https://doi.org/10.5664/jcsm.9314

JCSM | Journal of Clinical Sleep Medicine

CASE REPORTS

A case of Cheyne-Stokes breathing emerging in a patient with atrial fibrillation and an implanted hypoglossal nerve stimulator

Hanna Hong, MD[1]; Joel Oster, MD[2]; Aarti Grover, MD[1]; Khalid Ismail, MD[1]

[1]Division of Pulmonary, Critical Care, and Sleep Medicine, Tufts Medical Center, Boston, Massachusetts; [2]Division of Neurology, Tufts Medical Center, Boston, Massachusetts

Treatment emergent central sleep apnea (TECSA) can occur with positive airway pressure (PAP) therapy, mandibular advancement devices, and now recent cases with hypoglossal nerve stimulator (HNS) therapy during treatment for obstructive sleep apnea (OSA). There have been few published reports of Cheyne-Stokes breathing (CSB) emerging after implantation of an HNS. We present a case of a 76-year-old male with chronic atrial fibrillation and OSA who developed significant CSB after implantation of an HNS device. As popularity increases for alternative treatments of OSA, there should be close monitoring for emergence of CSB, especially in those who may have a propensity for high loop gain abnormalities contributing to central sleep apneas, such as patients with chronic atrial fibrillation. Further research is needed on CSA in patients with HNS implantation and atrial fibrillation, the prevalence of TECSA in the growing HNS therapy population, and the development of future management strategies.

Keywords: hypoglossal nerve stimulator, Cheyne-Stokes breathing, obstructive sleep apnea

Citation: Hong H, Oster J, Grover A, Ismail K. A case of Cheyne-Stokes breathing emerging in a patient with atrial fibrillation and an implanted hypoglossal nerve stimulator. *J Clin Sleep Med.* 2021;17(8):1731–1735.

INTRODUCTION

Treatment emergent central sleep apnea (TECSA) has been shown to occur with positive airway pressure (PAP) therapy and with mandibular advancement devices during treatment for obstructive sleep apnea (OSA). There have been few published reports of TECSA occurring with the use of the hypoglossal nerve stimulator (HNS) since the introduction of the use of upper airway stimulation for OSA.[1] Prevalence and predictive factors for TECSA have been studied in PAP therapy,[2] but little is known about TECSA occurring with HNS. With growing popularity of innovative treatments for PAP-refractory OSA, there may be a possibility of increasing incidence of TECSA and the need for unique management strategies. We present a patient with chronic atrial fibrillation (AF) and propensity for TECSA found to have the emergence of Cheyne Stokes breathing (CSB) after use of the HNS therapy for OSA.

REPORT OF CASE

A 76-year-old male with chronic AF and longstanding history of OSA with symptoms of nonrestorative sleep, excessive daytime sleepiness, snoring, and frequent nocturnal awakenings presented to our sleep clinic for evaluation for the HNS. His sleep history included severe OSA with a polysomnography (PSG) done in 2001, with an apnea-hypopnea index (AHI) of 82 events/h treated for 10+ years with good tolerance and improvement in his sleep symptoms; however, due to development of a spontaneous left pneumothorax followed by repeat pneumothorax with use of his bilevel PAP (BPAP) device, he was instructed to discontinue PAP therapy. Combination mandibular advancement device and nasal expiratory PAP were attempted, but PSG showed persistent mixed sleep apnea with an overall AHI of 35.5 events/h with a central apnea index (CAI) of 5.8 events/h (**Table 1**). As the patient had not responded adequately to these therapies, he was referred for HNS therapy evaluation. He had a diagnostic PSG done few months prior to our consultation, with an AHI of 18.6 events/h with a CAI of 0.7 events/h. Additional past medical history included AF; type 2 diabetes; asthma; rheumatoid arthritis; and hyperlipidemia, for which he was on medications of diltiazem, digoxin, dabigatran, glipizide, metformin, budesonide/formoterol, montelukast, tramadol, and atorvastatin.

