulmonary shunt (Glenn shunt) is a palliative surgery typically performed in children with cyanotic congenital heart disease to provide blood flow to the lungs and offload the right ventricle by diverting some of the venous return. Classic Glenn shunts are characterized by isolation of the pulmonary artery (PA) ipsilateral to the superior vena cava (SVC). Pulmonary arteriovenous malformations (PAVMs) are a known long-term complication of classic Glenn shunt. This case report highlights the role of saline contrast study in diagnosing PAVMs, treatment considerations after positive results on saline contrast study, and expected findings on saline contrast study for common congenital heart conditions.

CASE PRESENTATION

A 55-year-old woman presented with exertional cyanosis. She was born with D-transposition of the great arteries, ventricular septal defect (VSD), and pulmonary stenosis. She had a Blalock-Hanlon atrial septectomy at 6 weeks of age, classic (right) Glenn shunt at 5 years, and a Rastelli repair at 16 years. Rastelli repair consists of tunneling of left ventricular outflow tract to the aorta by closing the VSD with a baffle. In addition, a conduit is used to ensure continuity between the right ventricle and PA (Figure 1). After several years, she developed shortness of breath and exercise intolerance as a result of right ventricular (RV)–PA conduit stenosis. At age 31, she underwent replacement of the RV-PA conduit and repair of a small residual VSD. Her classic Glenn shunt is still in place and was left intact at the time of her Rastelli repair for unclear reasons (Figure 2).

For the past few months, the patient had been experiencing shortness of breath on exertion, accompanied by episodes of blue discoloration of her lips and nail beds. On physical examination, she appeared acyanotic, with a blood pressure of 110/70 mm Hg and a heart rate of 50 beats/min. She had an elevated jugular venous pressure and normal S1 with a widely split and loud S2. There was a grade 2/6 early peaking systolic ejection murmur, with a grade 2/4 diastolic component, best heard in the left upper sternal border. The lungs were clear to auscultation, and no peripheral edema was noted. Her resting oxygen saturation was 94% on room air. During a 6-min walk test, her oxygen saturation dropped to 89% on room air. After 1 min of rest, her oxygen saturation increased to 94%. Electrocardiography showed normal sinus rhythm with a right bundle branch block. Laboratory investigations were significant for hemoglobin of 14.6 g/dL and an N-terminal pro–brain natriuretic peptide level of 573 pg/mL. Renal and hepatic function test results were normal.

An echocardiographic examination was performed, showing no conduit stenosis with mild to moderate regurgitation of the bioprosthetic pulmonic valve (Video 1, Figure 3). No residual atrial septal defect or VSD detected. The left ventricle was normal in size, with an ejection fraction of 60% to 65% and a diastolic filling pattern consistent with elevated left atrial filling pressure. The right ventricle was normal in size and function (Video 2). The patient's RV systolic pressure was 36 mm Hg (assuming a right atrial pressure of 3 mm Hg; Figure 4). A saline contrast study was done through the left arm and showed appearance of saline contrast in the left atrium, followed by appearance of the saline contrast in the right atrium and right ventricle (Video 3, Figure 5). Computed tomography (CT) revealed micro–arteriovenous malformations in the right lung (Figure 6).

The patient underwent cardiac catheterization that showed a patent Glenn shunt, confirming flow to the right PA (RPA) with no continuity to the left PA. Injection of contrast in the Glenn shunt showed abnormal architecture of the right lung, with rapid venous transition after the injection suggesting micro–arteriovenous malformations in the right lung. No macro–arteriovenous malformations were visualized, so she was not a candidate for coil embolization (Video 4). Assessment of right heart hemodynamics revealed a mean RA pressure of 7 mm Hg, RV pressure of 49/11 mm Hg, left PA pressure of 46/15 mm Hg with a mean pressure of 24 mm Hg, and a mean wedge pressure of 14 mm Hg, with V waves to 19 mm Hg. Saturations

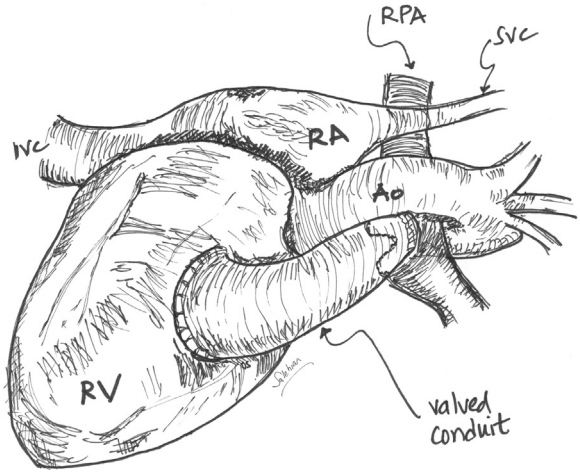

Figure 1 Diagram after Rastelli procedure, showing a conduit from the right ventricle (RV) to the PA. *Ao*, Aorta; *RA*, right Atrium; *IVC*, inferior vena cava.

