pii: jc-17-00291 http://dx.doi.org/10.5664/jcsm.7004

JCSM
Journal of Clinical Sleep Medicine

CASE REPORTS

Persistent High Residual AHI After CPAP Use

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Treatment-emergent central sleep apnea has recently been noted after various treatment modalities for obstructive sleep apnea. It often remits spontaneously or can be treated with continuous positive airway pressure. However, we encountered a pediatric patient with obstructive sleep apnea who presented with severe complications, including growth failure, attention-deficit hyperactivity disorder, poor school performance, daytime sleepiness, and urinary difficulty that required permanent cystostomy. His obstructive sleep apnea resolved after adenotonsillectomy. However, treatment-emergent central sleep apnea developed after adenotonsillectomy and was further aggravated after continuous positive airway pressure and bilevel positive airway pressure without a backup respiratory rate use. After bilevel positive airway pressure with a backup respiratory rate treatment for 3 months initially, all his symptoms improved, except growth failure. Later, after adaptive servoventilation was used for 10 months, the patient's growth began to improve.

Keywords: treatment-emergent central sleep apnea

Citation: Er LK, Lin SK, Yang SS, Lan CC, Wu YK, Yang MC. Persistent high residual AHI after CPAP use. *J Clin Sleep Med.* 2018;14(3):473–478.

INTRODUCTION

Complications of untreated pediatric obstructive sleep apnea (OSA) are serious, including learning and behavioral disturbance, attention-deficit hyperactivity disorder (ADHD), growth failure, cardiovascular disorder, and enuresis. Nevertheless, only half of pediatricians could recognize a relationship between these complications and OSA.[1] Enuresis caused by central sleep apnea (CSA) was reported in patients with Chiari malformation.[2] Treatment-emergent central sleep apnea (TECSA) is noted after various treatment modalities for OSA and often remits spontaneously, or can be treated with continuous positive airway pressure (CPAP).[3] However, we encountered a child with OSA presenting with refractory enuresis, growth failure, ADHD, daytime sleepiness, and poor school performance. TECSA developed after adenotonsillectomy (T&A) and was aggravated after CPAP and bilevel positive airway pressure (PAP) without a backup respiratory rate use.

REPORT OF CASE

This 17-year-old patient had a normal birth history. His mother was a costume designer, so cotton fiber (a potent allergen) was found everywhere in the house, resulting in his nasal obstruction and feeding difficulty. Severe snoring with mouth breathing and restless sleep at night were noted during his growth process. ADHD, poor school performance, and enuresis were discovered when he was 5 years old. Methylphenidate was prescribed, but he only took the medication for midterm tests or final examinations. Rehabilitation and psychotherapy were performed but failed.

When the patient was 8 years old, refractory enuresis and recurrent acute urine retention developed, which required intermittent catheterization program (ICP). The uroflowmetry revealed intermittent interrupted uroflow, poor maximal uroflow rate of 12.6 mL/s (normal range ≥ 25 mL/s), and increased postvoid residual urine volume of 38 mL (normal range < 20 mL). Dysfunctional voiding and nonanatomical obstruction were confirmed by subsequent videourodynamic studies. Because of refractory urinary retention needing frequent ICP, suprapubic cystostomy was performed. However, the patient still could occasionally void normally through the native urethra.

When the patient was 10 years old, polysomnography (PSG) revealed OSA with an apnea-hypopnea index (AHI) of 22.2 events/h, with 95% obstructive apnea (OA) events and 1.4% central apnea (CA) events. His body mass index (BMI) was only 14.1 with BMI z-score −1.9 and BMI percentile 3.1% (**Table 1**, study 1). The brain magnetic resonance imaging, thyroid and adrenal function, echocardiography, and comprehensive cardiopulmonary function test were all negative. Grade III tonsil enlargement, bilateral boggy inferior turbinates, and adenoid hypertrophy were noted. Standard T&A was performed. After T&A, the OSA resolved, but the CA progressed from 1.4% to 47.6%, resulting in an increasing AHI of 42.8 events/h (**Table 1**, study 2 and **Figure 1**). All

Table 1—Series of polysomnography results for this patient.

