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Posted Date: 10 May 2023

doi: 10.20944/preprints202305.0675.v1

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A Case of De Novo Positional Complex Sleep Apnea Syndrome (CompSAS)

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Abstract: Obstructive sleep apnea (OSA) is well known to often improve with non-supine positioning as opposed to supine positioning. Emerging research supports a role for sleep position management in patients with central sleep apnea (CSA) as well. We report a case of de novo Complex Sleep apnea Syndrome (CompSAS) in a 78-year-old female, who presented after a car accident due to unclear syncope. Diagnostic polysomnography (PSG) showed a moderate OSA. A CompSAS developed under Automatic positive airway pressure (APAP), while download data of 4 years showed a good adherence. No significant benefit was reported under Adaptive Servo Ventilation (ASV) and BiPAP-ST, while a reduction of CSA in non-supine position was noticed. Oxygen and sleep positional therapy (SPT) were considered resulting in a significant improvement of CSA and sleep quality. Further research on the prevalence of positional CSA is needed.

Keywords: central sleep apnea; adaptive servo ventilation; oxygen therapy; sleep positional therapy

1. Introduction

Central sleep apnea syndrome (CSAS) is a characterized by the cessation of ventilation lasting for ≥10 seconds due to transient loss of neural output to the ventilatory muscles. Central sleep apnea (CSA) occurs in less than 5% of subjects admitted to sleep clinics.(1) A distinction is made between hypercapnic CSA und non-hypercapnic CSA. Hypercapnic CSA is generally seen in neurlogical disorders with reduced central drive to the respiratory musculature or diminished muscle strength. Non-hypercapnic CSA occurs in connection with congestive heart failure (CHF) , high altitudes, hypothyrodism, and the idiopathic form of CSA.

The majority of patients with mild to moderate obstructive sleep apnea (OSA) have more apneic events in the supine position, as compared with non supine position. The most commonly used definition for positional OSA stipulates that the Apnea-Hypopnea-Index (AHI) must be at least twice as high in the supine position as compared with non supine positions. OSA is a more common and well-described form of sleep-disordered breathing (SDB) than CSA. Indeed supine-related OSA is a dominant phenotype of OSA with a prevalence of 20%–60% in the general population.(2)

It has been also reported that Cheyne-Stokes Respiration (CSR), a specific form of CSA characterized by a cyclic crescendo and decrescendo breathing pattern, is affected by body position during sleep. A study on patients with heart failure and CSR showed increasing severity of CSR in the supine position, with CSR becoming position-independent as cardiac dysfunction progressed.(3) There are few reports in the literature of positional central sleep apneas (PCSA) in patients without cardiac history or congestive heart failure (CHF). The association between CSA and positional sleep apnea (PSA) is also poorly understood.(4)

Patients with OSA may develop central apneas under application of positive airway pressure (PAP), especially during the first days or weeks after initiation. This phenomenon has been described as Complex sleep apnea syndrome (CompSAS). However it is of crucial importance to clearly define treatment-induced CSA and separate it from treatment-independent central apneas. CompSAS contribute often to a reduced response or adherence to continuous positive airway pressure (CPAP) and may lead to CPAP failure.(5)

 doi:10.20944/preprints202305.0675.v1

This is a case report of 78-year-old female with a severe de novo positional CompSAS.

2. Case Report:

A 78-year-old female presented to her primary doctor after a car accident due to unclear syncope in 2016.

A physical exam, basic laboratory investigation, including complete blood count, comprehensive metabolic panel, and thyroid stimulating hormone were normal. The patient had a history of hypertension and diabetes mellitus Type 2. Also, Scheuermann's disease is known since childhood. She had a normal weight with a BMI of 20 kg/m^2. The patient denied alcohol or illicit drug use. A full cardiological and neurological examination didn't show pathological findings. Also mental health history appeared to be noncontributory. As a next step, a diagnostic polysomnography (PSG) was recommended.

The patient was presented to the Sleep Medicine Center at the GZO Wetzikon in Switzerland in November 2016. Polysomnography showed a moderate OSA with an average AHI of 20/h. The Epworth Sleepiness Scale (ESS) showed a score of 3/24 indicating lower normal daytime sleepiness. A Maintenance of Wakeful Test (MWT) was performed on the next day and gave no evidence for excessive daytime sleepiness. There were periodic limb movements during sleep (PLMS) found with an average Index of 40/h. Otherwise no other unusual behaviors were noted. Automatic positive airway pressure (APAP) therapy with pressure (9-14 cm H2O) was recommended.

