Case Report / *Olgu Sunumu*

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Nocturnal Desaturation Due to Hereditary Thrombophilia: A Case Report

Nokturnal Desaturasyonun Ardındaki Kalıtsal Trombofili: Olgu Sunumu

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Abstract

Nocturnal hypoxemia is often attributed to obstructive sleep apnea syndrome (OSAS), but it may also reveal occult cardiopulmonary or thromboembolic disease. A 42-year-old woman with excessive daytime sleepiness and snoring underwent polysomnography, which showed mild OSAS. Despite her normal body mass index and absence of severe respiratory events she had nocturnal desaturation (mean SpO_2 88%). V/Q scintigraphy detected subsegmental defects indicating pulmonary embolism, and echocardiography revealed mild pulmonary hypertension. Genetic analysis demonstrated homozygous MTHFR C677T and PAI-1 (4G/4G) mutations. Anticoagulation and vitamin supplementation were initiated, resulting in normalized imaging. Nocturnal hypoxemia may be associated with thrombotic activity, especially in the presence of hereditary thrombophilia.

Keywords: Nocturinal hypoxia, OSAS, hereditary thrombophilia, chronic thromboembolic pulmonary hypertaension

Öz

Noktürnal hipoksemi genellikle obstrüktif uyku apne sendromu (OSAS) ile ilişkilendirilir; ancak altta yatan kardiyopulmoner ya da tromboembolik hastalıkların da göstergesi olabilir. Aşırı gündüz uykululuğu ve horlama yakınmasıyla başvuran 42 yaşında kadın hastada polisomnografide hafif OSAS saptandı. Normal vücut kitle indeksi ve belirgin solunumsal olayları olmamasına rağmen, noktürnal desaturasyon (ortalama SpO_2: %88) izlendi. Ventilasyon–perfüzyon sintigrafisinde pulmoner emboli ile uyumlu subsegmenter perfüzyon defektleri, ekokardiyografide hafif pulmoner hipertansiyon mevcuttu. Genetik analizde homozigot MTHFR C677T ve PAI-1 (4G/4G) mutasyonları tespit edildi. Antikoagülan tedavi ve vitamin desteği sonrası görüntüleme bulguları normale döndü. Noktürnal hipoksemi, özellikle kalıtsal trombofili varlığında, trombotik aktivite ile ilişkili olabilir.

Anahtar Kelimeler: Nokturinal hipoksi, OSAS, herediter trombofili, kronik tromboembolik pulmoner hipertansiyon

Introduction

Nocturnal hypoxemia is defined as a mean oxygen saturation level below 90% during sleep. While it is most frequently encountered in patients with obstructive sleep apnea syndrome (OSAS), it can also be observed in patients with chronic obstructive pulmonary disease (COPD), pulmonary hypertension (PH), obesity hypoventilation syndrome, congestive heart failure, neuromuscular disorders, or pregnancy, and in individuals living at high altitude (1).

Several mechanisms explain the relationship between OSAS and increased risk of thrombosis (2). Intermittent hypoxia induces oxidative stress and cellular injury, which in turn cause endothelial dysfunction, vascular inflammation, and enhanced platelet aggregation. Hypoxia-driven erythropoietin release results in elevated hematocrit and blood viscosity, ultimately promoting thrombosis. Recurrent episodes of desaturation also upregulate tissue factor, initiating the extrinsic coagulation cascade, while downregulating thrombomodulin, a cofactor required for activation of protein C in the anticoagulant pathway.

Beyond OSAS, nocturnal hypoxemia has also been described in patients with chronic thromboembolic pulmonary disease (CTEPD) and chronic thromboembolic PH (CTEPH). In these conditions, unresolved thromboembolic obstruction leads to persistent ventilation–perfusion mismatch, which may worsen during sleep and contribute to nocturnal desaturation independent of respiratory events (3). Importantly, nocturnal

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hypoxemia has been associated with right heart remodeling and impaired hemodynamics in patients with CTEPH, suggesting that sleep-related desaturation may serve not only as a clinical marker but also as a pathogenic driver of disease progression.