	Study No.						
	1	2	3	4	5	6	7
Condition	Before T&A	After T&A	Under CPAP titration	After CPAP use 3 months	After CPAP use 19 months	Under bilevel PAP without a backup respiratory rate titration	Under ASV titration
Height, cm	125.0	127.0	128.0	150.0	154.0	156.5	158.0
Height percentile, %	0.9	1.1	1.4	1.4	0.7	0.9	1.2
Weight, kg	22.0	21.0	22.0	32.0	36.0	37.8	45.6
Weight percentile, %	0.2	0.1	0.1	0.1	0.1	0.1	0.3
BMI, kg/m^2	14.1	13.0	13.4	14.2	15.2	15.4	18.3
BMI z-score	−1.9	−3.1	−2.7	−3.4	−3.1	−3.1	−1.5
BMI percentile, %	3.1	0.1	0.4	0.1	0.1	0.1	6.9
NC, cm	25.0	25.0	25.0	30.0	33.0	33.0	33.0
ESS score	3.0	2.0	2.0	1.0	1.0	1.0	1.0
Polysomnography results							
Sleep efficiency, %	85.5	65.0	48.2	48.4	85.3	86.6	88.5
Sleep latency, minutes	31.5	43.0	49.5	154.0	55.5	25.5	20.0
REM sleep latency, minutes	266.5	136.5	393	98.5	155.5	152.5	N/A
Supine posture, %	0.5	11.7	69.2	11.2	35.9	28.1	26.4
Stage N1 sleep, %	11.6	8.6	11.0	4.9	4.5	3.0	21.5
Stage N2 sleep,%	28.3	38.8	48.8	28.6	59.9	55.8	78.5
Stage N3 sleep, %	40.8	27.5	39.6	37.5	19.2	22.6	0.0
Stage R sleep, %	19.4	25.1	0.6	29.0	16.4	18.6	0.0
AHI, events/h	22.2	42.8	6.0	30.0	40.9	28.1	3.8
OA, %	95.9	13.2	0.0	3.5	14.3	0.0	0.0
CA, %	1.4	47.6	85.2	54.9	73.2	90.4	98.3
Mixed apnea, %	0.0	11.7	0.0	16.8	2.5	0.0	0.4
Hypopnea, %	2.7	27.5	14.8	24.8	10.0	9.6	1.3
Events duration, seconds							
Apnea, mean	14.0	16.0	19.0	24.0	29.0	31.0	15.0
Apnea, longest	27.0	26.0	28.0	58.0	74.0	70.0	35.0
Hypopnea, mean	16.0	20.0	18.0	29.0	29.0	36.0	22.0
Hypopnea, longest	19.0	34.0	21.0	53.0	47.0	44.0	33.0
DI, events/h	18.8	38.6	5.1	28.7	38.8	25.5	0.0
SaO_2 mean, %	97.0	94.0	98.0	94.0	95.0	96.0	97.0
SaO_2 nadir, %	88.0	85.0	88.0	80.0	76.0	81.0	94.0
SaO_2 < 92%, % TIB	0.5	16.1	1.1	19.7	23.2	16.5	0.0
Arousal index, events/h	17.9	29.7	18.1	23.7	35.5	25.1	5.5

