



## Uncommon late presentation of platypnea-orthodeoxia syndrome

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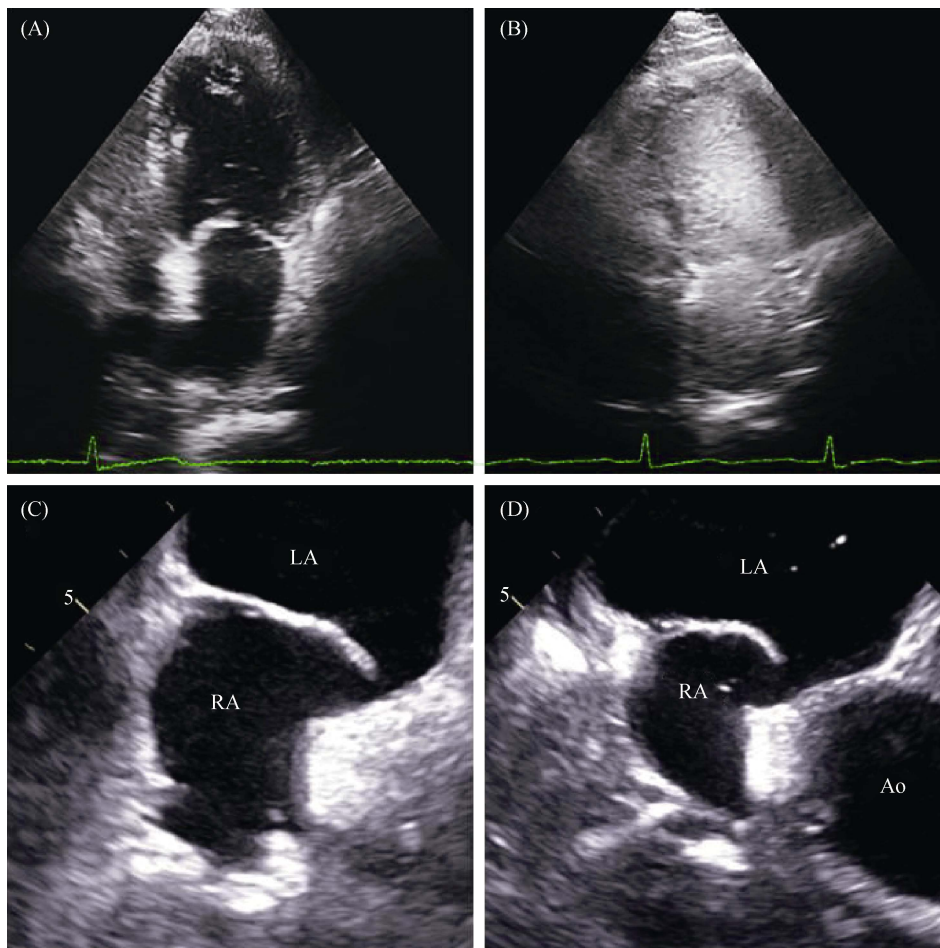
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A 79-year-old man presented with progressive dyspnea, gradually worsening over a period of several weeks. His past medical history included hypertension, chronic hepatitis C without cirrhosis, ischemic stroke occurred at the age of 68 and chronic obstructive pulmonary disease (COPD) caused by long-term cigarette smoking. The patient was alert and oriented and not in acute distress. The physical examination of the chest revealed decreased breath sounds at the bases of the lungs, without crackles or wheezes. Heart sounds were regular without murmurs. The respiration rate was normal. Extremities had no cyanosis, clubbing or oedema. The 12-lead electrocardiogram showed sinus rhythm with normal heart rate and non-specific T wave changes in D1, D2 and V5-V6. The chest radiograph revealed bilateral hilar prominence. Baseline peripheral capillary oxygen saturation (SpO<sub>2</sub>) measured by standard pulse oximetry was 89%. A face mask was placed, delivering oxygen at 6 L/min. The subsequent arterial blood gas analysis provided information on the following parameters: pH 7.41, PaCO<sub>2</sub> 34 mmHg, PaO<sub>2</sub> 64 mmHg, SaO<sub>2</sub> 91%. The full blood examination was normal, except for elevated C-reactive protein (50 mL/L, normal range < 10 mg/L) and D-dimer (782 ng/mL, normal range ≤ 270 ng/mL). A pulmonary embolism was suspected and a computed tomography pulmonary angiogram was then performed. No filling defects within the lumen of the pulmonary arterial branches were detected, neither were pleural effusion or pulmonary inflammatory infiltrates. A transthoracic echocardiogram (TTE) showed normal left ventricular ejection fraction, grade I diastolic dysfunction, normal heart valves, normal pulmonary pressure (systolic pulmonary artery pressure of 27 mmHg) and moderate enlargement of the ascending aorta (sinuses of

