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SLEEP MEDICINE PEARLS

A Case of Obstructive Sleep Apnea, Gastroesophageal Reflux Disease, and Chronic Hiccups: Will CPAP Help?

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A 60-year-old African American man with past medical history of coronary artery disease, diabetes mellitus, gastroesophageal reflux disease (GERD), hypertension, and asthma presented for evaluation of possible sleep disordered breathing. During the visit, frequent hiccups were noted. The hiccups started one year ago, were temporarily relieved with omeprazole 20 mg once a day, and became intractable in the last month. He denied nausea, vomiting, diarrhea, or weight loss.

Daily medications included amlodipine 10 mg, clopidogrel 75 mg, doxazosin 4 mg, lisinopril 10 mg, furosemide 20 mg, omeprazole 20 mg, pravastatin 40 mg, ranitidine 150 mg, glipizide 10 mg, metoprolol 25 mg, and albuterol metered dose inhaler. He smoked a half-pack of cigarettes per day for 40 years. He denied alcohol or drug use. Family history included hypertension, diabetes, and stroke.

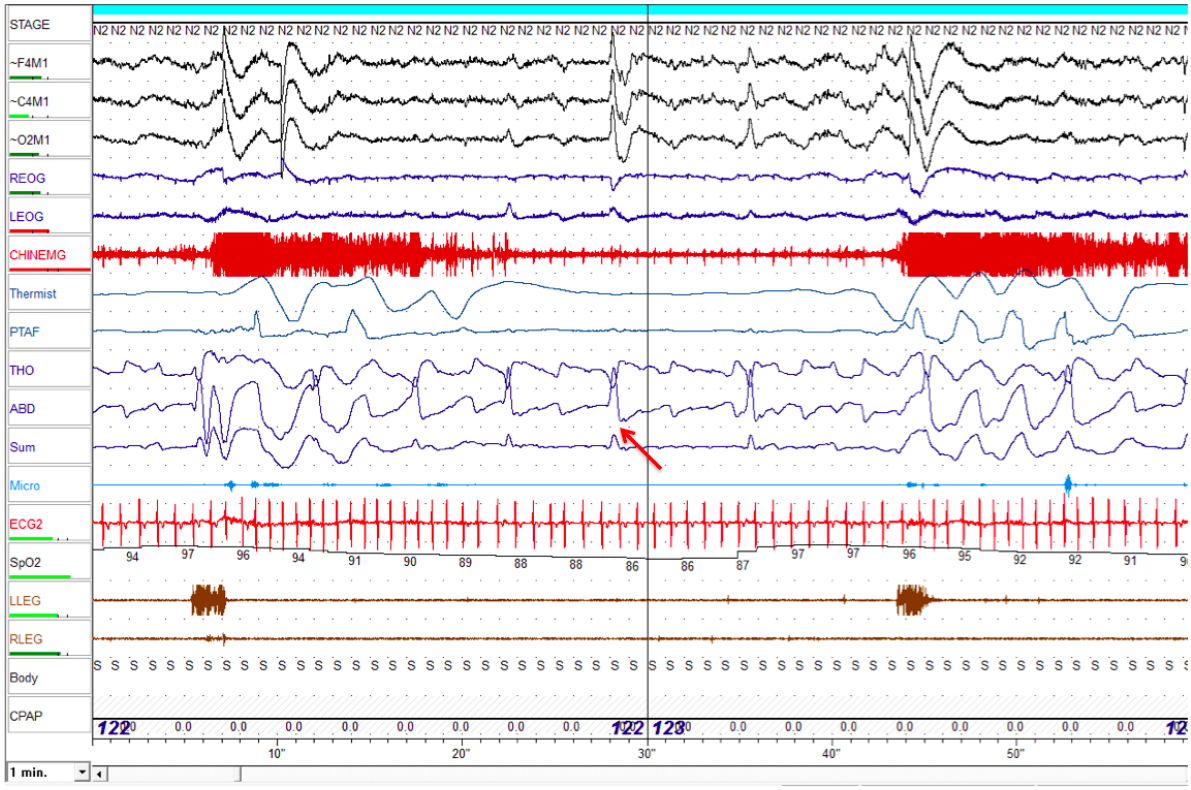
Physical exam revealed an obese male (body mass index 37) with hiccups approximately every 3 seconds. Mild inferior nasal turbinate hypertrophy was noted bilaterally. Oral airway evaluation showed an enlarged tongue with a Mallampati score of 4. The remainder of his physical examination and neurological examination was normal.

