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BRIEF COMMUNICATION

Platypnea-Orthodeoxia Syndrome in the Setting of Patent Foramen Ovale Without Pulmonary Hypertension or Major Lung Disease

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BACKGROUND: Patent foramen ovale (PFO)-associated platypnea-orthodeoxia syndrome is characterized by dyspnea and hypoxemia when upright. The pathogenesis is thought to involve an increase in right atrial pressure or change in degree of right to left shunting with upright posture.

METHODS AND RESULTS: We sought to characterize patients with platypnea-orthodeoxia syndrome related to PFO without pulmonary hypertension. We retrospectively reviewed databases at 3 tertiary referral hospitals in New South Wales, Australia from 2000 to 2019. Fourteen patients with a mean age of 69±14 years had a PFO with wide tunnel separation. Mean New York Heart Association Classification was II (±0.9) and 7 inpatients had been confined to bed (from postural symptoms). Baseline oxygen saturations supine were 93%±5% and 84%±6% upright. Two patients had a minor congenital heart defect and 4 had mild parenchymal lung disease with preserved lung function. The mean aortic root diameter was 37±6 mm and distance between aortic root and posterior atrial wall was 16±2 mm. Platypnea-orthodeoxia syndrome was preceded by surgery in 5 patients and 1 patient had mild pneumonia. Successful closure of the PFO using an Amplatzer device was performed in 11 of 14 patients. Post-closure, all patients had New York Heart Association Classification I (improvement 1.6±0.9, $P<0.003$) and semi-recumbent oxygen saturations increased by 13%±8% ($P<0.001$, n=10).

CONCLUSIONS: Platypnea-orthodeoxia syndrome is a debilitating condition, curable by PFO closure. Anatomical distortion of the atrial septum related to a dilated aortic root or shortening of the distance between the aortic root and posterior atrial wall may contribute to the syndrome.

Key Words: normal pulmonary pressures ■ patent foramen ovale ■ PFO closure ■ platypnea-orthodeoxia syndrome ■ right-to-left shunt

Patent foramen ovale (PFO) is common in the general population, with an estimated incidence at 25%–30%.[1] Platypnea-orthodeoxia syndrome (POS) however, is rare and likely to be underdiagnosed. PFO-associated POS is characterized by dyspnea and hypoxemia when upright, defined by a drop in PaO2 >4 mm Hg or SaO2 >5%.[1–3] The pathogenesis is thought to involve an increase in right atrial pressure or change in degree of right to left shunting with upright posture attributable to a structural change. Since the first reported case in 1949, there has been an increasing number of documented cases with attempts to define precipitants for POS in the absence of an elevated right-to-left pressure gradient.[1] These have typically

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been isolated case reports, with a small number of case series that have included patients with major lung pathology.[3–5]

We sought to characterize patients who were diagnosed with POS related to PFO without major structural heart disease, pulmonary hypertension (pulmonary vascular resistance >3 Wood units), or moderate/severe lung disease (lung volumes <80% predicted), to understand clinical features, PFO intracardiac anatomy and outcomes following PFO closure.

METHODS

We retrospectively reviewed databases at 3 tertiary referral hospitals (serving an adult population of 2.1 million) in New South Wales, Australia from 2000 to 2019. Continuous variables are expressed as mean±SD. Comparison within the study groups was assessed with Student *t*-test and a p-level of ≤0.05 was deemed significant. We declare that all supporting data are available within the article. The research conducted was minimal risk and written consent was waived. Ethics was approved by Sydney Local Health District Human Ethics Committee.

Findings

Patient characteristics, anatomical features and precipitating factors are detailed in Table. The mean New York Heart Association (NYHA) Classification was II (±0.92) with most patients presenting with dyspnea or found to have orthodeoxia during inpatient assessment. Seven inpatients had been confined to bed (because of postural symptoms) from 5 days up to 1 month. Of the patients without congenital heart disease, 30+33 days elapsed from onset of symptoms or signs of POS to diagnosis. In the 2 patients with minor congenital heart disease, symptoms had been present for several years.

