Is MRI Necessary in the Evaluation of Pediatric Central Sleep Apnea?

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Abstract

Objectives. (1) To determine the prevalence of central nervous system (CNS) pathology identified on head magnetic resonance imaging (MRI) scans in children with central sleep apnea (CSA); (2) to assess the yield of MRI in evaluation of CSA; and (3) to identify factors that predict CNS pathology in children with CSA.

Study Design. Case series with chart review.


Subjects and Methods. A chart review was conducted over 12 years. Patients 6 months to 18 years of age who underwent head MRI for evaluation of CSA were included. CSA was diagnosed on polysomnogram as central apnea index >1.

Results. Forty children were included in the CSA group. Twenty-two patients were male, and the mean age was 60 ± 41.5 months. The mean central apnea index was 3.8 ± 1.9, while the mean obstructive apnea hypopnea index was 3.4 (interquartile range, 0.7-3.8). Eighteen percent (7 of 40) of children with CSA had evidence of CNS pathology on MRI, with the most common finding (n = 3) being arachnoid cyst. Children with CSA who had gastroesophageal reflux disease or abnormal neurologic examination findings were more likely to have CNS pathology. Other factors, such as prematurity, did not improve the yield of MRI in children with CSA.

Conclusions. While routine evaluation of children with elevated central apnea index by MRI is not indicated, providers should consider neuroimaging in children with CSA and abnormal neurologic examination findings or gastroesophageal reflux disease. Further research is necessary to identify other tests with improved diagnostic yield for evaluation of pediatric CSA.

Keywords

pediatric, sleep apnea, Chiari malformation, polysomnogram

Pediatric sleep-disordered breathing is characterized by respiratory disturbances during sleep and daytime manifestations, such as sleepiness, hyperactivity, and poor attention. According to the International Classification of Sleep Disorders, pediatric sleep-disordered breathing can be divided into 2 major categories: obstructive sleep apnea (OSA) and central sleep apnea (CSA).¹ Pediatric OSA—which is associated with nocturnal hypoxemia, hypercapnia, and sleep fragmentation due to upper airway obstruction—affects 1% to 4% of preschool-aged children. The majority of literature on pediatric sleep-disordered breathing has focused on OSA, while there have been surprisingly few publications regarding the diagnosis and management of CSA. A recent study by Kritzinger et al² suggests that the prevalence of CSA in children may be higher than expected, thus highlighting the need for further research in this area.

CSA is characterized by episodes of apnea during sleep in the absence of airway obstruction. A central apnea on polysomnogram (PSG) is defined as the absence of chest and/or abdominal movement associated with cessation of airflow for >20 seconds or lasting >2 baseline respiratory cycles if the event is associated with an arousal, awakening, or oxygen desaturation of at least 3%.³ A central apnea index (CAI; number of central apneas per hour) >1 is considered diagnostic for CSA in children. CSA can be primary in nature or can be associated with other medical conditions, such as brainstem pathology, neurologic disorders, heart failure, and prematurity. While the exact cause of CSA is unknown, this disorder likely involves a disruption or dysfunction of ventilatory control in the central nervous system (CNS).⁴

Numerous case reports and small case series have been published describing the association between pediatric CSA.

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sleep-disordered breathing and Chiari malformation (CM).\textsuperscript{5-10} CM is characterized by herniation of a portion of the cerebellum through the foramen magnum. It is postulated that compression of respiratory centers in the brainstem may occur as a result of cerebellar herniation and cause sleep-disordered breathing.\textsuperscript{5} Manifestations of sleep-disordered breathing in patients with CM vary and can include OSA, CSA, and acute respiratory failure. Due to the association between CSA and CM, several publications have recommended obtaining magnetic resonance imaging (MRI) in children with CSA to rule out any brainstem pathology.\textsuperscript{2,5,7,8}

The prevalence of CSA in patients with CM ranges from 17.6\% to 48\%. Thus, it does seem prudent to consider screening CM patients for sleep-disordered breathing. However, the prevalence of CM or other CNS pathology in children presenting with CSA is unknown. Providers frequently obtain MRI when evaluating children with CSA. However, data are lacking that describe the utility of brain MRI in the evaluation in children with CSA. The objectives of this study are as follows: (1) to determine the prevalence of CNS pathology, including CM, identified on MRI scans in children with CSA diagnosed by full-night PSG; (2) to assess the utility of head MRI scans in the evaluation of pediatric CSA; and (3) to assess whether there are certain factors (eg, severity of CSA, history of developmental delay) that affect the yield of MRI in the evaluation of CSA.