Chest x-ray and non-contrast head computerized tomography (CT) were unremarkable. Magnetic resonance imaging of the brain with and without gadolinium contrast showed mild subcortical white matter ischemic changes. A non-contrast CT of the chest showed diffuse esophageal thickening, and esophagogastroduodenoscopy (EGD) revealed severe chronic esophagitis with a 5-cm ulcer.

A split-night polysomnogram showed evidence of severe obstructive sleep apnea (OSA). The apnea index was 107 events per hour. Hypopneas were not seen during the diagnostic portion of the study. A representative 60-sec epoch is shown in **Figure 1**. Continuous positive airway pressure (CPAP) titration with a full-face mask showed resolution of sleep disordered breathing at a pressure of 18 cm of water.

QUESTION
What is the cause of the event depicted by the red arrow in this 60-sec epoch (Figure 1)?

Figure 1—60-second epoch during sleep stage N2



This figure depicts an obstructive apneic event as noted by absence of flow in the thermistor for > 10 sec and paradoxical contractions in the thoracic and abdominal effort channels.

ANSWER
A hiccup during an obstructive apneic event.

DISCUSSION

Chronic persistent hiccups can be debilitating and have been associated with weight loss, insomnia, and fatigue. They can be caused by a wide variety of medical conditions, including central nervous system abnormalities, metabolic imbalances, and chest and abdomen pathology. Among the medications known to cause hiccups, the most common include corticosteroids, antidepressants, dopaminergics, and opioids.[1]

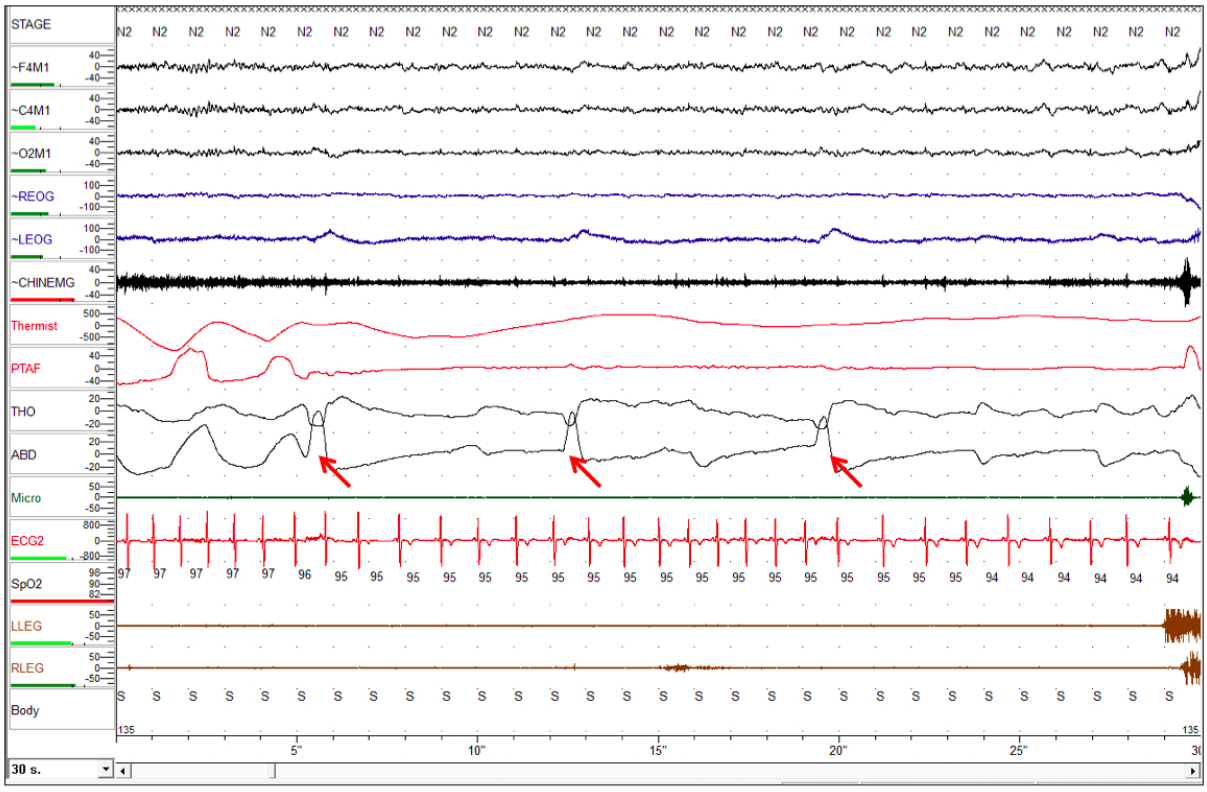
Chronic hiccups can persist during sleep and tend to decrease in frequency during N2, N3, and REM sleep.[2] In our patient hiccups during wakefulness occurred approximately every 3 seconds. During N1, hiccups occurred approximately every 4 to 5 seconds. During N2, the interval between hiccups gradually increased from 6 sec to > 20 sec. No hiccups were noted during REM sleep. The patient did not achieve N3. Hiccups were absent during the CPAP titration portion of the study, both during wakefulness and sleep. During obstructive apneas hiccups persisted and hiccup frequency was unaffected (**Figure 1**). Hiccups occurred during inspiration and were not usually associated with arousals (**Figure 2**). During the titration portion of the study, the frequency of apneas decreased and hypopneas became apparent. Hiccups were not seen during the CPAP titration. Even though a relationship between obstructive apneas and hiccups has not been established, the appearance of hypopneas after the resolution of hiccups may indicate an association between hiccups and complete upper airway closure.