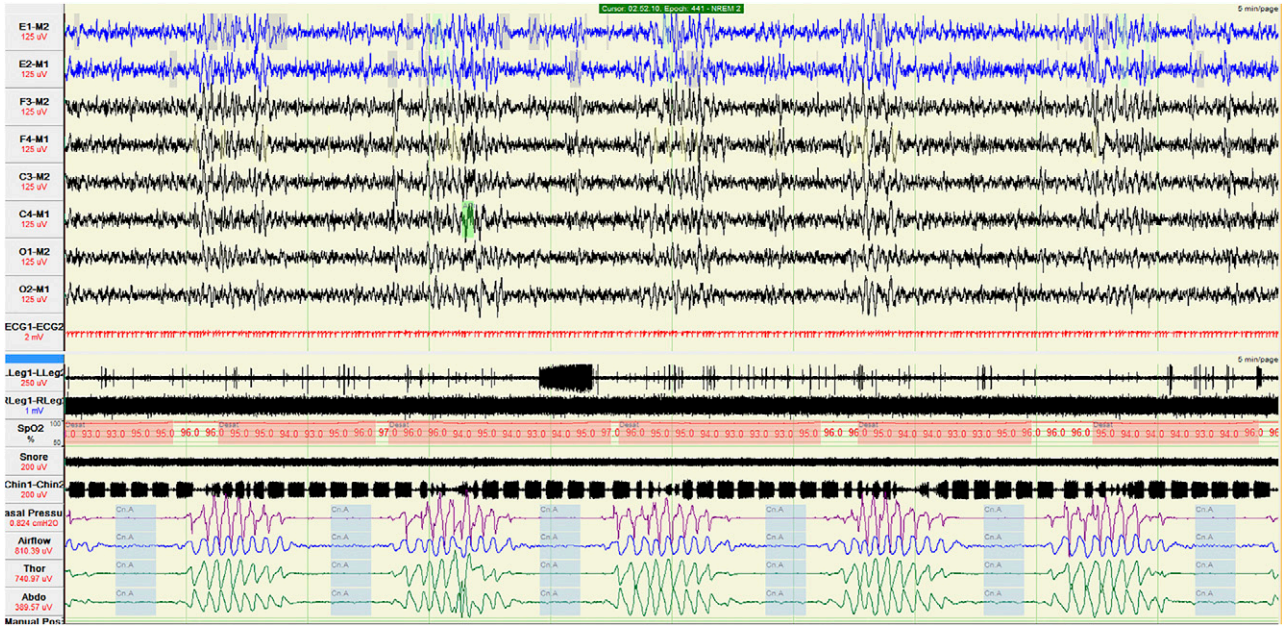
After HNS implantation and activation, the patient was instructed to use the device per protocol to develop acclimation of tongue muscle protrusion, followed by an HNS titration PSG to examine for efficacy of the device at varying levels of stimulation. Almost immediately upon falling asleep with initiation of the HNS, he had periodic breathing throughout the night on all settings studied. It appeared to have the classic CSB pattern with a cycle length of approximately 54 seconds, ventilatory phase of > 5 breaths, the arousals at the peak of the respiratory effort, and delayed oxygen desaturation nadirs (**Figure 1**). There was persistent mixed sleep apnea that night, with the majority of events being central apneas, with an overall AHI of 60.8 events/h (obstructive apnea-hypopnea index [OAHI], 11.3 events/h; CAI, 49.5 events/h). Because of his significant findings, he was recommended for a cardiac and neurologic evaluation for etiology of CSB. Echocardiography showed no evidence of decompensated heart failure, with an ejection fraction of 65–70%, mild aortic insufficiency, no left ventricular hypertrophy, and no valvular disease. He was in stable asymptomatic AF, rate controlled on

Table 1—Chronologic summary of PSG findings.

PSG Type	Date	AHI (events/h)	OAHI (events/h)	CAI (events/h)	O_2 Nadir (%)
Baseline diagnostic	April 2001	82	N/A	N/A	79
BPAP titration	August 2013				
	BPAP 12/08	74.7	20.4	54.4	90
	BPAP 14/10	54.9	8.1	46.8	92
	BPAP 16/12	0.0	0.0	0.0	93
	BPAP 17/13	1.2	0.0	1.2	95
MAD + NEPAP	July 2017	35.5	29.7	5.8	83
Baseline diagnostic	October 2017	18.6	17.9	0.7	92
HNS PSG titration	April 2018	60.8	11.3	49.5	90
Split-night PSG	June 2018				
	Diagnostic	55.7	45.8	9.7	90
	HNS therapy	59.4	6.3	53.1	90
Diagnostic HST without HNS*	May 2019	16.8	16.5	0.3	82

*Study performed while the patient was on acetazolamide and eszopiclone. AHI = apnea-hypopnea index, BPAP = bilevel positive airway pressure titration, CAI = central apnea index, HNS = hypoglossal nerve stimulator, HST = home sleep apnea test, MAD = mandibular advancement device, NEPAP = nasal expiratory positive airway pressure, OAHI = obstructive apnea-hypopnea index, PSG = polysomnography.

