Secondary nocturnal enuresis caused by central sleep apnea from Chiari malformation type 1

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Abstract Objective: To report a novel cause of nocturnal enuresis (NE) and highlight the literature giving insight into this novel mechanism.
Patient: A 12-year-old morbidly obese female with 2-year history of nightly secondary monosymptomatic NE.
Results: On evaluation, a history of severe sleep disturbed breathing was elicited. Anticipating obstructive sleep apnea (OSA), polysomnography was performed, detecting severe central sleep apnea (CSA) without OSA. Brain magnetic resonance imaging revealed severe Chiari malformation Type I (CM1) with abnormal cerebrospinal fluid dynamics. She had no other classic signs or symptoms of CM1. Neurosurgical decompression halted the NE and normalized nocturnal breathing and cerebrospinal fluid dynamics, confirming that the CSA was caused by the CM1 and resulted in the NE. A thorough literature review found no prior reports of CSA-induced NE. Since CSA and OSA differ by the absence of negative intrathoracic pressures in CSA, this case suggests that such pressures are not a key mechanistic component of SA-induced NE.
Conclusion: This first report of secondary NE caused by CSA from CM1 emphasizes obtaining a sleep history in the enuretic child, introduces a new cause of NE, and challenges hypotheses underlying SA-induced NE.

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Introduction

Nocturnal enuresis (NE) is the involuntary emission of urine during sleep more than twice a month beyond age 5 years. Affecting 2–15% of 5–15 year olds [1], NE is multi-factorial and incompletely understood. While primary NE has been continuous, secondary NE is the return of night-time wetting after 6 months of night-time dryness. Several significant medical disorders can present with secondary NE (such as diabetes insipidus, diabetes mellitus, depression, etc), which are typically uncovered by a thorough medical history, physical examination and urinalysis [2]. However, one serious cause of primary or secondary NE that often goes undetected is obstructive sleep apnea (OSA) [3,4]. Fortunately, NE can significantly abate or cease if the OSA is medically or surgically corrected [5].

In contrast to OSA, central sleep apnea (CSA) has never been reported in patients presenting with NE. We present such a case, providing evidence that secondary NE was caused by a significant Chiari malformation type 1 (CM1) and CSA. This case suggests that OSA per se may not induce NE, but some factor shared by both OSA and CSA could be the cause.

Patient presentation

A 12-year-old developmentally normal white female presented with a 2-year history of high-volume NE that occurred 7 nights per week. This was not associated with any past or current daytime urinary or bowel abnormalities. She had not tried any medications for bedwetting but had restricted night-time fluid intake without diminution of NE. On query of her breathing during sleep, her mother reported numerous episodes wherein she would stop breathing during sleep for 10–15 s followed by a loud gasp. She demonstrated no mouth breathing, loud snoring, choking sounds or congestion when sleeping, but did have excessive daytime somnolence when inactive. She had no history of chronic headaches, vision changes, nasal speech pattern, or chronic neck pain. Her past medical, surgical and family histories were unremarkable. Physical exam was remarkable for morbid obesity at 96 kg (body mass index = 40.7 kg/m²). She had no tonsilar hypertrophy or neurological abnormalities and her genitourinary exam was unremarkable. Urinalysis was normal.

Given the significant sleep disturbed breathing (SDB) history, a 15-channel polysomnography (Fig. 1) was performed. This showed highly abnormal sleep apneas and hypopneas without respiratory muscle effort during NREM sleep and frequent arousals. There were no signs of OSA and the apnea hypopnea index was equal to 50/h (abnormal ≥ 15/h). The episodes occupied 50% of her 7 h recording period and were associated with SaO2 drops to 84% with some apneic episodes. End tidal CO₂ (ETCO₂) ranged from 50 to 55 mmHg.

Given the diagnosis of CSA, a brain MRI was performed, revealing significant CM1 (Fig. 2). The cerebellar tonsillar tips were ectopically located at the posterior arch of C2 approximately 20 mm below the level of foramen magnum. There was effacement of the subarachnoid space both dorsal and ventral to the cervicomedullary junction with abnormal cerebrospinal fluid (CSF) flow dynamics. There was no hydrocephalus or syringomyelia in the visualized cervical spinal cord.

![Figure 1](image_url) A sample 5-min recording of patient’s polysomnogram at presentation reveals 11 consecutive CSAs during Stage I sleep. Each CSA episode lasted approximately 15 s with associated SaO₂ drops as low as 87%, changes in heart rate, and ETCO₂ elevations to as high as 55 mmHg.
Nocturnal enuresis caused by CSA from CM1

Figure 2  Sagittal T1-weighted MRI image shows elongated cerebellar tonsils with their tips extending approximately 20 mm below the level of foramen magnum (red bar). The CSF spaces around the cervicomедullary junction are effaced.

Her chest X-ray was normal without cardiomegaly. She was started on nocturnal bilevel positive airway pressure to achieve normal CO2 and O2 saturation, but she chose to not use it at home. Three weeks later, she underwent a successful neurosurgical suboccipital craniectomy, C1 laminectomy and duraplasty for posterior fossa decompression.

At 61 months postoperatively, her nocturnal breathing pattern is normal by history. Repeat polysomnography at 20 months after surgery revealed resolution of CSA with apnea hypopnea index < 2/h, but evidence of upper airway resistance syndrome reflected by moderate snoring, elevated ETCO2 (46–52 mmHg), intermittent paradoxical breathing and frequent respiratory effort-related arousals. Repeat head MRI confirmed successful posterior fossa decompression with normal CSF flow dynamics. Except for the two nocturnal enuretic episodes she had in the first week after surgery, her nightly secondary NE immediately ceased and has remained absent up to the 61-month follow up.

