Hypoplastic Posterior Leaflet Mitral Valve Associated with Bicuspid Aortic Valve

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INTRODUCTION

Agenesis or hypoplasia of the posterior leaflet of the mitral valve (HPMVL) is a rare congenital anomaly, and its finding in adulthood is even more extraordinary because of the high morbidity and mortality generated in childhood. Its association with other congenital heart defects has been reported. We present a clinical case of an adult from the Andes with HPMVL associated with a bicuspid aortic valve (BAV)—which generated severe and moderate valvar regurgitation—who underwent successful surgery.

CASE PRESENTATION

A 60-year-old male patient came for cardiology evaluation due to a heart murmur identified incidentally 4 years earlier. The patient reported no cardiovascular symptoms at the time of evaluation. Significant medical history included hypertension controlled with daily angiotensin receptor blocker 8 mg. On physical examination, blood pressure was 148/82 mm Hg, heart rate 80 beats/minute, and SpO_2 96% (without supplemental oxygen). A downward and outwardly displaced hyperdynamic apical impulse was palpated. On auscultation the first heart sound was soft and the second heart sound was normal. Additionally, 2 heart murmurs were auscultated: a blowing, high-pitched, holosystolic murmur of III/VI intensity best audible at the apex with radiation toward the left axillary area and a blowing, early diastolic murmur of II/VI intensity heard in the Erb area. There were no added pulmonary auscultation sounds or edema in the lower limbs.

The electrocardiogram showed sinus rhythm, signs of left atrial enlargement, right bundle branch block, and fragmented QRS complexes. Chest x-ray showed cardiomegaly and few signs of pulmonary congestion. Laboratory tests showed an elevated pro b-type natriuretic peptide (800 pg/mL). Transthoracic echocardiography (TTE) revealed mildly reduced left ventricular (LV) systolic function (LV ejection fraction 58% in the setting of severe mitral regurgitation [MR]) and preserved right ventricular systolic function (tricuspid annular plane systolic excursion 22 mm, S′ wave 15 cm/sec), with increased end-systolic and end-diastolic volumes (56 and 133 mL/m^2, respectively) and increased end-systolic and end-diastolic diameters (45 and 65 mm, respectively). In the evaluation of the mitral valve (MV), the anterior leaflet was severely elongated and myxomatous (Figure 1), while the posterior leaflet was hypoplastic with restricted motion (Figure 1, Videos 1 and 2), which generated a severe and eccentric MR. Likewise, TTE showed a BAV generating mild aortic regurgitation (AR). Transesophageal echocardiography (TEE) was performed to acquire more anatomical details of the MV and aortic valve. It confirmed the presence of a myxomatous and redundant anterior mitral leaflet with severe billowing prolapse and an undeveloped posterior mitral leaflet (Figures 1 and 2) that together generated severe MR with an eccentric jet directed toward the anterior atrial wall and with Coanda effect. In the analysis of MR severity, the effective regurgitation orifice area was 0.9 cm^2 and regurgitation volume was 112 mL calculated by quantitative Doppler, while the radius of convergence was 12 mm (Figure 1, Video 3). In the three-dimensional multiplanar reconstruction, the large anterior mitral leaflet and the functionally absent posterior mitral leaflet were corroborated, as seen from the atrial and ventricular view (Figure 2, Videos 4 and 5). Additionally, the presence of a type I BAV (Sievers classification) generating moderate AR (proximal isovelocity surface area [PISA] radius, 0.5 cm; vena contracta, 4 mm) was confirmed (Figure 3, Videos 6 and 7). This reclassification of severity could be because the exploration of the aortic valve in TTE may present limitations due to the acoustic window, even more so when studying AR with eccentric jets. In this sense, TEE at 120° exposes the valve better and gives more information on AR (PISA radius, vena contracta, jet width, and range). Coronary angiography and left heart catheterization revealed normal coronary arteries and isolated mild postcapillary pulmonary hypertension and corroborated the diagnosis of moderate AR (Figure 4).