Figure 1—HNS titration study revealed periodic breathing.

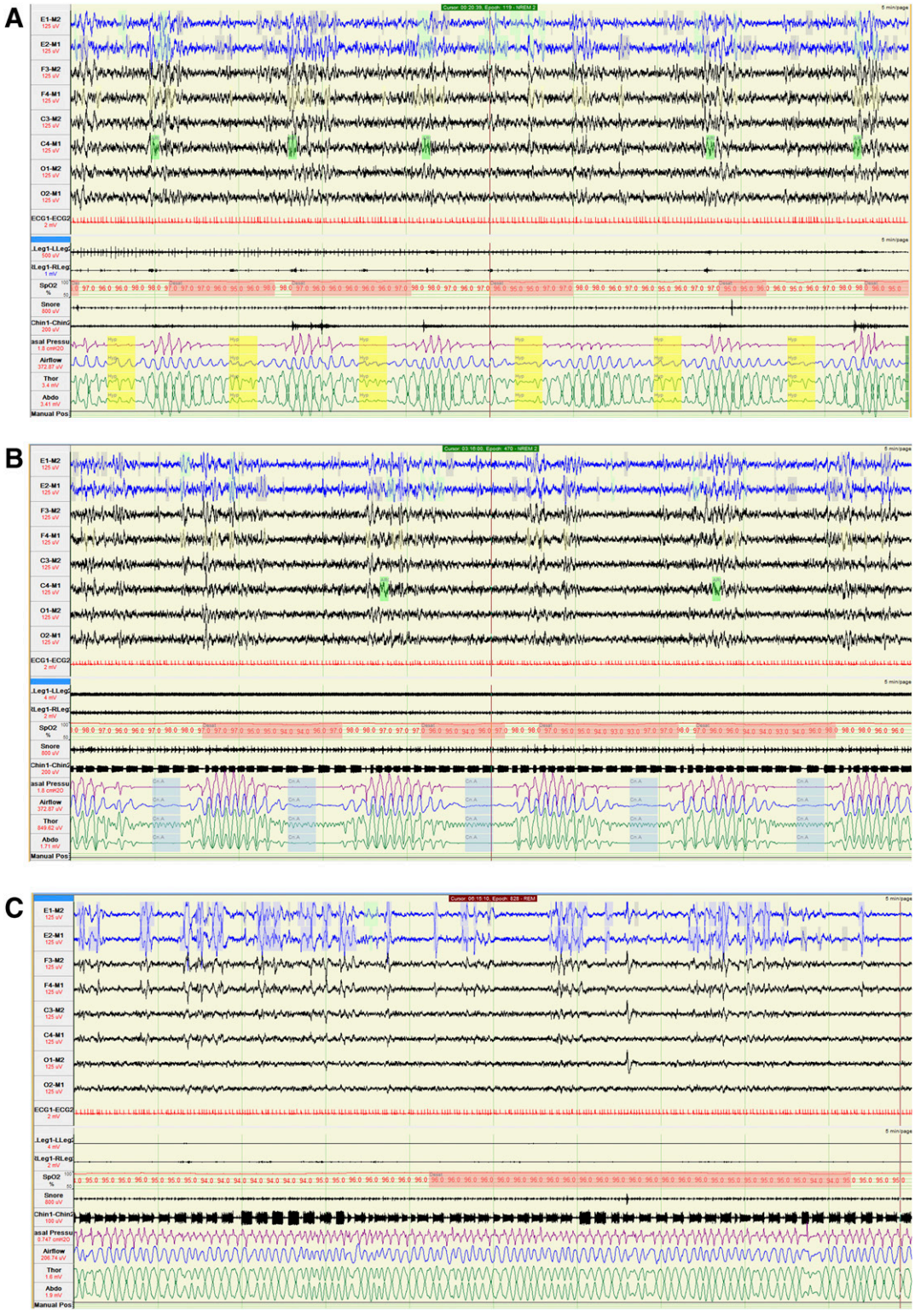


The HNS titration study appeared to have the classic CSB pattern with a cycle length here for 54 seconds (blue event box = 10 seconds), ventilatory phase of > 5 breaths, the arousals at the peak of the respiratory effort, and the desaturation nadir much delayed. This is a representative 5 minute epoch on an HNS setting of 3.5v, but the CSB was seen throughout the night on all settings tested. This chin lead here shows the tongue movement from the device as it activates the genioglossus muscle to thrust the tongue forward. During the apneic portion there is still activation of the tongue because of a feature of the device that will activate tongue protrusion if a breath trigger is not detected in 4 seconds. CSB = Cheyne-Strokes breathing, HNS = hypoglossal nerve stimulator.

