Journal Pre-proof

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PII: S0300-2896(26)00007-4

DOI: https://doi.org/doi:10.1016/j.arbres.2025.12.011

Reference: ARBRES 3938

To appear in: *Archivos de Bronconeumologia*

Received Date: 22 October 2025

Accepted Date: 11 December 2025

Please cite this article as: Herrera M, Zapata JJ, Dalmases M, Central sleep apnea in multiple sclerosis: an underrecognized comorbidity, *Archivos de Bronconeumología* (2026), doi: https://doi.org/10.1016/j.arbres.2025.12.011

Type of article: Clinical letter

Central sleep apnea in multiple sclerosis: an underrecognized comorbidity

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Although central sleep apnea (CSA) has been associated with neurologic conditions such as stroke, tumors and Arnold-Chiari malformation, its occurrence in multiple sclerosis (MS) is rarely reported. Sleep-disordered breathing (SDB) has been associated with fatigue, cognitive dysfunction and disease progression in MS. Nevertheless, it often remains under-recognized in the routine clinical practice. Early detection and treatment could improve quality of life and potentially modulate disease trajectory.

We report the case of a 69-year-old man diagnosed with primary progressive MS in 2011, presenting initially with progressive lower limb weakness and reduced walking distance. Baseline magnetic resonance image (MRI) revealed multiple supratentorial, periventricular and spinal cord demyelinating lesions at C4-C5. Throughout the following years, despite fampridine treatment, he developed progressive paraparesis and reduced mobility. Respiratory function tests were as follows: FEV_1/FVC ratio, 0.78; FEV_1 (forced expiratory volume in 1 second), 2.15 L (67% predicted); FVC (forced vital capacity), 2.75 L (65% predicted); TLC (total lung capacity), 5.48 L (79% predicted); DLCO (diffusing capacity for carbon monoxide), 62% predicted; and KCO (carbon monoxide transfer coefficient), 83% predicted. The maximal inspiratory and expiratory pressures were 51cm$H_2$0 (56% predicted) and 73 cm$H_2$0 (62% predicted), respectively. Arterial blood gas analysis revealed the following values: pH, 7.43; PaO_2, 79 mmHg; $PaCO_2$, 33 mmHg; bicarbonate, 23 mmol/L, and base excess of -1.7 mmol/L. In 2024, he was referred to the sleep unit for snoring and witnessed apneas without excessive daytime sleepiness. Polysomnography revealed frequent central sleep apneas (Figure 1-A), with an apnea-hypopnea index (AHI) of 40 events/hour, an oxygen desaturation index (ODI) of 41/hour, mean arterial oxygen saturation (SaO_2) of 92% and 0.9% of the time spent with SaO2 < 90% (CT90). According to the hypnogram, the distribution of sleep stages was as follows: stage 1 (2%), stage 2 (47%), stage 3 (39%), and REM sleep (12%). The overall arousal index was 46/hour, predominantly associated with respiratory events. Periodic limb movements (PLMs) were present, with a PLM index of 19/hour and a PLM-related arousal index of 5/hour. These findings indicate a moderate frequency of PLMs, which may have also contributed to sleep fragmentation; however, the overall architecture remained relatively preserved, with a normal proportion of light sleep. Follow-up MRIs demonstrated lesion progression involving infratentorial regions, including the cerebellum and the brainstem (Figure 1-B). The case was oriented as central apneas in the context of demyelinating lesions in the brainstem and a manual CPAP titration was performed. CPAP treatment failed to resolve the central apneas and adaptive servo-ventilation (ASV) was started with the following parameters: EPAP, 4-15 cmH_2O; support pressure, 0-15 cm$H_2$0 and auto backup rate. The treatment was well-tolerated and at the follow-up visit the overnight oximetry with ASV showed an ODI of 4 events/hour, mean SaO_2 of 93% and CT90 of 0.5%. The revision of the built-in software of the ASV device confirmed the adequate correction of respiratory events.

Sleep disturbances affect up to 50% of patients with MS, including SDB, insomnia, circadian rhythm disorders, restless legs syndrome, narcolepsy and REM sleep behavior disorder[1]. OSA is the most widely reported form of SDB in MS, whereas CSA is a rare finding, with a reported prevalence of 1%–4% and series negative for CSA[2-4]. A bidirectional relationship between the 2 conditions has been proposed. On the one hand, MS demyelinating lesions in the brainstem or spinal cord can impair upper airway muscle tone and favor OSA and/or disrupt respiratory control and produce CSA as it was the case with our patient. On the other hand, SDB-related intermittent hypoxia may aggravate neuroinflammation and neurodegeneration[2-4]. Therefore, screening for SDB should be considered in

patients with MS and CSA suspected in the presence of brainstem lesions[4]. Although evidence on the best treatment for CSA in MS is scarce and should be individualized, ASV may be an effective therapeutic option as occurred in our case[5].

In conclusion, CSA can occur in patients with MS, especially in those with infratentorial lesions, and may respond favorably to ASV treatment. Systematic screening for SDB, even in the absence of typical symptoms, should be considered in this population due to the possible impact of SBD in MS progression.

DECLARATIONS SECTION

ETHICAL CONSIDERATIONS: This study was conducted in full compliance with the ethical standards of the institutional research committee and the principles outlined in the Declaration of Helsinki.

INFORMED CONSENT: Informed consent was obtained from the patient.

FUNDING: None declared.

AUTHORS' CONTRIBUTIONS

M.H. and J.J.Z. collected the clinical data, created the figure, and drafted the manuscript. M.D. contributed to study conceptualization, manuscript planning, and critical review. All authors participated in critical revision of the manuscript and approved the final version.

CONFLICTS OF INTEREST: None declared.

ARTIFICIAL INTELLIGENCE INVOLVEMENT: This material was not partially or entirely produced with the assistance of artificial intelligence software or tools.

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Sí

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Figure 1. 1A. Conventional polysomnography showing frequent central apneas and periodic limb movements. **1B.** Brain MRI showing multiple demyelinating lesions in the brainstem.