Antihypertensive therapy was initially optimized by titrating the daily dose of angiotensin receptor blocker to 16 mg, and daily therapy with spironolactone 25 mg and empagliflozin 10 mg was instituted. Septic foci were ruled out in the patient and presurgical requirements were completed. During surgery, the presence of a large, thick, elongated anterior leaflet that constituted four-fifths of the MV was observed. The posterior leaflet, although present, was rudimentary and attached to the mitral annulus. The papillary muscles arose from the apical third of the left ventricle (LV) and protruded finger-like into the cavity. Most of the chordae tendineae extended from the heads of the papillary muscles into the anterior leaflet, with only a few anchored in the posterior leaflet. Regarding the aortic valve, we found the presence of 3 aortic sinuses, 2 cusps (with the presence of a poorly calcified raphe between the right and left cusps), and 2 commissures. All of these intraoperative findings corroborated what was identified in the

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VIDEO HIGHLIGHTS

Video 1: Two-dimensional TTE, apical 4-chamber view, demonstrates the redundant anterior MV with the HPMVL.

Video 2: Two-dimensional TTE, apical 3-chamber view, demonstrates the extensive mitral anterior leaflet and almost imperceptible HPMVL.

Video 3: Two-dimensional TEE, midesophageal, oblique 2-chamber (70°) view with color-flow Doppler, demonstrates an eccentric MR jet toward the anterior left atrial wall with associated moderate vena contracta and PISA radius.

Video 4: Three-dimensional TEE, volume-rendered reconstruction from the ventricular perspective, demonstrates the large anterior leaflet and the remnant of the embryologically HPMVL.

Video 5: Three-dimensional TEE, multiplanar reconstruction of 3 orthogonal long-axis views, demonstrates the elongated, redundant anterior leaflet with billowing A2 prolapse and the HPMVL. The three-dimensional volume-rendered reconstruction MV display from the surgeon's view (*bottom right*) demonstrates the functionally unicuspid MV anatomy.

Video 6: Two-dimensional TEE, midesophageal short-axis (51°) aortic valve view, demonstrates the BAV with raphe between right and left coronary leaflets.

Video 7: Two-dimensional TEE with color-flow Doppler, midesophageal long-axis (138°) view, demonstrates moderate AR without stenosis.

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echocardiographic studies, and the patient underwent mechanical bileaflet MV replacement (31 mm) and aortic valve replacement (25 mm) surgery. Postoperatively, the patient presented with third-degree atrioventricular block and the need for transient pacemaker support, finally requiring the implantation of a permanent pacemaker. At 1-month follow-up, the patient remained asymptomatic, while echocardiography showed a slight increase in LV systolic function (LV ejection fraction, 62%) and a decrease in LV volumes (systolic 50 mL/m^2 and diastolic 124 mL/m^2). In addition, the N-terminal pro b-type natriuretic peptide value improved (254 pg/mL).

DISCUSSION

Congenital MV malformations are rare, with an estimated incidence of 0.4% of patients with congenital heart disease;[1,2] this value may be underestimated due to inadequate reporting and the asymptomatic clinical pattern in many cases.

Valve progenitor cells originate from an endothelial-to-mesenchymal transition process, forming the endocardial cushions. Regarding the MV, the posterior leaflet derives from the lateral cushion, while the anterior leaflet develops from the extension of the upper and lower cushions. The semilunar valves emerge from the conotruncal and intercalated cushions of the outflow tract. The conotruncal cushions give rise to the right and left leaflets, and the right-posterior intercalated cushions develop into the posterior aortic (noncoronary cusp) leaflets.[3]

There exists a broad and intricate interplay among transcription factors (such as TGF-b, Notch, BMP, Gata, Nfatc1, Wnt/b-catenin, Twist-1, Sox9, and others) involved in the proper development of endothelial-to-mesenchymal transition and valvular progenitor cells. Alterations in these factors and their signaling mechanisms have been implicated in developing valve pathologies.[3] It remains unknown whether the co-occurrence of 2 pathologies, such as HPMVL and BAV, may be related to a disruption in a common signaling/transcription pathway.