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VIDEO HIGHLIGHTS

Video 1: Transthoracic echocardiography, parasternal view, showing RV-PA conduit (color Doppler) with mild to moderate regurgitation.

Video 2: Apical RV-focused view showing normal RV size and function.

Video 3: Saline contrast study (left upper extremity injection) showing bubbles first appearing in the left atrium. Bubbles are seen in the right atrium with some delay, because of a residual connection between the SVC and the right atrium.

Video 4: Cardiac catheterization showing injection of RPA through Glenn shunt. No macro–arteriovenous malformations (AVMs) are visualized. There is rapid venous transition, suggesting micro-AVMs in the right lung.

View the video content online at www.cvcasejournal.com.

included innominate vein (51%) → SVC (57%) → RPA (52%); inferior vena cava (59%) → main PA (52%) → left PA (61%); and femoral artery (91%). Pulmonary venous saturations were not directly measured.

The patient was started on 20 mg furosemide twice daily. On follow-up assessment 4 weeks later, her shortness of breath had diminished, with no further episodes of exertional cyanosis. Her oxygen saturation continued to be low normal. Given that her hypoxia was mild, and she felt well clinically, she preferred to be followed medically. She remained clinically stable at 1-year follow-up.

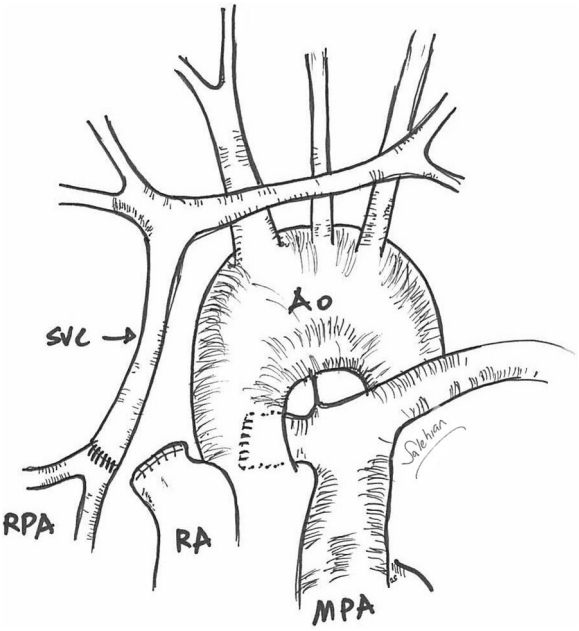

Figure 2 Diagram of classic Glenn shunt showing end-to-end anastomosis of the SVC to the RPA. *Ao*, Aorta; *MPA*, main pulmonary artery; *RA*, right atrium.

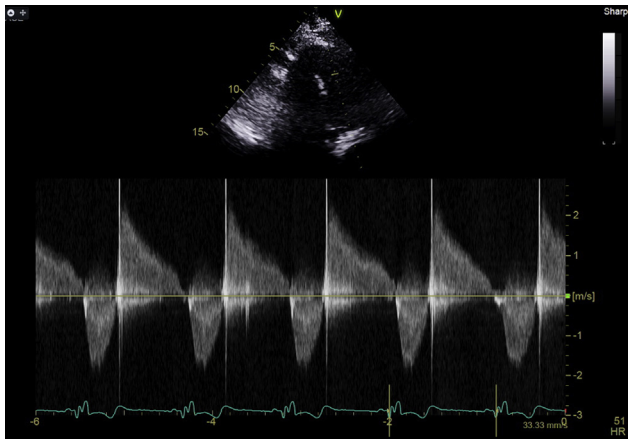

Figure 3 Transthoracic echocardiography, parasternal view, showing RV-PA conduit (continuous-wave Doppler) with no significant stenosis and a normal pulmonary insufficiency velocity.

