Sleep Disordered Breathing in Children and Adolescents with Chiari Malformation Type I

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Study Objectives: Chiari malformation Type I (CM-I) has been associated with sleep disordered breathing (SDB). The aim of this study was to evaluate the prevalence of SDB in CM-I and its clinical correlates in a population of children and adolescents.

Methods: Fifty-three consecutive children and adolescents affected by CM-I were enrolled (27 girls and 26 boys, mean age 10.3 ± 4.3 , range: 3-18 years). All patients underwent neurological examination, MRI, and polysomnography (PSG). Otorhinolaryngologic clinical evaluation was performed in patients with polysomnographic evidence of sleep-related upper airway obstruction.

Results: Mean size of the herniation was 9.5 ± 5.4 mm. Fourteen patients had syringomyelia, 5 had hydrocephalus, 31 presented neurological signs, 14 had epileptic seizures, and 7 reported poor sleep. PSG revealed SDB in 13 subjects. Patients with SDB, compared to those without SDB, had a higher prevalence hydrocephalus ($p = 0.002$), syringomyelia ($p = 0.001$),

and neurological symptoms ($p = 0.028$). No significant difference was observed in age, gender, prevalence of epilepsy, and size of the herniation. Obstructive SDB was associated with syringomyelia ($p = 0.004$), whereas central SDB was associated with hydrocephalus ($p = 0.034$).

Conclusions: In our population of CM-I patients the prevalence of SDB was 24%, lower than that reported in literature. Moreover, our findings suggest that abnormalities in cerebrospinal fluid dynamics in CM-I, particularly syringomyelia and hydrocephalus, are associated with SDB.

Keywords: Chiari malformation, sleep disordered breathing, obstructive sleep apnea, central sleep apnea, polysomnography, hydrocephalus, syringomyelia.

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Chiari malformation (CM) is a congenital or acquired abnormality of the craniocervical junction characterized by caudal herniation of the cerebellum, with variable extent, through the foramen magnum.¹ Five subtypes of CM are known, of which Type I (CM-I) is the most common.² CM-I presents as an isolated descent of the cerebellar tonsils into the craniovertebral junction; it can be caused by a small posterior fossa, occipito-atlanto-axial hypermobility, connective tissue weakness, or skull anomalies. CM-I is frequently associated with syringomyelia³ and occasionally with hydrocephalus.

Clinical presentation of CM-I may be heterogeneous and in many cases the diagnosis is made incidentally in asymptomatic patients. Usually, CM-I is diagnosed during the second or third decade of life. The symptoms most commonly associated with CM-I are neck pain, headache, lower cranial nerve signs, sneeze syncope, autonomic disturbances, and spinal cord disturbances.⁴ Pseudotumor-like episodes and Ménière disease-like syndrome are less frequent. Often the severity of the symptoms increases with the size of the herniation,⁵ but symptoms may not correlate with the severity of the malformation.

Sleep disordered breathing (SDB), with both central and obstructive sleep apneas, has been reported in association with CM-I. Although many reports of individual cases or small series are available, only few studies⁶⁻⁹ have systematically evaluated the prevalence of SDB in CM-I. These investigations enrolled patients with CM-I and CM-II and included both children and

BRIEF SUMMARY

Current Knowledge/Study Rationale: Chiari malformation has been associated with high prevalence of sleep-related respiratory disorders. The aim of the study was to evaluate the prevalence of SDB in a population of children and adolescent with CM type I.

Study Impact: The prevalence of obstructive SDB in our CM-I population is similar to that observed in the general population. In patients with SDB, obstructive events were associated with syringomyelia and sleep disturbances, whereas central events were associated with hydrocephalus.

adult subjects. These reports suggest that the prevalence of SDB is very high in patients with CM, both in children and adults.⁶⁻⁸

The aims of the present study were: (1) to evaluate the prevalence of SDB, both of central and obstructive origin, in a pediatric population of patients with CM-I; and (2) to define the relationships between SDB and the morphological abnormalities associated with CM-I, and in particular herniation of cerebellar tonsils, syringomyelia, and hydrocephalus.

