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Original Article

Sleep-disordered breathing in children with Chiari malformation type II and myelomeningocele

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Abstract ***Background***: The prevalence of sleep-disordered breathing (SDB) in children with Chiari malformation type II (CM-II), a known association of neural tube defects (NTD), has not been well documented. The aim of the present study was to assess the prevalence and possible predictive factors of SDB in patients with CM-II.

Methods: The study included all patients with documented CM-II who were routinely referred from the Neurosurgery Clinic to the University Sleep Disorders Centre at King Khalid University Hospital, Riyadh, Saudi Arabia, between January 2002 and July 2009. Overnight full polysomnography (PSG) was performed in all patients. Polysomnographic data were analyzed using descriptive statistics.

Results: Sixteen children (11 boys, five girls) were included in the study; their mean age was 4.7 years (range, 0.8–10 years) and their mean body mass index was 18.05 kg/m^2 (range, 15.4–25.4 kg/m^2). For the whole group, the mean apnea–hypopnea index (AHI) was 6.3/h (range, 0.2–24.5/h), with AHI recorded as >5/h in five patients (31.3%) and ≥10/h in three patients (18.8%). The mean central apnea–hypopnea index was 5.9/h (range, 0–24.5/h) and the mean obstructive apnea–hypopnea index was 0.4/h (range, 0–2.9/h). The mean arousal index was 15.1/h (range, 5–34/h).

Conclusion: The major assumption linking CM-II and NTD with potential brainstem compression and respiratory dysfunction during sleep was confirmed. Indeed, SDB is highly prevalent, and clearly underreported and undertreated in patients with CM-II associated with NTD.

Key words central apnea, Chiari, sleep, sleep apnea, spina bifida.

Chiari malformation type II (CM-II) is a congenital downward displacement of the posterior part of the cerebellum along with the lower medulla oblongata, through the foramen magnum, and into the cervical spinal canal (Fig. 1). CM-II is almost always associated with the presence of a neural tube defect (NTD). This anomaly may alter the anatomical relationships within the brainstem, and thus affect the functional integrity of both the respiratory nuclei and circuitry, as well as impinge upon the lower cranial nerves controlling the upper airway, thereby facilitating the occurrence of alterations in respiratory pattern and reflexes, particularly during sleep.[1–4] Under such circumstances, emergence of sleep-disordered breathing (SDB), such as central sleep apnea syndrome and obstructive sleep apnea syndrome, may lead to life-threatening conditions for which decompressive neurosurgery may be needed.[5]

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Chiari malformation type II is usually diagnosed shortly after birth, given that it is most frequently associated with the presence of myelomeningocele (MMC). Children are then usually investigated using magnetic resonance imaging (MRI) of the posterior fossa and brainstem, and are also assessed for the presence of high-pressure hydrocephalus, which then requires immediate treatment to prevent further cerebellar and brainstem herniation. Additional imaging of the spine is also necessary to examine whether additional abnormalities such as syringomyelia are present (Fig. 2). Of note, children with CM-II may present with a unique and dramatic form of apnea associated with painful or startling experiences, in which the child exhibits complete cessation of respiratory movements resulting in cyanosis.[6] This prolonged expiratory apnea with cyanosis (PEAC) has been associated with bradycardia and death, whereas non-fatal events can be mistaken for prolonged breath-holding spells.[6]

The outcome for patients with CM-II is usually guarded, with ≥15% dying by 3 years of age and ≥33% manifesting substantial neurological deficits. Even after surgical intervention, CM-II patients remain at risk for severe apneic events and PEAC is a common cause of death.[7] Although there is no single surgical approach for refractory patients who need neurosurgical intervention, most of the neurosurgical procedures rely on osseous