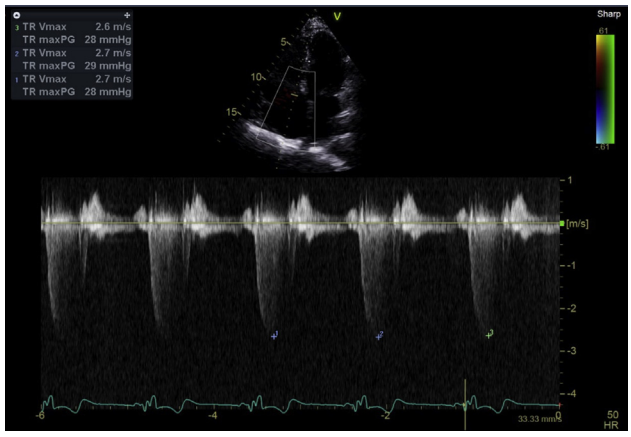

Figure 4 Transthoracic echocardiography, apical four-chamber view, continuous-wave Doppler of the tricuspid regurgitation jet showing tricuspid regurgitation (TR) jet velocity of 2.9 m/sec. Adding a right atrial (RA) pressure of 3 mm Hg, the RV systolic pressure (RVSP) is within the normal limits (36 mm Hg). Note that RVSP here reflects main PA and left PA pressure, but not RPA pressure.

DISCUSSION

The first successful cavopulmonary anastomosis was performed in 1958 by William Glenn in a 7-year-old patient with transposition of the great arteries and pulmonary stenosis.[1] The procedure created an end-to-end anastomosis of the SVC to the RPA. As a consequence, the RPA was disconnected from the main PA, and the SVC was disconnected from the right atrium. Six decades later, it continues to provide palliation to patients with cyanotic congenital heart disease. By ensuring low-pressure pulmonary blood flow directly from the SVC, it provides partial circulatory bypass of the right heart. A number of patients are living with classic Glenn shunts. Many of them are now adults, like our patient, and had the Glenn shunts placed decades ago. The bidirectional Glenn shunt is now preferred over the classic Glenn shunt and is used to palliate a variety of single-ventricle anatomies.

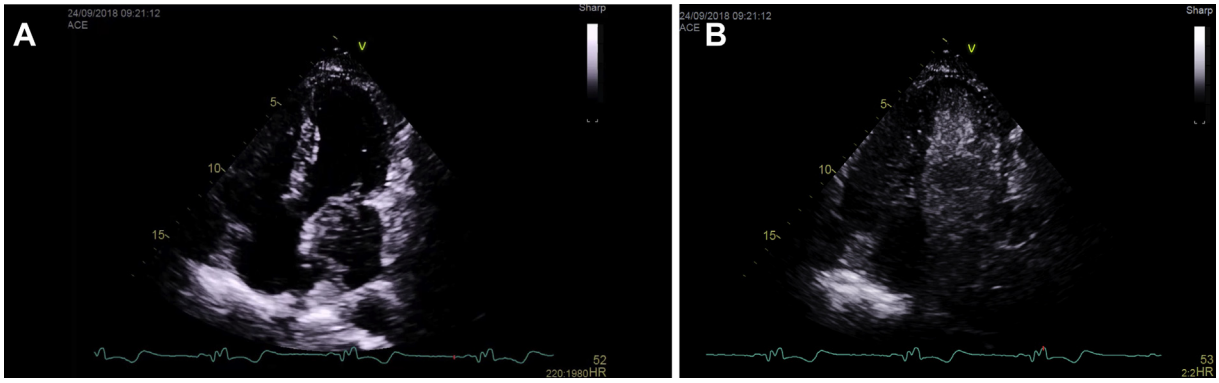

Figure 5 Still frame of saline contrast study, showing bubbles first appearing in the left atrium **(A)**, followed by opacification of the right heart **(B)**.

Right-sided PAVMs are a common problem after placement of a classic Glenn shunt.[2] They are usually located pleurally or subpleurally and range from microscopic telangiectasias to 1- to 5-cm vascular malformations. Right-to-left intrapulmonary shunting may occur in nearly all such patients at a microvascular level, though it manifests angiographically in about one third of patients on long-term follow-up.[3] Clinical implications of PAVMs include cyanosis, exercise intolerance, and potential to cause paradoxical emboli.

