Official Case Reports Journal of the Asian Pacific Society of Respirology
Respirology Case Reports
OPEN ACCESS
APSR

Rapidly evolving narcolepsy-like syndrome coinciding with severe OSA following pharyngoplasty in Prader-Willi syndrome

Gregory Blecher, Natalie Wainbergas, Michael McGlynn & Arthur Teng

Department of Sleep Medicine, Sydney Children's Hospital, Randwick, New South Wales, Australia

Keywords
Excessive daytime sleepiness, narcolepsy, obstructive sleep apnea, Prader-Willi syndrome, velopharyngeal incompetence.

Correspondence
Gregory Blecher, Department of Sleep Medicine, Sydney Children's Hospital, 61 High Street, Randwick, NSW 2031, Australia.
E-mail: greg.blecher@gmail.com

Received: 31 March 2014; Revised: 27 May 2014; Accepted: 30 May 2014.

Respirology Case Reports **2014; 2(3): 111–112**

doi: 10.1002/rcr2.65

Abstract

Our patient with Prader-Willi syndrome (PWS) not only displayed many typical syndromic features but also presented several unique challenges, with gross velopharyngeal insufficiency necessitating repair and severe obstructive sleep apnea developing thereafter, requiring ongoing non-invasive ventilation. This coincided with development of a narcolepsy-like syndrome, treated with dexamphetamine. Cataplexy, hypnogogic/hypnopompic hallucinations, sleep paralysis were absent and HLA-DQB1*06:02 was negative. Growth hormone (GH) therapy was commenced at 8 months of age and, as recommended, regular polysomnograms were conducted. Adenotonsillar growth on GH therapy is reported as well as several reports of sudden death in PWS patients on GH. Despite GH, lifestyle measures with regular dietician review, and an exercise program, there was progressive excessive weight gain. Our patient also developed moderate tonsil hypertrophy. To our knowledge, this is the first case report of severe obstructive sleep apnea secondary to sphincter pharyngoplasty coinciding with rapidly evolving narcolepsy-like syndrome.

Case Report

Prader-Willi syndrome (PWS) was diagnosed in a male term neonate when investigating hypotonia, feeding difficulties, hypothermia, and cryptorchidism, and genotyping confirmed 15q11.2–15q12 deletion. Growth hormone (GH) therapy was commenced at 8 months of age. Our patient had been reported to snore nightly, and as per protocol, a polysomnogram (PSG) prior to starting GH was performed. This showed mild obstructive sleep apnea (OSA), but was normal when repeated 3 months later.

Developmentally, there was significant global delay. Our patient was not walking independently at 3 years, remained hypotonic, and was communicating by vocal utterances and sign language. Since school entry, he has been in a support unit.

Gross velopharyngeal incompetence (VPI) was suspected due to virtually unintelligible speech, hyponasal resonance, intermittent nasal regurgitation, and difficulty in blowing out candles. This was confirmed at 6 years and 7 months after specialist ear nose and throat and speech pathology investigations. No cleft was detected. As there was little improvement despite maxillary expansion and intensive speech therapy, sphincter pharyngoplasty was performed at 7 years and 7 months. By this stage, there had been significant weight gain, the patient now weighing 50.5 kg (15 units >97th centile, body mass index [BMI] 27.5 kg/m^2).

Articulation markedly improved following surgery. However, our patient rapidly developed loud snoring with witnessed apneas and restless sleep and, on monitoring, was desaturating to 70%. He also was excessively sleepy and had new onset encopresis. Tonsils were midsize, 2/4. Severe OSA was confirmed on sleep study: there was desaturation to 52% at sleep onset; transcutaneous carbon dioxide (CO_2) rose abnormally from 41 mmHg to 82 mmHg. The obstructive and mixed apnea/hypopnea index was 9.5/h. Sleep onset rapid eye movement (REM) was noted.

Continuous positive airway pressure (CPAP) was commenced, but was insufficient as there was CO_2 retention. Bi-level positive pressure support (BPAP) with a full face mask (spontaneous timed mode inspiratory positive airway pressure 19 cmH_2O, expiratory positive airway pressure

14 cmH_2O, rate = 25 bpm) normalized transcutaneous carbon dioxide to 40 mmHg with no obstructive events. Compliance with BPAP was excellent, and over time, BPAP support could be weaned and transitioned to CPAP. Progressive weight gain required increasing CPAP pressures, currently at 14 cmH_2O.

