Clinical Vignettes

Platypnea-Orthodeoxia Syndrome: A Case of Chronic Paroxysmal Hypoxemia

C. Craig Rudy, B.S.^{1,4}, Cody Ballard, P.A.-C.^{2,4}, Craig Broberg, M.D., M.C.R.^{2,4}, and Alan J. Hunter, M.D.^{3,4}

¹School of Medicine, Oregon Health & Science University, Portland, OR, USA; ²The Knight Cardiovascular Institute, Oregon Health & Science University, Portland, OR, USA; ³Division of Hospital Medicine, Department of Medicine, Oregon Health & Science University, Portland, OR, USA; ⁴Oregon Health & Science University, Portland, OR, USA.

A 75-year-old man with chronic (30-year) unexplained paroxysmal hypoxemia presented with postural hypoxemia and desaturation consistent with a clinical manifestation of platypnea-orthodeoxia syndrome. His history included a lack of significant past pulmonary disease, yet with intermittent need for oxygen supplementation. On admission he was found to have an interatrial shunt through a patent foramen ovale. Device closure by percutaneous catheterization led to sustained resolution of symptoms. Platypnea-orthodeoxia syndrome is a rare but important consideration in the differential diagnosis of hypoxemia, as it represents a potentially curable cause of hypoxemia, with missed diagnosis leading to possible patient morbidity if untreated. Even more importantly, an astute and careful history and physical examination are integral to the diagnosis of this rare but likely unrecognized syndrome.

KEY WORDS: platypnea; orthodeoxia; hypoxemia; patent foramen ovale; intracardiac shunt.

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INTRODUCTION

Platypnea-orthodeoxia syndrome (POS) is a rare but important consideration in the differential diagnosis of unexplained dyspnea and hypoxemia. POS is defined by the presence of provoked dyspnea (platypnea) and objective hypoxemia (orthodeoxia) when moving from a supine to vertical position—a seeming paradox when contrasted with the more common orthopnea so often seen in congestive heart failure.¹

² With a complete history and basic tests, the identification of POS is relatively straightforward; however, identifying the underlying etiology can prove challenging. POS may originate in the setting of either intracardiac or intrapulmonary pathologies. The true incidence of intracardiac POS is uncertain, and is likely underdiagnosed given that the literature comprises primarily case reports.³

We present a man with a long history of unexplained paroxysmal dyspnea and hypoxemia, in whom the identification of platypnea and orthopnea ultimately led to a diagnosis of a reversible intracardiac cause. Additionally, we discuss the current understanding of the pathophysiology of the syndrome, with a focus on the intracardiac etiologies.

CASE

A 75-year-old man had a 30-year history of unexplained paroxysmal dyspnea and hypoxemia, first occurring in the 1980s following a diagnosis of severe pneumonia requiring supplemental oxygen at discharge. He continued to have multiple recurrent episodes of self-resolving hypoxemia without an identified cause. Five months prior to his current presentation, he was hospitalized at an outside institution for two sequential cerebrovascular accidents in the setting of newly diagnosed atrial fibrillation. He was again noted to have cryptic hypoxemia and was discharged with supplemental oxygen. He underwent two unsuccessful catheter ablation procedures for his atrial fibrillation. After the second ablation, he experienced acute worsening of hypoxemia requiring hospital readmission. CT pulmonary angiography was negative for a pulmonary embolism, and an agitated saline transthoracic echocardiogram (TTE) showed inconclusive evidence of a right-to-left shunt due to poor image quality. The patient was transferred to our institution for further evaluation of his hypoxemia. History revealed daily dyspnea that was severely disabling by midday, relieved only by recumbent rest. He denied recent history of fever, cough, chest pain, hemoptysis, lower extremity edema, or weight changes. Additional medical history included hypertension, hyperlipidemia, and sleep apnea, with nightly continuous positive airway pressure (CPAP) therapy. Home medications were atorvastatin, losartan, diltiazem, and warfarin. He had no history of tobacco use or significant environmental exposure. Investigation of prior records did not show conclusive evidence of right-to-left intracardiac shunt.

The intake physical examination was performed with the patient sitting in a semi-upright position off oxygen. His blood pressure was 102/71 mmHg, pulse 88 bpm, temperature

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36.5 °C, respiratory rate 18, and oxygen saturation 88 %. He appeared moderately dyspneic. His exam was notable for a non-elevated jugular venous pressure, regular rate and rhythm with a normal S1 and S2 without abnormal splitting, no murmurs, rubs, parasternal heaves, or gallops, and his lungs were clear bilaterally. His extremities were warm with 2+ pulses throughout. He had notable digital clubbing and cyanosis, but no hepatomegaly, ascites, gynecomastia, palmar erythema, spider angiomas, or edema. He was noted to have profound respiratory distress and oxygen desaturation to less than 88 % when sitting up on room air that was unchanged with supplemental oxygen administration. His hypoxemia and need for supplemental oxygen completely resolved upon returning to the supine position but recurred on provocative challenge. Chemistries, liver enzymes, and blood count analyses were normal. A single anterior–posterior chest radiograph showed only minimal left lower lobe atelectasis. An electrocardiogram revealed a first-degree atrioventricular (AV) block (248 ms) and borderline left axis deviation (QRS axis -17°), but otherwise normal conduction. Arterial blood gas demonstrated acute respiratory alkalosis with a PaO₂ of 74. His presentation was thus consistent with POS.

