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Research Article

Sleep Disordered Breathing in Children with Genetic and Craniofacial Syndrome

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Abstract

Sleep-disordered breathing is common in children with genetic and craniofacial syndromes, but its mechanisms and polysomnographic patterns vary by diagnosis. This case series and narrative review describes five children evaluated for suspected sleep-disordered breathing and places their findings in the context of syndrome-specific evidence. The cases included a 7-year-old girl with Down syndrome and severe obstructive sleep apnea, a 7-year-old girl with Morquio syndrome and moderate obstructive sleep apnea, a 5-month-old girl with Prader-Willi syndrome and both obstructive and central events, a 6-year-old boy with Crouzon syndrome and severe obstructive sleep apnea with hypoxemia and hypoventilation, and a 10-year-old boy with achondroplasia and moderate obstructive sleep apnea. Adenotonsillectomy improved symptoms in the children with Down and Morquio syndromes, although the literature indicates that residual obstruction is common in several of these conditions. The child with Crouzon syndrome had residual obstructive sleep apnea after surgery and difficulty adhering to continuous positive airway pressure. The infant with Prader-Willi syndrome received nocturnal oxygen while growth hormone therapy was started cautiously. Across the cases, structural upper-airway narrowing, hypotonia, altered ventilatory control, and skeletal or neurologic abnormalities contributed in different combinations. Symptoms alone may not identify the type or severity of sleep-disordered breathing in these populations. Polysomnography is therefore important for diagnosis, treatment planning, and follow-up, with additional airway or neurologic evaluation when central events or persistent obstruction suggest an underlying lesion.

Keywords

Sleep-disordered Breathing, Obstructive Sleep Apnea, Central Sleep Apnea, Polysomnography, Genetic Syndromes, Craniofacial Syndromes

1. Introduction

Sleep-disordered breathing (SDB) encompasses abnormalities of respiration during sleep that can fragment sleep and cause oxygen desaturation [1]. It includes obstructive sleep apnea (OSA), central sleep apnea (CSA), and nocturnal hypoventilation. OSA is the most frequently reported form in children, but clinicians should also consider central events and sleep-related hypoventilation.

The American Thoracic Society defines pediatric OSA as prolonged partial upper-airway obstruction or intermittent complete obstruction during sleep that disrupts gas exchange and normal sleep patterns [2]. Untreated OSA is associated with cardiovascular, cognitive, behavioral, and psychiatric complications [3-6]. Because symptoms do not reliably pre-

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dict OSA, overnight polysomnography (PSG) remains the diagnostic standard [7].

CSA occurs when airflow ceases in the absence of respiratory effort. In children, the American Academy of Sleep Medicine defines a central apnea as absent chest and abdominal movement with cessation of airflow for more than 20 seconds, or for at least two baseline respiratory cycles when accompanied by arousal, awakening, or oxygen desaturation of at least 3% [8].

Sleep disorders are common in children with genetic and chromosomal syndromes associated with craniofacial abnormalities, hypotonia, neurologic impairment, or developmental delay. Presentations may include snoring, witnessed apnea, difficulty initiating sleep, frequent waking, restless sleep, or excessive daytime sleepiness. This article presents five illustrative cases and reviews syndrome-specific mechanisms, prevalence, and management considerations.

2. Methods

This article presents five illustrative clinical cases with recorded symptoms, polysomnographic findings, and available management outcomes. We retrospectively reviewed the sleep laboratory database during the period of May 2019 to March 2024. Comorbidities were classified based on patient's medical diagnoses recorded in their hospital files. The patients underwent standard overnight PSG using Alice 6 diagnostic sleep system by Philips Respironics (USA). PSG measurements included electroencephalogram, electro oculogram, submental electromyogram (EMG), and bilateral anterior tibialis EMG. Respiratory measurements included chest wall and abdominal movement using chest wall and abdominal belts; nasal airflow measurements using nasal air pressure transducer and oronasal thermal sensor, oxygen saturation (SaO_2) (Masimo, Irvine, CA, USA).