medication, having failed cardioversion and cardiac ablation attempted 4 years prior. He underwent magnetic resonance imaging of his brain, which was negative for significant pathology. His tramadol was discontinued in case of potential contribution for central sleep apnea (CSA). In addition, his previous PSGs were reviewed in detail with the referring provider. The most recent diagnostic PSG did not show CSB or periodic breathing; however, during previous PSGs with sleep apnea therapy, the patient was found to have a pattern of predisposition to TECSA with evidence of frequent central apneas. During a BPAP titration on varying pressure settings (without a backup rate), the patient developed a CAI as high as 54.4 events/h (**Table 1**).

To investigate the CSB further, the patient underwent a split-night PSG with and without the use of the HNS device. The first half of the night was performed as a diagnostic study without

Figure 2—Split-night PSG with and without the use of the HNS device.



(A) First half of split-night PSG performed as diagnostic without the use of the HNS, demonstrating mixed obstructive apneas and hypopneas (yellow/blue event boxes = 10-second length). There was still the presence of periodic breathing, but there was clear respiratory effort with paradoxical movements in the thoracic and abdominal belts and clear flow in the thermistor tracing. **(B)** With the HNS device turned on, there was continued periodicity but now unmasking central apneas, the absence of paradoxical breathing, and the crescendo/decrescendo ventilatory portion of CSB. **(C)** During REM sleep later in the PSG with the HNS device on, there was the absence of both obstructive and central events. HNS = hypoglossal nerve stimulator; PSG = polysomnography, REM = rapid eye movement.

the use of the HNS, which demonstrated mostly mixed obstructive apneas and hypopneas, as shown (**Figure 2A**), with clear respiratory effort, paradoxical movements in the thoracic and abdominal belts, and clear flow in the thermistor tracing. During the second half of the study with the HNS device turned on, it demonstrated a periodic breathing pattern with central apneas, absence of paradoxical breathing, and the crescendo/decrescendo ventilatory portion of CSB (**Figure 2B**). During rapid eye movement sleep with the HNS device on, there was the absence of both central and obstructive respiratory events (**Figure 2C**). Overall, the diagnostic portion had an AHI of 55.7 events/h (OAHI, 45.8 events/h; CAI, 9.7 events/h) and the HNS treatment portion had an overall AHI of 59.4 events/h (OAHI, 6.3 events/h; CAI, 53.1 events/h).

We speculated that, due to the patient's chronic AF in combination with clinical signs of elevated loop gain, he developed worsening symptomatic CSA that was unmasked by treatment for OSA with the HNS device. Management was directed toward treating his symptomatic TECSA, borrowing concepts from the PAP literature. To treat his OSA, he was recommended to continue HNS therapy, and an awake endoscopy with the HNS device was performed to confirm adequate anatomical movement of velopharyngeal opening, supraglottic opening, and tongue protrusion. In addition, the settings were decreased to avoid overtitration of the therapy. To treat his CSA, he was prescribed acetazolamide and eszopiclone with referral to cardiac electrophysiology to consider benefit from restoration into sinus rhythm. He was successfully cardioverted back into sinus rhythm during the procedure. After cardioversion, he returned 1 week later for a home sleep apnea test without the use of the HNS device but still on acetazolamide and eszopiclone, which demonstrated an overall AHI of 16.8 events/h (OAHI, 16.5 events/h; CAI, 0.3 events/h), very similar to the patient's initial diagnostic PSG prior to HNS implantation (**Table 1**). Electrocardiography performed the same day revealed the patient had unfortunately reverted back into AF rhythm. With this current medical therapy regimen, the patient felt symptomatically slightly improved as he was sleeping longer with less nocturnal awakenings; however, he continued to endorse persistent excessive daytime sleepiness.

DISCUSSION

The mainstay of treatment for OSA has been PAP therapy since its invention in 1980.[3,4] For those with PAP-refractive OSA there have been alternative therapies, including oral appliances, positional therapy, upper airway surgery, and bariatric surgery. HNS therapy was developed as another alternative option for patients who could not tolerate PAP therapy.