The presentation of congenital MV malformations includes a wide spectrum of abnormal morphologies, which were classically classified in 1971 by Davachi and collaborators[4] according to the affected area within the MV apparatus (leaflets, commissures, chordae tendineae, or papillary muscles). Most frequently, more than 1 segment of the MV apparatus is compromised within their presentation.[4]

The anomalies linked to the leaflets include leaflet aplasia or hypoplasia, valve cleft, accessory valve tissue, or subdivision into smaller cusps.[5,6] Leaflet aplasia or hypoplasia is, within this spectrum, one of the rarest entities, with fewer than 30 cases reported worldwide,[6] and an incidence of approximately 1:8,800 patients according to a prospective study involving 26,484 participants in a routine echocardiographic examination.[6] This pathology has been most frequently observed in infants and children with symptomatic MR, either in isolation or in association with other cardiac lesions, with a tendency to be incompatible with life in many cases beyond the neonatal period. However, some cases have been described in adults,[3,7-12] with ages ranging between 17 and 76 years, without a relationship linked to sex; usually, these adults have mild MR and relatively preserved hemodynamic parameters. Therefore, it is known that the progression of MR over the years and the clinical symptoms that develop are the main factors that lead to diagnosis.[13] Within the group of symptomatic patients, some reports indicate the presence of dyspnea, deterioration in functional class,[1,10] dizziness,[11] palpitations,[6] or chest pain,[6] which are nonspecific but become the first clue to diagnosis.

Usually, HPMVL is associated with a compensatory myxomatoid elongated anterior leaflet. It must be distinguished from other pathologies that have certain particular characteristics, such as parachute MV[1,4] (characterized by unifocal attachment of the MV chordae to a single or fused papillary muscle), arcade valve[14] (thickened and short chordae tendineae, with reduction of the interchordal spaces and development of a fibromuscular band in severe cases, which can produce stenosis or MR), or the cleft mitral leaflet[1,4] (a division of the leaflets that looks like a slit-like hole on echo), and special attention should be given to differentiate it from Barlow's disease[4,13] (pronounced annular dilatation, bileaflet prolapse and/or billowing, hooding, and the presence of thick, spongy leaflets due to excessive myxomatous tissue proliferation with or without calcification).

Even less frequent is the association of this MV disease with other cardiac anomalies. Congenital defects associated with HPMVL include the presence of BAV, atrial septal defects, congenital lung anomalies, and Williams-Beuren's syndrome.[6,14] Establishing the percentage of occurrence of each of these associated defects remains elusive because there have only been anecdotal reports of the concomitant occurrence of these anomalies. Our patient presented with a concurrent BAV, a condition that has only been reported in 3 cases.[8]

For MV leaflets' congenital malformations there are no specific guidelines regarding treatment; therefore, we assumed the parameters