The patient returned 10 months later for follow-up after using APAP. The downloaded data showed an effective treatment of her sleep apnea. Adherence data showed a regular device usage of 6 hours on average per night. Therapy data showed an average residual AHI of 1.2/h. She reported a subjective benefit regarding night sweats. The next follow-up visit was in February 2018 showed again a regular device usage, and an average residual AHI of 2.0/h. The ESS showed a score of 3/24, while the patient reported no subjective benefit from the therapy. The therapy data from the next follow-up in September 2019 showed a slight elevated AHI of 9.6/h in spite of the regular usage without significant air leaks. The patient denied excessive daytime sleepiness as well as sleep disturbances. The APAP therapy with pressure (9-14 cm H2O) was continued without any change.

In March 2021 the downloaded data showed ineffective treatment of her sleep apnea with an average residual AHI of 40/h. The patient returned for an overnight titration study at the sleep laboratory. APAP pressures (9-14 cm H2O) were tested. This study showed a CompSAS with an average residual AHI of 32.1/h. The respiratory events were central with an average central AHI of 32.1/h. Also, the transcutaneous capnography registered a mild hypercapnia with an average transcutaneous CO2 Pressure (PtcCO2) of 53.1 mmHg and maximum PtcCO2 of 73.8 mmHg probably due to Scheuermann's disease with kyphoscoliosis (Table 1). According to these findings and also in view of the patient`s clinical condition we considered a change to Adaptive Servo Ventilation (ASV) therapy. Echocardiography showed a normal left ventricular ejection fraction (LVEF) of 64%.

Follow-up visits were performed in March, June, and July 2021. The downloaded data of the ASV device showed an ineffective treatment with an average AHI of 18.3/h, 20.2/h, and 15.6/h respectively. Adherence data showed a regular device usage, with an average of 5.5 h, 5 h, and 5.5 h of usage per night respectively. No significant air leaks were noted using the Airtouch Mask F20. Again, the patient reported no subjective benefit from the therapy. Also, the downloaded data from October 2021 showed persistent ineffective treatment with an average residual AHI of 23/h. However, adherence data showed a regular device usage with an average of 5.3 h usage per night. As a next step, we considered a device change using an ASV-device from another producer. In June 2022 the patient experienced an acute myocardial infarction. Echocardiography showed a reduced LVEF (44%). Therefore, we stopped the ASV-therapy according to the recommendation of the American Academy of Sleep Medicine (AASM).

The patient returned for an overnight titration study with capnography. Bilevel positive airway pressure-spontaneous/Timed (BiPAP-ST) of 16/8 cm H2O was tested. A mean oxygen saturation of 94%, minimum oxygen saturation of 83%, and an average AHI of 19.3/h were observed at this

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pressure setting. The transcutaneous capnography registered a normocapnia with an average PtcCO2 of 38.7 mmHg and maximum PtcCO2 of 46 mmHg.

Since the respiratory events were predominantly central events in supine position (Figure 1) we considered the initiation of sleep positional therapy (SPT) accompanied by nocturnal oxygen therapy with a flow rate of 2 Liters/minute.

The ambulatory nocturnal polygraphy on SPT and oxygen therapy showed an effective treatment of the respiratory events with an average AHI of 0/h and mean oxygen saturation of 97,8% (Figure 2). The patient reported also a significant improvement of her sleep quality.

Table 1. Results of PSG on APAP-therapy (9-14 cmH20) in sleep laboratory.

Total Recording Time	**466 minutes**
Total Sleep Time	428 minutes
Sleep Efficiency	91.1%
Sleep Latency	0.9 minute
REM Latency	65 minutes
REM Periods	4
N1	2.6%
N2	47.8%
N3	25.9%
REM	15.7%
Supine	428 minutes
Prone	0 minutes
Left	0 minutes
Right	0 minutes
AHI	32,1/h
Central AHI	32,1/h (Supine 32.1/h)
Obstructive AHI	0/h
Mean Sleep Oxygen Saturation	93.4%
Minimum Sleep Oxygen Saturation	77%
Transcutaneous CO2 Mean	53.1 mmHg
Transcutaneous CO2 Maximum	73.8 mmHg

PSG: Polysomnography, **APAP:** Automatic Positive Airway Pressure, **AHI**: Apnea- Hypopnea-Index, **CO2**: Carbon dioxide.