Methods

This study was approved by the Institutional Review Board of Eastern Virginia Medical School and the Hospital Research Coordination Committee of the Children’s Hospital of The King’s Daughters. A retrospective chart review was conducted at this tertiary children’s hospital between December 2000 and December 2012. Approximately 4200 full-night PSGs were performed during the study period. Children aged 6 months to 18 years who were diagnosed with CSA (CAI >1) on PSG were eligible for inclusion. Those children with CSA that subsequently had head MRI performed as part of their evaluation for an elevated CAI were included in the study. Children with medical comorbidities, such as seizures, developmental delay, and hydrocephalus, were eligible for inclusion. Children with CSA that failed to complete the head MRI were excluded.

Subjects that underwent full-night PSG were identified by searching hospital billing records using Current Procedural Terminology codes 95810 and 95811. This list of patients was cross-referenced with children that had undergone head MRI at our institution during the study period. Such patients were identified using code 327.27 of the International Classification of Diseases, Ninth Revision.

All full-night PSGs were performed in dedicated pediatric sleep laboratories in accordance with the American Academy of Sleep Medicine guidelines\textsuperscript{3} and scored by pediatric sleep medicine specialists. Standard procedure included a 6-lead electroencephalogram, 2 bilateral electrooculogram leads, and 1 submental and 2 tibial electromyograms. Respiratory measurements were recorded by the following means: airflow by a nasal pressure transducer, oxygen saturation by pulse oximetry, and carbon dioxide by a carbon dioxide sensor. Information obtained from each PSG included total time in bed, total sleep time, sleep efficiency, time spent in each sleep stage, number and classification of arousals and respiratory events, and oxygen and carbon dioxide levels. Recorded respiratory data included counts and indexes of the following events: obstructive apneas, obstructive hypopneas, central apneas, and mixed apneas recorded in non–rapid eye movement sleep, rapid eye movement sleep, and total sleep.

One of the difficulties in evaluating sleep-disordered breathing in children involves the controversy regarding definitions of sleep events and sleep disorders. The following definitions (based on the American Academy of Sleep Medicine guidelines\textsuperscript{3}) were used in the analysis of PSG data in our study. An obstructive apnea occurs if there is an absence of airflow for \geq 2 respiratory cycles with the presence of persistent abdominal and thoracic movements. A central apnea is defined as the absence of chest and abdominal movement associated with cessation of nasal airflow and 1 of the following: the event lasts >20 seconds, or the event occurs for at least 2 baseline respiratory cycles and is associated with an arousal, an awakening, or an oxygen desaturation of at least 3\%. Postsigh, postmovement central apneas <20 seconds in duration were not scored unless associated with either an arousal or oxygen desaturation. A hypopnea is defined as a 50\% reduction in airflow that is associated with a 3\% drop in oxygen saturation, an arousal, or an awakening.

The CAI is the number of central apneas per hour of sleep. Central apneas and periodic breathing during sleep are normal events in healthy infants in the first weeks after birth. Typically, with increasing age, there is greater stability in the respiratory control system with fewer central respiratory events.\textsuperscript{11} There is no accepted classification for pediatric CSA. Children with a CAI >1 on PSG were considered to have CSA. We defined mild CSA as a CAI between 1 and 5. Moderate CSA was defined as a CAI between 5 and 10, while children with CAI \geq 10 were considered to have severe CSA. The obstructive Apnea-Hypopnea Index (AHI) is the number of obstructive and mixed apneas and hypopneas per hour of sleep. OSA was diagnosed in children with an obstructive AHI >1. Pediatric OSA can be further categorized as mild (AHI, 1 to 5), moderate (AHI, 5 to 10), or severe (AHI >10).