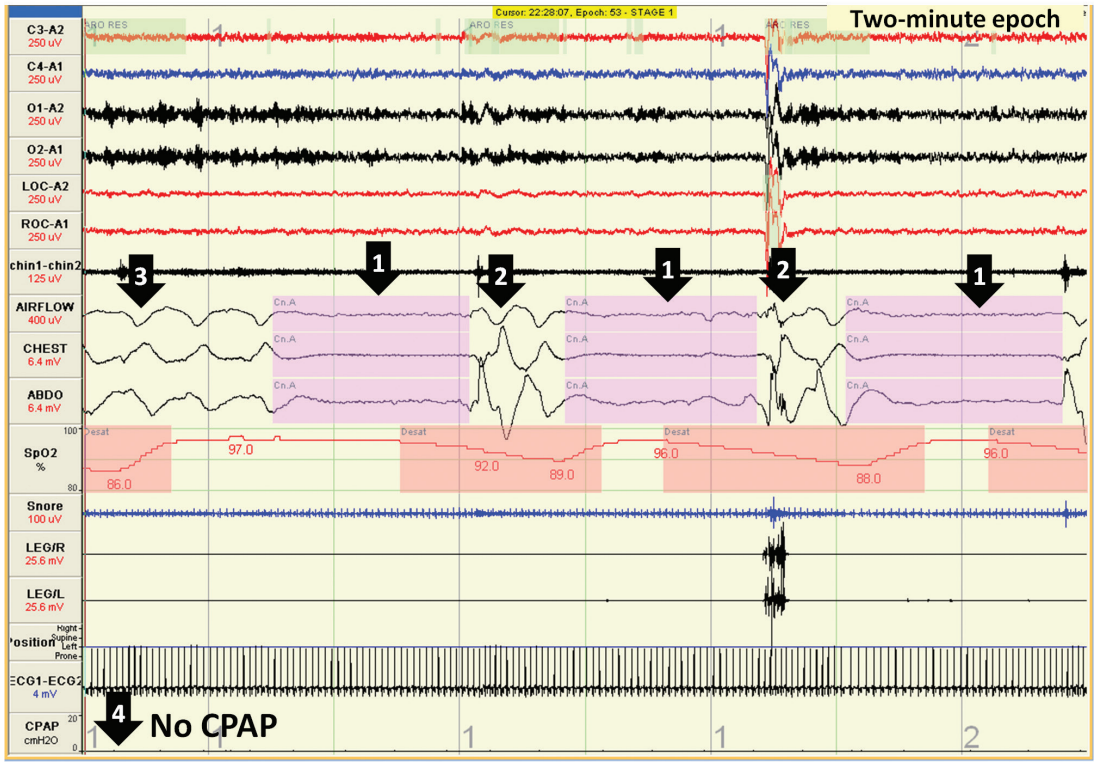
AHI = apnea-hypopnea index, APAP = auto-adjusted CPAP, ASV = adaptive servoventilation, BMI = body mass index, CA = central apnea, CPAP = continuous positive airway pressure, DI = desaturation index, ESS = Epworth sleepiness scale, N/A: not available, NC = neck circumference, OA = obstructive apnea, PAP = positive airway pressure, REM = rapid eye movement, SaO_2 = oxygen saturation, T&A = adenotonsillectomy, TIB = total time in bed.

of the patient's symptoms persisted. CPAP titration was performed, but the CA component further increased to 85.2% (**Table 1**, study 3). Thus, he was referred to our chest clinic.

The patient was noted as very thin and he had an obvious growth failure (BMI z-score of −2.7, at a BMI percentile of only 0.4%). He was unable to concentrate or talk fluently. His parents stated that he was very difficult to awaken, and always required several naps in school. A poor parent-child relationship between him and his father was also noted. His father was stubborn, which resulted in the child being fearful of his father. After a reviewed series of PSG results, TECSA was favored. We suggested CPAP for him because most TECSA will remit spontaneously or after CPAP treatment. His parents refused CPAP and the patient was lost to follow-up.

He later returned when he was 15 years old because all of his symptoms worsened after regular CPAP treatment (Fisher & Paykel, Auckland, New Zealand) with a nasal mask for 3 months at another medical center. His BMI z-score further decreased to −3.4 with a BMI percentile of 0.1%. After downloading the CPAP usage profile, his residual AHI (rAHI) under CPAP use was high and with a wide range (from 5 to 65.1 events/h). The PSG follow-up showed that the CA component

Figure 1—Polysomnography results after adenotonsillectomy.



