CASE BASED DISCUSSIONS

Platypnoea–orthodeoxia syndrome: beware of investigations undertaken supine

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ABSTRACT

Platypnoea–orthodeoxia syndrome (POS) is a rare disorder, manifesting as deoxygenation occurring when the patient is in the upright position. Four broad mechanisms for the condition have been described: intracardiac shunts, intrapulmonary shunts, hepatopulmonary syndrome and pulmonary ventilation–perfusion mismatch. Here, we present the first case of POS in a patient with a proven right to left intracardiac shunt occurring in the context of postural hypotension and normal right heart pressures. We highlight the need to carry out investigations in the upright position before discounting intracardiac shunting as a cause for the syndrome. Short-term improvement of the syndrome was obtained with medical management of the patient's orthostatic hypotension and as such suggests a conservative management strategy for similar patients, which may delay the need for invasive procedures to close the anatomical defect.

RP (Senior House officer): An 85-year-old man presented with 2 weeks of intermittent shortness of breath. His medical history included bilateral pulmonary emboli, for which he was taking apixaban 5 mg twice daily, Parkinson's disease, benign prostatic hypertrophy and overactive bladder. He had never smoked.

On examination, his chest was clear, heart sounds were normal and he was clinically euvolaemic. Fingertip oxygen saturation (SpO_2) was 75% seated and he had type 1 respiratory failure with a PaO_2 of 6.7 kPa and $PaCO_2$ of 4.3 kPa breathing room air. D-dimer was raised at 1111 ng/mL and he underwent CT pulmonary angiography which excluded recurrent thromboembolic disease and did not indicate another cause for respiratory failure.

SDR (Consultant Cardiologist): Contrast-enhanced echocardiography revealed good biventricular function and a haemodynamically insignificant left to right shunt at the atrial level. Cardiac MRI confirmed the presence of a patent foramen ovale (PFO) but again did not demonstrate a significant shunt. Left and right heart catheterisation showed unobstructed coronaries and normal pulmonary pressures, respectively. The calculated pulmonary to systemic blood flow ratio was within the normal range for the methodology used (0.9).

Our investigations failed to demonstrate a cause for respiratory failure and as intracardiac shunting seemed unlikely, we considered the possibility of an intrapulmonary shunt. The patient was transferred to the regional respiratory centre.

FL (Respiratory Senior House Officer): Interestingly, the patient desaturated primarily when sitting upright. Specifically, when supine and breathing room air, his SpO_2 was 98%; however, he desaturated to 77% after sitting upright for 10 min. Arterial blood gases revealed a supine PaO_2 of 10.8 kPa but a sitting PaO_2 of 6.59 kPa with corresponding $PaCO_2$ of 4.4 kPa and 4.5 kPa. We observed that his deoxygenation occurred in combination with a fall in systolic blood pressure of 36 mm Hg. The patient's positional deoxygenation was suggestive of POS. However, given the absence of a right to left intracardiac shunt on previous investigations, the cause of his POS remained unclear. We did, however, suspect that his orthostatic hypotension played a role in the pathophysiology of his syndrome.

MIP (Consultant Respiratory Physician): It is important to note that all of the investigations so far had been carried out in the supine position, and this was particularly true of the cardiac MRI and right heart catheterisation which had been used to 'rule out' intracardiac shunting. Thus, relying on these tests to exclude a shunt which occurs only when upright might provide false reassurance.

I therefore arranged an anatomical shunt study to be performed in the upright position. We have previously shown that a shunt greater than 8% is associated with a high likelihood of a functionally significant defect.[1]

SW (Principal Respiratory Physiologist): The anatomical shunt investigation was carried out with the patient seated upright. The patient breathed 100% oxygen from a Douglas bag via a two-way non-rebreathing valve and tightly sealed mouthpiece until complete equilibrium was identified by stable oxygen end tidal measurements. A further arterial blood gas was measured at this point. The ideal PaO_2 breathing 100% oxygen was calculated to be 89.5 kPa. The patient's PaO_2 in equilibrium with 100% oxygen was 12.5 kPa. A fall of 2.66 kPa from the ideal PaO_2 value equates to a 1% shunt and thus this patient demonstrated a sizeable anatomical shunt of 28.9% of his cardiac output.

MH (Consultant respiratory physician) and MIP: To locate the anatomical position of the shunt he underwent, a second contrast-enhanced echocardiogram while seated at 60 degrees. This revealed a Grade 3 right to left shunt across his PFO (figure 1; online supplementary video 1). Expert review of his imaging failed to disclose evidence of pulmonary

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/thoraxjnl-2019-213258)

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Received 20 February 2019
Revised 5 April 2019
Accepted 30 April 2019
Published Online First 30 May 2019

Check for updates

To cite: Liew F, Gargoum F, Potter R, *et al*. *Thorax* 2019;**74**:917–919.

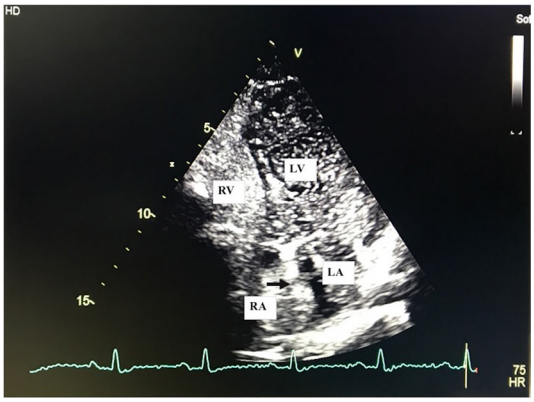

Figure 1 Apical four chamber view of transthoracic echocardiogram after intravenous injection of bubble contrast. The latter can be seen to cross the atrial septum from right to left (arrow). LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

arteriovenous malformation (AVM) or liver disease and circulating liver enzymes were normal.