There is evidence for two major etiologic factors that contribute to the development of PAVMs: (1) the loss of pulsatile pulmonary blood flow and, perhaps more important, (2) the lack of hepatic venous effluent directly perfusing the pulmonary arteries.[4] Isolation of the lungs from hepatic venous return results in decreased exposure to angiogenesis inhibitors originating in the liver. This alteration in angiogenesis results in vascular proliferation and vasodilatation, resulting in PAVMs.[5]

The diagnosis of PAVMs has traditionally been made by pulmonary angiography. However, pulmonary angiography is invasive, and therefore contrast echocardiography with agitated saline is usually the preferred initial test. In patients without PAVMs, the microbubbles are too large to pass through the normal pulmonary vasculature, resulting in no bubbles being observed in the left atrium. In the presence of PAVMs, however, the bubbles rapidly transit through large-caliber blood vessels, resulting in arteriovenous shunting. Hence, bubbles are seen in the left atrium. In patients with PAVMs, bubbles typically appear in the left atrium with a delay of two to eight cycles after they appear in the right atrium, related to pulmonary transit time.[6] In addition, there is a steady and persistent appearance of microbubbles in the left atrium in the setting of PAVMs, as opposed to a "puff" of microbubbles seen with a patent foramen ovale. The appearance of bubbles in the left heart can be further quantified on the basis of the maximum number of bubbles counted in the left ventricle in one still frame. A pulmonary shunt can be graded as grade 1 (≤29 bubbles), grade 2 (30–100 bubbles), or grade 3 (>100 bubbles).[6] However, in our patient, upon injection of saline contrast in the upper extremity, the saline contrast first reached the right lung through the Glenn shunt and then appeared in the left atrium via PAVMs. Bubbles were seen in the right atrium with some delay, because of a residual connection between the SVC and the right atrium. Alternatively, the delayed appearance of bubbles in the right atrium could be due to venovenous collateral vessels from the SVC to inferior vena cava or flow from the SVC to inferior vena cava via the azygous vein. However, CT did not show any evidence of a prominent azygous vein or venovenous collateral vessels. Expected findings on saline contrast study (injected in a left upper extremity vein) for common congenital heart conditions are summarized in Table 1.[7]

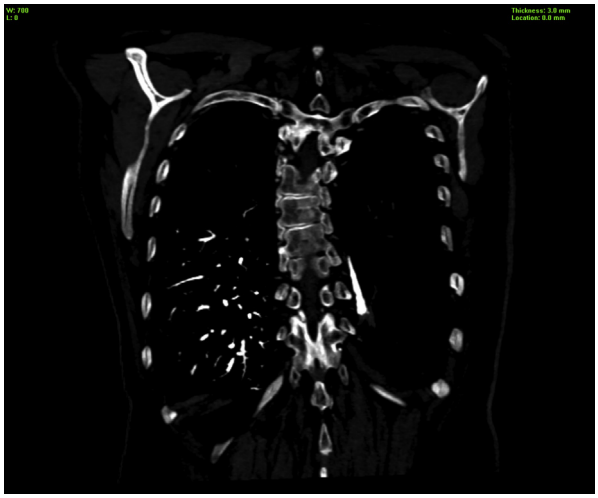

Figure 6 Coronal slice of contrast-enhanced computed tomographic scan showing micro–arteriovenous malformations in the right lung. Homogenous, well-circumscribed nodules can be seen in the right middle and right lower lobes. There is enhancement of the feeding artery, the aneurysmal part, and the draining vein. No macro–arteriovenous malformations are visualized.

In comparison with pulmonary angiography, contrast echocardiography with agitated saline has higher sensitivity for detecting PAVMs. In one series of 14 patients with Glenn shunts who underwent both pulmonary angiography and contrast echocardiography, 21% of patients had positive findings on pulmonary angiography, compared with 71% who had positive findings on contrast echocardiography.[8] However, many such patients with positive findings on contrast echocardiography have no pulmonary vein desaturation at rest.[9] The likely explanation for this discrepancy is that contrast echocardiography can detect PAVMs at an early stage, before a significant decrease in pulmonary vein saturation. However, the clinical relevance of this early-stage disease is unclear, as the timeline for progression to clinically relevant desaturation can vary. Our patient, despite PAVMs evident on contrast echocardiography, CT, and cardiac catheterization, had only mild desaturation. An additional difference between contrast echocardiography and pulmonary angiography is greater interobserver agreement for interpretation of contrast echocardiographic studies

Table 1 Expected findings on saline contrast study (injected in a left upper extremity vein) for common congenital heart conditions (including postsurgical patients)

