Title

A 38-Year-Old Man With Well Treated OSA on CPAP With Persistent Nocturnal Hypoxemia

Journal

CHEST Journal, 157(1)

ISSN

0012-3692

Authors

Culpepper, David J
Hong, Deborah
Ryden, Armand
et al.

Publication Date

2020

DOI

10.1016/j.chest.2019.06.045

CHEST

A 38-Year-Old Man With Well Treated OSA on CPAP With Persistent Nocturnal Hypoxemia

David J. Culpepper, MD; Deborah Hong, MD; Armand Ryden, MD; Jesse Currier, MD; Jonathan M. Tobis, MD; Sharon De Cruz, MD; and Michelle R. Zeidler, MD

CASE PRESENTATION: A 38-year-old male with a prior diagnosis of severe OSA (apnea-hypopnea index [AHI] 99/h) presented for transfer of care. He was successfully titrated to CPAP of 10 cm H_2O at an outside laboratory and was compliant with therapy with residual AHI 1.9/h. On presentation, he was polycythemic, with negative evaluation for primary polycythemia, and evaluation for hypoxemia was initiated. CHEST 2020; 157(1):e1-e3

Medical history was significant for hypertension, hyperlipidemia, gastroesophageal reflux disease, and obesity. He had a 4 pack-year smoking history. His medications included amlodipine, lisinopril, omeprazole, and simvastatin. The patient lived at sea level.

Physical Examination Findings

Vitals on presentation: afebrile, heart rate 85 beats/min, BP 128/83 mm Hg, respiratory rate 18 breaths/min, and oxygen saturation (Sa_{O_2}) 94% on room air. His BMI was 38. Pertinent findings on physical examination included oropharynx with a Mallampati class IV airway, breath sounds clear to auscultation bilaterally, cardiac regular rate and rhythm without a murmur, and no clubbing or cyanosis.

Laboratory Findings

Hemoglobin level was 18.0 g/dL. Arterial blood gas showed daytime room air Pa_{O_2} 67 mm Hg and PaC_{O_2} 36.3 mm Hg with an A-a gradient of 37.4 mm Hg. Pulmonary function testing and chest radiograph were normal. Initial 3-night oximetry showed 88 min $<$ 88% Sa_{O_2} (oxygen nadir 81%, oxygen desaturation index 4.4/h) while on CPAP (residual AHI $<$ 5/h). Transthoracic echocardiogram (TTE) revealed left ventricular ejection fraction 65%, right ventricle with normal systolic function, no evidence of right heart pathology, and a negative bubble study. Right heart catheterization showed pulmonary artery pressure 32/10 mm Hg. Supplemental oxygen with CPAP was initiated at 2 L/min; however, significant nocturnal hypoxemia persisted. Repeat 3-night oximetry showed 91 min $<$ 88% Sa_{O_2} (oxygen nadir 80%, oxygen desaturation index 2.1/h, 0 min $<$ 80% Sa_{O_2}) with no specific pattern of desaturation.

What is the cause of the hypoxemia? What intervention should be done next?

What is the diagnosis?

AFFILIATIONS: From the Department of Medicine (Drs Culpepper, Hong, Ryden, Currier, and Zeidler), Greater Los Angeles Veterans Affairs Healthcare System, Los Angeles, CA; and Department of Medicine (Drs Culpepper, Hong, Ryden, Currier, Tobis, De Cruz, and Zeidler), University of California, Los Angeles, Los Angeles, CA.

Dr Culpepper is currently at Franciscan Medical Group (Federal Way, WA).

CORRESPONDENCE TO: David J. Culpepper, MD, Franciscan Medical Group, 34503 9th Ave S, Ste 230, Federal Way, WA 98003; e-mail: davidculpepper@chifranciscan.org

DOI: https://doi.org/10.1016/j.chest.2019.06.045

Cause and next step: Subsequent transcranial Doppler revealed a high-grade right-to-left shunt at rest, increasing with Valsalva maneuver. Transesophageal echocardiography showed a patent foramen ovale (PFO). The patient underwent PFO closure.

Diagnosis: Persistent sleep-related hypoxemia secondary to OSA in the setting of a PFO.

Discussion

The differential diagnosis of sleep-related hypoxemia includes reduced inspired oxygen tension with altitude, sleep-related hypoventilation, V/Q mismatch, and shunt. The patient lived at sea level. He did not carry a diagnosis of pulmonary or neuromuscular disease. Awake pCo_2 was low normal, arguing against obesity hypoventilation, but not fully excluding it. Lack of improvement in oxygenation with supplemental oxygen with CPAP therapy argues against V/Q mismatch, leaving shunt as the most likely diagnosis.

Sleep pulse oximetry is a valuable tool for the detection of hypoxemia. It should be considered for patients with severe obesity or those with other evidence of possible hypoxemia during sleep, such as polycythemia, regardless of whether the AHI has normalized on CPAP therapy.

OSA is a common condition in the general population, occurring in 24% of men and 9% of women. Similarly, PFO is seen in approximately 20% to 25% of the general population. PFO is more prevalent in patients with OSA, occurring in up to 65% of patients with sleep apnea. Concurrent OSA and PFO can lead to more severe nocturnal desaturation compared with those without a PFO. The pathophysiology results from a transient increase in right-sided heart pressure with sleep. In the setting of a PFO, this elevated pressure can result in temporary right-to-left shunting depending on the pressure gradient across the septum. Furthermore, the prevalence of right-to-left shunting is reinforced by hypoxic pulmonary vasoconstriction that occurs during the apneic episode. Asking patients with OSA to perform a Valsalva maneuver can demonstrate this phenomenon by simulating the increased right-sided filling pressures. Patients with both OSA and a PFO will be more likely to have a significant drop in Sao_2 compared with those without a PFO. The presence of a PFO results in patients with OSA becoming symptomatic at a younger age as well as a greater arterial desaturation relative to the number of respiratory disturbances.