All head MRIs were read by pediatric radiologists. MRI reports were reviewed and classified as “normal” if no pathologic findings were identified. Reports were designated “abnormal” if pathologic findings were identified, such as CM or hydrocephalus.

Patient demographic data, PSG variables, and MRI results were recorded. Charts were reviewed for comorbid medical conditions, such as developmental delay and seizures, as well as abnormal neurologic examination findings, such as nystagmus, cranial nerve deficits, or extremity weakness. Children were considered to have gastroesophageal reflux disease (GERD) if their caregivers reported a clinical history of GERD. In our practice, a history of reflux is routinely solicited
as part of the review of systems on the initial clinical intake. Descriptive statistics were utilized to determine the baseline characteristics of the subject population and were calculated using SAS 9.3 (SAS Institute, Cary, North Carolina). Proportions were compared with the Fisher’s exact test. P < .05 was considered significant.

### Results

Forty children underwent head MRI after CSA was identified on PSG. The mean age of the subjects was 60.0 ± 41.5 months (range, 8 to 190), and the majority of children (55%, n = 22) were male. Thirty percent of subjects (n = 7) were obese as defined by a body mass index percentile >95th. Comorbid medical conditions were common among children with CSA. Fourteen children (36%) had a history of developmental delay. Asthma (n = 13), prematurity (n = 10), seizure disorder (n = 10), and GERD (n = 9) were other frequently identified medical problems in this population (Table 1). Three children had abnormal neurologic examination findings: 1 had ptosis, and 2 had hypotonia and distal extremity weakness. Table 2 shows the PSG findings of the subjects. The mean CAI was 3.8 ± 1.9, while the mean obstructive AHI was 3.4 (median, 1.7; interquartile range, 0.7-3.8). The majority of children in the study (n = 27, 68%) had mild CSA, as defined by a CAI between 1 and 5. Fifty-eight percent (n = 23) of children with CSA also had OSA (obstructive AHI >1). The mean nadir oxygen saturation was 88% ± 4%.

Of the 40 children with CSA, 7 (18%) had abnormal head MRI, with the most common finding (n = 3) being arachnoid cyst. One child had CM. Other abnormal findings in children with CSA included pineal cyst (n = 1), bilateral subcortical white matter changes (n = 1), and tectum and thalamic lesions concerning for neurofibromatosis type 1 (n = 1). Only 2 of the 7 children with abnormalities identified on MRI required further evaluation or treatment (Table 3).

In bivariate analysis, abnormal neurologic examination findings in subjects with CSA increased the likelihood (P = .03; odds ratio, 29.5; CI, 1.2 to 702.0) of abnormal head MRI. A history of GERD was also associated with increased odds (odds ratio, 11.2; CI, 1.6 to 78.4) of having CNS pathology on MRI. Other demographic factors, such as a history of prematurity, asthma, obesity, or seizures, did not predict which children with CSA had abnormal head MRI findings. Interestingly, rates of CNS pathology on head MRI were similar between children with mild CSA and those with moderate/severe CSA (odds ratio, 0.8; CI, 0.1 to 4.8). Thus, children with severe CSA were not more likely to have MRI abnormalities than were children with mild disease. Similarly, the presence of OSA (obstructive AHI >1) did not increase the likelihood (P = .68) of having abnormal head MRI.

### Discussion

While otolaryngologists typically order PSGs in children to evaluate for OSA, other disease processes—such as CSA, hypventilation, seizures, and periodic limb movement disorder—can be identified during this testing. Numerous studies have focused on the appropriate management of children with OSA, as defined by an elevated AHI on PSG. However, few studies have reported on the evaluation and treatment of children with an elevated CAI.2,9 Thus, it can be challenging for providers to determine which children with CSA on PSG require further evaluation, such as neuroimaging.