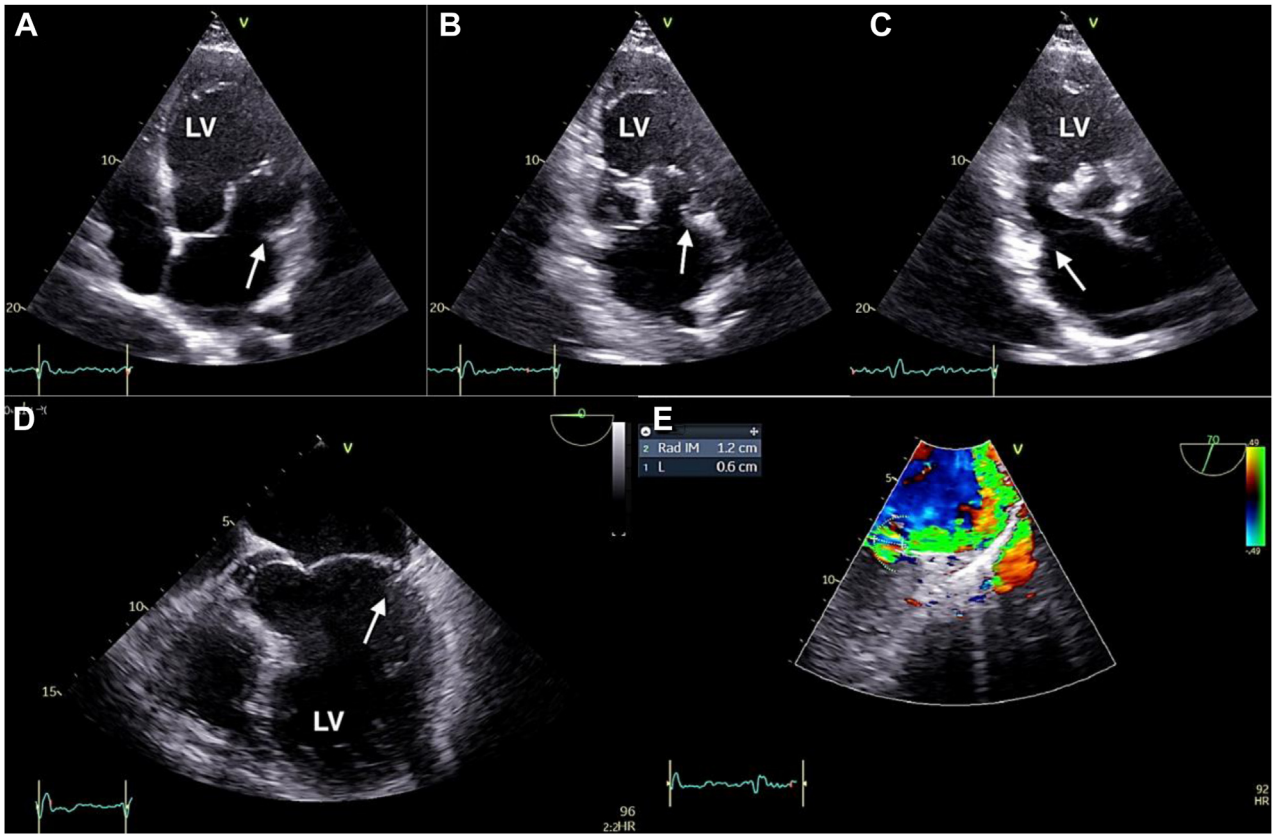

Figure 1 **(A)** Two-dimensional TTE, apical 4-chamber diastolic view, demonstrates the redundant anterior mitral leaflet with the HPMVL (*arrow*). **(B)** Two-dimensional TTE, apical 2-chamber view, mid diastole, demonstrates the poorly developed posterior leaflet with restricted motion (*arrow*). **(C)** Two-dimensional TTE, apical 3-chamber view, early diastole, demonstrates the barely visible posterior leaflet (*arrow*). **(D)** Two-dimensional TEE, 4-chamber (0°) view, demonstrates the large anterior MV leaflet extending to the lateral annulus and the HPMVL (*arrow*). **(E)** Two-dimensional TEE, midesophageal, oblique 2-chamber (70°) view with color-flow Doppler, demonstrates an eccentric MR jet toward the anterior left atrial wall with a moderate vena contracta and PISA radius.

set for the management of primary MR according to the 2021 European Society of Cardiology guidelines, since part of the valve apparatus is affected (posterior leaflet). In this guideline, valve repair or replacement is considered as indication IB for asymptomatic individuals with ventricular dysfunction, established as an end-systolic diameter >40 mm and/or an ejection fraction <60%.[15] These parameters were clearly met by our patient. In this case, valve repair is always the first treatment option, as long as it is anticipated that it will be successful and long-lasting.[15] Arasaratnam and collaborators,[7] in Australia, propose a technique based on mitral posterior leaflet augmentation with collagen bioscaffold patch associated with annuloplasty with ring.