An increase in central apneas were seen after adenotonsillectomy (from 1.4% to 47.6%). The central apnea (arrow 1) was terminated with augmented respiratory efforts (arrow 2) compared with normal respiratory efforts (arrow 3) without CPAP use (arrow 4). CPAP = continuous positive airway pressure.

was still high (**Table 1**, study 4). Severe nasal obstruction with mouth breathing and mask leakage was suspected, and a full-face mask was used. Antihistamine and intranasal steroid were also administered.

After CPAP treatment for 19 months, high rAHI and all of the patient's symptoms still persisted. The PSG showed his CA component progressed with a longer duration (**Table 1**, study 5). Another attended PSG under the physician's supervision was performed. We observed that the duration of CA became longer under CPAP and bilevel PAP without a backup respiratory rate (**Figure 2** and **Figure 3**). Bilevel PAP with a backup respiratory rate of 12 was changed, and his CA completely disappeared and he could breathe smoothly (**Figure 4**). The morning after the first night of bilevel PAP with a backup respiratory rate of 12, he urinated normally from his native urethra. He spoke fluently and said he had never slept so well.

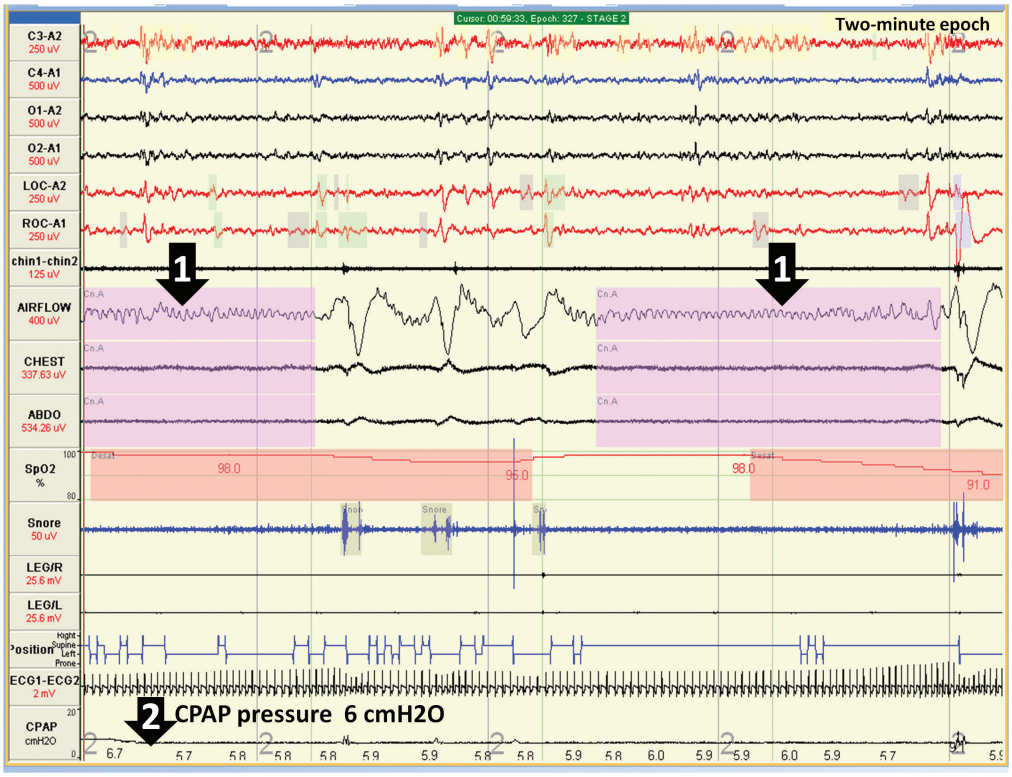
Because of severe complications, adaptive servoventilation (ASV) was strongly suggested. However, initially, his father rented a bilevel PAP with a backup respiratory rate of 12 for 3 months, ICP and cystostomy were withdrawn, the patient's ADHD improved, and normalized school performance was observed. However, the patient's growth failure remained even with regular bilevel PAP with a backup respiratory rate of 12 with a BMI z-score of −2.6, at a BMI percentile of 0.5%. Finally, the patient's father purchased an ASV for him. After ASV treatment for 10 months, his growth was improving (height percentile from 0.7% to 1.2%, weight percentile from 0.1% to 0.32%, BMI z-score from −2.6 to −1.5, and BMI percentile from 0.5% to 6.9%) (**Table 1**, study 7).