METHODS

Patients

Fifty-three consecutive unrelated patients were enrolled in the study (27 girls and 26 boys, mean age 10.3 ± 4.3 , range: 3-18 years). The enrollment period lasted 12 months. All pa-

tients underwent MRI study either for the presence of head or neck pain (23 subjects) or for the presence of neurologic disturbances (31 cases, including epilepsy, lower cranial nerves impairment, dizziness, and swallowing difficulties). The inclusion criteria were: age > 1 and ≤ 18 years and presence of CM-I. Exclusion criteria were: presence of other neurological diseases or craniofacial malformations, previous cranial or cervicovertebral surgery, and heart failure. Patients did not receive central nervous system active drugs in the 2 weeks prior to the study, with the exception of antiepileptic treatment for those patients who had seizures. All patients underwent physical and neurological examination, brain and spinal cord MRI, and polysomnography (PSG). The study was approved by the local ethics committee, and patients (when applicable) or parents gave their written consent to participate.

MRI Study

All patients underwent the same MRI protocol, including, 1.5 T sagittal-axial T1-T2 sequences of the brain and spinal cord. CM-I was defined as tonsillar herniation to a point at least 5 mm below the foramen magnum on coronal sequences.⁴ Syringomyelia or syringobulbia were defined as spinal cord or medulla cavitation with CSF-like content on T1-T2 sequences.¹⁰

Polysomnography

Laboratory-based polysomnographies were recorded in soundproof rooms. Full-night recordings were obtained in 40 patients; in the remaining 13, because of poor compliance to an overnight exam, a diurnal polysomnography (nap) was performed. In these cases the recording was performed with the same technique applied to the night studies; the duration of the recording and sleep stages composition fulfilled the guidelines established by the AASM.¹¹ A statistical comparison was made between the group of patients who underwent a full-night recording and those who were studied during a daytime nap. The variables analyzed were the following: age, gender, presence of neurological symptoms, epilepsy and sleep disturbances, snoring, size of herniation, presence of syringomyelia, hydrocephalus, and epilepsy, O-AHI, C-AHI, ODI, presence of SDB, and type of SDB. For numerical variables, a nonparametric test was used (Mann-Whitney U-test); for categorical variable the Fisher two-tailed exact test was adopted. Due to multiple comparisons, the level of significance was set at $p < 0.01$.

Recording montage included EEG leads filled with electrolyte applied to following locations: Fp1, Fp2, C3, C4, T3, T4, O1, O2; reference electrodes applied to the left (A1) and right (A2) mastoids; 2 EOG electrodes applied to the outer ocular canthus and referred to the contralateral mastoid, surface EMG of submental and intercostal muscles, airflow measured by a nasal-cannula pressure transducer, thoracic and abdominal effort, EKG, and peripheral hemoglobin saturation measured by a sensor placed on a finger. Continuous audio and video recording were performed by means of infrared cameras. Sleep recordings were analyzed on computer monitor, and sleep stages were visually classified according to the criteria of the American Academy of Sleep Medicine (AASM, 2007) in all patients.¹² We applied the AASM rules also for the scoring of sleep-related respiratory events. As suggested by the AASM

scoring manual, we applied criteria for children to patients below age 13 years, and adult criteria to patients older than 13 years. This difference may be particularly relevant for the scoring of hypopneas.

The analysis of the SpO₂ parameters was made with dedicated software (Rembrandt SleepView-Medcare). Oxygen desaturation events were scored when a fall in SpO₂ $\geq 3\%$ was observed. The parameters considered were: baseline SpO₂, lowest SpO₂, oxygen desaturation indexes (ODI) in total sleep, in NREM, and in REM. The presence of snoring or loud breathing was detected by means of a specific microphone. Snoring was quantified according to a 4 point score: 0 = (no snoring), 1 = (snoring dependent on sleep stages *and simultaneously* on body position, that is, snoring which occurs in slow wave sleep or REM *and* in supine position), 2 = (snoring dependent on sleep stages *or* on body position, that is snoring occurring in slow wave sleep or REM, regardless of the position, *or* in supine position, regardless of the sleep stage), 3 = (snoring occurring in all positions and in all sleep stages). SDB was defined by the presence of at least one of the following findings: (1) obstructive apnea-hypopnea index ([AHI] including obstructive and mixed events) above the cutoff values; (2) central AHI above the cutoff values; (3) oxygen desaturation index ([ODI] independently from the presence of obstructive, central, or mixed events) above the cutoff values.