A recumbent transesophageal echocardiogram (TEE) revealed a 1-cm communication across the atrial septum, with right-to-left shunting confirmed with both color Doppler and appearance of agitated saline in the left atrium within three cardiac cycles (Fig. 1). The septum had a large flap-like component partially covering a defect, consistent with a large stretched patent foramen ovale (PFO). With no other explanation for the patient's POS, it was believed that this PFO was contributing to his protracted hypoxemia.

Right heart catheterization confirmed normal intracardiac pressures. The PFO was closed percutaneously with a 30-mm

Amplatzer™ Cribiform device. The post-procedure TTE with agitated saline and Doppler visualized the device with minimal residual right-to-left shunting. Clinically, our patient experienced complete resolution of his platypnea and orthodeoxia following the procedure. There was no change in his first-degree AV block. He was discharged 2 days later without oxygen, and remains asymptomatic 1 year later. He is also recovering from his prior strokes, exercising 4 days weekly, and traveling with his wife.

DISCUSSION

This case describes a man with a 30-year history of unexplained dyspnea and hypoxemia, ultimately determined to be POS, who experienced complete resolution upon closure of his identified PFO. Observations during bedside assessment contributed to the diagnosis. While it is difficult to explain how this syndrome was masked or intermittently exacerbated over the years, its complete resolution with repair of the PFO certainly supports a causative role.

Platypnea describes the subjective sensation of shortness of breath in the sitting or standing position that is relieved in the supine position. Likewise, orthodeoxia describes objective hypoxemia in the sitting or standing position that is relieved when supine. The diagnosis of POS is a clinical diagnosis without consensus diagnostic criteria.⁴ Diagnostic evaluation consists of a physical exam in both the supine and upright position with corresponding oxygen saturation monitoring. Further investigative studies, such as echocardiography, can subsequently be targeted to finding the underlying etiology. Importantly, because many imaging studies are performed with patients in a supine position, they may not demonstrate

Figure 1 Transesophageal echocardiogram demonstrating right-to-left shunt with Doppler and agitated saline. Panel a shows a large patent foramen ovale (PFO) communicating between the right atrium (RA) and left atrium (LA). Panel b shows the PFO, with color demonstrating shunting across the PFO from RA to LA. Panel c demonstrates agitated saline in both the RA and LA, with saline bubbles visualized in transit across the PFO. Specifically demonstrated in the left panel: more than five bubbles appearing in the LA in less than three cardiac cycles, which is diagnostic of an intracardiac shunt.

the same desaturation seen in different body positions.⁵ In the case of this patient, although a supine TEE demonstrated right-to-left shunt, its magnitude was likely less than when he was sitting. Furthermore, introducing agitated saline through a lower extremity IV can optimize shunt detection owing to venous return from the inferior vena cava directed at the atrial septum.³ An important and non-invasive alternative in the shunt work-up is the ^{99m}Tc-macroaggregated albumin nuclear medicine study, which can detect and calculate the total shunt percentage.⁶ Classically, intracardiac POS shunt work-up has been initiated with echocardiography; however, careful consideration should be given to patient-specific factors when determining which shunt study is appropriate.

Pathology in either the heart or the lungs can lead to POS, with three separate pathophysiologic mechanisms: intrapulmonary arteriovenous shunts, pulmonary disorders associated with V/Q mismatch, and intracardiac shunts.³ Clinicians are often far more familiar with hepatopulmonary syndrome (HPS), which is found in up to 10–30 % of patients with cirrhosis.⁴ In HPS, the positional hypoxemia occurs when one assumes an upright position, leading to preferential blood flow through the lung bases where pathologic arteriovenous malformations predominate, resulting in right-to-left shunting.¹ Similarly, in pulmonary conditions resulting in apical V/Q mismatch, patients experience diminished pulmonary arteriole blood flow at the lung apices without associated ventilatory compensation, which is exacerbated in the upright position.¹ POS can also occur in non-cirrhotic liver disease, although it is less commonly recognized.⁴ The remainder of this discussion will focus on intracardiac POS.