The PSGs were scored using the AASM acquisition and scoring standards. All PSG studies were interpreted by pe-diatric sleep physicians. An obstructive apnea event was scored when airflow dropped at least 90% from the baseline with chest and/or abdominal motion throughout the entire event; the duration of which was at least a minimum of two baseline breaths. A hypopnea event was scored when airflow dropped at least 30% from baseline, the duration of which was at least a minimum of two baseline breaths. Central apnea event was defined as the absence of chest and/or abdominal movement associated with a cessation of airflow for more than 20 s or lasting more than 2 baseline res-piratory cycles if it was associated with an arousal, an awakening or an oxygen desaturation of at least 3%. The de-saturation index was calculated on the basis of the number of oxygen desaturation events ≥3%.

3. Case Series

Table 1. *Clinical features and sleep-study findings in the five cases.*

Case	Syndrome	Main findings	Management and outcome
1	Down syndrome 7 years, female	Snoring, suspected apnea, daytime sleepiness; BMI 26; OAHI 13/h	Positional therapy and adenotonsillectomy; daytime symptoms and activity improved
2	Morquio syndrome 7 years, female	Snoring, attention difficulty, hyperactivity; BMI 16; OAHI 8/h	Positional therapy and adenotonsillectomy; nocturnal and behavioral symptoms improved
3	Prader-Willi syndrome 5 months, female	Hypotonia; OAHI 2/h; CAI 5.5/h; oxygen desaturation	Growth hormone started cautiously; nocturnal oxygen produced a good response
4	Crouzon syndrome 6 years, male	Snoring, gasping, enuresis; AHI 30/h; transcutaneous CO_2 50 mmHg; desaturation to 68%	Adenotonsillectomy reduced OAHI to 10/h; CPAP adherence was difficult
5	Achondroplasia 10 years, male	Snoring; BMI 24; OAHI 6/h; CAI 2/h	Further management was not reported

AHI: apnea-hypopnea index; BMI: body mass index; CAI: central apnea index; CPAP: continuous positive airway pressure; OAHI: obstructive apnea-hypopnea index; PSG: polysomnography.

3.1. Case 1: Down Syndrome

A 7-year-old girl with trisomy 21 was referred for snoring, suspected apnea, and excessive daytime sleepiness. Two years before presentation, her sleep duration had increased and daytime naps had resumed. Her Epworth Sleepiness Scale score was 14. Examination showed grade 2 tonsillar hypertrophy and a body mass index (BMI) of 26. PSG showed an obstructive apnea-hypopnea index (OAHI) of 13 events/h, including

a hypopnea index of 9 events/h and an obstructive apnea index of 4 events/h, consistent with severe OSA. Positional therapy was started, and she was referred for otolaryngologic assessment. After adenotonsillectomy, her parents reported improvement in daytime symptoms, school performance, and physical activity.

Down syndrome (DS) occurs in approximately 1 in 800 infants in the United States [9]. Obesity and generalized hypotonia increase the risk of OSA compared with typically developing children [10-12]. Macroglossia, midface hypoplasia, and adenotonsillar hypertrophy also contribute to upper-airway obstruction [13-15]. Central apnea may occur because of hypotonia and immature ventilatory control [16-18], although structural causes such as Chiari malformation and atlantoaxial subluxation should be considered [19].

Reported OSA prevalence in children with DS varies across studies [10, 12, 20-22]. A meta-analysis of 18 studies involving more than 1,000 children reported OSA in approximately 70% when defined by an apnea-hypopnea index greater than 1 event/h, and in approximately 50% when defined by an index greater than 5 events/h [21]. OSA is also common in infants with DS [23, 24]. The American Academy of Pediatrics recommends PSG for all children with DS by 4 years of age [22].

Adenotonsillectomy is generally the first-line treatment for OSA in children with DS [25-27]. Residual OSA is common, so follow-up PSG and additional treatment may be needed [28, 29]. Relevant complications include neurodevelopmental impairment and pulmonary hypertension [30, 31].

3.2. Case 2: Morquio Syndrome

A 7-year-old girl with Morquio syndrome presented with snoring, attention difficulty, and hyperactive behavior. Her Epworth Sleepiness Scale score was 6. Examination showed coarse facial features, a broad nose, pectus carinatum, grade 3 tonsillar hypertrophy, and a BMI of 16. PSG showed an OAHI of 8 events/h, including a hypopnea index of 3 events/h and an obstructive apnea index of 5 events/h, consistent with moderate OSA. She received positional therapy and was referred for adenotonsillectomy. After surgery, her parents reported improvement in nocturnal symptoms, behavior, and school performance.