Anatomic Evaluation of Upper Airway

A detailed otorhinolaryngologic (ORL) evaluation of upper airways anatomy was performed in all patients who presented PSG findings consistent with sleep-related upper airway obstruction (alone or associated with central sleep apneas). The ORL evaluation included: evaluation of nasal septum deviation, hypertrophic turbinates, adenoidal hypertrophy, tonsils size, macroglossia, uvular hypertrophy or prolapse, and Mallampati score.¹³

Statistical Analysis

Based on the PSG findings, the study population was divided in two groups: with SDB (SDB+) or without SDB (SDB-). Clinical and morphological parameters were compared between these two groups. Moreover, SDB+ was further divided into 3 subgroups: purely obstructive (O-SDB), purely central (C-SDB), and combined (CO-SDB). These subgroups were compared with the SDB- group. Due to the small number of subjects in the subgroups of SDB (purely central, purely obstructive, or combined), no further comparison among these subsets of patients was performed.

The variables considered were: age, gender, presence of neurological symptoms, presence of symptoms of sleep disturbances (snoring or apneas witnessed by the parents), size of herniation, and presence of syringomyelia, hydrocephalus, and epilepsy. All variables included in the study were compared between groups; for numerical variables, a nonparametric test was used (Mann-Whitney U-test); for categorical variables, the Fisher two-tailed exact test was adopted. In case of multiple comparisons, in order to avoid family-wise type-I errors, a formal Bonferroni correction was applied to each family of comparisons, by dividing the limit of significance by the number

Table 1—Demographic, clinical, and polysomnographic data in CM-I patients

	Age	Gender	Neurologic signs	Sleep symptoms	Cerebellar herniation	Epilepsy	Syringomyelia	Hydrocephalus
Total (n = 53)	10.3 ± 4.3	26 M 27 F	31	7	9.5 ± 5.4	14	14	5
SDB− (n = 40)	10.6 ± 4.3	20 M 20 F	20	4	9.5 ± 4.1	11	6	1
O-SDB (n = 6)	11.7 ± 4.1	3 M 3 F	5	3	8.3 ± 3.8	1	4	1
C-SDB (n = 5)	7.8 ± 4.2	2 M 3 F	4	0	15.8 ± 11.2	0	2	1
CO-SDB (n = 2)	7.0 ± 0.0	1 M 1 F	2	0	6.5 ± 2.1	2	2	2

SDB+, patients with SDB; SDB−, patients without SDB; O-SDB, patients with purely obstructive SDB; C-SDB, patients with purely central SDB; CO-SDB, patients with both obstructive and central SDB; M, males; F, females. Age is expressed in years (mean ± SD); cerebellar herniation is expressed in mm (mean ± SD). All other data are expressed as number of patients for each category.

of comparisons. All statistics were performed by means of the SYSTAT 12 software version 12.02.00 for Windows (copyright SYSTAT Software Inc. 2007).

RESULTS

All patients fulfilled the MRI diagnostic criteria for CM-I. The mean length of hindbrain herniation was 9.5 ± 5.4 mm. Five patients had hydrocephalus, 14 had syringomyelia, EEG abnormalities were detected in 25 patients, and epileptic seizures were reported in 14 cases. Detailed clinical and morphological data of the population are reported in **Table 1**.

Useful PSG recordings were obtained in all patients. The comparison between the 13 patients who received a diurnal nap PSG exam and the 40 who underwent a full-night sleep study did not show significant differences in any of the parameters considered (**Table 2**). On the basis of the scoring of respiratory events in PSG, the patients were classified into 4 subgroups: patients without SDB (SDB−); patients with purely obstructive SDB (O-SDB), patients with purely central SDB (C-SDB), and patients with both obstructive and central SDB (CO-SDB).

SDB was detected in 13 patients (24%). Six patients had O-SDB (11%), 5 patients had C-SDB (9%), and 2 patients had CO-SDB (3%). SDB was of mild-to-moderate severity in most patients; only 2 patients showed AHI > 10 events/h (one O-SDB and one C-SDB). Results of the statistical comparison between SDB+ and SDB− groups are in **Table 3**. Results of the scoring of sleep-related respiratory events are reported in **Table 4**. Results of the ORL evaluation in children with obstructive events during sleep are reported in **Table 5**. Finally, in **Table 6**, PSG results in the CM population, divided into age groups, are reported.

