A case report of a triad causing platypnoea–orthodeoxia syndrome

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Background
Platypnoea–orthodeoxia syndrome (POS) is a rare condition characterized by hypoxaemia and dyspnoea when changing from a recumbent to an upright position. Diagnosis requires a high clinical suspicion and is often underdiagnosed.

Case summary
We report a case of POS in a 50-year-old woman with dyspnoea and new-onset atrial fibrillation. Oxygen saturation and dyspnoea worsened as she changed from a supine to a sitting position (96 vs. 86%, respectively). Transoesophageal echocardiography demonstrated enlargement of both atria and right ventricle with reduced systolic function and a large Chiari network (CN). Colour Doppler discovered severe tricuspid regurgitation with tenting and tethering of the valve leaflets. Finally, a bubble test revealed the cause of POS to be a patent foramen ovale along with the severe tricuspid regurgitant jet moving into the left atrium and favoured by the CN. Surgical closure of the foramen ovale resulted in the resolution of symptoms.

Discussion
Platypnoea–orthodeoxia syndrome is most commonly caused by a right-to-left shunt through an anatomical defect of the interatrial septum, typically a patent foramen ovale, combined with elevated right atrium pressure. This case illustrates an uncommon cause of POS in the absence of elevated atrium pressure due to the interplay of three key elements: a patent foramen ovale, tricuspid regurgitation, and the CN. Our aim is to alert physicians to the possibility of an intracardiac shunt as the cause of unexplained and/or refractory hypoxaemia related to position changes. Early recognition of this syndrome promotes timely treatment, greatly improving patient outcomes.

Keywords
Platypnoea–orthodeoxia syndrome • Patent foramen ovale • Chiari network • Tricuspid regurgitation • Dyspnoea • Atrial septal defect • Case report

Learning points
• Platypnoea–orthodeoxia (POS) syndrome should be suspected with hypoxaemia and dyspnoea of unknown origin that worsens in the upright position and is relieved in the supine posture.
• Our study demonstrates an uncommon cause of POS due to the combination of foramen ovale, Chiari network, and tricuspid regurgitation without elevated right atrial pressure.
• Closure of the atrial shunt has been shown to be an effective treatment. Therefore, early diagnosis is crucial for improving the quality of lives of these patients.

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Introduction

Platypnoea–orthodeoxia syndrome (POS) is a rare condition characterized by hypoxaemia and dyspnoea in the upright position that is relieved in the supine posture. Since it was first described in 1949, cases of POS have increased as it is becoming more familiar to the medical community. Nevertheless, its underlying mechanisms still mystifies physicians and poses a diagnostic challenge. We report a case of POS in a 50-year-old woman due to the combination of a patent foramen ovale (PFO), severe tricuspid regurgitation (TR), and a large Chiari network (CN).

Timeline

Case presentation

A 50-year-old female with a history of hyperparathyroidism and hypertension was admitted to our hospital with new-onset atrial fibrillation (AF) and dyspnoea that commenced after parathyroidectomy surgery a month prior to hospitalization. She denied chest pain, fever, cough, wheezing, and sputum production.

Physical examination showed an irregular heart rhythm at 120 b.p.m. and worsening dyspnoea and arterial blood oxygen saturation (SpO2) from 98% to 86% when she changed from a supine to a sitting position, therefore, we suspected POS. Hypoxaemia was refractory to oxygen administration, and no finger clubbing, jugular venous distention, or peripheral oedema was observed.

The electrocardiogram demonstrated the presence of AF and signs of right ventricle overload with inverted T-waves in the right precordial leads (V1-3) (Supplementary material online, Figure S1). Chest X-ray showed cardiomegaly and pulmonary congestion (Supplementary material online, Figure S2). NT-proBNP (6029 pg/mL, reference values < 300 pg/mL) and D-dimer (4.24 μg/mL, reference values < 0.4 μg/mL) were elevated. Other laboratory parameters were unremarkable.

An emergent computed tomography pulmonary angiogram excluded pulmonary embolism and pulmonary function tests revealed no evidence of lung disease.

Transthoracic echocardiography showed enlargement of both atria and a dilated right ventricle (right ventricular end-diastolic diameter of 46 mm) with reduced systolic function (Supplementary material online, Video S1). Left ventricular size was normal with a mild reduction of the ejection fraction (50%). Severe TR and tenting of the tricuspid valve were identified (Video 1).

Right heart cardiac catheterization results included a normal mean pulmonary artery pressure (15 mmHg), right atrium pressure (7 mmHg), and a pulmonary capillary wedge pressure (8 mmHg). The net pulmonary-to-systemic shunt ratio performed in the supine position was normal (Qp/Qs: 1.04). Coronary angiogram excluded significant stenosis.

