Platypnoea-orthodeoxia syndrome: more than just a PFO

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Summary

Platypnea-orthodeoxia syndrome (POS) is a rare condition characterised by episodes of dyspnoea and desaturation when changing from a recumbent to a sitting or standing position, due to a right-to-left shunt through the atrial septum (cardiac POS) or a pulmonary vascular shunt. A consistent finding among patients with cardiac POS is an interatrial communication (patent foramen ovale [PFO] or atrial septal defect [ASD]), but these often-congenital anatomies, alone, do not account for development of massive right-to-left shunt, which frequently occurs later in life leading to severe hypoxaemia. We present the case of an 84-year-old woman known for evolutive right breast carcinoma with successive loco-regional progressions, which over several years, despite local and systemic therapy, eventually invaded the right pectoral muscle, with skin infiltration of the right chest wall and right diaphragmatic paralysis. She subsequently developed rapidly progressive dyspnoea: a cardiac workup including contrast examinations (trans-cranial duplex and trans-thoracic echocardiography) showed a massive intra-cardiac right-to-left shunt, while transoesophageal echocardiography confirmed the presence of a large PFO. Based on these findings, the patient was diagnosed with POS and PFO closure was performed with immediate normalisation of oxygen saturation, and at 6–month follow-up no further episodes of desaturation were reported. The aim of this case discussion was to underline the mechanisms leading to significant right-to-left shunt among patients with PFO, especially when in an upright position, and to elucidate the therapeutic options.

Key words: cardiac platypnoea-orthodeoxia syndrome; patent foramen ovale; percutaneous closure

Case presentation

An 84-year-old woman, known for osteoporosis with multiple vertebral fractures and secondary kyphoscoliosis, had been diagnosed 10 years earlier with grade 2, ductal right breast carcinoma. Several years later she suffered a pulmonary embolism. Thereafter the evolution of the cancer was characterised by successive loco-regional progressions, despite local radiation, chemo- and hormone therapy. She subsequently developed invasion of the right pectoral muscle and right diaphragmatic paralysis (fig. 1A and 1B). During the four months prior to her most recent admission, she had been admitted three times to our institution for grade 3 dyspnoea, but each time without fever or cough. The workup showed no pulmonary oedema or obstructive syndrome, and diuretic administration did not lead to any clinical improvement.

Physical examination at this new admission for dyspnoea revealed reduced respiratory sounds in the right inferior pulmonary area with dullness upon percussion, and blood oxygen desaturation with ambient air when she was in an upright position (82%, but above 90% when recumbent). Chest computed tomography showed no pulmonary embolism, but confirmed right diaphragmatic elevation, and spirometry revealed a restrictive syndrome due to kyphoscoliosis. Blood gas analysis performed at 100% oxygen was compatible with a right-to-left shunt (shunt calculation 21.3%, N: <5) [1]. The shunt was confirmed with transthoracic echocardiography (TTE) (fig. 2A), which showed early and massive right-to-left shunt following contrast administration. Transoesophageal echocardiography (TEE) interestingly showed an aspect of compression of the right atrium with a hypermobile interatrial septum and a large PFO (fig. 2B and 3). These findings allowed the final diagnosis of cardiac POS, with the shunt through the PFO being favoured by diaphragmatic paralysis and chest deformity due to kyphoscoliosis. After multidisciplinary discussion including the oncologists, PFO closure was performed with immediate normalisation of oxygen saturation (from 92% to 98% under general anaesthesia) and complete relief of symptoms with no further episodes of desatu-