Due to the rarity of descriptive literature, the incidence of intracardiac POS is unknown, with most discussions limited to case reports. The most comprehensive review of POS discussed features of 188 patients from 105 case reports, where 167 patients (89 %) were found to have POS due to an intracardiac shunt.³ Among those involving a right-to-left intracardiac shunt with normal pulmonary artery and right atrial pressures, 88.3 % had a PFO.³

While the pathophysiology of intracardiac POS is not completely elucidated or uniformly endorsed, there appear to be two, slightly differing theories: the dynamic structural-mediated^{1, 2} and dynamic pressure-mediated hypotheses.⁷ In both hypotheses there is an assumption of a “two-hit” process, consisting of both an underlying anatomic defect and an additional acquired cardiac or pulmonary abnormality associated with a variety of anatomic and systemic processes.⁷

In the *structural* hypothesis, intracardiac POS requires the presence of an interatrial communication, which is most typically a PFO, but may also be an atrial septal defect or fenestrated atrial septal aneurysm.^{2, 3} In healthy individuals with a PFO, left atrial pressure is slightly higher than right atrial pressure, resulting in a pressure gradient sufficient to functionally close the PFO by abutting the flap of tissue against the septal wall. However, in some individuals, shunting of deoxygenated blood from the right atrium to the left atrium can

occur, bypassing the pulmonary circulation, which can result in cryptogenic stroke, paradoxical embolism, or POS.^{3, 5} This may occur in the setting of elevated right atrial pressures, but intracardiac POS can also occur in the setting of normal right atrial pressures, suggesting reliance on an underlying “functional component” of the shunt.² It has been hypothesized that, instead of changes in pressure, physical changes in the shape and orientation of the atrial septum and inferior vena cava, dependent on body position, cause a streaming of flow from the inferior vena cava directly towards the interatrial communication. A right-to-left jet results despite normal right atrial pressures.³ Factors leading to these changes are diverse and are not completely understood, but from the only complete review, the most common associated anatomic abnormalities that could explain flow-related changes were aortic changes (23.4 %—aneurysm, dilation, or distortion), pneumonectomy (15.6 %), and diaphragm paralysis (10.6 %).³ Other described changes included a prominent eustachian valve, Chiari network, localized emphysema, kyphoscoliosis, right hydrothorax, and chest trauma.^{3, 5}

In the *pressure-mediated* hypothesis, an interatrial abnormality must similarly be present; however, the *second hit* may be due to a dynamic pressure gradient created by a multitude of factors, including postural changes in atrial chamber volumes causing shunt reversal, decreased left-sided filling pressures when orthostatic, and right atrial compression from nearby structures (e.g. dilated aortic root).⁷ Notably, this article indicates that medical symptomatic management focused on controlling right atrial pressure may be possible, whereas therapies previously described in the literature were targeted at closure of the atrial communication.

Reconciliation of these two distinct hypotheses has not yet been addressed in the literature. It seems plausible that both are independent, or even interdependent, mechanisms of POS. Clinically, our patient had POS with concomitant normal right-sided pressures in the supine position. An upright measurement of right atrial pressure by angiocatheter would be prohibitively difficult, and short of that, we cannot prove that his right atrial pressures are unchanged in the upright position. However, intracardiac POS has been detected in a patient with sequential recumbent and upright TEE, demonstrating clinically significant exaggeration of the shunt in a patient with severe aortic root dilation.⁸ Consistent with previous reviews, our patient had a number of findings that have been associated with intracardiac POS in prior reports, including kyphosis and mild dilation of the ascending aorta.^{3, 5}

Regardless of the associated anatomic abnormalities, the definitive treatment of POS with an identified interatrial communication is surgical or percutaneous closure of the defect. Untreated, the patient would likely continue to experience significant dyspnea and hypoxemia. In a retrospective trial of 78 patients, percutaneous closure was shown to provide statistically significant improvement in New York Heart Association scores.⁹ Successful closure of an atrial defect has been shown to produce symptomatic improvement in more than 95 % of

patients, and percutaneous intervention is the preferred method of closure.^{9, 10} In patients where closure cannot be achieved or is medically unsafe, medical therapy can be considered.⁷

In summary, this patient's 30-year history of cryptic hypoxemia may be attributable to POS due to an unrecognized PFO. Identification and closure resulted in resolution of a 30-year history with significant impact on his livelihood. Although it is unlikely that the resolution of his symptoms was mere coincidence, this alternative cannot be completely eliminated, given the atypical course of the disease and protracted intermittent symptoms. This case highlights the importance of considering POS when evaluating unexplained hypoxemia, since the treatment for such may dramatically improve daily function and quality of life. A directed history and physical exam is a simple way to diagnose POS, which is likely more prevalent than currently recognized.

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Corresponding Author: Alan J. Hunter, M.D.; Oregon Health & Science University, 3181 SW Sam Jackson Park Road Mail Code: BTE119, Portland, OR 97239, USA (e-mail: huntera@ohsu.edu).

Compliance with Ethical Standards:

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