A transoesophageal echocardiography with agitated saline (bubble study) showed the early appearance of contrast in the left atrium during Valsalva manoeuvre, suggesting the presence of a PFO with right-to-left shunting (Supplementary material online, Video S2). During the test, we identified an extensive membrane in the right atrium consistent with CN (Videos 2 and 3).Colour Doppler revealed the CN aiding the direction of the TR jet to the left atrium through the PFO (Figure 1 and Supplementary material online, Video S2).
Cardiac magnetic resonance (MR) imaging revealed a significant jet of TR and a shortening of the subvalvular apparatus and adherence of the posterior leaflet to the myocardium causing tethering. No apical displacement of the annulus was found (Supplementary material online, Figures S3 and S4).

A heart rate strategy was adopted, and the patient was started on beta-blockers and anticoagulation. She finally underwent open-heart surgery with PFO closure, resection of the CN (Figure 2), and bio-prosthetic tricuspid valve replacement.

The post-operative recovery was satisfactory, symptoms remitted and SpO2 levels returned to normal (98%) with no variation between the supine and sitting position. The patient remained asymptomatic during the follow-up and resumed an active life.

**Discussion**

The pathophysiology of POS remains poorly understood. Causes can be classified into three categories: intracardiac shunting, pulmonary shunting, or ventilation-perfusion mismatch. It has been suggested that both an anatomic and a functional component are required. The anatomical shunt could be located in the heart [PFO or atrial septal defect (ASD)], or in the lungs (intra-pulmonary arteriovenous malformations). As for the functional component, it is caused by an elevated right atrium pressure causing left-to-right shunt reversal as seen in pulmonary hypertension. However, it may also occur in the presence of a prominent CN or in conditions that distort the cardiac anatomy (aortic aneurysms, kyphoscoliosis, or hemidiaphragmatic paralysis).

In our patient, the right-to-left shunt is caused by the combination of the severe TR and CN which directs the regurgitant jet through

**Video 1** Transoesophageal echocardiography with colour Doppler using a mid-oesophageal four-chamber view showing severe tricuspid regurgitation with tenting of the valve. Note the apical origin of the tricuspid regurgitation jet in the right ventricle.

**Video 2** Transoesophageal echocardiography using a mid-oesophageal four-chamber view showing the Chiari network. We can also appreciate the restrictive movement of the posterior leaflet due to tethering.

**Video 3** Three-dimensional echocardiography reconstruction of the right atrium, showing the Chiari network and foramen ovale.

**Figure 1** Still frame image from Supplementary material online, Video S3. Transoesophageal echocardiography with colour Doppler using a mid-oesophageal bicaval view that shows how the Chiari network guides the direction of the tricuspid regurgitant jet through the patent foramen ovale.
the PFO. Symptoms worsen in an upright position because it stretches the interatrial septum increasing the degree of shunting.

The dynamic interplay of PFO, TR, and CN is a rare cause of POS. Previously reported cases include an isolated CN, an acute TR related to trauma or endocarditis or the combination of PFO and CN. To the best of our knowledge, this is the first case of POS due to the interplay of PFO, TR, and CN.

The importance of TR in the development of right-to-left shunts has been documented in the literature. A study concluded that the severity and direction of the TR jet towards the ASD determined the appearance of shunting.8

The most probable cause of TR in our patient is a combination of tricuspid valve dysplasia and AF. There are two types of TV dysplasia: (i) Ebstein's anomaly which is characterized by apical displacement of the annulus and (ii) TV dysplasia without septal leaflet displacement nor atrialization of the right ventricle. They both share tethering of the leaflets to the underlying myocardium and there can be shortening of TV chordae. The MR and echocardiography imaging of our patient concurs with the characteristics of TV dysplasia, namely the shortening of the subvalvular apparatus that explains the severe tenting and the adherence of the posterior leaflet to the myocardium causing its restrictive movement. This anomaly could have caused a pre-existing TR that over time dilated the right ventricle. Although this defect is congenital, the patient remained asymptomatic until adulthood. We speculate that the development of AF after parathyroidectomy surgery contributed to tricuspid ring dilation, greater TR, and more severe shunting, which triggered the onset of symptoms.