CSA can be primary in nature. However, CSA is more commonly associated with other medical conditions, including neurologic disorders such as CM or Prader-Willi syndrome, gastroesophageal reflux, prematurity, and hypothyroidism.2 Several studies have described an association between sleepdisordered breathing and CM.5-8,10,12 For example, Dauvilliers et al12 reported sleep apnea in 12 of 20 children (60%) diagnosed with CM. Thirty-five percent (n = 7) of these patients had OSA, while 25% (n = 5) had CSA. Thus, routine screening for sleep apnea in patients with CM is now recommended. Based on this association between CSA and CM, head MRI is frequently obtained in children with central apnea to identify CNS pathology. However, data to support this practice are lacking.

There has been only 1 previous study that described the utility of obtaining head MRI in a population of children with CSA diagnosed on PSG.2 Eighteen patients in the analysis by Kritzinger et al2 had head MRI after PSG showed

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**Table 2. Subject Polysomnogram Data.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central apnea index</td>
<td>3.79 ± 1.93</td>
</tr>
<tr>
<td>Obstructive AHI (interquartile range)</td>
<td>3.37 (0.70-3.75)</td>
</tr>
<tr>
<td>Presence of OSA (obstructive AHI &gt;1), n (%)</td>
<td>23 (58)</td>
</tr>
<tr>
<td>Nadir oxygen saturation, %, mean ± SD</td>
<td>87.9 ± 4.4</td>
</tr>
<tr>
<td>Oxygen saturation, %, mean ± SD</td>
<td>96.5 ± 1.2</td>
</tr>
</tbody>
</table>

Abbreviations: AHI, Apnea-Hypopnea Index; OSA, obstructive sleep apnea.

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**Table 1. Subject Demographic Data.**

<table>
<thead>
<tr>
<th>Number of Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Age, mean ± SD, mo</td>
</tr>
<tr>
<td>Race</td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Black</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Body mass index, mean, kg/m²</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Developmental delay</td>
</tr>
<tr>
<td>Asthma</td>
</tr>
<tr>
<td>Prematurity</td>
</tr>
<tr>
<td>Gastroesophageal reflux</td>
</tr>
</tbody>
</table>

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"Values presented as No. (%) unless noted otherwise. Obesity is defined as a body mass index percentile >95th."
CSA. Fifty-six percent (10 of 18) of children with an elevated CAI had abnormal findings on head MRI. The majority of these children had a history of multiple medical problems, including cerebral palsy, hypotonia, Prader-Willi syndrome, and prematurity. The authors reported that 4 new diagnoses amenable to treatment were made after MRI. However, 3 of the 4 children had known CNS pathology (CM and brainstem glioma) prior to undergoing PSG and MRI.

In the current study, the prevalence of CNS pathology found on head MRI in children with CSA was 18% (7 of 40). Most findings identified on MRI in our study were benign and not likely related to the patients’ central apnea. Only 2 patients (5%) required further evaluation or intervention.

Why was the prevalence of CNS pathology in our subjects lower than that previously described? The explanation is likely related to different study populations. Kritzinger et al.2 focused on children with primary CSA. In their study, children with concurrent OSA on PSG were excluded. The most common sleep problem that otolaryngologists evaluate in children is OSA. Thus, we chose to include children in our analysis that had OSA in addition to an elevated CAI. Our initial hypothesis was that children with CSA and comorbid OSA (AHI >1) would have a lower prevalence of CNS pathology than would children with isolated CSA. We presumed that isolated CSA was more likely to be associated with CNS pathology, while CSA in the setting of OSA was due to sleep disruption and fragmentation caused by obstruction. Interestingly though, when we compared children with isolated CSA with those that had both CSA and OSA, the prevalence of MRI abnormalities was similar. Our sample size, however, may have been inadequate to detect a difference between the 2 groups. Further research is needed to address whether CSA associated with OSA is a different clinical entity than isolated CSA in children.