DISCUSSION

Initially, it was thought that all the symptoms (growth failure, enuresis, poor school performance, ADHD, daytime sleepiness) were because of the patient's OSA. However, when TECSA developed after OSA was relieved by T&A, all of the patient's symptoms remained. His symptoms improved only after adequate treatment for TECSA. This suggested that both OSA and CSA may cause complications in children with sleep-disordered breathing. Most known causes of CSA were investigated, but all were found to be negative. Thus, we believed his TECSA was caused by T&A initially, and CPAP and bilevel PAP without a backup respiratory rate treatment later.

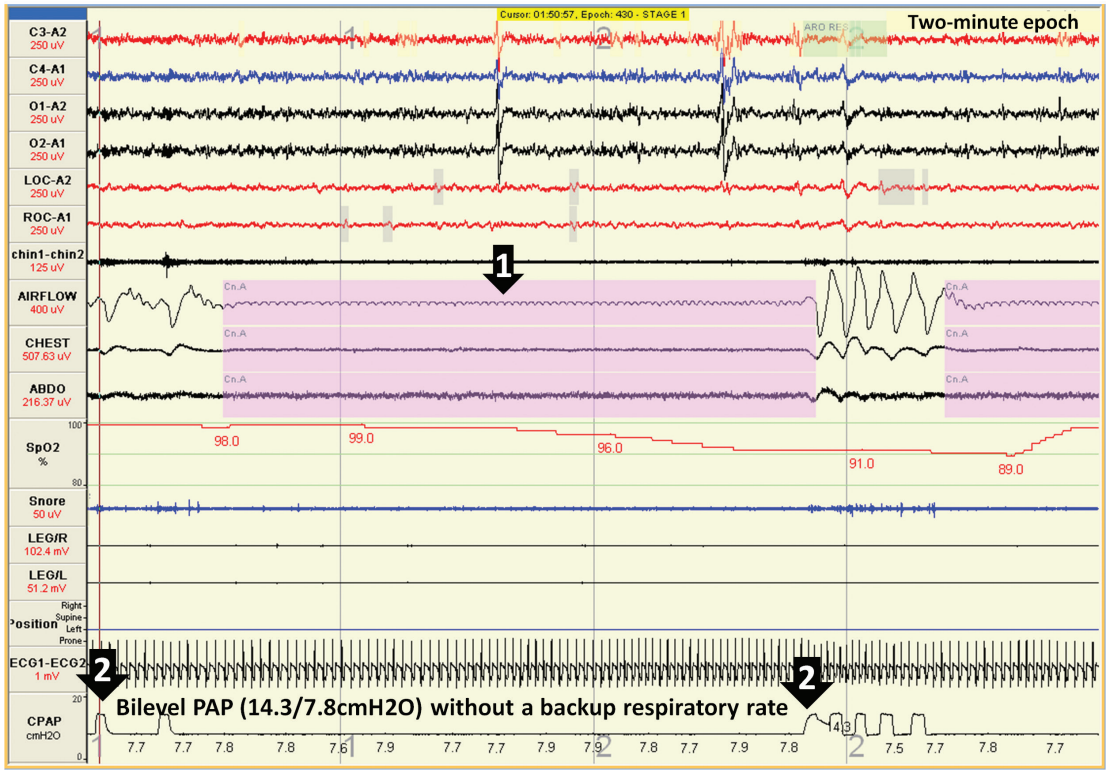
Several possible pathogeneses of TECSA have been suggested: (1) severe OSA with higher loop gain and ventilatory instability at baseline, and PAP therapy augmented the loop gain and ventilatory instability, leading to CSA[4]; (2) intermittent hypoxia increased central and peripheral chemoreceptor sensitivity and then increased the propensity to develop CSA[5]; (3) air leakage during PAP use led to CO_2 washout from the mask and anatomic dead space[6]; and (4) PAP therapy activated the stretch receptors and inhibited central respiratory output.[7] Initially, we thought this patient had nasal obstruction with mouth breathing and severe mask leakage; therefore, his nasal

Figure 2—Polysomnography results under CPAP.