Taken together, nocturnal hypoxemia is a clinical finding that may either reflect the presence of established cardiopulmonary disease or reveal an undiagnosed condition. Here, we present a patient, after obtaining informed consent, initially evaluated for OSAS symptoms, in whom further investigation led to the diagnosis of pulmonary embolism and hereditary thrombophilia. This case highlights the importance of considering thromboembolic disease in the differential diagnosis of unexplained nocturnal desaturation.

Case Report

A 42-year-old hypertensive female smoker who did not live at high altitude presented with excessive daytime sleepiness, fatigue, and snoring. Polysomnography revealed mild OSAS [Apnea–Hypopnea Index (AHI): 13/h], a mean nocturnal oxygen saturation of 88%, and T90 (time below 90% oxygen saturation) of 45%. Despite a normal body mass index (24 kg/m^2) and absence of severe respiratory events, she exhibited marked nocturnal desaturation.

The patient's systemic physical examination and postero-anterior chest X-ray were normal. Pulmonary function testing of the patient showed no obstruction and hemoglobin was 13.7 g/dL. Echocardiography demonstrated preserved left ventricular ejection fraction (60%), mild PH (37 mmHg), and mild tricuspid regurgitation with a tricuspid annular plane systolic excursion (TAPSE) of 20 mm. V/Q scintigraphy revealed heterogeneous perfusion with subsegmental defects in the right lower lobe, consistent with pulmonary embolism (Figure 1).

The patient had no conventional risk factors for thrombosis; however, genetic testing revealed homozygous MTHFR C677T and PAI-1 (4G/4G) polymorphisms. Laboratory evaluation showed vitamin B12 of 208 ng/L, folate of 6.8 mg/L, and homocysteine of 11.8 µmol/L. Following B12 (1 mg/day) and folate (5 mg/day) supplementation, homocysteine decreased to 8 µmol/L in 12 weeks. Anticoagulation with warfarin was administered for 6 months. Follow-up imaging confirmed resolution of perfusion defects, while echocardiography showed mild improvement in right ventricular function (TAPSE 22