The statistical comparison between the SDB+ and SDB− groups showed, in the SDB+ group, a higher prevalence of hydrocephalus ($\chi^2 = 9.177$, $p = 0.002$), syringomyelia ($\chi^2 = 10.932$, $p = 0.001$), and neurological symptoms ($\chi^2 = 4.842$, $p = 0.028$). No differences between the SDB+ and the SDB− groups were observed in age and gender composition, prevalence of epilepsy, or size of the hindbrain herniation. In the obstructive group (O-SDB+), compared to normals (SDB−) we observed an increased prevalence of syringomyelia ($\chi^2 = 8.186$, $p = 0.004$) and sleep disturbances ($\chi^2 = 6.470$, $p = 0.011$). Finally, the C-SDB+ group showed, compared to SDB−, a greater prevalence of hydrocephalus (U-test: 4.493, $p = 0.034$).

Table 2—Results of statistical comparison between patients who received a full-night study and patients who received a nap study

	Full-night PSG vs Nap			
	Mann-Whitney		Fisher test	
	U-test	p	χ^2	p
Age	162.5	0.043		
Gender			0.058	0.810
Herniation	249.5	0.827		
Syringomyelia			1.078	0.299
Hydrocephalus			1.794	0.180
Epilepsy			0.099	0.753
Sleep disturbances			0.457	0.499
Neurological symptoms			2.846	0.092
Snoring			1.405	0.236
SDB+			0.778	0.378
O-SDB			2.199	0.138
C-SDB			0.714	0.398
CO-SDB			0.675	0.411
O-AHI	317.5	0.159		
C-AHI	237.0	0.623		
ODI	264.5	0.925		

O-SDB, patients with purely obstructive SDB; C-SDB, patients with purely central SDB; CO-SDB, patients with both obstructive and central SDB; O-AHI, obstructive apnea-hypopnea index; C-AHI, central apnea-hypopnea index; ODI, oxygen desaturation index. All indexes are expressed as number of events per hour of sleep (mean ± SD). Snoring refers to the number of patients with PSG evidence of snoring for each category.

DISCUSSION

The present study addresses two issues: the prevalence of SDB in a population of children and adolescents affected by CM-I and its anatomical and clinical correlations.

Regarding the prevalence of SDB, 24% of the patients in our CM-I population had abnormal PSG indexes (SDB+). Obstructive SDB was slightly prevalent (6 of 13 cases of SDB); central SDB was observed in five cases, and two patients had a combination of obstructive and central respiratory events. SDB was in most cases asymptomatic: sleep-related symptoms were observed in only seven patients in the sample, of whom four were SDB−, and three had obstructive SDB. Central SDB was not symptomatic in any patient of the sample.

Table 3—Results of statistical comparison between patients with SDB+, O-SDB, and C-SDB versus patients without SDB

	SDB+ vs SDB–				O-SDB vs SDB–				C-SDB vs SDB–			
	Mann-Whitney		Fisher test		Mann-Whitney		Fisher test		Mann-Whitney		Fisher test	
	U-test	p	χ^2	p	U-test	p	χ^2	p	U-test	p	χ^2	p
Age	297.5	0.436			98.50	0.481			122.5	0.132		
Gender			0.058	0.810			0.001	1.000			0.008	0.927
Herniation	243.0	0.723			133.5	0.657			45.5	0.130		
Syringomyelia			10.932	0.001			8.186	0.004			0.177	0.674
Hydrocephalus			9.177	0.002			2.518	0.113			4.493	0.034
Epilepsy			0.099	0.753			0.318	0.573			1.546	0.214
Sleep disturbances			1.464	0.226			6.470	0.011			0.534	0.465
Neurological symptoms			4.842	0.028			2.337	0.126			0.753	0.385

SDB+, patients with SDB; SDB–, patients without SDB; O-SDB, patients with purely obstructive SDB; C-SDB, patients with purely central SDB.