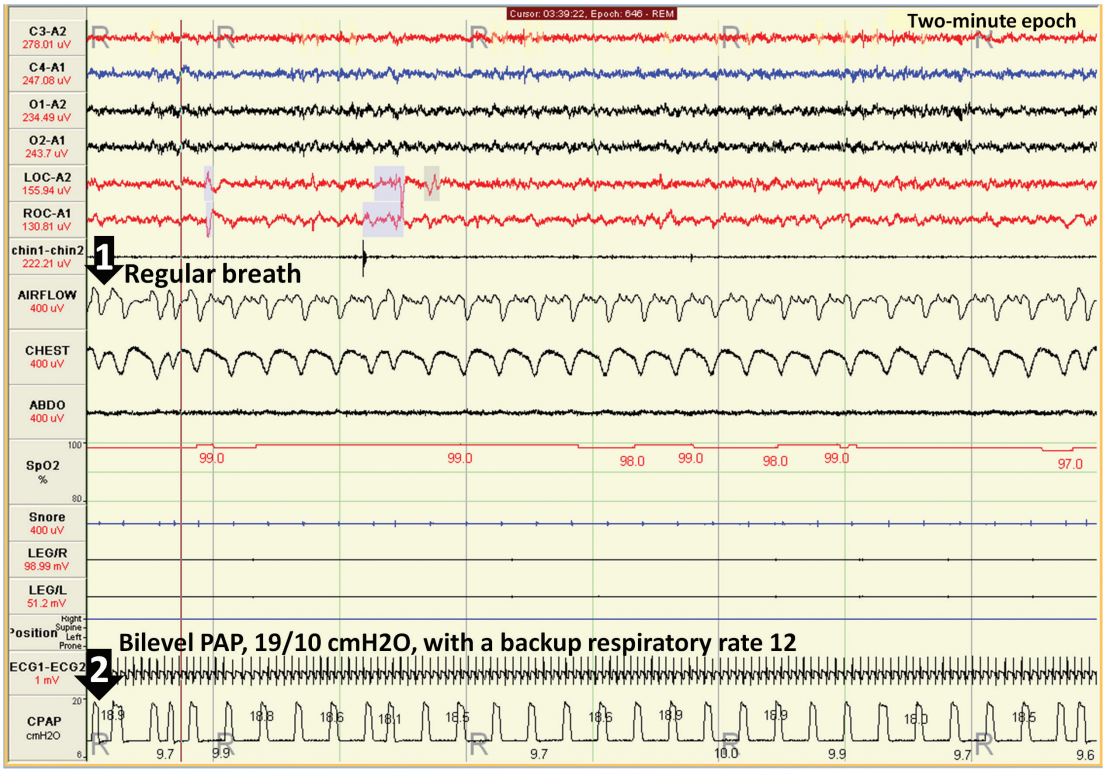
The central apneas (arrow 1) became longer in duration while under CPAP use (arrow 2). CPAP = continuous positive airway pressure.

Figure 3—Polysomnography results under bilevel PAP without a backup respiratory rate.



The central apneas (arrow 1) became longer in duration while under bilevel PAP use without a backup respiratory rate (arrow 2). PAP = positive airway pressure.

Figure 4—Polysomnography results under bilevel PAP with a backup respiratory rate of 12.