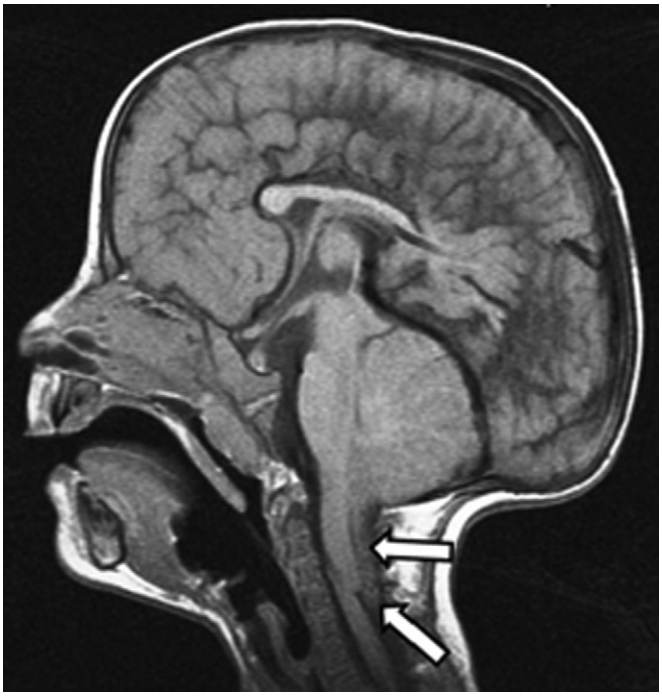

Fig. 1 Mid-sagittal magnetic resonance imaging (T1-weighted image) of Chiari malformation type II patient showing herniation of the cerebellar tonsil down to C4 level (arrows), brainstem towering, and small posterior fossa.

decompression and dural grafting, with more aggressive decompression and intradural dissection being reserved for patients with presence of a syrinx.[8]

Methods

This study was performed at the King Khalid University Hospital University Sleep Disorders Centre, Riyadh, Saudi Arabia, between 2002 and 2009. The study involved 16 patients with CM-II and NTD, as confirmed on MRI, and who were referred from the Neurosurgery Clinic for an overnight sleep test.

Overnight full polysomnography (PSG) was conducted in all patients, and consisted of multichannel recordings in the sleep laboratory for determination of sleep stages (using electroencephalography, chin muscles electromyography and electrooculography), video recording, as well as measurements of oronasal airflow (thermistor and nasal pressure cannula), snoring (microphone), respiratory effort (inductance plethysmogrpahy) and oxygen saturation (SaO_2) using a finger pulse oximeter (Biox 3740, Ohmeda, GEHC, Waukesha, WI, USA).

Tests were scored and interpreted using age-appropriate criteria.[9–12] Central, obstructive, and mixed apneic events were counted. Obstructive apnea was defined as the absence of airflow with continued chest wall and abdominal movement with duration of ≥2 s breaths. Hypopneas were defined as a decrease in oronasal flow of ≥50% with a corresponding decrease in SpO_2 of ≥4% or more and/or an arousal. The obstructive apnea–hypopnea index (OAHI) was defined as the number of obstructive apneas and hypopneas per hour of total sleep time (TST). Arousals were defined according to the American Academy of Sleep Medicine Scoring Manual. The respiratory indices that were recorded were the total apnea–hypopnea index (TAHI), central apnoea–hypopnea index (CAHI) and OAHI along with sleep efficiency, sleep latency, sleep architecture/staging, snoring, number of arousals and leg movements. Mild SDB was defined as TAHI ≥1/h of total sleep time (hTST) and TAHI < 5/hTST, and moderate–severe SDB as TAHI ≥5/hTST and >10/hTST, respectively.

Statistical analysis

Statistical analysis was performed using SPSS for Windows version 16 (SPSS, Chicago, IL, USA). All data were summarized using descriptive statistics and expressed as mean and range.

Results

Sixteen children (11 boys, five girls) were enrolled in the study (Table 1); their mean age was 4.7 years (range, 0.8–10 years) and their mean body mass index was 18.05 kg/m^2 (range, 15.4–25.4 kg/m^2). The mean sleep efficiency was 83% (range, 47–100%). For the whole group, the mean TAHI was 6.3/h (range, 0.2–24.5/h), with TAHI >1/hTST recorded in 11 children (68%), TAHI >5/hTST in five children (31.3%), and TAHI >10/hTST in three children (18.8%). The mean CAHI was 5.9/hTST (range, 0–24.5/hTST) and mean OAHI was 0.4/hTST (range, 0–2.9/hTST). Eleven of 16 patients (68%) were diagnosed with