FG (Respiratory Specialist Registrar): Orthostatic hypotension was a new feature in this man. Although orthostatic hypotension can be a feature of parkinsonism, the patient had recently been started on several medications which also could have contributed to its development. These included tamsulosin, finasteride, mirabegron and mirtazapine. In view of the clear relationship between episodes of hypotension and periods of deoxygenation, these medications were slowly tapered. In doing so, the episodes of desaturation became less frequent and profound.

Percutaneous closure of the PFO was considered. However, this procedure is not without risk. Death or massive haemorrhage complicates 1.5% of cases, while 'minor' complications including cardiac arrhythmias, device thrombosis and arteriovenous fistula formation occur in 7.9%.[2] Furthermore, the patient had become increasingly frail as a result of a long period of hospitalisation with debilitating positional dyspnoea. Therefore, we explored managing him conservatively by treating his orthostatic hypotension. Following withdrawal of all causative medications, we initiated treatment with fludrocortisone 200 µg.

FL: Following 1 week of fludrocortisone treatment, the patient no longer reported positional dyspnoea. His upright SpO_2 was 88% and blood pressure was 101/66 mm Hg. He returned to the referring hospital. To further support his blood pressure, fludrocortisone was increased to 400 µg and he commenced treatment with midodrine. These medications were tolerated well and attenuated the severity of his POS for 3 months, allowing the patient to receive physiotherapy and restore his functional status. However, the improvement proved unsustained and the patient underwent percutaneous closure of his PFO, with complete resolution of his syndrome.

DISCUSSION

FL, FG, MIP: POS is a rare clinical syndrome which describes deoxygenation and dyspnoea when the patient is in the upright position. To date, less than 200 cases have been described in the literature. Four broad mechanisms for this syndrome have been described: intracardiac shunts, intrapulmonary shunts, hepatopulmonary syndrome and pulmonary ventilation–perfusion (VQ) mismatch. The pathophysiology of the latter three is straightforward. The majority of AVMs occur in the lung bases. In an upright position, more blood is diverted to the base of the lung thereby increasing movement of deoxygenated blood into the systemic circulation. The same gravitational mechanisms could explain increased blood flow through hepatic collaterals in the case of hepatopulmonary syndrome, or pulmonary anastomoses which are also a feature of that condition. Similarly, in cases of VQ mismatch, the upright position augments the physiological deadspace in the upper zones of the lungs, which may be sufficient to cause deoxygenation in cases of severe lung parenchymal or thromboembolic disease.[3]

Although the most commonly described, POS in the context of an intracardiac shunt is more challenging to explain. The right to left shunt occurs despite normal right heart pressures, as seen in the present case. Some authors have proposed that the upright position results in a transient rise in right atrial pressure when the patient has a less compliant right ventricle (RV).[3] RV filling pressures reduce on standing but flow through the left ventricle increases causing it to become more compliant relative to the stiff RV, which resists filling from the right atrium. Thus, blood flows preferentially via the septal defect into the more compliant left side of the heart. Consistent with this theory, POS caused by intracardiac shunts has mostly been reported in the elderly population, and compliance of the RV is known to reduce with age. Cases have also been reported in patients with RV infarcts, eosinophilic endomyocardial disease and constrictive pericarditis,[3] all of which could preferentially reduce RV compliance.

We describe the first case of POS in a patient with a proven right to left intracardiac shunt occurring in the context of postural hypotension. Although not a well-recognised association, three cases of POS in the context of orthostatic hypotension secondary to autonomic failure, diabetes and Parkinson's disease have been described.[4 5] Interestingly, none of these patients had evidence of an intracardiac shunt, although this was not sought directly by Fox and colleagues.[5] These authors did, however, use transient fluid loading to confirm that the shunting could be corrected by resolving hypotension, although we did not feel ethically able to attempt this in our patient.

Furthermore, we have demonstrated that shunting only occurred when upright and that its severity could be attenuated by manipulating medications to raise his blood pressure. We hypothesise that as a result of orthostatic hypotension, his systemic vascular resistance failed to rise sufficiently on standing to maintain his mean arterial pressure (MAP). When combined with age-related stiffness of his RV, this fall in MAP could cause a transient rise in right atrial pressure relative to the left atrium, resulting in a significant shunt. The improvement of his POS on treatment of his orthostatic hypotension supports this.

In summary, POS is a rare clinical syndrome which can be challenging to recognise. Although most cases are associated with a PFO, this is the first to suggest postural hypotension as a key driving factor for right to left shunting of blood. Furthermore, this is the first case to show improvement, although temporary, with conservative strategies, delaying the need for invasive interventions to close the defect. Importantly, intracardiac shunts should not be discounted as a cause for POS unless the investigations which do so are undertaken in the appropriate body position.

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Contributors FL and FG were involved in the clinical care of the patient at the Royal Brompton Hospital and co-wrote the manuscript. RP was involved in the clinical care of the patient at Ealing Hospital and co-wrote his section of the manuscript. SDR was the patient's lead clinician while at Ealing hospital. He selected the images and supplementary video for this case report and co-wrote his section of the manuscript. SW performed and reported the anatomical shunt study. He co-wrote his section of the manuscript. MH was involved in the clinical care of the patient at the Royal Brompton Hospital and co-wrote the manuscript. MIP was the lead clinician responsible for the patient's care at the Royal Brompton Hospital and co-wrote the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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