The other central component in this case is the CN, a reticulated web of fibres in the right atrium that originates from incomplete resorption of the embryonic right valve of sinus venosus.11 Imaging studies report a prevalence between 2–15% and a mean length of 3 cm.12 Compared to this measurement, the CN in this case is unusually large (5 cm). This remnant has no clinical significance, albeit it has been associated with thrombus formation, endocarditis, arrhythmias, and congenital defects like PFO, with 83% of patients affected by both.13 The CN could even favour the persistence of PFO and potentiate the risk of embolic events.14

Definitive treatment for POS is the closure of the atrial shunt. In one of the largest case series to date,15 76 of 78 patients with POS underwent successful PFO closure with resolution of symptoms. The percutaneous approach is preferred over surgery because of lower morbidity, except in the presence of co-existing anatomic defects.

Despite the availability of an effective treatment, patients with POS still suffer from delayed diagnosis. This case should raise awareness among physicians of POS in patients with hypoxaemia of unknown origin and increase the understanding of its underlying mechanisms. Early recognition and timely treatment are paramount to improve the quality of life of these patients.

**Lead author biography**

Dr Laura Fuertes Kenneally is a cardiology resident at the General University Hospital of Alicante, Spain. She received her Medical Degree from the Miguel Hernández University in Elche. She has an interest in general cardiology and basic cardiovascular science.

**Supplementary data**

Supplementary material is available at European Heart Journal—Case Reports online.
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Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as Supplementary data.

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References

1. Burchell HB, Helmholz HF, Wood EH. Reflex orthostatic dyspnea associated with pulmonary hypertension. Am J Physiol 1949;159:563–564.
2. Rodrigues P, Palma P, Sousa-Pereira L. Platypnea-orthodeoxia syndrome in review: defining a new disease! Cardiology 2012;123:15–23.
3. Cheng TO. Mechanisms of platypnea-orthodeoxia: what causes water to flow uphill? Circulation 2002;106:e47.
4. Sirt R, Youssef GS. Acute right to left shunt—combination of tricuspid valve endocarditis, Chiari network, and ostium secundum atrial septal defect. J Cardiol Cases 2017;16:151–153.
5. Garg R, Wark T, Dudley J, Robertson J. Obstructing Chiari network facilitating blood flow across a patent foramen ovale causing hypoxia. J Am Coll Cardiol Case Rep 2020;2:1025–1028.
6. Hatami Y, Tanaka H, Kajura A, Tsuda D, Matsuoka Y, Kawamori H et al. Sudden onset of platypnea-orthodeoxia syndrome caused by traumatic tricuspid regurgitation with ruptured chordae tendineae after blunt chest trauma. Can J Cardiol 2018;34:1088.e11–1088.e13.
7. Patel AD, Abo-Auda WS, Nekkanti R, Ahmed S, Razmi RM, Pohost GM et al. Platypnea-orthodeoxia in a patient with ostium primum atrial septal defect with normal right heart pressures. Echocardiography 2003;20:299–303.
8. Kai HK, Koyanagi S, Hirooka Y, Sugimachi M, Sadowa J, Suzuki S et al. Right-to-left shunt across atrial septal defect related to tricuspid regurgitation: assessment by transesophageal Doppler echocardiography. Am Heart J 1994;127:578–584.
9. Qureshi MY, Sonnmer RJ, Cabalak AK. Tricuspid valve imaging and intervention in pediatric and adult patients with congenital heart disease. JACC Cardiovasc Imaging 2019;12:637–651.
10. Utsunomiya H, Harada Y, Susawa H, Ueda Y, Izumi K, Iakura K et al. Tricuspid valve geometry and right heart remodeling: insights into the mechanism of atrial functional tricuspid regurgitation. Eur Heart J Cardiovasc Imaging 2020;21:1068–1078.
11. Loukas M, Sullivan A, Tubbs RS, Weinhaus AJ, Derderian T, Hanna M. Chiari’s network: review of the literature. Surg Radiol Anat 2010;32:895–901.
12. Moral S, Ballesteros E, Huguet M, Panaro A, Palet J, Evangelista A. Differential diagnosis and clinical implications of remnants of the right valve of the sinus venosus. J Am Soc Echocardiogr 2016;29:183–194.
13. Schneider B, Hofmann T, Jussen MH, Meierertz E. Chiari’s network: normal anatomic variant or risk factor for arterial embolic events? J Am Coll Cardiol 1995;26:203–210.
14. Rigatelli G, Dell’avvocata F, Braggion G, Giordan M, Chinaglia M, Cardiaci P. Persistent venous valves correlate with increased shunt and multiple preceding cryptogenic embolic events in patients with patent PFO: an intracardiac echocardiographic study. JACC Cardiovasc Interv 2008;2:72–973.
15. 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;28:164–168.