The mucopolysaccharidoses (MPS) are a heterogeneous group of inherited metabolic disorders caused by deficiencies in enzymes responsible for glycosaminoglycan degradation [32]. Accumulated glycosaminoglycans affect multiple tissues, including the lungs and upper airway, and can produce SDB, particularly OSA [33, 34]. Deposits in the tongue, adenoids, tonsils, larynx, and hypopharynx narrow the airway, while skeletal abnormalities further increase airway resistance.

OSA is sufficiently common in MPS that evaluation at diagnosis is recommended regardless of age [35-38]. Symptoms alone may not correlate with PSG findings. Reported nonrespiratory sleep problems include insomnia, altered sleep-stage distribution with reduced rapid eye movement sleep, and restless legs symptoms [39, 40]. Enzyme replacement therapy may reduce some mucosal narrowing of the larynx and hypopharynx, but it may not resolve adenotonsillar hypertrophy [41].

3.3. Case 3: Prader Willi Syndrome

A 5-month-old girl presented with hypotonia, low activity, a weak cry, and dysmorphic features. Methylation-specific polymerase chain reaction analysis of the SNRPN locus supported a diagnosis of Prader-Willi syndrome (PWS). Before growth hormone treatment, she was referred for PSG. Apart from occasional possible apnea, no sleep symptoms were reported. Her BMI was 17. PSG showed mild OSA, with an OAHI of 2 events/h, and an elevated central apnea index (CAI) of 5.5 events/h. Flexible nasopharyngoscopy showed a normal airway with evidence of laryngopharyngeal reflux, and echocardiography was normal. Growth hormone therapy was initiated cautiously, and nocturnal oxygen was started for episodic oxygen desaturation with a good response.

PWS is a complex genetic disorder occurring in approximately 1 in 25,000 live births. Infants typically have marked hypotonia, hypophagia, hypogonadism, and failure to thrive. Sleep disorders include excessive daytime sleepiness, secondary narcolepsy, altered sleep architecture, and SDB. OSA is common, while CSA is particularly relevant in infancy [42-45]. Sleep disturbance and sleep apnea are included among the minor diagnostic criteria for PWS [46].

Adenotonsillar hypertrophy, hypothalamic and central nervous system dysfunction, muscle weakness, and nasopharyngeal narrowing can contribute to SDB [42]. Because sudden deaths have been reported in association with growth hormone treatment, PSG before treatment initiation and continued clinical surveillance are recommended [47]. OSA prevalence varies across studies [48-52]. Among affected children, approximately half of cases have mild OSA, 22.35% have moderate OSA, and 24.58% have severe OSA. CSA is common in infants but often improves with age [53]. Hypersomnia and narcolepsy have also been reported, with an estimated prevalence near 35% [54].

3.4. Case 4: Crouzon Syndrome

A 6-year-old boy with genetically confirmed Crouzon syndrome was referred for snoring, mouth breathing, gasping, and nocturnal enuresis. His family reported that he slept better while sitting upright. PSG showed an apnea-hypopnea index of 30 events/h, a mean transcutaneous carbon dioxide level of 50 mmHg, and oxygen desaturation to 68%. Adenotonsillectomy reduced the OAHI to 10 events/h, indicating residual OSA. Continuous positive airway pressure was attempted, but adherence was difficult.

Craniofacial disorders include nonsyndromic and syndromic conditions. Craniosynostosis results from premature

fusion of one or more cranial sutures and may be associated with variants in fibroblast growth factor receptor genes. Syndromic forms include Apert, Crouzon, Pfeiffer, Muenke, and Saethre-Chotzen syndromes.

OSA is the most common sleep disorder in syndromic craniosynostosis. Reported prevalence ranges from 40% to 70%; most identified cases are mild, but moderate and severe disease also occur [55-59]. Midface and maxillary hypoplasia, adenotonsillar hypertrophy, and choanal atresia contribute to obstruction [56, 60, 61]. Upper-airway obstruction may coexist with raised intracranial pressure and requires careful evaluation [62, 63]. Central apnea can occur in association with hindbrain compression [64, 65]. Residual OSA after treatment is common, so continued follow-up is important.