Traditionally, evaluation for PFO requires the use of a TTE with an agitated saline bubble study. Unfortunately, because of the imprecision of this study, a negative result in the setting of a high clinical suspicion would prompt further evaluation with an invasive transesophageal echocardiogram for confirmation. More recently, transcranial Doppler has been proven to have the same sensitivity and specificity as a transesophageal echocardiogram for the diagnosis of PFO. Additionally, this procedure is noninvasive and thus better tolerated by patients.

CPAP is the accepted primary therapy for OSA. In most cases, appropriate treatment of OSA with CPAP improves nocturnal hypoxemia; the effect of closure of PFO on nocturnal hypoxemia remains unclear. CPAP actually helps reduce the amount of right-to-left shunting that occurs in patients with concurrent OSA and PFO. The theory behind this effect is that CPAP limits the variation of intrathoracic pressure throughout the respiratory cycle and diminishes hypoxemia and pulmonary arterial pressure, thus decreasing right-to-left shunting through the valve-like PFO. As noted, CPAP alone does not seem to be adequate in resolving hypoxemia for all patients. In these cases, it appears the PFO is directly responsible for ongoing symptoms. It remains unclear what factors of the PFO causes some patients to continue to be symptomatic while on appropriate CPAP therapy. It is likely that the size of the PFO is an important factor, but this alone does not account for the differences seen between cases. In patients with concurrent OSA and PFO, the percutaneous closure of the PFO can have therapeutic purposes because it decreases the passage of deoxygenated blood into the left atria, which limits intermittent hypoxemia and the risk of periodic breathing. This in turn can have dramatic improvements on the overall control of a patient's sleep-disordered breathing and daytime symptoms. Further studies are needed to better delineate which patients would benefit from preemptive closure of PFO in addition to the conventional CPAP therapy.

Clinical Course

The patient presented with laboratory findings suggestive of hypoxemia, which was confirmed on nocturnal oximetry. Hypoxemia occurred in the setting of concurrent OSA with PFO despite adequate CPAP

treatment and 2 L of supplemental oxygen. He underwent successful percutaneous PFO closure. Repeat polysomnogram 4 months after PFO closure on CPAP and room air showed resolution of nocturnal hypoxemia (AHI 1.5/h, oxygen nadir 90%). Supplemental nocturnal oxygen was discontinued. Hemoglobin at an interval follow-up 9 months after oxygen was discontinued, was 16.4 g/dL, and has remained normal. The patient's weight remained stable throughout his clinical course.

Clinical Pearls

1. *The prevalence of PFO is much higher in patients with OSA compared with the general population.*
2. *Nocturnal desaturations are more severe in those patients with concurrent OSA and PFO compared with those with OSA alone.*
3. *Transcranial Doppler is more sensitive for detection of PFO compared with traditional TTE and may be indicated in patients with a negative bubble study if clinical suspicion remains high.*
4. *Additional studies are needed to better predict which patients would benefit from preemptive closure of PFO, in addition to conventional CPAP therapy.*
5. *Sleep pulse oximetry monitoring should be considered in obese OSA patients even in the setting of normalization of the AHI on CPAP therapy or in those patients with the risk of sleep-related hypoventilation, intrinsic pulmonary disease, or other causes of hypoxemia.*

Acknowledgments

Financial/nonfinancial disclosures: None declared.

Other contributions: *CHEST* worked with the authors to ensure that the Journal policies on patient consent to report information were met.

Suggested Readings

Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. *Mayo Clinic Proc*. 1984;59:17-20.

Shanoudy H, Soliman A, Raggi P, et al. Prevalence of patent foramen ovale and its contribution to hypoxemia in patients with obstructive sleep apnea. *Chest*. 1998;113:91-96.

Beelke M, Angeli S, Del Settle M, et al. Prevalence of patent foramen ovale in subjects with obstructive sleep apnea: a transcranial Doppler ultrasound study. *Sleep Med*. 2003;4:219-223.

Agnoletti G, Iserin L, Lafont A, Sidi D, Desnos M. Obstructive sleep apnoea and patent foramen ovale: successful treatment of symptoms by percutaneous foramen ovale closure. *J Interv Cardiol*. 2005;18:393-395.

Johansson MC, Eriksson P, Peker Y, et al. The influence of patent foramen ovale on oxygen desaturation in obstructive sleep apnoea. *Eur Respir J*. 2006;29:149-155.

Silver B, Greenbaum A, McCarthy S. Improvement in sleep apnea associated with closure of a patent foramen ovale. *J Clin Sleep Med*. 2007;3:295-296.

Lau EM, Yee BJ, Grunstein RR, Celermajer DS. Patent foramen ovale and obstructive sleep apnea: a new association? *Sleep Med Rev*. 2010;14:391-395.

Pellaton C, Heinzer R, Michel P, Eeckhout E. Patent foramen ovale and obstructive sleep apnoea: from pathophysiology to diagnosis of a potentially dangerous association. *Arch Cardiovasc Dis*. 2011;104:242-251.

Mojadidi MK, Bohkoor PI, Gevorgyan R, et al. Sleep apnea in patients with and without a right-to-left shunt. *J Clin Sleep Med*. 2015;11:1299-1304.

Beelke M. CPAP treatment promotes the closure of a patent foramen ovale in subjects with obstructive sleep apnea syndrome - results from a pilot study. *SM J Neurol Disord Stroke*. 2017;3:1015-1021.