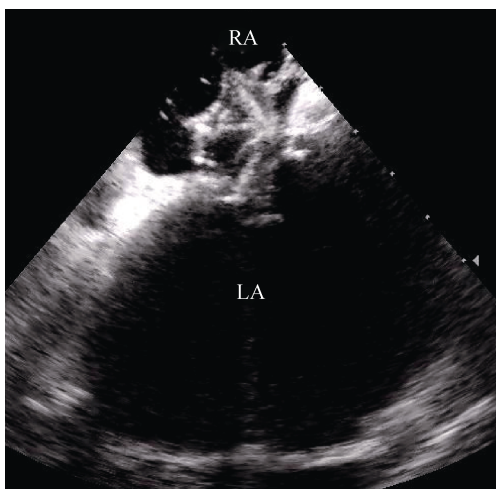
Valsalva diameter of 49 mm). The patient was treated with a standard therapy for the acute exacerbation of COPD. Serum inflammatory markers progressively decreased. Nevertheless, episodes of dyspnea, central cyanosis and fluctuating hypoxia persisted. In clinostatism, SpO<sub>2</sub> was 90% breathing ambient air. In the orthostatic position, it decreased to 70% with face mask delivering 10 L/min oxygen. The patient became cyanotic, but breath and heart sounds remained unremarkable in both supine and standing positions. A right-to-left shunt was suspected. A TTE and a transcranial Doppler ultrasound with agitated saline contrast showed a mild right-to-left shunt across the interatrial septum (Figure 1A). Contrast-enhanced echocardiography and contrast-enhanced transcranial Doppler ultrasound in both supine and sitting position were then performed. At 60 degrees incline, there was a dramatic shunt increase (Figure 1B). The patient underwent a 2D and 3D transesophageal echocardiography (TEE) in both supine and sitting position. It showed an aneurismal interatrial septum with patent foramen ovale (PFO) (Figure 1C & D). After the intravenous injection of agitated saline, the TEE documented a small right-to-left shunting across the PFO in the supine position. However, the TEE showed larger PFO size associated with significant shunt increasing in the upright position. The patient underwent successful percutaneous PFO closure with GORE<sup>®</sup> HELEX<sup>®</sup> Septal Occluder (W.L. Gore & Associates, Flagstaff, Arizona, USA). Subsequent right heart catheterisation demonstrated normal pulmonary pressures. The patient experienced progressive relief from dyspnea. Before discharge arterial saturation was 95% breathing room air without orthodeoxia. A strict clinical and echocardiographic follow-up was scheduled.

Platypnea-orthodeoxia (POS) is a rare clinical syndrome characterized by dyspnea and deoxygenation in the sitting or

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**Figure 1. Transthoracic and transesophageal echocardiographic images.** (A): TTE (apical 4 chambers view) with agitated saline contrast showing few microbubbles crossing atrial septum in the supine position; (B): TTE (apical 4 chambers view) with agitated saline contrast demonstrating massive right-to-left shunting with complete left chambers opacification in the upright position; (C): TEE without contrast showing PFO with a direct communication between LA and RA in the supine position; and (D): TEE without contrast showing larger PFO size with slightly compressed RA due to enlargement of extra-rotated ascending aorta (Ao) in the sitting position. Ao: ascending aorta; LA: left atrium; PFO: patent foramen ovale; RA: right atrium; TTE: transthoracic echocardiogram.



**Figure 2. Intracardiac echocardiographic image showing the GORE® HELEX® Septal Occluder device placement through the PFO.** LA: left atrium; PFO: patent foramen ovale; RA: right atrium.

upright position, relieved by the assumption of the supine position. Two conditions must coexist to cause POS: an anatomical defect (i.e., the interatrial communication) and a functional component that cause right-to-left shunt. The physiopathological explanation is still under debate. As matter of fact, the POS is characterized by dynamic right-to-left shunting in the absence of pulmonary hypertension. In 2002 this paradox has been described as “water flowing uphill”.<sup>[1]</sup> The possible mechanism could be an extrinsic compression of the right atrium, causing an increase of the atrial filling pressure and a right-to-left shunting across the atrial septum in the upright position.<sup>[3,4]</sup> Positional modification of the atrial septum due to a different anatomical relationship of the inferior caval vein (IVC) with PFO or atrial septal defect may also cause a right-to-left shunting in the standing posture.<sup>[5]</sup> In the case presented, why a significant right-to-left shunting developed in a 79-year-old man with PFO? The PFO was apparently an “innocent bystander”

during childhood, youth and adulthood of the patient. An ischemic stroke occurred when he was 68 years old. It can't be ruled out that the PFO may have played a role in the etiology of the ischemic stroke. However, at that time hypertension and cigarette smoking were assumed to be responsible for this. Subsequently, the PFO was proved "guilty" in old age. The association between POS and a number of conditions causing distortion of the interatrial septum has been described: kyphoscoliosis, pneumonectomy, aortic aneurysm or elongation.<sup>[6]</sup> The patient had a moderate enlargement of the ascending aorta that may have altered the intra-cardiac anatomical relationships stretching the right atrial septum. The co-existing atrial septal aneurysm could have caused a "spinnaker effect" redirecting the IVC flow through the PFO. As matter of fact, it is assumed that a prominent Eustachian valve could become redirected to the foramen ovale guiding the blood directly from the IVC to the foramen in elderly.<sup>[7]</sup> The proper diagnosis of POS may be difficult because the symptoms are non-specific. However, the POS should be considered in patients with unexplained dyspnea and deoxygenation related to postural changes. The most readily available and non-invasive diagnostic method is supine and upright contrast TTE.<sup>[8]</sup> TTE imaging in standing position is technically more difficult than in the standard left lateral one. Assessment of the anatomical correlation by TEE should be performed if an intra-cardiac shunt is detected.<sup>[9]</sup> The detection of this rare clinical syndrome has important therapeutic implications. Surgical or transcatheter percutaneous approaches to close atrial septal defect or PFO may be considered.<sup>[10]</sup> Percutaneous closure of PFO has been proposed as the treatment of choice for patients with POS.<sup>[11]</sup> However, there are no randomized controlled studies assessing the effectiveness of PFO closure in patients aged 75 years or older. Our case suggests that the diagnosis of POS is challenging in older patients complaining dyspnea. Percutaneous closure of PFO can be feasible, safe and effective in elderly with POS, comorbidities and frailty.

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