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Rhino-Sinus Involvement in Children With Obstructive Sleep Apnea Syndrome

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Summary. Objective: Obstructive sleep apnea syndrome (OSAS) is commonly associated with adenotonsillar hypertrophy. We hypothesized that respiratory perturbations extend to other regions of the upper respiratory tract in such children, particularly to rhino-sinus regions. Study Design: A prospective case control study using Magnetic Resonance Imaging (MRI) of the upper airway and surrounding tissues of OSAS and controls. Magnetic resonance imaging was used to evaluate radiographic changes within the: paranasal sinuses, middle ear and mastoid air cells, and the nasal passages. Results: We studied 54 OSAS (age 5.7 ± 3.0 years) and 54 controls (age 6.2 ± 2.0 years, $P =$ NS). Children with OSAS had significantly more opacification of: maxillary sinuses ($P < 0.05$), sphenoid sinuses ($P < 0.01$), and mastoid air cells ($P < 0.01$). They also had significantly more: middle ear effusions, ($P < 0.001$), prominence of inferior nasal turbinate(s) ($P < 0.05$), and deviation of the nasal septum ($P < 0.05$). Conclusions: Childhood OSAS is associated with a wide range of upper respiratory tract perturbations and is not limited to adenoid and tonsillar hypertrophy. **Pediatr Pulmonol. 2010; 45:993–998.**

Key words: obstructive sleep apnea syndrome (OSAS); magnetic resonance imaging (MRI); upper airway; Rhino-sinus disorders.

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INTRODUCTION

The association between adenotonsillar hypertrophy and obstructive sleep apnea syndrome (OSAS) in children is well-established. However, the pathophysiology of this hypertrophy is not well understood,[1] nor is the exact nature of the relationship between OSAS and a group of other inflammatory conditions along which it frequently presents in children, including allergic rhinitis, rhinosinusitis, and chronic otitis media.[2–5]

There are two important reasons to suggest an association between adenotonsillar hypertrophy and a broader respiratory tract perturbation in children with OSAS. First, the adenoid and tonsils have afferent lymphatic pathways extending from more remote regions of the nasopharynx and oropharynx. This could suggest that adenotonsillar hypertrophy may be secondary to an inflammatory process in more distant regions. Second, in young children, all the anatomical structures surrounding the upper airway are in close proximity and lined with a similar respiratory epithelium. Thus, any inflammatory process at one end is likely to affect substantial areas of the upper airway. However, while OSAS may represent a manifestation of a broader respiratory disorder involving the upper airway in children, objective evidence of such an association is limited.

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An important radiographic method for studying the above relationship in an objective manner is to utilize magnetic resonance imaging (MRI) of involved structures of the head and neck in children with and without OSAS. MRI has excellent soft tissue resolution and is both accurate and reliable and has been used previously to perform volumetric analysis of the upper airway, with particular emphasis on the role of the adenoid and tonsils on airway morphology and risk for OSAS.[6,7] However, to date, a detailed analysis of surrounding structures, such as the nasal cavity, paranasal sinuses, and middle ear has not been performed.

In this study we hypothesized that upper respiratory tract involvement in young children with OSAS is not limited to the adenoid and tonsils, and a broader upper respiratory tract perturbation may exist. To this end, we applied MRI to evaluate the: paranasal sinuses, middle ears and mastoid air cells, and intranasal structures, in children with OSAS and controls.

METHODS

The study was approved by the Institutional Review Board of the Children's Hospital of Philadelphia and Informed consent was obtained from each subject's parents.

OSAS Subjects

Subjects with OSAS without a history of adenotonsillectomy were recruited from the pool of patients evaluated for sleep disordered breathing at the Sleep Disorders Center. After OSAS was confirmed by polysomnography, patients underwent MRI of the upper airway under sedation.

Controls

Controls were selected from patients who underwent head or neck MRI for a clinical indication such as: seizures, headaches, trauma, and to rule out a brain or neck lesion. Exclusion criteria included prior adenotonsillectomy or OSAS. In addition, controls with evidence of paranasal sinus findings on MRI who presented with headaches were excluded from analysis. Controls had normal growth and development and were matched to OSAS subjects by: age, gender, ethnicity, weight, and height.

History of Allergic Rhinitis and/or Asthma

All subjects were asked about presence of allergic rhinitis and/or asthma, the above diagnoses did not exclude them from participation. They were also asked about the daily use of any of the following medications: nasal steroids, nasal antihistamines, leukotriene inhibitors, β-agonists, inhaled steroids, and antibiotic therapy.