Baseline oxygen saturations when supine were 93%±5% and 84%±6% when upright. All patients had a PFO with wide tunnel separation and a strongly positive bubble study at rest. Two patients had a minor congenital heart defect (invasively confirmed mild pulmonary stenosis or repaired ventricular septal defect) and 4 had mild parenchymal lung disease on imaging, with preserved lung function. Other anatomical features noted were a shortened distance between the aortic root and posterior atrial wall distance (16±2 mm) compared with expected normal values (>26 mm)[5] and ascending aortic root dilatation (37±6 mm, 20±5 mm/m^2) that may alter aortic arch curvature (Figure S1).

Successful closure of the PFO using an Amplatzer device was performed in 11 of 14 patients, the remainder declined or had major comorbidities precluding closure. Post-closure all patients had New York Heart Association Classification of I (improvement of 1.6±0.9, *P*<0.0034, n=11). Oxygen saturations increased by 13%±8% (*P*<0.001, n=10, post procedural oxygen saturations were presumed to have been recorded in the semi-recumbent position). The saturations were missing for 1 patient who underwent closure. There were no procedural complications.

Table 1. Patient Characteristics (n=14)

Age, y	69±14
Women (%)	7 (50)
Body surface area (m^2)	1.9±0.2
Inpatients (%)	9 (64)
Presenting complaint	
Dyspnea/platypnea	10 (71)
Hypoxemia/orthodeoxia	14 (100)
Paradoxical embolus	2 (14)
Erythrocytosis	1 (7)
Flushing/headache	1 (7)
Syncope	1 (7)
Congenital heart disease	2 (14)
Lung disease, mild (lung volumes >80% predicted)	4 (29)
Precipitant	5 (36)
Coronary artery bypass grafting	1 (7)
Sub-diaphragmatic/other surgery	4 (29)
Aortic sinus diameter (mm)	37±6
Aortic sinus indexed (mm/m^2)	20±5
Aortic root to posterior atrial wall distance (mm)	16±2
Closure with Amplatzer device (25–35 mm)*	11 (79)
Aneurysmal septum (%)	13 (92)
Mean hemoglobin (g/L)	143±32

Values are mean+SD or n (%).
*3 subjects opted not to proceed with closure.

DISCUSSION

In our cohort, focused on patients with preserved lung and pulmonary vascular function, the diagnosis of POS was frequently delayed because the condition was underrecognized as a potential diagnosis in the absence of pulmonary hypertension. Other potential contributors to delay in diagnosis include multiple comorbidities that confuse the clinical presentation and the difficulty in diagnosing orthodeoxia in hospitalized patients - when patients are semi-recumbent, oxygen saturations are less obviously deranged. In our cohort, the delay to diagnosis had important clinical implications with prolonged hospital stays and long periods of recumbency.

All patients in this series had a highly mobile atrial septum with a gaping PFO. Other typical anatomical cardiac features were a shortened distance between the posterior aortic root and posterior atrial wall distance; and ascending aortic root dilatation or

elongation resulting in increased aortic arch curvature. The elongation or dilatation of the ascending aorta can cause compression on the right atrium and allows the PFO to gape open when upright.[4,6]

Over one third of the patients in our series had an inciting event that may have altered intrathoracic pressure and/or structure. When there are changes to the aortic anatomy, it tilts the axis of the inter-atrial septum causing the defect to be placed in line with the highest flow from the inferior vena cava. The defect gapes wider, and there is preferential streaming of flow across the inferior vena cava. This distortion may also be the culprit following intra-thoracic or abdominal surgery. A prominent Eustachian valve or a highly mobile aneurysmal septum may also contribute to preferential streaming across the defect in the absence of an inter-atrial pressure gradient (right>left).[3–6]

POS is a debilitating condition, treatable at low procedural risk by PFO closure. Consideration of this uncommon and likely underdiagnosed syndrome may prevent delay in diagnosis and allow for early, curative intervention.

ARTICLE INFORMATION

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Disclosures

None.

Supplemental Material

Figure S1

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SUPPLEMENTAL MATERIAL

Figure S1. Transesophageal echocardiogram demonstrating a highly mobile and aneurysmal atrial septum and the method for measuring the posterior atrial wall distance (dotted line from posterior margin of aortic root to inner edge of posterior atrial wall at septal anchor-point).