3.5. Case 5: Achondroplasia

A 10-year-old boy with achondroplasia was referred for snoring. His parents denied other nocturnal symptoms, and no neurologic symptoms were reported. His medical history included rickets, and his BMI was 24. PSG showed moderate OSA, with an OAHI of 6 events/h, and a CAI of 2 events/h.

Achondroplasia is an inherited skeletal disorder characterized by disproportionate short stature [66, 67]. It occurs in approximately 1 in 25,000 to 30,000 individuals and results from abnormal fibroblast growth factor receptor 3 signaling that impairs endochondral bone growth [68]. Craniofacial anatomy and altered musculoskeletal growth increase the risk of neurologic and cardiorespiratory complications [69].

Reported OSA prevalence in achondroplasia ranges from 40% to 87% [69-73]. Adenotonsillar hypertrophy, airway malacia, and midface hypoplasia contribute to obstruction. Infants are at particular risk and require comprehensive respiratory and neurologic evaluation [74]. Respiratory dysfunction is associated with abnormal PSG findings [75], and persistent OSA may remain after surgery [76].

Spinal deformity and altered respiratory mechanics can impair gas exchange and contribute to nocturnal hypoventilation or CSA [66]. Central events may indicate foramen magnum stenosis and should prompt neurologic and neurosurgical assessment when clinically appropriate [77].

4. Discussion

These cases show that SDB in children with genetic and craniofacial syndromes has several overlapping mechanisms. Adenotonsillar hypertrophy and craniofacial narrowing favor obstruction, whereas hypotonia and impaired ventilatory control can produce obstructive or central events. Skeletal abnormalities may further reduce respiratory reserve or impair gas exchange. The resulting PSG phenotype therefore cannot be predicted from the diagnostic label alone.

Symptoms improved after adenotonsillectomy in children with Down and Morquio syndromes, but the Crouzon syndrome case demonstrates that substantial residual OSA may remain. Published studies similarly report persistent disease after upper-airway surgery in DS, syndromic craniosynostosis, and achondroplasia [28, 29, 56, 76]. Post-treatment PSG is important when symptoms persist, when the underlying syndrome carries a high risk of residual obstruction, or when treatment response is uncertain. Positive airway pressure may be needed, although adherence can be difficult, as illustrated by Case 4.

Central events require particular attention in infants and in children with conditions associated with neurologic or craniocervical abnormalities. In PWS, CSA is prominent in infancy and may improve with age [53]. In DS, craniosynostosis, and achondroplasia, central apnea may warrant evaluation for Chiari malformation, hindbrain compression, atlantoaxial instability, or foramen magnum stenosis [19, 64, 65, 77]. Clinical interpretation should integrate respiratory pattern, gas exchange, age, neurologic examination, airway findings, and planned therapies.

This article describes five illustrative cases rather than a consecutive cohort. It does not estimate prevalence, compare treatments, or establish causal relationships. The cases support a practical approach centered on early recognition, objective sleep testing, syndrome-specific evaluation, and reassessment after treatment.

In conclusion Children with genetic and craniofacial syndromes are at high risk of obstructive sleep apnea, central sleep apnea, and sleep-related hypoventilation. Presenting symptoms may be subtle and do not reliably define severity. Polysomnography should guide diagnosis and follow-up, while persistent obstruction or central events should prompt targeted airway, neurologic, or craniocervical evaluation. Treatment should address the dominant mechanism and include repeat assessment because residual disease is common.

Abbreviations

AHI	Apnea-Hypopnea Index
BMI	Body Mass Index
CAI	Central Apnea Index
CPAP	Continuous Positive Airway Pressure
CSA	Central Sleep Apnea
DS	Down Syndrome
MPS	Mucopolysaccharidoses
OAHI	Obstructive Apnea-Hypopnea Index
OSA	Obstructive Sleep Apnea
PSG	Polysomnography
PWS	Prader-willi Syndrome
SDB	Sleep-disordered Breathing

Author Contributions

Abdullah Khayat: Conceptualization, Data curation, Methodology, Writing – original draft, Writing – review & editing

Data Availability Statement

The clinical information supporting the case presentations is contained in this article.

Conflicts of Interest

The author declares no conflicts of interest.

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