Obstructive sleep apnea syndrome as a rare presentation in a young girl with a central nervous system tumor.

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Title: Obstructive sleep apnea syndrome as a rare presentation in a young girl with a central nervous system tumor

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Abstract

Sleep related breathing disorders (SRBDs) are a common problem in infancy and childhood. The most common type of SRBD in this age group is obstructive sleep apnea syndrome (OSAS), generally caused by factors affecting airway patency, such as tonsillar hypertrophy or obesity. However, in adults OSAS can also be caused by processes affecting the brainstem, such as central nervous system tumors. This report describes a 2-year-old girl who presented with symptoms of snoring, restless sleep, repeated night-time waking, and apneic events whilst asleep. She had no co-morbidities, and examination revealed normal sized tonsils. A sleep study demonstrated severe OSAS with an obstructive apnea/hypopnea index of 34. Her OSAS completely resolved on excision of the tumor. The case highlights the importance of neurological examination as part of evaluation of OSAS, especially in cases where tonsils are not enlarged and there are no other risk factors for OSAS.

Main text

Introduction

Sleep related breathing disorders (SRBDs) are a common problem in infancy and childhood. They can be broadly categorized as being due to processes that affect airway patency, resulting in increased breathing effort and inadequate ventilation (obstructive sleep apnea syndrome, OSAS), or disorders where respiratory effort is diminished or absent as a result of central nervous system dysfunction - central apnea[1] (which can occur with or without hypoventilation).

OSAS is caused by disruption to ventilation during sleep, due to partial or complete obstruction within the airway. It is characterized by repetitive episodes of complete cessation of breathing (apnea) or partial upper airway obstruction (hypopnea); these events often lead to episodes of low blood oxygen saturations. Features such as snoring and sleep disruption are a common feature [2]. OSAS is common in childhood, affecting up to 5.7% of children[3]. Recognized risk factors for OSAS include obesity, adenotonsillar hypertrophy, chromosomal disorders such as Down syndrome, and craniofacial or nasal abnormalities[3].

Central sleep apnea in childhood is less common, and represents an absence of airflow due to a lack of respiratory effort. It can be caused by immaturity of respiratory control, or may form part of a hypoventilation syndrome, causes of which may be congenital (e.g. congenital central hypoventilation syndrome) or acquired, with causes including Arnold Chiari malformation, spinal injury, or central nervous system tumors[4].

Here we report the case of a girl with a posterior fossa tumor presenting with severe OSAS, which resolved after surgical excision of the tumor.

Report of case

A 2-year-old girl presented to her Family Physician with 12-month history of snoring, restless sleep, repeated night-time waking, and observation of apneic events by her mother. She had no other significant medical history of note. Due to COVID-19 restrictions in place at the time, she was reviewed as a telephone consultation 2 months later by a pediatric ear, nose and throat (ENT) specialist – the history was confirmed and the child was referred for a sleep study which was later expedited and performed urgently (5 weeks from ENT review) due to a worsening of symptoms following the initial referral. Tonsils were confirmed as Brodsky grade 1-2[5] (on a scale of 0-4, where 0 represents no tonsillar enlargement) at subsequent hospital admission (detailed below).

The patient underwent a domiciliary cardiorespiratory polygraphy study using the SOMNOtouch device (SOMNOmedics, Germany) comprising: chest and abdominal respiratory inductance plethysmography bands, pulse oximetry, nasal pressure flow with integral snore sensor, body position sensor and actigraphy. The study was manually scored using Domino software (SOMNOmedics) in accordance with the American Academy of Sleep Medicine manual for the Scoring of Sleep & Associated Events (version 2.6)[6]. The study demonstrated severe obstructive sleep apnea. A total of 353 obstructive events were scored with a nadir SpO_2 of 66% and an obstructive apnea/hypopnea index (oAHI) of 34 per hour of estimated sleep [Figure 1a]. Not a single central event was scored.

3 weeks following her sleep study, the patient presented to the emergency department with a short (<24 hour) history of dysphagia and effortless vomiting on waking, visual disturbance, and possible absence-like seizure, against a background of unsteady gait (around 4 weeks). A neurological examination revealed a broad based ataxic gait and dysdiadochokinesia. Computed tomography (CT) and magnetic resonance imaging (MRI) of her head during this admission demonstrated a midline posterior fossa space occupying lesion, 3.5x3.2x3.7cm in dimension (Figure 2a). She underwent a midline sub-occipital craniotomy with a telo-velar approach enabling tumour resection. Gross total resection of the tumour was achieved with minimal brain retraction and no intra-operative complication (Figure 2b). Histopathology confirmed a WHO Grade 1 Pilocytic astrocytoma, with no pathogenic variants or gene fusion identified. Due to a post-operative pseudomeningocoele and persistent cerebrospinal fluid leak, a ventriculo-peritoneal shunt was ultimately inserted. Her vomiting and gait unsteadiness resolved following surgery. After a period of inpatient and outpatient rehabilitation there were no long-term ongoing neurological deficits.