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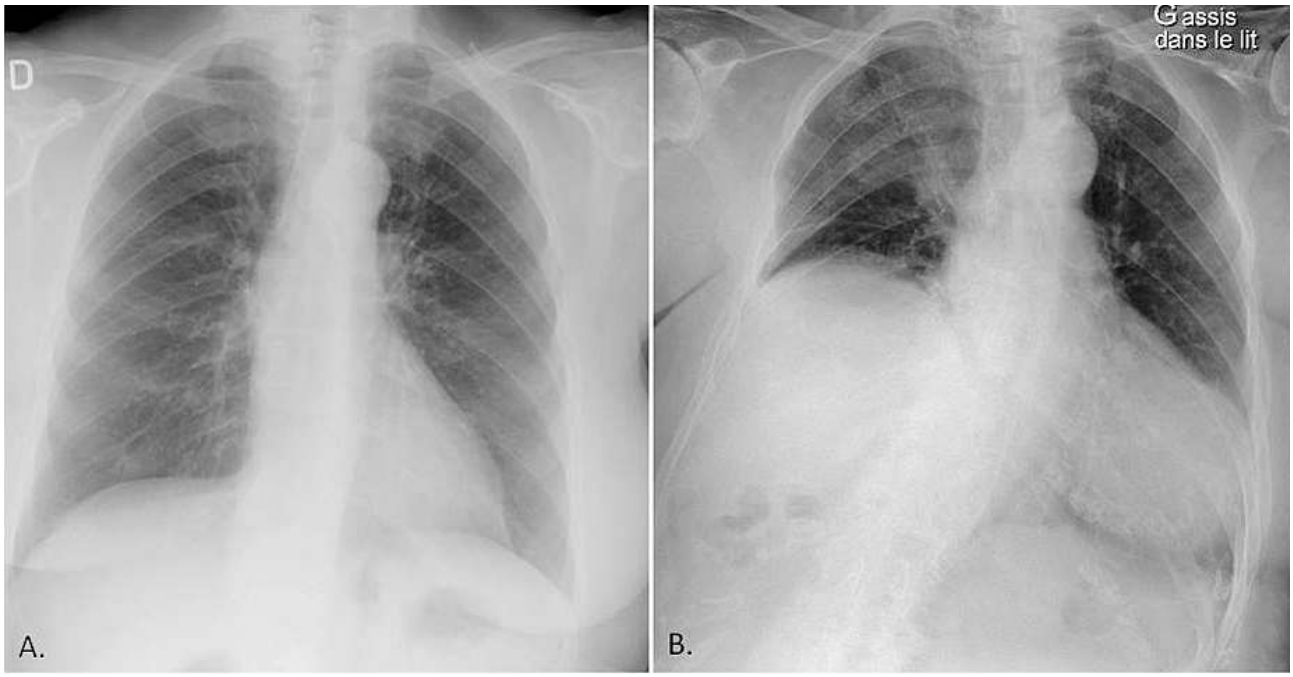

Figure 1
A Chest x-ray in 2004.
B Chest x-ray at presentation.

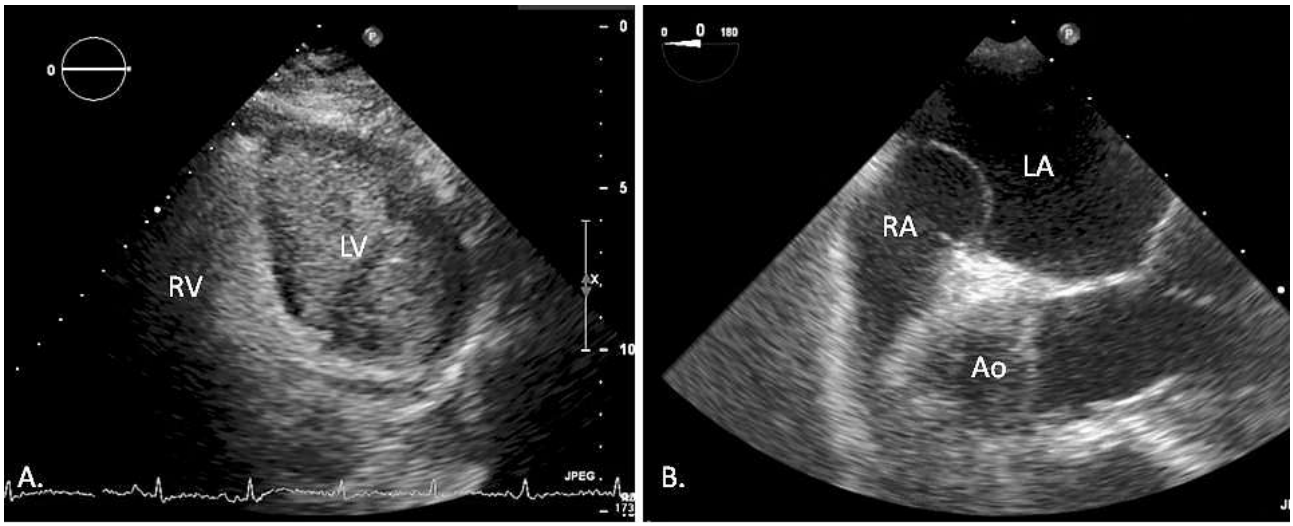

Figure 2
A Transthoracic echocardiography showing an important right-to-left shunt on contrast examination. RV = right ventricle; LV = left ventricle.
B Transoesophageal echocardiography mid-oesophageal view at 0° showing compression and deformity of the right atrium. RA = right atrium; LA = left atrium; Ao = aorta.

ration at 6 months. The pulmonary pressures recorded invasively during PFO closure were normal, the saturation measurements were as follows: mixed venous calculated by the Flamm formula 62%, pulmonary artery 65%, pulmonary vein 97%, and femoral artery 92%, with a Qp/Qs (92–62/97–65) within the normal range at 0.97, in the supine position.