Finally, our patient underwent replacement with mechanical prosthesis of both valves, after being evaluated by the surgical team of our hospital.

CONCLUSION

Malformations of the MV apparatus are rare, and agenesis or hypoplasia of the posterior leaflet is among the most infrequent. Its association with other congenital anomalies has been reported and increases the complexity of the case. A pathophysiological basis that explains these findings has not yet been established. The differential diagnosis should be made with other anomalies of the mitral apparatus. Echocardiography, particularly the three-dimensional transesophageal approach, is determinant for the diagnosis of complex mitral pathologies and surgical planning.[14]

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

CONSENT STATEMENT

Complete written informed consent was obtained from the patient (or appropriate parent, guardian, or power of attorney) for the publication of this study and accompanying images.

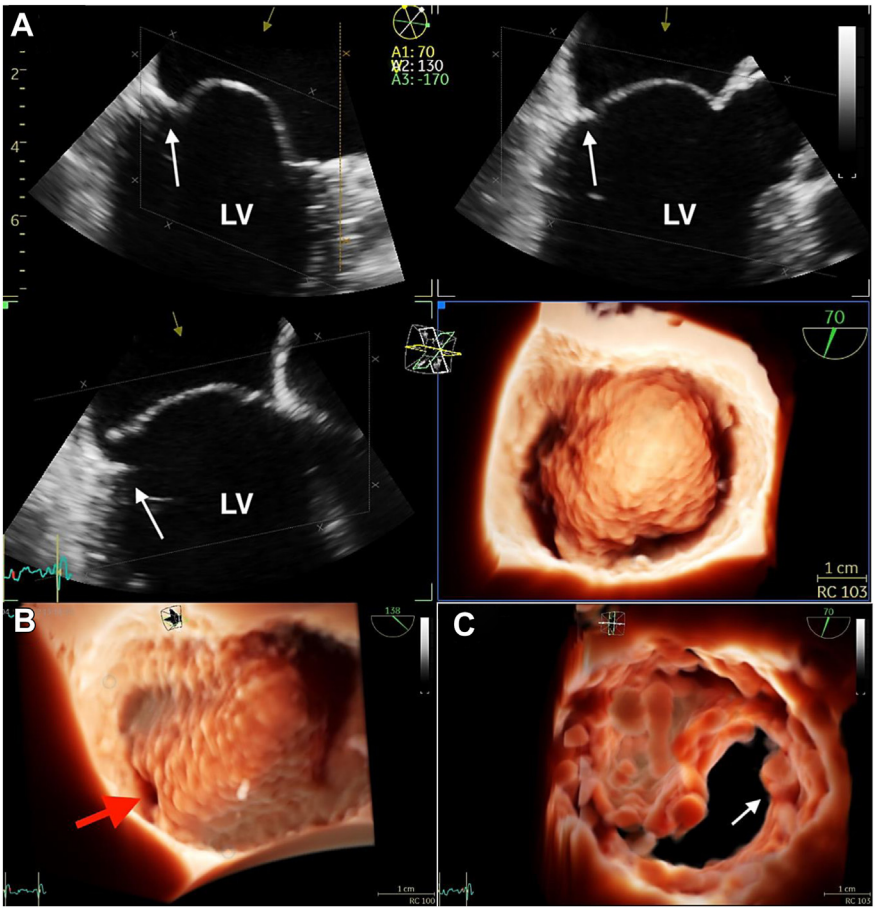