Discussion

While NE afflicts 2–15% of 5–15 year olds [1], secondary NE accounts for 15–26% of enuresis cases [6] and has classically been ascribed to new psychosocial stressors precipitating the symptoms [7]. Another common disease of childhood is SDB, which includes the spectrum from habitual snoring to OSA, affecting 10% of preschoolers [8]. Habitual snoring, a milder form of SDB, has been associated with a four times increased risk of NE [8]. One to three percent of children with SDB manifest OSA [9] and 46% of children with OSA have NE [10].

Unlike adulthood OSA which is associated with thick neck or tongue, snoring, and body mass index > 30 [11], most cases of childhood OSA are due to adenotonsillar hypertrophy [12]. Adenoidectomy and tonsillectomy for pediatric OSA yields an impressive 61–71% and 100% NE cure rate in primary and secondary enuretics, respectively [5,12]. The pathophysiological basis of NE in OSA has been ascribed to: 1) a lack of diurnal variation in vasopressin [13], and 2) an increase in atrial natriuretic factor release secondary to negative intrathoracic pressures generated during breathing attempts against an obstructed airway and/or hypoxia/hypercarbia from apneic episodes [14,15].

In our patient, the working diagnosis was OSA, given the child’s morbid obesity. However, the startling finding of CSA led to prompt diagnosis and surgical decompression of the CM1. CM1 is the congenital or acquired herniation of the cerebellar tonsils below the foramen magnum into the upper cervical canal. The cerebellar tonsils and/or brainstem are compressed and a medullary kink may disturb CSF flow. Its true prevalence has been estimated at 1:1000 [16]. Despite mainly being a congenital anomaly, CM1 can present in infants and children, with symptomatic onset depending upon the progression and possibly somatic growth. It can manifest a broad and variable range of signs and symptoms suggesting cerebellar, cranial nerve, high cervical spinal cord, and forebrain lesions [17]. CM1 has been detected in infants and children with CSA [18,19] and OSA [20], and unfortunately at the time of autopsy in asymptomatic children with sudden death [21]. Factors contributing to CSA in CM patients include: 1) mechanical compression of the lower medulla or upper cervical cord, 2) reduced vascular supply to the lower medulla, 3) reduced sensitivity to O2 and CO2, and 4) loss of peripheral chemoreceptor function by stretching of the IXth and Xth cranial nerves [22]. During sleep, the voluntary system of respiratory control is not functional so the integrity of the brainstem’s automatic respiratory control becomes critical.

Due to its life-threatening nature, CSA is the only clearcut neurological indication for posterior fossa CM1 decompression [23]. In most patients, benefits of posterior fossa decompression far outweigh the risks [24]. The dramatic resolution of our patient’s CSA and NE after neurosurgical decompression suggests that the malformation was responsible for her NE.

The first major point to take away from this case is that the child was referred to urology without appropriate evaluation by her pediatrician; an obese child with nocturnal enuresis should have been questioned for abnormal breathing and/or snoring by her pediatrician and referred for sleep study rather than to urology. However, not all pediatricians are aware of this relationship between sleep apnea and NE, and thus urologists too must investigate sleep habits.

The second major point from this case report is that CSA from CM1 can cause bedwetting. Theoretically, CM1 could cause lesser forms of SBD, inducing NE without other classic CM1 signs or symptoms. This child’s case was unusual in that she did not manifest any other signs or symptoms of CM1 except CSA. Her case raises questions such as: How many children with CSA have NE? How many children with CM1 have NE?

The third major point from this case is that OSA per se may not induce NE, but some factor shared by both OSA and CSA could be causal. Since no other signs and symptoms of CM1 and no daytime urinary symptoms were present in this patient, the NE in our patient was not due to direct...
compression of the pontine micturition center but instead resulted from a mechanism shared by OSA and CSA. Candidate factors include intermittent hypoxemia/hypercarbia, central nervous system microarousals seen on electroencephalogram, and sympathetic arousals which show a brady-tachycardic pattern on electrocardiogram. Furthermore, it is unknown whether vasopressin release is decreased and/or atrial natriuretic factor release is increased in CSA due to episodic hypoxia and hypercarbia. However, since CSA and OSA differ by the absence of negative intrathoracic pressures in CSA, this case suggests that negative intrathoracic pressures are not a key mechanical component to SA-induced NE.

Since we are continually searching for solutions to NE, this case report becomes quite important. Although the CM1 probably was congenital in this child, she must have had progression of her CM1 2 years prior to presentation, possibly growth related. After her surgery, she was cured both of her wetting AND her sleep apnea, all because she came for evaluation of her bedwetting. She could have died in her sleep from her CSA! In addition, the long-term neurological and psychosocial implications of CSA are significant, including increased risk of cardiovascular disease, stroke, and death. This case suggests that negative intrathoracic pressures are not a key mechanical component to SA-induced NE.

"What we see depends mainly on what we look for."—Sir John Lubbock (British biologist and politician, 1834–1913)

Conflict of interest statement

All authors have no professional affiliation, financial agreement or conflicts of interest to report. The authors affirm that this manuscript is being submitted only to Journal of Pediatric Urology and that it will not be submitted elsewhere while under consideration. It has not been published elsewhere, and, should it be published in Journal of Pediatric Urology, it will not be published elsewhere—either in similar form or verbatim—without permission of the editors. In addition, all authors are responsible for reported research. They have participated in the concept and design; analysis and interpretation of data; drafting or revising of the manuscript, and have approved the manuscript as submitted.

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Ethical approval

As an educational article/case report, approval was not required.

References