These results are different, in several aspects, from those previously reported in the literature. Compared to previous studies, we observed a lower prevalence of SDB, and particularly, a lower prevalence of central sleep apneas. Gagnadoux et al.,¹⁴ in a case series including only adult patients, observed sleep apnea syndrome (SAS) in 12 of 16 patients (prevalence: 75%); almost half the events were central. Dauvilliers et al., who enrolled a large sample of CM-I and CM-II patients (26 adults and 20 children)⁶ reported that SAS was present in 31 of the patients with CM (67.4% of the total sample; 70% of CM-I, 50% of CM-II, including mainly children). Sixty per cent of children with CM exhibited SAS, including 35% with obstructive (OSAS) and 25% with central (CSAS) sleep apnea syndrome. SAS was observed in 73% of CM adults (57.7% OSAS, 15.4% CSAS). Severe SAS was found in 23% of CM adults. Finally, a Brazilian polysomnographic study including patients of all ages (from childhood to elderly), affected by CM-I and CM-II, reported a prevalence of SDB reaching 63%, almost in all cases of central type.⁸ Notably, this study observed a high prevalence of REM behavior disorder (RBD), which we never observed in our series, probably due to the younger age of our patients.

A possible source of discrepancies in the interpretation of pediatric PSG is the definition of hypopneas. The AASM provides a definition which requires the simultaneous presence of a flow limitation and hemoglobin desaturation and/or EEG arousal. It has been demonstrated that a more extensive definition of hypopneas, based on the simultaneous application of nasal cannula pressure transducers and oral thermistors, and which does not include desaturations or arousals, leads to the scoring of a much greater number of respiratory events.¹⁵ In the present study we decided to score hypopneas and other respiratory events according to AASM criteria, in order to obtain data which could be compared to those reported in previous literature.

The age and the composition of our sample could explain, at least in part, the discrepancy from previous reports. In fact, our population is exclusively pediatric, with an age ranging from 3 years to 18 years. Moreover, we included only patients with CM-I; we decided to exclude CM-II, which is generally associated with a more severe neurologic impairment. On the other hand, it is well known that SDB, particularly OSAS, has a peak of prevalence in the first decade.¹⁶ The prevalence of OSAS in pediatric age is debated, and it varies according to the age limits

and the criteria adopted for the diagnosis. In an epidemiological study which enrolled a population of 399 children and adolescents 2 to 18 years of age, Redline et al.¹⁷ reported a prevalence of OSAS of 10.3%. Seen in this view, the prevalence of obstructive SDB in our CM-I population is not far from that observed in the general population.

An alternative possible source of difference is the severity of the neurological symptoms or signs. In previous studies, most patients presented neurological symptoms and signs, as well as sleep disturbances. Conversely, we enrolled patients who presented neurological symptoms or signs (essentially: headache, epilepsy, dizziness or vertigo) but also patients (about half the sample) in whom CM resulted as an occasional finding in MRI studies. Moreover, only three patients in the series complained about sleep apnea. This relatively high number of asymptomatic patients may represent an important contribution to the knowledge of the natural history of CM-I.

The second endpoint of the study was to look for correlations between morphological and clinical abnormalities of CM-I patients and SDB. In particular, we explored the relationships between PSG findings and entity of cerebellar herniation, the presence of syringomyelia, hydrocephalus, epilepsy, and neurological and hypnological symptoms. The results demonstrate that the presence of SDB is associated with presence of syringomyelia, hydrocephalus, and neurological symptoms, whereas it is independent of the size of herniation. In the analysis of SDB+ subgroups, obstructive SDB was associated with syringomyelia and sleep disturbances, whereas central SDB was associated with a greater prevalence of hydrocephalus.

Few data are available concerning the pathophysiological mechanisms underlying SDB in patients affected by CM. Respiratory manifestations during sleep are generally ascribed to two types of abnormalities: upper airway dysfunction and abnormalities of respiratory control centers. Upper airway dysfunction is mainly associated with obstructive apneas, whereas abnormalities of respiratory control play a pivotal role in the pathophysiology of central sleep apneas.^{6,7} There are several hypotheses concerning the possible mechanisms of central apnea in CM: physical compression of the brainstem and consequent depression of the respiratory center or reticular activating system,¹⁴ abnormal chemosensitivity due to damaged peripheral chemoreceptors,¹⁸ and stretching of lower cranial nerves