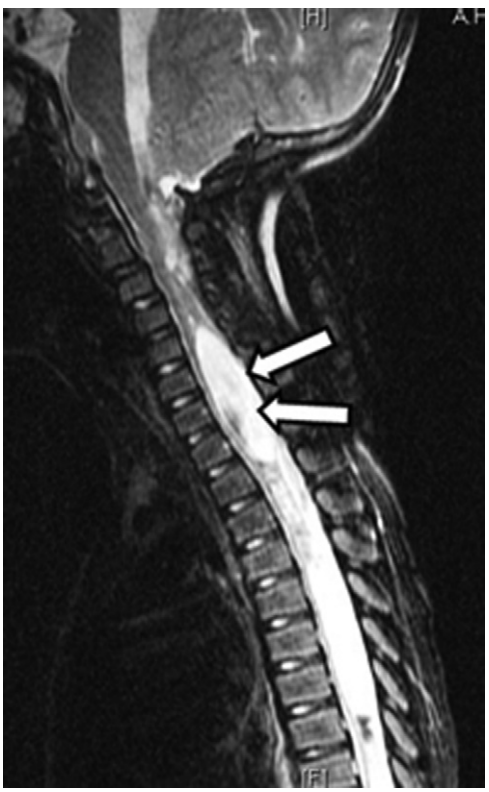

Fig. 2 Sagittal T2-weighted magnetic resonance imaging of a Chiari malformation type II patient with hydro-syringomyelia of the cervical and thoracic spinal cord (arrows).

Table 1 CM-II and NTD subject characteristics and sleep findings ($n = 16$)

Variables	Mean ± SD
Age (years)	4.7 ± 2.8
BMI	18.05 ± 3.7
TIB (min)	380.9 ± 31.8
TST (min)	312.8 ± 58
Sleep efficiency (TST/TIB [%])	83.7 ± 12.8
TAHI (events/h TST)	6.3 ± 7.3
TAHI for NREM (events/h TST)	3.5 ± 6.2
TAHI for REM (events/h TST)	2.8 ± 4.0
CAHI (events/h TST)	5.9 ± 7.3
OAHI (events/h TST)	0.4 ± 0.8
Desaturation index (% of total sleep time)	8.92 ± 17.34
Minimum O_2 saturation (%)	84.79 ± 15.27
Mean O_2 saturation (%)	96.5 ± 2.98
Arousal index (/h TST)	15.11 ± 8.39
Stage I–II (% of total sleep)	51.42 ± 12.28
Stage III (% of total sleep)	29.67 ± 12.07
REM (% of total sleep)	18.07 ± 7.6

BMI, body mass index; CAHI, central apnea–hypopnea index; NREM, non-rapid eye movement; OAHI, obstructive apnea hypopnea index; REM, rapid eye movement; stages I–III, non-REM sleep stages; TAHI, total apnea–hypopnea index; TIB, time in bed; TST, total sleep time.

central sleep apnea. The mean arousal index was 15.1/hTST (range, 5–34/hTST), with respiratory arousal index being 5.0 + 7.6/hTST and spontaneous arousals being 10.1 + 8.4/hTST.

Of note, the majority of the children predominantly had central apneas and hypopneas, with obstructive events contributing very little to the TAHI.

Discussion

This study shows that SDB is a common condition in children with CM-II associated with MMC, most likely due to compression and dysplasia of the brainstem. Central apneas and hypopneas are the most common respiratory abnormality during sleep, and these events lead to hypoxemia and at times hypercarbia. Occasionally, these children can also present with obstructive apneas.[12] Although the exact mechanisms underlying these respiratory abnormalities during sleep are not completely understood, dysfunction of respiratory control centers in the medulla, and/or cranial nerve dysfunction involving either the vocal cords or bulbar muscles mediating airway patency, are likely to be involved.[1–3] Although these children appear to breathe normally during wakefulness, the potential occurrence of PEAC points to the presence of underlying abnormalities in control of ventilation, which then is more likely to manifest during sleep.[2–4] Furthermore, infants and adolescents with CM-II have not only central chemoreceptor dysfunction, but are also at higher risk for peripheral chemoreceptor abnormalities, as evidenced by arousal deficits to respiratory stimuli.[13–16] In addition to SDB, children with MMC may also have restrictive lung disease secondary to scoliosis and to ventilatory muscle weakness, which may further exacerbate the hypoxemic events that develop during sleep.[17] Indeed, these children are at a relatively high risk for aspiration pneumonia and atelectasis as a result of the pharyngeal and laryngeal functional abnormalities. But despite severe problems with ventilatory control, affected children appear to have normal cognitive and intellectual functioning, and also are surprisingly happy individuals.