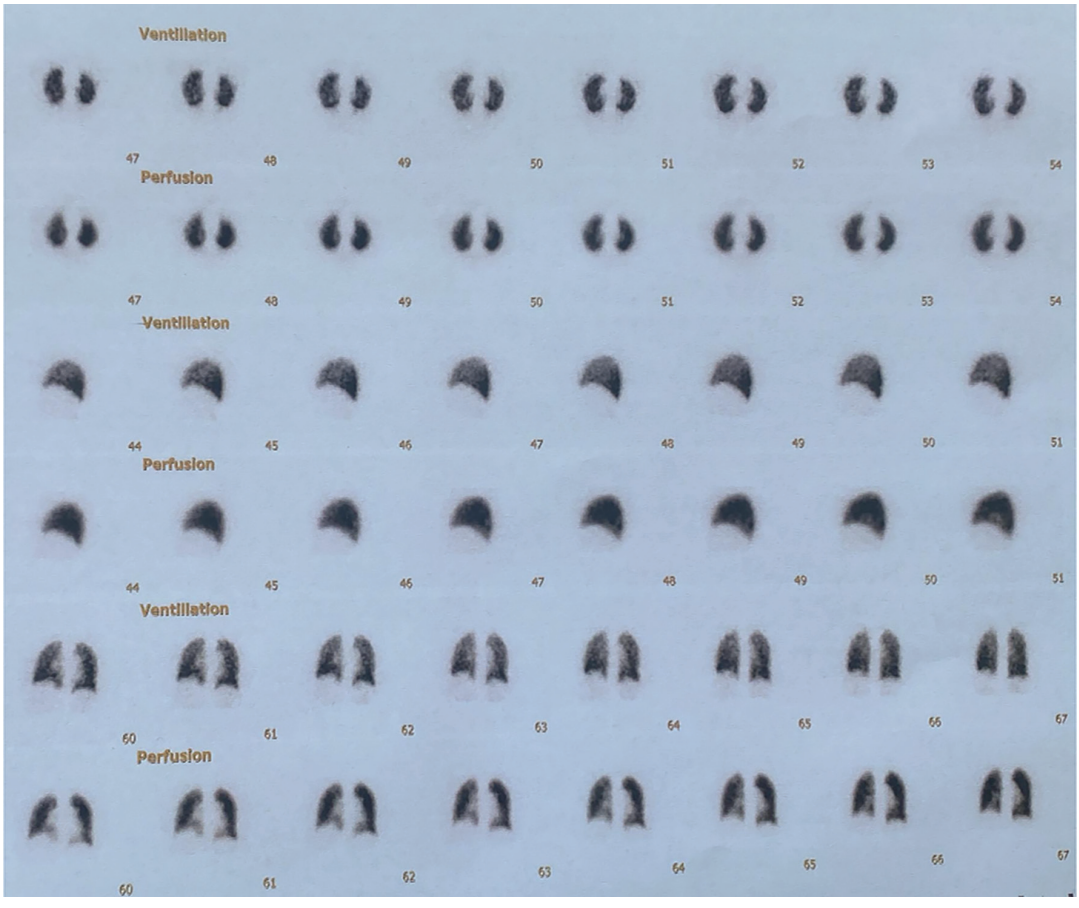

Figure 1. Perfusion images: partially heterogeneous involvement in both lungs; subsegmental hypoperfusion areas in the superior and posterior basal segments of the right lung's lower lobe. Ventilation images: hypoperfused areas are ventilated and compatible with high probability of pulmonary thromboembolism.

mm) and stable pulmonary pressure (35 mmHg). The patient remains under observation.

Discussion

Nocturnal hypoxemia is a multifactorial phenomenon most frequently caused by OSAS, but may also result from other causes. In COPD, hypoventilation and ventilation–perfusion mismatch contribute, while in heart failure, pulmonary congestion and Cheyne–Stokes respiration exacerbate desaturation.

The incidence of CTEPD following acute pulmonary embolism ranges from 0.5% to 9% (4). Risk factors include diagnostic delay, recurrent embolism, and right ventricular dysfunction. In CTEPD, indices such as mean SpO_2 and T90 are stronger predictors of PH than AHI (5). Importantly, nocturnal hypoxemia has been correlated with right heart structural changes and impaired hemodynamics, even in the absence of overt OSAS (6).

Pronounced nocturnal hypoxia in these patients may result from ventilation–perfusion mismatch due to organized thrombus and from hypoxia-related increases in tumor necrosis factor alpha, which may augment thrombophilia (7).

Methylenetetrahydrofolate reductase (MTHFR) C677T polymorphism decreases enzyme activity, leading to hyperhomocysteinemia in folate deficiency, predisposing individuals to venous thrombosis and cardiovascular disease (8). In patients carrying an MTHFR mutation, supplementation with vitamin B12 (0.5 mg/day) and folate (0.5–5 mg/day) is indeed a reasonable and evidence-based strategy to lower plasma homocysteine levels and to reduce the risk of hyperhomocysteinemia-related complications (9). Plasminogen activator inhibitor-1 (PAI-1) 4G/5G variant increases PAI-1 expression and inhibits fibrinolysis, further promoting thrombus formation (10). While systematic reviews suggest that these mutations alone may not consistently predict clinical thrombotic events (11), their coexistence with intermittent hypoxia, as in OSAS, may amplify thrombotic risk.