We were able to identify 2 factors—abnormal neurologic examination findings and a clinical history of GERD—that predicted abnormal head MRI in patients with CSA. The association between abnormal neurologic examination findings and CNS pathology on head MRI is not surprising. The link among GERD, CSA, and abnormal MRI is less clear. In Kritzinger’s review,2 GERD was identified as the most common comorbid medical condition in children with CSA. There are physiologic protective reflexes, such as the esophageal and laryngeal chemoreceptor reflex, that may be responsible for apnea events in children with GERD.13 The role of GERD in children with CSA, however, is still being investigated, with some studies demonstrating improvement in apnea with GERD treatment and others refuting this link.13 In our study, the association between abnormal head MRI and GERD may have been confounded by other factors, such as neurologic disease.

Neuroimaging is frequently performed in the evaluation of 2 additional pediatric conditions: migraine and sensorineural hearing loss. How does the prevalence of MRI abnormalities in children with CSA compare with the prevalence of MRI abnormalities in children with migraine and sensorineural hearing loss? The prevalence of CNS pathology found on head MRI in children with migraines ranges from 4% to 20%.14-16 In Lewis’s review of neuroimaging in children with migraines,16 54 of 107 children underwent neuroimaging. Four children (7%) had abnormalities. While none of the abnormal neuroimaging findings were apparent clinically, their discovery did not influence the diagnosis, management, or outcome of the patients. Thus, the authors concluded that neuroimaging is not warranted in children and adolescents with migraine whose neurologic examinations yield normal findings. In a recent study, the prevalence of abnormal findings on MRI in children with sensorineural hearing loss was significantly higher at 40%.17 Children with unilateral hearing loss had a greater percentage of inner ear anomalies diagnosed on MRI than children with bilateral sensorineural hearing loss. Thus, the authors concluded that neuroimaging is indicated in children with unilateral sensorineural hearing loss.

One of our aims was to identify the utility of head MRI in children with a history of sleep-disordered breathing and elevated CAI. The findings of this study do not support routine ordering of head MRI in all children with an elevated CAI on PSG. MRI is not without risk in the pediatric...
population, as children often require sedation or even general anesthesia to tolerate the scan. Providers must take into account the entire clinical picture, including history, physical examination findings, and PSG results when determining whether to obtain MRI. Head MRI should be considered in children with CSA that also have a history of abnormal neurologic examination findings or GERD. Neuroimaging should also be considered in any child in whom CM is suspected. In children with CSA for whom the necessity of neuroimaging is unclear, a neurology consult may be useful. While we did not address the timing of neuroimaging in relation to surgical therapy, we have studied rates of resolution of CSA following adenotonsillectomy at our institution. In children with OSA and mild CSA (CAI <5), providers can safely proceed with adenotonsillectomy, with the majority of patients experiencing resolution of their disease. While it may be prudent to obtain imaging preoperatively in children with severe disease (CAI >10), further research is needed to address this question.

To our knowledge, this is the first study to examine the prevalence of head MRI abnormalities in patients with CSA and to identify factors that are associated with CNS pathology in this population. One of the strengths of this study was the utilization of PSG to diagnose sleep apnea in all the subjects. Limitations include a small subject population and the retrospective nature of the study design. The decision to obtain MRI in the evaluation of subjects with CSA was at discretion of the provider. Thus, we may be overestimating the prevalence of MRI abnormalities if providers were more likely to order MRI in children with additional clinical findings, such as neurologic examination abnormalities or severe comorbid medical conditions. Future research needs to focus on determining the prevalence and etiology of CSA in children. A better understanding of this disease process will enable us to develop paradigms for evaluation and treatment.

Conclusion
The majority of CNS abnormalities noted on head MRI in children with an elevated CAI are benign. Routine neuroimaging in this group is not indicated. Head MRI should be considered for children with CSA that have abnormal findings on neurologic examination or a history of GERD.

Author Contributions
Meghan Woughter, data collection, manuscript preparation; Amy M. Perkins, statistical analysis, manuscript revision; Cristina M. Baldassari, study design, manuscript preparation and revision.

Disclosures
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References