A hiccup center has been postulated in the brainstem. Efferent pathways travel mainly to the diaphragm, glottis, and esophagus[3]; with activation of these pathways resulting in forceful respiratory muscle contraction, followed by closure of the glottis and a rapid drop in intrathoracic pressure. This drop in intrathoracic pressure may cause air to move out of the stomach into the esophagus and/or food to move from the oral cavity/upper esophagus into the lower esophagus.

Esophageal pathology including erosive esophagitis secondary to GERD has been associated with hiccups and when appropriately treated, has been reported to resolve hiccups. It has also been postulated that hiccups can worsen GERD by increasing gastric pressure secondary to diaphragmatic contractions or by negative esophageal pressure with decreased lower esophageal sphincter (LES) tone during the hiccups.[4] The most likely cause of persistent hiccups in our patient is erosive esophagitis. Persistent hiccups have also been reported as the initial presentation of esophageal carcinoma making EGD evaluation and esophageal biopsy critical in these patients.

CPAP alters esophageal function by increasing intrathoracic pressure, compressing the esophagus, and decreasing the pressure gradient associated with the diaphragm. CPAP increases basal LES pressure, esophageal pressure, and gastric pressure, while simultaneously decreasing the duration of LES relaxation

Figure 2—30-sec epoch during sleep stage N2



Red arrows indicate thoracic-abdominal movements secondary to hiccups as confirmed by review of the video monitoring. Note that the hiccups are not associated with arousals.

when swallowing. This results in a decreased number of reflux events with CPAP use.[5] CPAP induced intrathoracic pressure elevation may prevent the pressure drop responsible for hiccups, thereby resulting in either reduced hiccup frequency or complete resolution.[6] The common practice of breath holding with the mouth and nose closed may also alleviate hiccups through a similar mechanism. Our patient is stable on CPAP and is taking omeprazole 20 mg twice a day. Nighttime hiccups have resolved and daytime hiccups are now rare.

CLINICAL PEARLS

1. Hiccups can persist during sleep; however, hiccup frequency decreases compared to wakefulness.
2. Hiccups occur during inspiration.
3. Gastroesophageal reflux is a common cause of chronic hiccups; however, other causes of chronic persistent hiccups should also be evaluated
4. CPAP eliminated hiccups in this patient with obstructive sleep apnea and severe esophagitis

CITATION

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DISCLOSURE STATEMENT

The authors have indicated no financial conflicts of interest.