In the present case, the combination of OSAS-related intermittent hypoxia and genetic thrombophilia likely increased her thrombotic susceptibility, leading to pulmonary embolism. As reported by Han et al. (5), nocturnal hypoxemia, independent of AHI, has been identified as an independent determinant of elevated mean pulmonary artery pressure, as in our case. Although anticoagulation and vitamin supplementation normalized perfusion and homocysteine levels in 12 weeks, mild PH persisted, possibly due to delayed recognition. Current guidelines (12) do not support lifelong anticoagulation or antiplatelet therapy in such cases, emphasizing the importance of individualized follow-up.

Conclusion

Nocturnal hypoxemia should not be regarded solely as a marker of sleep-disordered breathing. It may indicate occult cardiopulmonary or thromboembolic disease and can contribute to disease progression if unrecognized. Patients with disproportionate nocturnal desaturation should undergo a thorough evaluation, including V/Q imaging and echocardiography. Early identification of underlying causes enables timely management and may prevent long-term complications.

Ethics

Informed Consent: Written informed consent was obtained from a 42-year-old female patient.

Footnotes

Conflict of Interest: No conflict of interest was declared by the authors.

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References

1. Hajipour M, Labarca G, Ayas N, et al. Nocturnal hypoxemia in respiratory medicine: pathophysiology, measurement, and association with outcomes. Semin Respir Crit Care Med. 2025;46(2):221-232.
2. Raj R, Paturi A, Ahmed MA, et al. Obstructive sleep apnea as a risk factor for venous thromboembolism: a systematic review. Cureus. 2022;14(2):e22729.
3. Li HT, Yuan P, Jiang R, et al. Sleep-disordered breathing and nocturnal hypoxemia in chronic thromboembolic pulmonary disease. Intern Med J. 2024;54(8):1292-1301.
4. Valerio L, Mavromanoli AC, Barco S, et al. Chronic thromboembolic pulmonary hypertension and impairment after pulmonary embolism: the FOCUS study. Eur Heart J. 2022;43(36):3387-3398.
5. Han T, Huang Q, Zhai Z, et al. Nocturnal hypoxemia is associated with poor pulmonary hemodynamics in patients with chronic thromboembolic pulmonary disease. Respir Res. 2025;26(1):239.
6. Spiesshoefer J, Herkenrath S, Harre K, et al. Sleep-disordered breathing and nocturnal hypoxemia in precapillary pulmonary hypertension: prevalence, determinants, and clinical consequences. Respiration. 2021;100(9):865-876.
7. Naito A, Sakao S, Terada J, et al. Nocturnal hypoxemia and high circulating TNF-α levels in chronic thromboembolic pulmonary hypertension. Intern Med. 2020;59(15):1819-1826. doi:10.2169/internalmedicine.4458-20.
8. Mazokopakis EE, Papadomanolaki MG, Papadakis JA. Association of methylenetetrahydrofolate reductase (MTHFR) gene polymorphisms with serum folate, cobalamin, and homocysteine concentrations in Greek adults. Scand J Clin Lab Invest. 2023;83(2):69-73.
9. McCaddon A, Miller JW. Homocysteine-a retrospective and prospective appraisal. Front Nutr. 2023;10:1179807.
10. Maghsudlu M, Noroozi Z, Zokaei E, et al. Association between plasminogen activator inhibitor-1 4G/5G polymorphism and recurrent pregnancy loss: an updated systematic review and meta-analysis. Thromb J. 2024;22(1):44.
11. Valeriani E, Pastori D, Astorri G, et al. Factor V Leiden, prothrombin, MTHFR, and PAI-1 gene polymorphisms in patients with arterial disease: a comprehensive systematic review and meta-analysis. Thromb Res. 2023;230:74-83.
12. Middeldorp S, Nieuwlaat R, Baumann Kreuziger L, et al. American Society of Hematology 2023 guidelines for management of venous thromboembolism: thrombophilia testing. Blood Adv. 2023;7(22):7101-7138.