Central apneas disappeared and the breathing was normalized (arrow 1) under bilevel PAP use with a backup rate of 12 (arrow 2). PAP = positive airway pressure.

mask was changed to a full-face mask and he was prescribed an antihistamine and intranasal steroid. However, his TECSA persisted. Under PSG examination under our supervision, we determined that his mask leakage was caused by mask dislocation during frequent changes in sleep postures and the "augmented respiratory effect after CA events" (such as "gasping"). As shown in **Figure 1**, we noted the regular smooth respiratory efforts before CA and augmented respiratory efforts after CA, and suggested the presence of high loop gain and ventilator instability in this patient. As shown in **Figure 2** and **Figure 3**, his CA was further aggravated under CPAP and bilevel PAP without backup respiratory rate use, suggesting that PAP therapy might have activated the stretch receptors and inhibited central respiratory output.

In most cases, TECSA remits spontaneously or after CPAP treatment for 2 to 3 months, especially among patients with good CPAP use in adult studies.[8] Although CPAP could be effective and generally well tolerated in children with OSA,[9] another study showed a high dropout rate of CPAP therapy (approximately one-third within 6 months) in children with OSA.[10] Routine downloads of the CPAP usage date are essential. In our sleep center, CPAP usage data is always downloaded to ensure treatment efficiency because both adults and children with OSA have very poor long-term CPAP compliance in Taiwan. This strategy helped to note that even when the patient had good CPAP use, his sleep-disordered breathing still persisted because of the developed TECSA.

The frequency of TECSA in children is unknown because there is a paucity of literature, with only a few case reports published.[3,11] Many studies related to TECSA prevalence and its natural course are adult studies.[12] Thus, for children with TECSA, the treatment options are unknown. It was only known that the TECSA in our patient did not remit with time and was even aggravated after CPAP and bilevel PAP without a backup respiratory rate use with worsened symptoms and growth. We suggested that TECSA should be closely monitored. When TECSA progresses, it should be treated promptly because it can still cause serious complications, just as in this patient.

Both bilevel PAP with a backup respiratory rate or ASV are effective for patients with TECSA who do not respond to CPAP or bilevel PAP without a backup respiratory rate therapy.[8] However, ASV has a superior long-term advantage over bilevel PAP with a backup respiratory rate and is proved to be well tolerated.[13] Because our patient had very serious complications, ASV was strongly advised. His ADHD, poor school performance, enuresis, and daytime sleepiness improved after bilevel PAP with a backup respiratory rate. His growth did not improve after bilevel PAP with backup respiratory rate use, but significantly improved after ASV use.

We concluded that an increased awareness of OSA and its complications in pediatric practices may result in earlier treatment and less morbidity for children with OSA. Careful review of the raw data of PSG and routine downloads of CPAP usage

data are crucial, especially for children with severe complications. Once TECSA has developed, it should be monitored until it remits. ASV can be successfully used to treat TECSA in a teenager.

ABBREVIATIONS

ADHD, attention-deficit hyperactivity disorder
AHI, apnea-hypopnea index
APAP, auto-adjusting continuous positive airway pressure
ASV, adaptive servoventilation
BMI, body mass index
CA, central apnea
CPAP, continuous positive airway pressure
CSA, central sleep apnea
DI, desaturation index
ESS, Epworth Sleepiness Scale
ICP, intermittent catheterization program
NC, neck circumference
OA, obstructive apnea
OSA, obstructive sleep apnea
PAP, positive airway pressure
PSG, polysomnography
rAHI, residual apnea-hypopnea index under positive airway pressure treatment
REM, rapid eye movement
T&A, adenotonsillectomy
TECSA, treatment-emergent central sleep apnea
TIB, total time in bed

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ACKNOWLEDGMENTS

The authors thank Editage (www.editage.com) for English language editing. Author contributions: Leay Kiaw Er: English editing, article revision; Shinn-Kuang Lin: article revision; Stephen Shei-Dei Yang: critical revision; Chou-Chin Lan: data and reference collection; Yao-Kuang Wu: data and reference collection; Mei-Chen Yang: article writing, critical revision, corresponding author.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication June 3, 2017
Submitted in final revised form October 15, 2017
Accepted for publication October 19, 2017
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DISCLOSURE STATEMENT

All authors have seen and approved the manuscript. The study was supported by a grant from the Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation (TCRD-TPE-106-RT-1). The authors report no conflicts of interest.