Sleep Apnea Questionnaire

The Brouillette sleep questionnaire[8] was used for initial screening of sleep disordered breathing in all subjects.

Overnight Polysomnography

Subjects and controls were studied in the Sleep Disorders Center at the Children's Hospital of Philadelphia. Studies were performed on a computerized polysomnography acquisition and analysis system (Somnostar; SensorMedics, Yorba Linda, CA). The following cardio-respiratory variables were recorded: Chest and abdominal wall movement by respiratory inductance plethysmography (Respitrace Systems; Ambulatory Monitoring, Inc., Ardsley, NY); heart rate by ECG; inspired and expired end-tidal CO_2 tension ($P_{ET}CO_2$) by capnography (Novametrix 7000; Novametrix, Wallingford, CT); arterial oxygen saturation (SpO_2) assessed by pulse oximetry (Novametrix 7000); oral/nasal airflow with a thermistor (Thermistor 3 port; Nihon Kohden, Tokyo, Japan). Sleep stage was monitored with electroencephalogram (EEG: C4-A1, C3-A2, O1-A2, and O2-A1 positions), electro-oculogram (EOG: ROC/A1 and LOC/A2), and submental electromyogram (EMG). Body movements were monitored by visual observation by the technologist and recordings using a low-light camera (Javelin, CCTV/camera).

Scoring of respiratory variables was performed based on standards set by the American Thoracic Society and previously published data in children.[9,10] We used the definition of obstructive apnea as cessation of airflow at the nose and mouth associated with out-of-phase movement of the rib cage and abdomen. Hypopnea was defined as a decrease of 50% or more in oral/nasal thermistor signal and a concurrent fall in 3% or more of basal oxygen saturation or an arousal.

MRI Protocol

MRI was performed under sedation with intravenous pentobarbital of 2 mg/kg, in increasing increments of 2 mg/kg until sleep. A maximum of three doses, or a total dose of 200 mg were given.

MRI was performed with a 1.5T Siemens Vision system (Iselin, NJ). Images were acquired using a commercially available anterior–posterior volume head coil. The patient's head was positioned supine with the soft tissue Frankfort plane (tragus of the ear to orbital fissure) perpendicular to the table.

Sequential T1 and T2-weighted spin echo axial sections were obtained, spanning from the roof of the orbit to the level of cricoid. The following parameters were used for the T1-weighted images; (TR = 650 msec, TE = 14 msec, 192×256 matrix, slice thickness 3 mm with distance factor 0, 1 acq, FOV = 20–24 cm, RECFOV 6/8). For the

T2-weighted images; (TR = 6,000 msec, TE = 90 msec, 192 × 256 matrix, slice thickness 3 mm with distance factor 0, 1 acq, FOV = 20–24 cm, RECFOV 6/8). Sagittal images spanning bilaterally from the midline T1; (TR = 650 msec, TE = 14 msec, 192 × 256 matrix, slice thickness 3 mm with distance factor 0, 1 acq, FOV = 20–24 cm, RECFOV 8/8). T2; (TR = 6,000 msec, TE = 90 msec, 132 × 256 matrix, slice thickness 3 mm with distance factor 0, 1 acq, FOV = 20–24 cm, RECFOV 8/8). Coronal images spanning from the anterior nares back to the spinal cord T1; (TR = 6,000 msec, TE = 97 msec, 150 × 202 matrix, slice thickness 4 mm with distance factor 0, 1 acq, FOV = 20–24 cm). Following acquisition of the MR studies, image data were transferred via the Radiology Department's Picture Archival and Communication System (PACS) and stored for analyses on a Sun Workstations in the Pulmonary Imaging Lab in a DICOM format.

Rhino-Sinus Evaluation

Analysis was performed using the raw MR images of each subject. Images were reviewed and scored by a neuroradiologist (KS) blinded to the patient's history and diagnosis.

Paranasal Sinuses and Mastoid Air Cells

We used a modified form of the Lund-Mackay staging system to score the degree of opacification of the paranasal sinuses[11] including: anterior and posterior ethmoid sinuses, maxillary sinuses, frontal sinuses, and sphenoid sinuses. This methodology was also applied to score the mastoid air cells. Accordingly, degree of opacification was determined unilaterally and a bilateral total score was calculated; (0) no opacification, (1) mucosal thickening, (2) partial opacification, (3) complete opacification. Significant sinus opacification was determined with a total score of $\geqslant 3$, or with a score of $\geqslant 2$, noted unilaterally.