Discussion

Platypnea-orthodeoxia syndrome is rare and of unknown prevalence within the general population. As only a few case-series and case-reports have described this syndrome, it is likely under-diagnosed and probably under-reported [2–4]. Diagnosing POS is challenging, and our case confirms that in patients presenting with dyspnea POS is usually a "rule-out diagnosis"

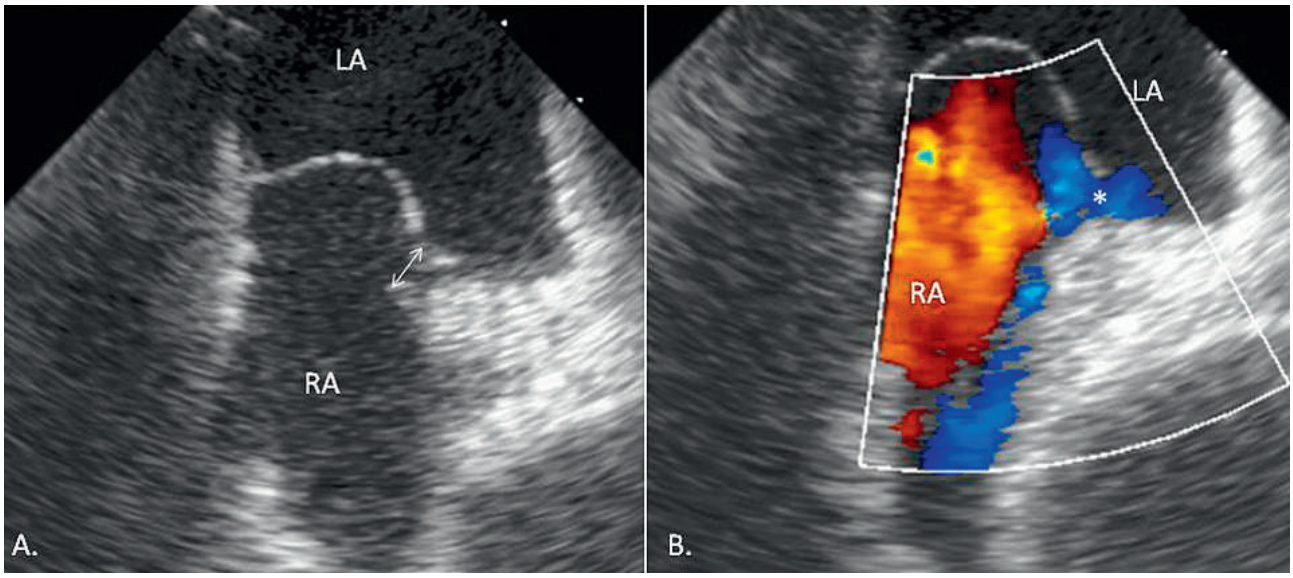

Figure 3
A Transoesophageal echocardiography showing the PFO in open position (double headed arrow). RA = right atrium; LA = left atrium.
B Transoesophageal echocardiography showing the PFO with right-to-left shunt on colour-Doppler examination (*). RA = right atrium; LA = left atrium.

Table 1
Causes of cardiac platypnoea-orthodeoxia syndrome (in the presence of patent foramen ovale or atrial septal defect).

Intrinsic
Pericardial effusion
Ascending aortic enlargement/aneurism
Extrinsic
Diaphragmatic paralysis and ascension
Pneumectomy
Pleural effusion
Kyphoscoliosis
Restrictive pulmonary syndrome

which is suspected only when other causes to the dyspnea have been excluded. When the diagnosis of POS has been confirmed, and in order to decide upon a treatment strategy, the exact cause must be identified: (1.) intracardiac shunt (cardiac POS), (2.) intrapulmonary shunt (e.g. pulmonary arteriovenous malformation) or (3.) ventilation-perfusion mismatch.

Our patient presented with cardiac POS caused by a right-to-left intracardiac shunt, without pulmonary hypertension. In typical cardiac POS, when the patient is in an upright position, the net right-to-left driving forces are not usually due to pulmonary hypertension, but rather due to congenital or acquired favourable atrial anatomy causing a redirection of blood flow from the vena cava through the PFO, even when no significant pressure gradient is present. In fact, approximately 25% of the general population is born with a PFO, but more often exhibit no POS, suggesting that a PFO alone does not lead to POS. Additionally although an interatrial communication (PFO or atrial septal defect) must exist for POS to develop, and an atrial septal aneurysm (ASA) or a prominent Eustachian valve contribute to the likelihood of POS developing, it is the modification of right atrial chamber anatomy often acquired in later adulthood [5], which is the main cause of the right-to-left shunt.