Figure 2 **(A)** Three-dimensional TEE, multiplanar reconstruction of 3 orthogonal long-axis midsystolic views, demonstrates the elongated, redundant anterior leaflet with billowing prolapse and the HPMVL. The three-dimensional volume-rendered reconstruction image of the MV from the surgeon's view (*bottom right*) demonstrates the functionally unicuspid MV anatomy. **(B)** Three-dimensional TEE, volume-rendered systolic reconstruction from the atrial perspective, demonstrates the functionally unicuspid, prolapsing anterior MV leaflet that does not completely cover the P1 segment (*red arrow*). **(C)** Three-dimensional TEE, volume-rendered mid-diastolic reconstruction from the ventricular perspective demonstrates the HPMVL (*white arrow*).

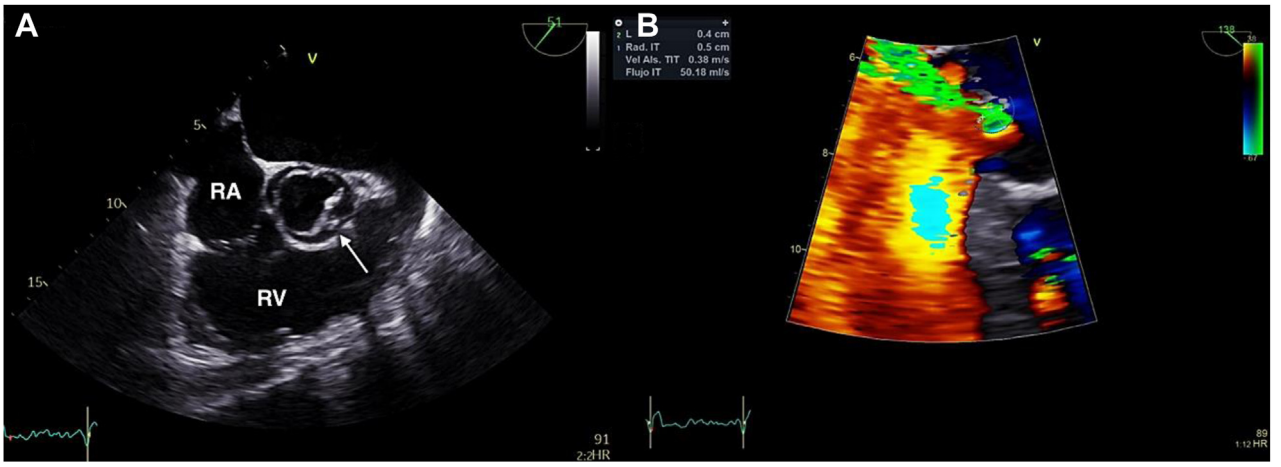

Figure 3 **(A)** Two-dimensional TEE, midesophageal short-axis (51°) view, midsystolic phase, demonstrates BAV with raphe between right and left coronary leaflet (*white arrow*). **(B)** Two-dimensional TEE, midesophageal long-axis (138°) view with color-flow Doppler focused on the aortic valve, systolic phase, demonstrates a moderate regurgitation jet (PISA radius, 0.5 cm; vena contracta, 0.4 cm). *RA*, Right atrium; *RV*, right ventricle.