Middle Ear

The presence or absence of a middle ear effusion was determined for each subject on each side; (0) no effusion, (1) effusion. A bilateral total score was calculated.

Intranasal Structure

(a) The presence of lower nasal turbinae prominence was determined; (0) no turbinate prominence, (1) unilateral or bilateral turbinate prominence, and (b) The presence of nasal septum deviation was determined; (0) no deviation, (1) 1–2 mm deviation, (2) >2 mm deviation.

Data Analysis

Data are presented as Means ± SD and proportions. With regard to demographic and sleep data, *t*-tests for independent samples were used to compare groups with regard to normally distributed continuous variables, and Chi-square and Fisher's Exact tests were used regard to categorical variables. For radiographic findings, groups were matched according to anthropometric measures, and Fisher's Exact and McNemar's tests were applied. MATLAB statistical package was used for all analyses. All tests of significance were two-tailed and performed at $P < 0.05$.

RESULTS

We studied 54 OSAS subjects, mean age 5.7 ± 3.0 years (range 2.0–12.1 years) and 54 matched controls, mean age 6.2 ± 2.0 years (range 2.0–9.4 years). Three additional controls were excluded from analysis since they had radiographic evidence of rhino-sinus involvement in conjunction with headaches. Subjects with OSAS were not significantly different from controls with respect to age, gender, ethnicity, height, weight, or BMI (Table 1).

History of Allergic Rhinitis and/or Asthma

There were no significant differences in the prevalence of allergic rhinitis or asthma between groups. Eleven OSAS and 5 controls had a history of allergic rhinitis, and 11 OSAS and 7 controls had asthma. Similarly, we did not find significant differences in the number of subjects consuming nasal steroids, nasal antihistamines, leukotriene inhibitors, β-agonists, and inhaled steroids, between groups. None of the subjects were treated for acute rhinosinusitis with any antibiotic during the period of the study.

Polysomnography

Polysomnography studies were performed in all 54 OSAS subjects and in 45/54 (83%) controls (Table 2). All controls had respiratory values within normal accepted range. The mean respiratory values for OSAS subjects were: apnea index: 3.7 ± 5.0, apnea/hypopnea index: 10.5 ± 9.2, base-line SpO_2: 96.3 ± 1.1%, and SpO_2 nadir: 82.6 ± 8.4%. These data suggest moderate OSAS in this group.

TABLE 1— Demographics

	OSAS (n = 54)	Controls (n = 54)	*P*-Value
Age (years)	5.7 ± 3.0	6.2 ± 2.0	NS
Gender (male/female)	32/22	32/22	NS
Ethnicity (AA/Caucasian)	32/22	28/26	NS
Height (cm)	114.1 ± 19.8	116.9 ± 14.2	NS
Weight (kg)	26.6 ± 16.0	24.4 ± 8.8	NS
BMI (kg/m^2)	18.8 ± 5.1	17.4 ± 3.2	NS
BMI Z-score	0.8 ± 1.3	0.5 ± 1.2	NS

Mean ± SD. AA; African American.

TABLE 2— Polysomnography

	OSAS (n = 54)	Controls (n = 45)	*P*-Value
Total sleep time (hr)	7.4 ± 0.9	7.6 ± 0.9	NS
Sleep efficiency (%)	87.6 ± 7.4	89.0 ± 6.3	NS
Apnea index	3.7 ± 5.0	0.1 ± 0.2	<0.001
Apnea hypopnea index	10.5 ± 9.2	0.4 ± 0.8	<0.001
Baseline SpO_2 (%)	96.3 ± 1.1	96.9 ± 0.8	<0.01
SpO_2 nadir (%)	82.6 ± 8.4	91.8 ± 3.3	<0.001
Baseline $ETCO_2$ (mm Hg)	39.9 ± 3.9	36.8 ± 5.2	<0.01
Peak $ETCO_2$ (mm Hg)	49.6 ± 6.9	41.6 ± 6.7	<0.001
Arousal-wakening index	15.4 ± 6.8	11.3 ± 4.2	<0.001

Mean ± SD.

Sleep Apnea Questionnaire

Sleep apnea scores were available for all OSAS and controls. The mean scores were 2.8 ± 1.5 and -3.0 ± 1.0, respectively ($P < 0.001$). There was no significant difference in scores for controls who underwent polysomnography (n = 45) and those who did not (n = 9), -2.9 ± 1.1 and -3.4 ± 0.8, respectively.