In our case, this favourable anatomic modification was due to right diaphragmatic ascension, and kyphoscoliosis. In the presence of atrial chamber or septal deformity, the anatomic relationship between the atrial septum and inferior vena cava is altered, thus facilitating the flow of systemic venous blood through the PFO, particularly when the patient is in an upright position. This may be caused by a number of mechanical conditions, the most common of which are listed in table 1.

The method of choice for evaluating the presence and magnitude of a right-to-left shunt is contrast TTE. On the other hand, atrial and interatrial anatomies (e.g. large PFO ± ASA ± Eustachian valve) are best assessed by TEE. To measure the extent and in particular the position-dependency (e.g., supine, sitting) of the right-to left shunt, a series of oxygen saturation measurements should be taken using standard pulse oximetry, blood gas analysis, or even during cardiac catheterisation. In order to make the diagnosis of POS of cardiac origin, the presence of a right-to-left shunt should be definitively confirmed by a “step down” of oxygen saturation between the pulmonary veins and the left atrium. However, such serial measurements are not of-

ten performed as a matter of routine since the non-invasive work-up (echocardiography, oximetry) usually establishes the diagnosis, and because invalidity experienced by the patient rather than the precise extent of the shunt is the deciding factor for PFO closure. Moreover, due to the intermittent and position-dependent nature of the shunt, invasive shunt calculation in the supine position may not reflect the true shunt magnitude as seen during episodes of positional desaturation. Our case illustrates the latter since the invasive shunt calculation showed normal Qp/Qs at 0.97. However, right heart catheterisation plays a crucial role in measuring pulmonary pressures, as even when the right-to-left shunt has been corrected severe pulmonary hypertension can be responsible for a clinical deterioration. The treatment of choice for cardiac POS is percutaneous closure of the defect on the atrial septum. Therefore before initiating a procedure, it is of particular importance to be sure of the cardiac origin of the POS, as well as to assess the extent to which the cardiac shunt is relevant in the mixed form of POS. Since this syndrome is relatively rare [3], there only exist a few retrospective series and case reports in the medical literature [2, 4, 6]. These reports all confirm clinical improvement after closure, but also underline the importance of making the correct diagnosis, and in particular the need to exclude other causes of hypoxaemia before initiating intervention.

Conclusion

POS is a rare syndrome that can be suspected in the context of positional hypoxaemia of unknown cause. To establish the diagnosis of cardiac POS, TTE ± TEE must show a right-to-left shunt, and positional desaturation must be confirmed with pulse oximetry or blood gas analysis. Since it is acquired, anatomical modifications which intrinsically (e.g. pericardial effusion, aortic dilatation) or extrinsically (e.g. kyphoscoliosis, diaphragmatic paralysis, pneumonectomy) lead to redirection of inferior vena cava flow directly through a PFO when the patient is upright, such anatomical causes should be actively sought when cardiac POS is suspected. Percutaneous PFO closure is the treatment of choice for this condition, since this intervention has been reported to be safe, while instantaneously correcting hypoxaemia and relieving dyspnea.

References

1 Chiang ST. A nomogram for venous shunt (Qs/QT) calculation. Thorax. 1968;23(5):563–5.
2 Guerin P, Lambert V, Godart F, Legendre A, Petit J, Bourlon F, et al. Transcatheter closure of patent foramen ovale in patients with platypnea-orthodeoxia: Results of a multicentric french registry. Cardiovasc Intervent Radiol. 2005;28:164–8.
3 Cheng TO. Platypnea-orthodeoxia syndrome: Etiology, differential diagnosis, and management. Catheter Cardiovasc Interv. 1999;47:64–6.
4 Blanche C, Noble S, Roffi M, Testuz A, Muller H, Meyer P, et al. Platypnea-orthodeoxia syndrome in the elderly treated by percutaneous patent foramen ovale closure: A case series and literature review. Eur J Intern Med. 2013;24:813–7.
5 Rodrigues P, Palma P, Sousa-Pereira L. Platypnea-orthodeoxia syndrome in review: Defining a new disease? Cardiology. 2012;123:15–23.
6 Meier B. Catheter-based closure of the patent foramen ovale. Circulation. 2009;120:1837–41.