2 months following tumor resection, a repeat home respiratory polygraphy study was performed which demonstrated complete resolution of OSA, with mean SpO_2 98%, a nadir of 94%, and an oAHI of 0 [Figure 1b]. An MRI Head 3 months following surgery showed no evidence of recurrence or residual disease.

Discussion

Whilst central abnormalities of sleep breathing are well-documented in children with intracerebral tumors, our case of a child with a brain tumor presenting as severe OSAS demonstrates that obstructive SRBD can also arise as a result of intracerebral pathology. This phenomenon is little-

reported in children, and we believe this case to be the first one to confirm resolution of OSAS following tumor resection.

CNS tumors are the commonest solid tumors in children with an average incidence of 4.4 per 100,000 per year in 0-14 year olds in the United Kingdom[10]. They are the commonest cause of death from all childhood cancers[7]. Tumors of the posterior fossa (or infratentorial tumors) most often present with signs and symptoms of raised intracranial pressure and cerebellar signs; such as, headache, vomiting, ataxia and impaired coordination[8]. Diagnostic delay for children and teenagers with brain tumors may compromise long term outcome.

There are few cases reported in the literature of children with brain tumors and SRBD. Children are documented as mainly presenting with a mixed SRBD pattern[9–11], and to our knowledge there is only one previous case report of a child presenting with isolated OSA[12], although there was no follow-up sleep study to confirm resolution of OSAS after resection of the tumor, and the child was noted to have severe obesity, an independent risk factor for OSAS. In adults, a case series reported polysomnographic (PSG) findings in patients admitted for surgical excision of an intracranial tumour (both supra-tentorial and infra-tentorial)[13]. Aligned with our case report, the authors reported a high proportion (6/11) of the patients had OSAS prior to surgery, with a decrease in mean oAHI after removal of the tumour. Similarly, in a case series of adult patients with operated Arnold Chiari malformation, post-operative PSG showed a decrease in the mean apnea-hypopnea index[14].

The MRI of our case demonstrated a posterior fossa tumor, exerting mass effect on the cerebellar parenchyma resulting in tonsillar descent with anterior displacement of the brainstem. Compression of structures at the craniovertebral junction can disrupt respiratory control centres, predisposing to central events, as the brainstem is the primary source of ventilatory pattern generation. However, compression in this context does not explain a presentation with an obstructive pattern.

The glossopharyngeal (IX) nerve arises from the medulla (a key region of the brainstem); consisting of sensory, motor, and parasympathetic fibers. Its branches consist of and innervate the carotid sinus (via peripheral chemoreceptors), muscles of the pharynx, tonsillar complex and tongue; thereby maintaining upper airway patency[15]. Thus dysfunction of glossopharyngeal nerve branches may result in a deleterious effect on upper airway patency, and this is the putative mechanism for OSA in our case. In a related case of a teenage boy with Chiari type I malformation, the patient presented with parasomnia, an elevated apnea hypopnea index, and a high pitched voice[16]. Similarly

to our case, the symptoms (including the high-pitched voice) resolved with surgical intervention, supporting a pathologic mechanism of increased pressure on cranial nerve nuclei/branches.

A potential limitation to our case report is the use of limited-channel recordings (respiratory polygraphy) as compared with polysomnography for the diagnosis of sleep-disordered breathing. The utility of home respiratory polygraphy whilst allowing the scoring of respiratory events in the presence of desaturation, does not allow for the scoring of events that have led to arousal or awakening due to the absence of EEG measurements. Thus respiratory polygraphy may lead to underscoring and/or misclassification of OSAS in mild/moderate disease[17]. In the case of our patient, she had demonstrably severe OSAS, making issues of underscoring less relevant.

Conclusion

Our case highlights the potential for intracerebral pathology including brain tumors to present with OSAS. Since brain tumors are the most common solid tumors of childhood, we believe that this case is important to report. Specifically, the case highlights that one may wish to consider the role of neurological examination as part of evaluation of OSAS causation, especially in cases where tonsils are not enlarged and there are no other apparent risk factors (obesity, other co-morbidities) for OSAS.

Abbreviations

SRBD: Sleep-related breathing disorder

OSAS: Obstructive sleep apnea syndrome

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Figure captions

Figure 1. Pre-and post-operative sleep study results. Screenshots of overnight SpO2 profile over 11 hours (a) and a 2-minute sleep epoch (b) demonstrating obstructive events. Screenshots of overnight SpO2 profile over 11 hours (c) and a 2-minute sleep epoch (d) demonstrating complete resolution of obstructive events. The SOMNOtouch device includes a nasal cannula which monitors respiratory flow and snore signals; in this case there was extensive mouth breathing, which limited the utility of this channel.

Figure 2. Pre- and post-operative MRI scans of the brain. Pre-operative sagittal (a) and axial (b) scans showing a mixed solid cystic lesion within the posterior fossa and effacement of the fourth ventricle. Post-operative sagittal (c) and axial (d) scans showing increased enhancement within the resection cavity with no definite evidence of disease recurrence.

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