Paranasal Sinuses and Mastoid Air Cells

With the exception of the frontal sinuses, opacification of all paranasal sinuses was seen with greater frequency in OSAS subjects than in control subjects (Table 3). However, these findings only reached significance for the maxillary ($P < 0.05$) and sphenoid ($P < 0.01$) sinuses. Mastoid cells opacification was noted with greater frequency in OSAS patients than in controls ($P < 0.01$), as was the presence of a middle ear effusion ($P < 0.001$).

Intranasal Structure

Prominence of the nasal turbinates and the presence of a nasal septum deviation were both seen with greater frequency in OSAS patients than in control subjects ($P < 0.05$ for both) (Fig. 1).

DISCUSSION

We applied MRI to study the extent of upper respiratory tract involvement in young children with OSAS. Our results suggest that the paranasal sinuses, middle ears and mastoid air cells, and intranasal structures, are affected in a high proportion of these children. Thus, OSAS in young children is associated with a significantly respiratory tract perturbation that is not limited to the adenoid and tonsils.

In regard to our radiographic method evaluating the paranasal sinuses, few methodological issues deserve an initial comment. CT is commonly used to evaluate paranasal sinus disease and is considered to be more sensitive than MRI to detect mucosal changes, though involves radiation to the head and neck. However, recent studies using MRI with the Lund-Mackay scoring system, as we did, support the use of this methodology in various rhino-sinus disorders in both adults and children.[12–16] A recent study has shown that Lund-Mackay scoring by MRI correlates well with CT and has a high sensitivity and specificity for detecting paranasal sinus disease.[12]

Our results suggest significantly more involvement of the paranasal sinuses in children with OSAS as compared to controls, despite the fact that a history of allergic rhinitis requiring treatment was equally common in both groups. Of particular interest is the finding of sphenoid involvement, not previously reported in OSAS. The paranasal sinuses are mucosal-lined bony cavities which lie adjacent to the nasal cavity. The epithelium of the nasal cavity and the paranasal sinuses is histologically identical and is anatomically continuous with it; inflammation and infectious conditions of both regions are therefore referred at times as rhinosinusitis.[17] We cannot ascertain the cause of rhino-sinus involvement in our subjects and if this represents an infection or non-infectious inflammatory condition. However, other studies have shown that children with adenoid hypertrophy and chronic rhinosinusitis had improved outcomes when treated with a combination of adenoidectomy and antibiotics,[18–20] compared to children treated with adenoidectomy alone.[21]

TABLE 3— Rhino-Sinus Findings

	N/n (%)		
	OSAS (n = 54)	Controls (n = 54)	*P*-Value
(1) Significant sinus opacification			
Maxillary	15/54 (28%)	6/54 (11%)	<0.05
Anterior ethmoid	11/54 (20%)	4/54 (7%)	NS
Posterior ethmoid	12/54 (22%)	4/54 (7%)	NS
Sphenoid	15/54 (28%)	5/54 (9%)	<0.01
Frontal	2/31 (6%)	4/32 (13%)	NS
Mastoid air cells	16/54 (30%)	2/54 (4%)	<0.01
(2) Middle ear effusion	17/54 (31%)	3/54 (6%)	<0.001
(3) Inferior turbinate prominence	44/54 (81%)	31/54 (57%)	<0.05
(4) Nasal septum deviation	21/54 (39%)	9/54 (17%)	<0.05