Anatomy	Definition	Expected finding on saline contrast study
Patent foramen ovale	It is a flaplike valve between the right and left atria, occurring in 25%–30% of the general population.	Initial appearance of bubbles in right atrium, followed by appearance in left atrium (within three to five cardiac cycles). Appearance may be delayed in the presence of atrial septal aneurysm.
PAVMs	These are abnormal communications between pulmonary arteries and veins.	Initial appearance of bubbles in right atrium, followed by appearance in left atrium (usually after a delay of two to eight cardiac cycles). Early appearance may be seen with extensive PAVMs or rapid pulmonary transit (as seen in hepatopulmonary syndrome).
Secundum atrial septal defect	It is a defect in the foramen ovalis, resulting from poor growth of the secundum septum or excessive absorption of the primum septum.	Bubbles appear in the right atrium, with negative contrast from left-to-right shunting. In addition, bubbles may cross into the left atrium.
Persistent left SVC with intact coronary sinus	It drains the left subclavian vein into the coronary sinus. Usually accompanied by a normal right-sided SVC.	Bubbles appear in the coronary sinus, followed by the right atrium
Persistent left SVC with an unroofed coronary sinus	In addition to the description above, part or all of the common wall between the coronary sinus and left atrium is absent.	Bubbles appear in the coronary sinus, followed by the left atrium/ventricle. Bubbles may also appear in right atrium via coronary sinus.
Classic Glenn shunt	Anastomosis of the SVC to the RPA.	No bubbles in left or right atrium. In the presence of PAVMs, bubbles appear in left atrium.
Bidirectional Glenn shunt	End-to-side anastomosis of the SVC to the central PA.	No bubbles in left or right atrium. In the presence of PAVMs, bubbles appear in left atrium.
Extracardiac Fontan (no fenestration)	Bidirectional anastomosis of the SVC to the right PA and a conduit to connect the IVC to the PA.	No bubbles in the atrium.
Extracardiac Fontan (with fenestration)	In addition to the description above, a small communication is created between the conduit and atrium, allowing for a small, persistent right-to-left atrial shunt.	Bubbles appear in the atrium (the atrial septum is usually resected in single-ventricle patients).

IVC, Inferior vena cava.

compared with pulmonary angiography.[9] CT and magnetic resonance imaging are additional imaging modalities to diagnose PAVMs. Typical appearance on CT is a smooth nodule with a feeding artery and a draining vein. Contrast is not necessary for diagnosis on CT but can be helpful in patients with atypical nodules on nonenhanced CT with high clinical or echocardiographic suspicion for PAVMs.[10] Disadvantages of CT include occasional mischaracterization of vascular tumors as PAVMs and need for prolonged breath holding.

Treatment options for PAVMs depend on the clinical indication and type of PAVM. Common indications for treatment include hypoxia, followed by paradoxical embolism. Coil embolization can be used to treat large or macro-PAVMs, which generally requires a feeding artery diameter ≥ 3 mm.[11] However, many patients after Glenn shunts have diffuse PAVMs that are not amenable to coil embolization, as in our patient. In this case, redirection of hepatic venous blood flow to the affected lung (without crossing a capillary bed) can effectively treat, and often eliminate, PAVMs. This redirection of blood flow can be done in three ways. First, patients can undergo conversion to complete Fontan circulation, if they are suitable candidates. However, in some cases, PAVMs have been shown to persist despite conversion to Fontan circulation, which may be due to streaming of hepatic venous blood toward the healthy lung. Redirection of hepatic venous blood toward the diseased lung can result in resolution of PAVMs. Second, removing the Glenn shunt and restoring PA continuity can restore hepatic vein flow in the right lung and lead to resolution of PAVMs. However, this procedure necessitates a repeat sternotomy. Third, an arteriovenous fistula can be created in the arm, either at the axillary level or the brachiocephalic level.[12] This allows hepatic venous blood to be introduced into the right lung without crossing a capillary bed and can lead to resolution of cyanosis and hypoxia.[13] However, this requires the hepatic venous blood to empty directly into the systemic ventricle (without crossing the pulmonary capillary bed), a condition our patient did not meet. Creation of an arteriovenous fistula does not improve PAVMs in patients with unilateral hepatic venous streaming.[12] Complications of these fistulas can include fistula occlusion and upper extremity complications such as pain or edema.

In our patient, given that she had no large PAVMs amenable to coil embolization, and that her symptoms were relatively mild, it was elected to continue conservative management at this point.

CONCLUSION

We report a case of PAVMs diagnosed on a saline contrast study in a patient presenting with exertional cyanosis. This case demonstrates the ability of saline contrast to detect micro-PAVMs and the unusual appearance of saline contrast in the left side of the heart due to the presence of a Glenn shunt. Transthoracic echocardiography, CT, and cardiac catheterization played complementary roles in the diagnosis and management of this patient.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2020.09.002.

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