Table 4—Detailed PSG results in study population

Patient #	Age	Gender	PSG study	O-AHI	C-AHI	ODI	Snoring	Type of SDB
1	11	F	Full night	0.00	0.58	0.00	No	SDB–
2	4	F	Full night	0.56	0.56	0.00	Yes	OSA
3	5	M	Full night	0.86	0.00	4.31	No	SDB–
4	7	M	Nap	0.00	0.00	0.85	No	SDB–
5	7	F	Nap	0.00	0.00	0.61	No	SDB–
6	9	M	Full night	0.90	1.10	2.50	No	CSA
7	4	M	Full night	0.10	1.60	1.60	No	CSA
8	10	F	Full night	2.20	0.00	19.70	Yes	OSA
9	7	F	Full night	1.40	8.70	10.20	Yes	OSA+CSA
10	10	F	Full night	0.60	0.00	0.40	No	SDB–
11	4	M	Nap	0.00	0.70	0.00	No	SDB–
12	18	M	Full night	0.00	0.00	0.00	No	SDB–
13	13	F	Nap	0.00	0.00	0.70	No	SDB–
14	15	M	Full night	8.00	0.00	11.20	No	OSA
15	18	F	Full night	0.00	0.00	0.00	No	SDB–
16	7	M	Full night	1.93	1.93	0.00	Yes	OSA+CSA
17	15	F	Full night	1.00	0.00	3.60	No	SDB–
18	7	F	Full night	0.00	0.60	0.48	No	SDB–
19	10	F	Nap	0.00	0.90	0.00	No	SDB–
20	13	F	Full night	0.00	11.46	6.70	No	CSA
21	3	F	Nap	0.00	0.38	17.60	Yes	CSA
22	18	M	Full night	0.00	0.30	0.90	No	SDB–
23	16	F	Nap	0.00	0.00	0.00	No	SDB–
24	14	M	Full night	1.40	0.00	1.70	Yes	OSA
25	10	F	Full night	0.34	0.85	0.34	No	SDB–
26	15	F	Full night	0.00	0.30	0.00	No	SDB–
27	6	M	Full night	0.00	0.00	0.00	No	SDB–
28	15	M	Full night	0.00	1.00	1.00	No	SDB–
29	13	M	Full night	23.90	0.00	31.90	Yes	OSA
30	18	F	Full night	0.00	0.70	3.12	No	SDB–
31	12	M	Full night	0.00	0.72	0.14	No	SDB–
32	13	M	Nap	0.00	0.00	0.00	No	SDB–
33	10	F	Nap	0.00	0.54	1.09	No	SDB–
34	10	F	Nap	0.00	1.63	10.61	No	CSA
35	14	M	Full night	0.00	0.90	1.30	No	SDB–
36	4	M	Full night	1.00	0.00	0.00	No	SDB–
37	4	F	Full night	0.00	0.90	0.00	No	SDB–
38	11	F	Full night	0.00	0.70	0.50	No	SDB–
39	6	F	Full night	0.00	0.43	0.85	No	SDB–
40	13	M	Full night	0.00	0.90	0.50	No	SDB–
41	8	F	Full night	0.00	0.00	4.00	No	SDB–
42	14	F	Full night	0.76	0.15	1.86	No	SDB–
43	12	M	Full night	0.10	0.40	0.90	Yes	SDB–
44	12	M	Nap	0.00	0.00	0.00	No	SDB–
45	8	F	Full night	0.00	0.50	0.97	No	SDB–
46	12	M	Full night	0.60	0.60	3.40	No	SDB–
47	14	M	Nap	0.00	0.00	0.98	No	SDB–
48	14	F	Full night	5.60	0.00	4.00	Yes	OSA
49	8	M	Full night	0.00	0.90	0.00	No	SDB–
50	4	M	Full night	0.00	0.12	0.98	No	SDB–
51	8	M	Nap	0.00	0.00	0.00	No	SDB–
52	4	M	Full night	0.00	0.86	0.43	Yes	SDB–
53	11	F	Full night	0.00	0.38	0.38	No	SDB–

SDB–, patients without SDB; O-SDB, patients with purely obstructive SDB; C-SDB, patients with purely central SDB; CO-SDB, patients with combined obstructive and central SDB; M, males; F, females.

