



# Continuous Positive Airway Pressure Therapy in a Patient with Pantothenate-Kinase-Associated Neurodegeneration

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Dear Editor,

Pantothenate-kinase-associated neurodegeneration (PKAN), also known as Hallervorden-Spatz Disease, is the most common form of neurodegeneration involving brain iron accumulation. Most patients with classic PKAN are wheelchair-bound by their midteens.<sup>1</sup> The first-line treatment for obstructive sleep apnea (OSA), one of the most common sleep disorders, is continuous positive airway pressure (CPAP) therapy. Dystonia or dyskinesia hinders the application of CPAP therapy. There have been a few reports on the treatment of OSA by using invasive procedures including intrathecal baclofen or tracheostomy in patients with laryngeal dystonia and severe bulbar dysfunction.<sup>2</sup> However, evidence is lacking for the usefulness of CPAP in patients with severe dystonia and OSA. Herein we report a case of PKAN and OSA treated with CPAP, with favorable acceptance and compliance.

A 12-year-old boy presented at our sleep clinic with the frequent cessation of breathing during sleep. Recurrent falling with generalized dystonia had started from 2 years of age, and the patient had been wheelchair-bound since the age of 8 years. His younger brother presented similar symptoms. The patient was diagnosed with PKAN caused by gene mutation (R440P and N501I; compound heterozygote) at 9 years of age (Fig. 1A, B). He had a history of deep brain stimulation of the bilateral globus pallidus interna due to severe dystonia. The patient showed progressive retrocollic dysphagia with dystonia, and underwent percutaneous endoscopic gastrostomy. Frequent snoring and cessation of nocturnal breathing was observed during the previous 2 years. His body mass index was 14.6 kg/m<sup>2</sup> (weight, 36 kg; height, 157 cm), and his neck circumference was 34 cm. Overnight polysomnography (PSG) was successfully completed despite severe dystonia, which revealed moderate OSA with an apnea-hypopnea index (AHI) of 16.2/h. His lowest oxygen level was 69%, and desaturation with the level below 90% accounted for 84.4% of the total sleep time (Fig. 1C). The AHIs in supine and nonsupine positions were 18.0/h and 0/h, respectively. The AHI was markedly higher during rapid eye movement (REM) sleep (31.4/h) than during non-REM sleep (16.2/h). The patient showed no abnormal limb movements or parasomnia. Following a second PSG session, snoring and OSA completely disappeared at a CPAP of 7 cm H<sub>2</sub>O (Fig. 1D). After 1 month of CPAP therapy his daytime sleepiness improved and the mean AHI during CPAP therapy decreased to 1.3/h. The patient used CPAP therapy every day; the proportion of days with >4 h/night usage was on 97% of days, and the mean duration was 6.7 h/day.

Our patient presented severe dystonia and dysphagia, possibly associated with the development of OSA.<sup>3</sup> OSA accelerates neurocognitive deterioration and increases mortality rates via various mechanisms such as intermittent hypoxia, sleep fragmentation, and hemodynamic fluctuation.<sup>4</sup> Although there is no evidence for the development of sleep-related breathing disorder in PKAN,<sup>5</sup> adequate respiratory support is recommended if stridor or laryngeal dystonia is observed.<sup>6</sup> The present patient received CPAP therapy due to the presence of moderate OSA and profound desaturation (down to 69%). His acceptance of and compliance with