There was excessive daytime sleepiness (EDS) but no cataplexy, hypnogogic/hypnopompic hallucinations, or sleep paralysis. A multiple sleep latency test (MSLT) was performed at 7 years and 10 months and demonstrated sleep onset rapid eye movement (SOREM) in three of four nap opportunities with mean sleep latency of 9 min, consistent with a narcolepsy-like syndrome. HLA-DQB1*06:02 was not detected. Patient was commenced on dexamphetamine (currently 10 mg am, 5 mg midi). A magnetic resonance imaging of the brain at age 7 years and 8 months was normal.

Despite regular dietician follow-up and an exercise program, on six monthly endocrine review, there had been progressive weight gain (most recent – BMI 32 kg/m^2, waist circumference to height ratio = 0.64) necessitating serial GH dose increases (currently 9.5 mg/week).

Discussion

Our patient not only displays many features typical of PWS, but also had several unique challenges with gross VPI necessitating repair, severe OSA developing thereafter, and a narcolepsy-like syndrome evolving.

Many of the features of PWS can be explained by hypothalamic dysfunction: failure to thrive and feeding problems in the neonatal period, with a switch to insatiable hunger in early childhood resulting in morbid obesity, short stature because of GH deficiency, temperature instability, central hypogonadism, and sometimes central hypothyroidism. Other features are yet to be explained: hypotonia, behavioral issues, intellectual disability, and dysmorphism. Like the majority of patients with PWS, our patient had a microdeletion of 15q11. He initially fed poorly, but then developed polyphagia and developed morbid obesity. He requires significant support at school.

Central hypoventilation/apnea is often seen in infancy or early childhood years in children with PWS. OSA then predominates secondary to obesity, facial configuration (micrognathia, small oronasopharynx), hypotonia, and sticky secretions [1]. Adenotonsillar hypertrophy compounds this. Early central apnea was not evident in our patient. Although morbidly obese by age 7 years, he had no symptoms of OSA. It was only after sphincter pharyngoplasty, presumably because of the narrowing of the oropharynx, that he rapidly developed severe OSA, requiring ongoing non-invasive ventilation. OSA following sphincter pharyngoplasty has been described [2].

There is evidence of partial GH deficiency in PWS and there is increasing interest in GH therapy which has been demonstrated to increase lean body mass, decrease percent body fat, and improve physical strength and agility. However, concern has been raised about its safety in PWS because of several reports of sudden death after commencement, often within the first few months [3]. Adenotonsillar hypertrophy, possibly mediated through insulin-like growth factor-1, has been associated with GH therapy. PSG is recommended before GH initiation, within 2–3 months after starting therapy and if OSA symptoms develop. Our patient has enlarged tonsils, 2/4. He has had regular PSGs/titration studies as recommended.

Abnormalities of REM sleep and EDS are frequently seen in PWS. Patients may display narcolepsy-like features such as SOREM and cataplexy, independent of obesity-related symptoms [4, 5]. Diagnosis of narcolepsy involves the tetrad of EDS, cataplexy, hypnogogic/hypnopompic hallucinations, and sleep paralysis. On MSLT, the mean sleep latency is <8 min and >2 SOREM. HLA-DQ*B1:0602 or *A1:0102 is present in the majority of narcoleptic patients with cataplexy. EDS is usually the first symptom in the pediatric group. Our patient developed a narcolepsy-like syndrome around the time of the sphincter pharyngoplasty.

This is to our knowledge the first case report of rapidly evolving severe OSA secondary to sphincter pharyngoplasty coinciding with the development of a narcolepsy-like syndrome in a patient with PWS.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

References

1. Nixon GM, and Brouillette RT. 2002. Sleep and breathing in Prader-Willi syndrome. Pediatr. Pulmonol. 34:209–217.
2. Ettinger RE, Oppenheimer AJ, Lau D, et al. 2012. OSA after dynamic sphincter pharyngoplasty. J. Craniofac. Surg. 23:1974–1976.
3. Nagai T, Obata K, Tonoki H, et al. 2005. Cause of sudden, unexpected death of Prader-Willi syndrome patients with or without growth hormone treatment. Am. J. Med. Genet. 136:45–48.
4. Goh DYT, Galster P, and Marcus C. 2000. Sleep architecture and respiratory disturbances in children with obstructive sleep apnea. Am. J. Respir. Crit. Care Med. 162:682–686.
5. Nevsimalova S, Vankova J, Stepanova I, et al. 2005. Hypocretin deficiency in Prader-Willi syndrome. Eur. J. Neurol. 12:70–72.