Table 5—Results of ORL evaluation in the 8 patients with obstructive events during sleep

Patient #	Septum deviation	Turbinate hypertrophy	Adenoid hypertrophy	Tonsil size (0 - 5)	Uvula	Macroglossia	Mallampati score
2	No	Yes	No	0	No	Mild	1
8	Yes	No	Mild	0	No	No	1
9	Yes (left)	No	Mild	0	Mild prolapse	No	1
14	No	No	Mild	2	No	No	2
16	No	Yes	No	0	No	No	1
24	No	No	No	0	No	No	1
29	No	No	Mild	0	No	No	1
48	Yes (right)	Yes	No	0	No	No	1

Patient numbers refer to the consecutive number of enrollment (see **Table 4**). Tonsils size is expressed on a scale ranging from 0 (invisible tonsils) to 5 (tonsils touching on the midline, "kissing tonsils"). Uvula indicates presence of uvular hypertrophy or prolapse.

Table 6—Prevalence of SDB in the population of CM-I patients by age

Age range, y	n	Gender	SDB+	SDB–	O-SDB	C-SDB	CO-SDB
3-5	9	6M 3F	3	6	1	2	0
6-8	11	5M 6F	2	9	0	0	2
9-11	10	1M 9F	3	7	1	2	0
12-14	14	10M 4F	4	10	3	1	0
15-18	9	4M 5F	1	8	1	0	0
< 13	34	16M 18F	8	26	2	4	2
≥ 13	19	10M 9F	5	14	4	1	0

n, number of patients in each age group; M, males; F, females; SDB+, patients with SDB; SDB–, patients without SDB; O-SDB, patients with purely obstructive SDB; C-SDB, patients with purely central SDB; CO-SDB, patients with combined obstructive and central SDB.

that carry inputs from the carotid bodies to medulla.¹⁸ Besides, in case of associated malformations, such as syringomyelia, the medullar compression may also compromise blood flow, resulting in delayed feedback to the respiratory chemoreceptors. Also, the pathophysiological mechanisms underlying OSA in CM are not clear.⁶ Probably obstructive respiratory events, due to sleep-related upper airway collapse, may be related to an alteration in nervous control of upper airway patency during sleep and to impairment of the pathways involving the IX and X pairs of cranial nerves and muscles dedicated to inspiration and expiration.⁶

Raised intracranial pressure and hydrocephalus are known pathogenic mechanisms of SDB, and particularly of OSAS.¹⁹⁻²³ On the other hand, obstructive apneas during sleep have been considered the cause of transient, severe increase in intracranial pressure.^{24,25} In one report, the authors speculated that episodic airway obstruction and concurrent intracranial hypertension may have contributed to the development of syringomyelia.²⁴ Therefore, the association between hydrocephalus and SDB could be bidirectional: it could be hypothesized that OSAS may contribute to the development of syringomyelia and hydrocephalus in patients with CM.^{24,25}

Whatever the pathophysiologic mechanism that correlates SDB and cerebrospinal fluid (CSF) dynamic in CM-I patients, respiratory disturbances during sleep should be systematically investigated in these patients, in order to evaluate the role of SDB in the clinical course of CM-I, syringomyelia, and hydrocephalus. SDB may worsen clinical symptoms and, in epileptic patients, the frequency of seizures. For these reasons, an evaluation

of the sleep-related respiratory pattern should be routinely performed in CM-I children. Moreover, longitudinal studies are necessary to evaluate the indications and the efficacy of surgical treatment in CM patients with SDB.