Sleep-disordered breathing was reported as being present in 62% of patients who underwent overnight sleep tests in one center, and these findings are remarkably similar to those presented herein.[17] In that study, sudden unexplained deaths occurred in 9% of patients during sleep, but only 13% of patients who died were known to have SDB, suggesting that underrecognition of the respiratory abnormalities during sleep is rampant and widespread. Similarly, in a survey of American and Canadian Spina-Bifida Clinics, 11% of deaths were due to respiratory failure.[15] Evaluation for SDB was, however, done in only 8% of that group of patients. Thus, SDB remains underrecognized despite its high prevalence in CM-II, and the known well established risk for death either during sleep or during cyanotic/apneic spells in infants with MMC.[18] Although history can be used as a screening tool, it does not appear to be helpful in differentiating patients with or without SDB.[19] The high incidence of SDB reported in the present study indicates that respiratory disturbances during sleep in patients with CM–II should alert health professionals dealing with children diagnosed with MMC to conduct overnight sleep tests as a routine screening procedure.

As shown in the present patients, SDB consisted predominantly of central sleep apnea syndrome (Fig. 3). Nevertheless, the present group of patients, who were referred to a tertiary care center, might represent only a small percentage of the total number of patients with CM-II and MMC being evaluated and

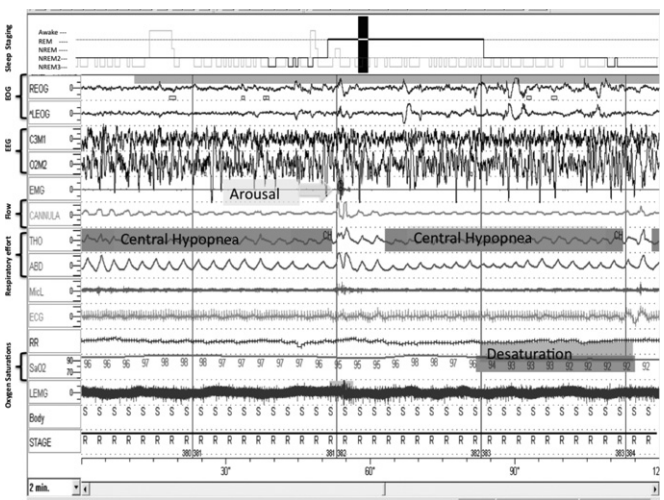

Fig. 3 Portion of a polysomnogram from a Chiari malformation type II patient with epoch of 2 min. The patient had two very long central hypopneas, the first one resulting in arousal and the second one resulting in desaturation. ABD, abdominal respiratory movement; Body, body position; C3M1, O2M2, electroencephalography (EEG) channels; CANNULA, oronasal airflow; Chin EMG, submental/chin electromyogram; LEG1, LEG 2, leg electromyogram; REOG, LEOG, right and left electro-oculograms; SaO_2, oxygen saturation; Stage, sleep stage; THO, thoracic respiratory movement. Sleep stages: Awake; REM, rapid eye movement; NREM: non-rapid eye movement.

treated by similar tertiary services in Riyadh or Saudi Arabia. There are two other neurosurgical centers in the city of Riyadh that offer pediatric surgical services for MMC patients, but the present center is the only one that has the ability, and also routinely implements sleep tests in these patients. The childhood population of Riyadh is approximately 1.8 million, but the catchment area is not well defined because patients may choose the center for their treatment. Thus, the absence of a centralized database of all children with CM-II and the current inability to implement routine sleep tests in all patients with this condition preclude any accurate estimates on the incidence of SDB. Notwithstanding, the present findings and those of other centers lead us to surmise that the incidence of SDB in CM-II is likely to be alarmingly high.

Conclusions

Early recognition of the symptoms and consequences of SDB is important for practitioners involved in the care of children with CM-II. While in a clinical setting, it might be tempting to downplay the significance of sleep disturbances in these children, given the other serious health problems that affect these children, it should also be recognized that SDB, when left untreated, may lead to serious complications including sudden death. In this series, the prevalence of SDB in children with CM-II was high. We therefore propose that all children with this condition should be screened at regular intervals using polysomnography to detect SDB as early as possible. This approach should better identify children at risk, and also guide in the decision process on the need for surgical intervention, as well as identifying children at risk for postoperative respiratory complications.

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