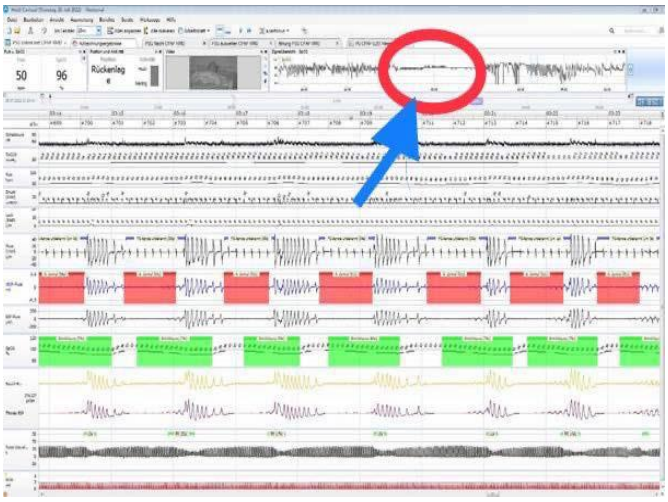

Figure 1. Central apneas in supine sleep on Bilevel-ST (Spontaneous-Timed).

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The central apneas are marked in **red** while the oxygen desaturations are marked in **green**. The arrow also refers to the significant improvement of oxygen desaturations in non-supine position in the overview of the oxygen saturation during the whole study.

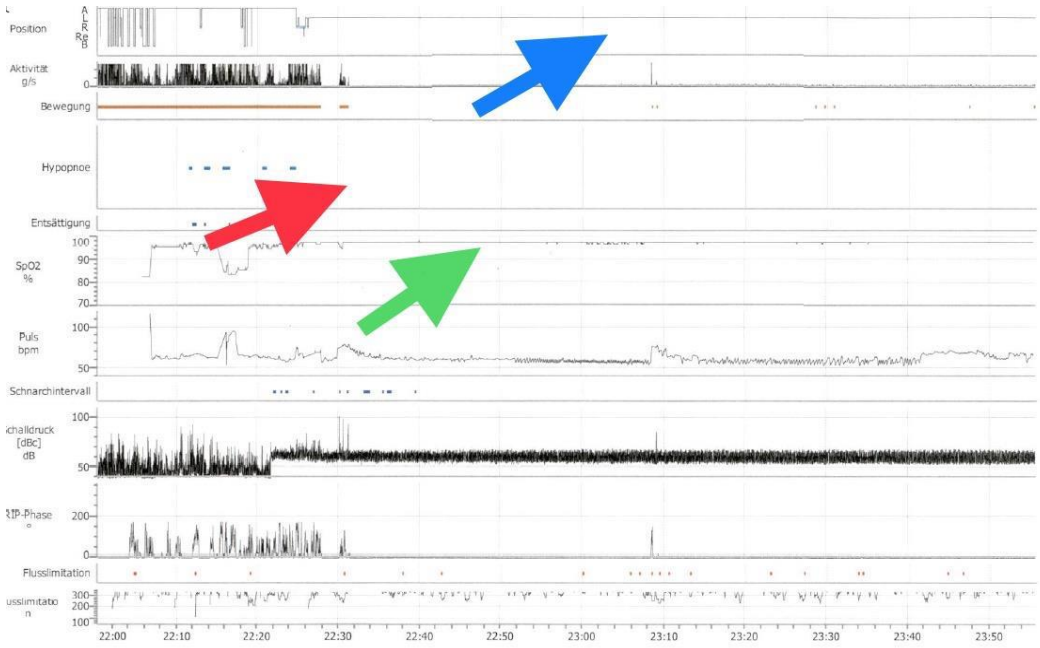

Figure 2. Ambulatory nocturnal Polygraphy on Sleep Positional Therapy (SPT) and oxygen-therapy.

The figure above shows the improvement of the oxygen desaturations (green arrow) and hypopneas (red arrow) during sleep on the left side (blue arrow).

3. Discussion

Sleeping position could be an aggravating factor for the sleep apnea. Specifically, sleeping in the supine position can lead to a significant worsening of OSA which is believed to be related to relaxation of muscles in the jaw and throat under the influence of gravity leading to narrowing of the upper airways. This is frequently seen in patients with less severe OSA and smaller neck circumference.