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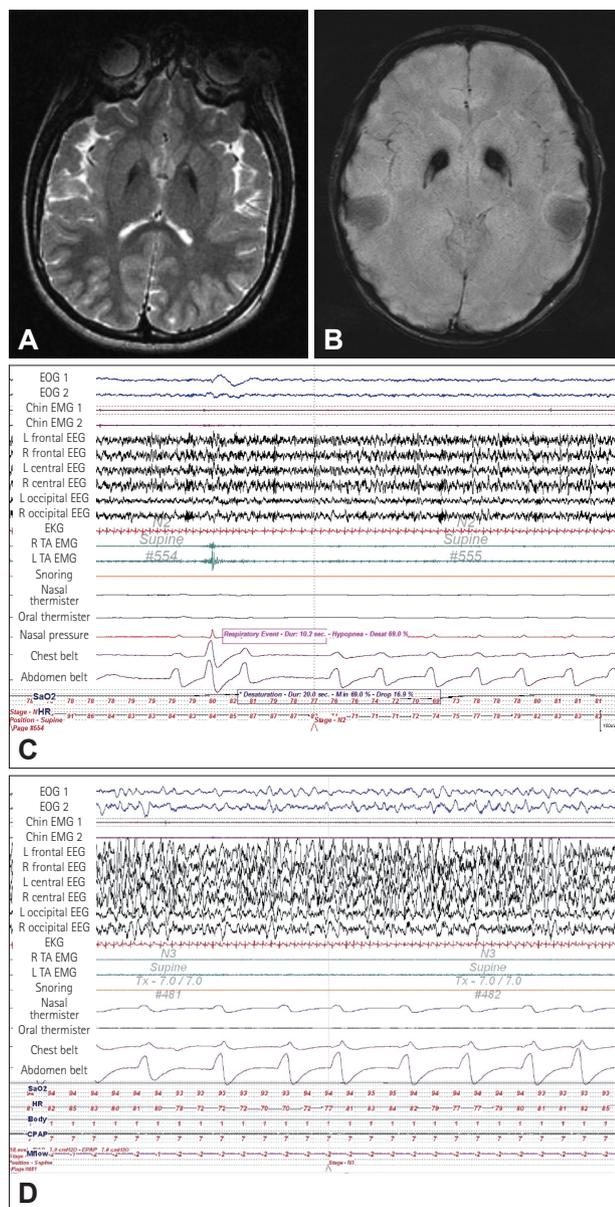
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CPAP usage were excellent, and no complications (e.g., air leakage or skin irritation) were reported.

Neuronal loss and iron accumulation in the globus pallidus



**Fig. 1.** Magnetic resonance imaging and polysomnography features of the patient. T2-weighted (A) and T2\* susceptibility-weighted images showing a hyperintense center with a dense hypointense rim (eye-of-tiger sign) (B). C: Baseline polysomnography image revealing recurrent episodes of obstructive sleep apnea and the lowest oxygen saturation (down to 69%). D: Complete elimination of snoring and sleep apnea was confirmed at a continuous positive airway pressure of 7 cm H<sub>2</sub>O by polysomnography. CPAP: continuous positive airway pressure, EEG: electroencephalography, EKG: electrocardiogram, EMG: electromyography, EOG: electrooculography, HR: heart rate, L: left, R: right, SaO<sub>2</sub>: peripheral oxygen saturation, TA: tibialis anterior.

interna could reduce inhibitory outputs to the pedunculopontine nuclei, which are the muscle tone regulators of REM sleep in patients with PKAN.<sup>5</sup> In our patient, AHI during REM sleep was twice as high as that during non-REM sleep. Thus, the phenotype of OSA in patients with PKAN could differ from that in patients without dystonia. This is the first report on the usefulness of CPAP therapy in a patient with PKAN. Clinicians should diagnose and treat OSA despite the presence severe dystonia or the disabled state of patients. Further studies are needed to elucidate the pathogenesis and efficacy of CPAP therapy in patients with PKAN and OSA.

**Author Contributions**

Conceptualization: Dae Lim Koo. Data curation: Hyung Seok Guk, Dae Lim Koo. Formal analysis: Dae Lim Koo. Investigation: Hyung Seok Guk, Dae Lim Koo, Hyunwoo Nam. Methodology: Dae Lim Koo. Supervision: Dae Lim Koo, Hyunwoo Nam. Writing—original draft: Hyung Seok Guk, Dae Lim Koo. Writing—review & editing: Hyung Seok Guk, Dae Lim Koo, Hyunwoo Nam.

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**Conflicts of Interest**

The authors have no potential conflicts of interest to disclose.

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