With the increasing popularity of using neurostimulator devices for the treatment of OSA, it would be reasonable to see increased cases of TECSA with HNS use. There has been a report of treatment-emergent CSB after HNS in a patient with a history of mixed sleep apnea with PAP therapy.[5] However, unlike PAP therapies, there is currently no available HNS mode for those patients in whom symptomatic TECSA does not resolve with continued therapy. In the PAP literature, risk factors for increased risk of developing TECSA include higher baseline AHI on diagnostic PSG, higher CAI, extremely high continuous PAP settings, and male sex.[6] Further research is needed to investigate if these predictive factors could be translated to the HNS population, and how to approach those patients presenting for implantation evaluation who have had a history of developing TECSA with PAP.

There is a growing body of literature suggesting an intricately tied physiologic mechanism between AF and idiopathic CSA.[7] Aggressive management of chronic AF with cardioversion into sinus rhythm has been shown to reduce nocturnal central respiratory events[8] but little is known if patients with AF who specifically develop TECSA may also experience a benefit. Future management strategies such as avoiding overtitration of HNS and concomitant treatment for CSA should be investigated to see if they would be effective treatment pathways in patients receiving HNS therapy with a high propensity for loop gain instability.

Care must be taken to closely monitor patients with chronic AF and history of TECSA on OSA therapy as these patients may potentially develop CSA with HNS, especially those with a history of medical risk factors. Further research is needed on CSA in patients with HNS implantation and AF, the prevalence of TECSA in the growing HNS therapy population, and the development of future management strategies.

ABBREVIATIONS

AF, atrial fibrillation
AHI, apnea-hypopnea index
BPAP, bilevel positive airway pressure
CAI, central apnea index
CSA, central sleep apnea
CSB, Cheyne-Stokes breathing
HNS, hypoglossal nerve stimulator
OAHI, obstructive apnea-hypopnea index
PAP, positive airway pressure
PSG, polysomnography
TECSA, treatment-emergent central sleep apnea

REFERENCES

1. Strollo PJ Jr, Soose RJ, Maurer JT, et al; STAR Trial Group. Upper-airway stimulation for obstructive sleep apnea. *N Engl J Med*. 2014;370(2):139–149.
2. Nigam G, Riaz M, Chang ET, Camacho M. Natural history of treatment-emergent central sleep apnea on positive airway pressure: a systematic review. *Ann Thorac Med*. 2018;13(2):86–91.
3. Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. *Lancet*. 1981;317(8225):862–865.
4. Epstein LJ, Kristo D, Strollo PJ Jr, et al; Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med*. 2009;5(3):263–276.
5. Sarber KM, Ishman SL, Patil RD. Emergence of Cheyne-Stokes breathing after hypoglossal nerve stimulator implant in a patient with mixed sleep apnea. *JAMA Otolaryngol Head Neck Surg*. 2019;145(4):389–390.

6. Nigam G, Pathak C, Riaz M. A systematic review on prevalence and risk factors associated with treatment- emergent central sleep apnea. *Ann Thorac Med*. 2016; 11(3):202–210.
7. Leung RS, Huber MA, Rogge T, Maimon N, Chiu KL, Bradley TD. Association between atrial fibrillation and central sleep apnea. *Sleep*. 2005;28(12): 1543–1546.
8. Fox H, Bitter T, Horstkotte D, Oldenburg O. Cardioversion of atrial fibrillation or atrial flutter into sinus rhythm reduces nocturnal central respiratory events and unmasks obstructive sleep apnoea. *Clin Res Cardiol*. 2016; 105(5):451–459.

ACKNOWLEDGMENTS

Author contributions: Dr. Hong conceptualized and drafted the initial manuscript and approved the final manuscript as submitted; Dr. Oster reviewed the manuscript and approved the final manuscript as submitted; Dr. Grover reviewed the manuscript and approved the final manuscript as submitted; Dr. Ismail conceptualized and reviewed and revised the manuscript, and approved the final manuscript as submitted.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication October 18, 2020
Submitted in final revised form March 22, 2021
Accepted for publication March 23, 2021
Address correspondence to: Hanna Hong, MD, Division of Pediatric Pulmonology and Sleep Medicine, Children's Hospital Orange County, 1201 W. La Veta Ave, Orange, CA 92868; Telephone: 714-509-8709; Email: HHong@choc.org

DISCLOSURE STATEMENT

All authors have approved the manuscript as submitted. The authors report no conflicts of interest.