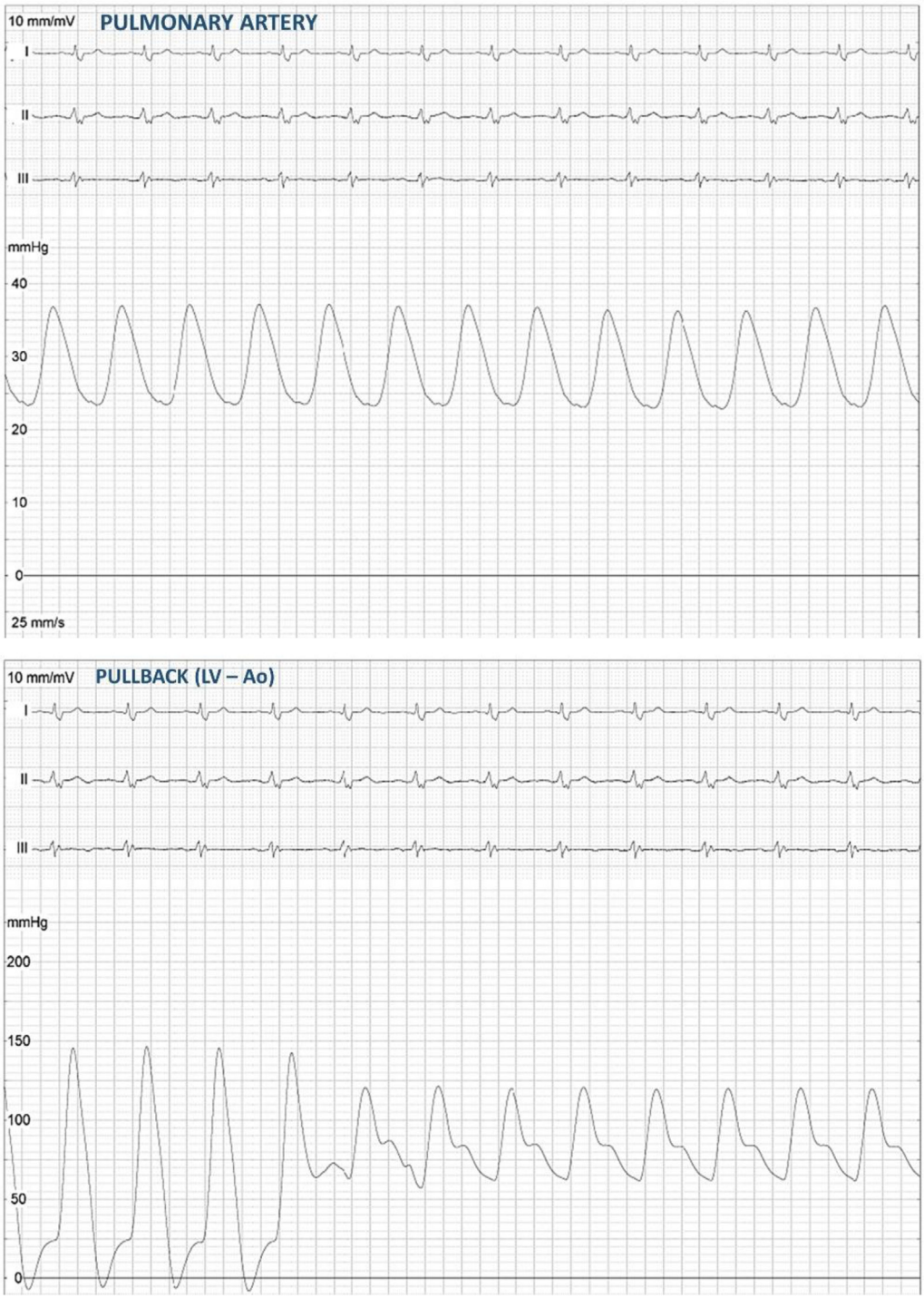

Figure 4 Invasive pressure tracing during right heart catheterization demonstrates the pulmonary artery (*top*) and the LV to aortic pullback (*bottom*) pressure waveforms with a systolic/diastolic pulmonary artery pressure (PAP) of 37/24 mm Hg, LV systolic/diastolic pressure of 145/24 mm Hg, aortic systolic/diastolic pressure of 122/55 mm Hg, calculated mean PAP of 28 mm Hg, pulmonary capillary wedge pressure of 24 mm Hg, cardiac output of 6.5 L/min, cardiac index of 3.33 L/min/m^2, and pulmonary vascular resistance of 0.61 Woods units. *Ao*, Aorta.

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DISCLOSURE STATEMENT

The authors report no conflicts of interest.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2023.12.025.

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