REFERENCES

- Paul KS, Lye RH, Strang FA, Dutton J. Arnold-Chiari malformation. Review of 71 cases. *J Neurosurg* 1983;58:183-7.
- Fernandez AA, Guerrero AI, Martinez MI, et al. Malformations of the craniocervical junction (Chiari type I and syringomyelia: classification, diagnosis and treatment). *BMC Musculoskelet Disord* 2009;10 Suppl 1:S1.
- Strahle J, Muraszko KM, Kapurch J, Bapuraj JR, Garton HJ, Maher CO. Chiari malformation Type I and syrinx in children undergoing magnetic resonance imaging. *J Neurosurg Pediatr* 2011;8:205-13.
- Milhorat TH, Chou MW, Trinidad EM, et al. Chiari I malformation redefined: clinical and radiographic findings for 364 symptomatic patients. *Neurosurgery* 1999;44:1005-17.
- Wu YW, Chin CT, Chan KM, Barkovich AJ, Ferriero DM. Pediatric Chiari I malformations: do clinical and radiologic features correlate? *Neurology* 1999;53:1271-6.
- Dauvilliers Y, Stal V, Abril B, et al. Chiari malformation and sleep related breathing disorders. *J Neurol Neurosurg Psychiatry* 2007;78:1344-8.
- Gosalakkal JA. Sleep-disordered breathing in Chiari malformation type 1. *Pediatr Neurol* 2008;39:207-8.
- Henriques-Filho PS, Pratesi R. Sleep apnea and REM sleep behavior disorder in patients with Chiari malformations. *Arq Neuropsiquiatr* 2008;66:344-9.
- Botelho RV, Bittencourt LR, Rotta JM, Tufik S. Adult Chiari malformation and sleep apnoea. *Neurosurg Rev* 2005;28:169-76.
- Koyanagi I, Houkin K. Pathogenesis of syringomyelia associated with Chiari type 1 malformation: review of evidences and proposal of a new hypothesis. *Neurosurg Rev* 2011;33:271-84; discussion 84-5.
- Owens JA, Mindell JA. Pediatric sleep medicine: priorities for research, patient care, policy and education. *J Clin Sleep Med* 2006;2:77-88.

12. Iber C, Ancoli-Israel S, Chesson A, Quan SF. *The AASM manual for scoring of sleep and associated events: rules, terminology and technical specifications*. Westchester, IL: American Academy of Sleep Medicine, 2007.
13. Mallampati SR, Gatt SP, Gugino LD, et al. A clinical sign to predict difficult tracheal intubation: a prospective study. *Can Anaesth Soc J* 1985;32:429-34.
14. Gagnadoux F, Meslier N, Svab I, Menei P, Racineux JL. Sleep-disordered breathing in patients with Chiari malformation: improvement after surgery. *Neurology* 2006;66:136-8.
15. Lin CH, Guilleminault C. Current hypopnea scoring criteria underscore pediatric sleep disordered breathing. *Sleep Med* 2011;12:720-9.
16. Bonuck KA, Chervin RD, Cole TJ, et al. Prevalence and persistence of sleep disordered breathing symptoms in young children: a 6-year population-based cohort study. *Sleep* 2011;34:875-84.
17. Redline S, Tishler PV, Schluchter M, Aylor J, Clark K, Graham G. Risk factors for sleep-disordered breathing in children. Associations with obesity, race, and respiratory problems. *Am J Respir Crit Care Med* 1999;159:1527-32.
18. Nogues MA, Roncoroni AJ, Benarroch E. Breathing control in neurological diseases. *Clin Auton Res* 2002;12:440-9.
19. Kristensen B, Malm J, Rabben T. Effects of transient and persistent cerebrospinal fluid drainage on sleep disordered breathing in patients with idiopathic adult hydrocephalus syndrome. *J Neurol Neurosurg Psychiatry* 1998;65:497-501.
20. Pollak L, Shpirer I, Rabey JM, Klein C, Schiffer J. Polysomnography in patients with intracranial tumors before and after operation. *Acta Neurol Scand* 2004;109:56-60.
21. Shaffer N, Martin B, Loth F. Cerebrospinal fluid hydrodynamics in type I Chiari malformation. *Neurol Res* 2011;33:247-60.
22. Shah S, Haughton V, del Rio AM. CSF flow through the upper cervical spinal canal in Chiari I malformation. *AJNR Am J Neuroradiol* 2011;32:1149-53.
23. Tran K, Hukins CA. Obstructive and central sleep apnoea in Arnold-Chiari malformation: resolution following surgical decompression. *Sleep Breath* 2011;15:611-3.
24. Pasterkamp H, Cardoso ER, Booth FA. Obstructive sleep apnea leading to increased intracranial pressure in a patient with hydrocephalus and syringomyelia. *Chest* 1989;95:1064-7.
25. Sugita Y, Iijima S, Teshima Y, et al. Marked episodic elevation of cerebrospinal fluid pressure during nocturnal sleep in patients with sleep apnea hypersomnia syndrome. *Electroencephalogr Clin Neurophysiol* 1985;60:214-9.

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