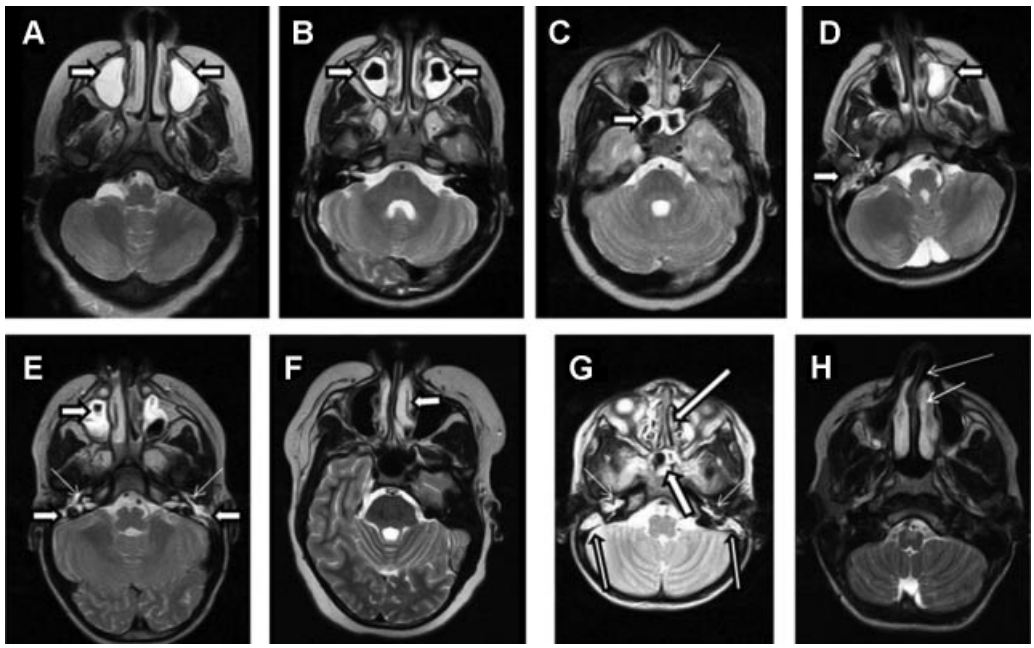

Fig. 1. Rhino-sinus findings in OSAS. (A) Bilateral complete maxillary sinus opacification. (B) Bilateral partial maxillary sinus opacifications with air-fluid level. (C) Bilateral partial opacification of sphenoid sinus (large arrow), complete posterior ethmoid sinus opacification (thin arrow). (D) Complete left maxillary sinus opacification (top large arrow), complete right mastoid sinuses opacification (low large arrow), right ear effusion (thin arrow). (E) Bilateral partial maxillary sinus opacification, bilateral complete mastoid sinus opacification (low large arrows), bilateral middle ear effusion (thin arrows). (F) Unilateral prominence of the left inferior turbinate. (G) Bilateral: ethmoid, sphenoid, and mastoid sinus opacification, bilateral middle ear effusion (thin arrows). (H) Nasal septum deviation (upper arrow) and prominence of inferior turbinates (lower arrow).

Such studies support the concept of co-infection of the adenoid and paranasal sinuses in these children.

Our findings of middle ear opacification noted in about a third of OSAS subjects are likely to represent middle ear effusion. This is supported by a recent study by Gozal et al.[5] demonstrating a high prevalence of recurrent otitis media in children with OSAS. Such findings were also noted by Cengel and Akyol[22] who in a randomized controlled study prescribed nasal steroid to children with adenoid hypertrophy and middle ear effusion. They have demonstrated that nasal steroids significantly reduced adenoid size and the frequency of middle ear effusion. However, we also noted opacification of the mastoid cells. The significance of this finding in the absence of clinical symptoms is unclear but may represent a site of increased inflammation along with the middle ear manifestation in these subjects.

Several sites of upper airway obstruction should be considered in children with OSAS. Nasal airway resistance is particularly high in infants and young children and tends to decline towards adolescent years[23,24] Complete or partial nasal obstruction due to congenital anomalies such as choanal atresia, stenosis, and deformities such as nasal septal deviation, and acute or chronic inflammatory conditions as: rhinitis, nasal polyps, and adenoid hypertrophy are well known risks for OSAS in young children.

In addition to the finding of prominence of the inferior turbinate(s) we noted that nasal septum deviation was more common in OSAS subjects. It is not possible from these static images to determine the degree to which these irregularities in nasal anatomy contribute to actual nasal airflow obstruction. However, studies of anterior rhinomanometry demonstrate higher resistance in both adults and children with OSAS.[25,26] In addition, surgical and non-surgical approaches to reduce nasal resistance such as: septoplasty and turbinectomy,[27] rapid maxillary expansion,[28] and nasal steroids,[29,30] were all shown to be beneficial to children with OSAS.

It should be emphasized that the radiographic findings in our study suggest an association rather than causality. In addition, our findings cannot indicate with certainty the type of inflammatory or infectious cause(s). Our findings would have been strengthen if were supported by concomitant serum and local biomarkers indicating such processes. However, recent studies in children with OSAS document inflammatory processes both locally in the tonsils and adenoid[31] and systemically.[32,33] Thus, we believe the current study provides the radiographic

evidence for such processes involving other important regions of the upper airway in children with OSAS and may supports the rationale of considering adding anti inflammatory treatment modalities to some children with primary OSAS or for children with residual OSAS after adenotonsillectomy.[29–31]

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