There are only a few reports in the literature of PCSA in patients with not known cardiac history or CHF. One study did show a change in sleep-disordered breathing (SDB) pattern from obstructive to almost all mixed and central apneas on both diagnostic and CPAP titration studies with change to supine sleeping position in 8 patients who had no cardiac history (one patient had a history of cerebral hemorrhage, and one had cerebral ischemia).[6] Another study showed significant supine worsening of sleep apnea in patients with treatment-emergent CSA or CompSAS on both CPAP and ASV.[7] Another case report from Zaharna et al. showed idiopathic CSA in an otherwise healthy young man with significant worsening in supine sleep.[4]

Benosit L. et al. published a prospective multicenter trial of 16 patients, in whom 4 patients suffered from Hypertension and Arrythmia, which showed that SPT is effective and can be considered as a new treatment modality in PCSA. Long-term follow-up and compliance monitoring is ongoing.[8]

This case report showed a CompSAS that was significantly worse in supine position. While ASV and BIPAP-ST are the first choice in such cases, no significant improvement in residual AHI was seen in this case. Therefore, we have considered a SPT using a sleep pillow. An additional therapy with oxygen was recommended. The ambulatory nocturnal polygraphy after nearly 6 weeks showed a significant improvement of the average AHI without significant oxygen desaturations. The patients reported a better sleep quality without any excessive daytime sleepiness.

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Treatment of CSA is generally based on the underlying cause. In our case we assume that the central apneas were not due to CHF, even with mild reduced LVEF of 44% after the myocardial infarction in June 2022. However, CSA were reported already in APAP overnight titration in 2021 followed by echocardiography showing normal LVEF of 64% before the beginning of ASV therapy. Additionally, CSR pattern and periodic breathing were absent on both the diagnostic and titration studies. Also, the patient did not tolerate opioids and was receiving nonsteroidal anti-inflammatory drugs (NSAIDs) for her chronic pain.

Sleeping in the supine position reduces cardiac output, which delays the transfer of blood gas information from the pulmonary capillary bed to the chemoreceptors and can lead to sustained fluctuations in respiratory output (i.e. CSA). In addition to reducing cardiac output sleeping in the supine position can result in a reduction of both the functional residual capacity and the metabolic rate, which consequently enhance plant gain, which is defined as a large change in carbon dioxide levels relative to a small change in ventilation. This is another proposed mechanism in the development of CSA.

Although CSA is usually associated with hypocapnia, it is not compulsory. This patient's PtcCO2 was slightly elevated (mean 53.1 mmHg) in the capnography measurement during overnight titration study on APAP therapy in March 2021 und normal (mean 38.1 mmHg) during the BiPAP-ST overnight titration study in July 2022. More important is the proximity of the central apnea threshold to the carbon dioxide (CO2) level. The slightly elevated PtcCO2 corresponds to the fact that hypoventilation is the predominant SDB in kyphoscoliosis patients. Eupneic patients with CHF may also have CSA.

The prevalence of CompSAS seems to vary among different studies, ranging between 18% and 56%. However, it is not easy to assume the prevalence of CompSAS in a clinical setting, because of the dynamic nature of this condition, with improvement or disappearance of the central respiratory events during sleep in some patients, and its *de novo* appearance in others. CompSAS may occur de novo in 4% of patients with OSA under CPAP during follow up.[9] Only those central apneas that do not disappear under CPAP fulfill the criteria of treatment-induced CSA (CompSAS).

We assume that our patient represented a case of de novo positional CompSAS, which improved significantly on nocturnal oxygen therapy (NOT) and SPT. NOT is still indicated for CSA-CSR. While the exact mode of action is unknown, it is believed that supplemental oxygen dampens the respiratory drive, thus reducing the minute ventilation and increasing partial pressure of carbon dioxide. However, the possibility of coexisting obstructive respiratory events in the overnight titrations studies under APAP and BiPAP-ST cannot be ruled out due to the absence of esophageal pressure, which is seen as a gold standard in identification of obstructive and central respiratory events during sleep.[10] Other causes for worsening of OSA like reduced adherence, significant air leaks and weight gain have been already excluded.

4. Conclusions

The present case suggests that SPT should be taken in consideration as a treatment option of CSA or CompSAS, especially in those patients who have difficulties in tolerating other treatment options for CSA including CPAP, BiPAP, and ASV therapy. In some cases, patients view SPT as a more tolerable alternative treatment. However, high scientific evidence for SPT as viable treatment option for CSA is lacking till now.

5. Patents

This research was performed in Sleep Medicine Center (GZO Wetzikon) in Zurich Oberland, Switzerland.

Author Contributions: Conceptualization, KA; methodology KA; investigation, KA, SM; resources, KA, SM; data curation, KA; writing—original draft preparation, KA writing—review and editing, KA, SM. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

 doi:10.20944/preprints202305.0675.v1

Institutional Review Board Statement: Not applicable for studies not involving humans or animals.

Informed Consent Statement: Written informed consent has been obtained from the patient to publish this paper.

Data Availability Statement: The data presented in this study are available in this article.

Acknowledgments: We sincerely thank our patient for her willingness to share the details of her sleep breathing disorder in this case report.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviation:

AASM	American Academy of Sleep Medicine
AHI	Apnea-hypopnea index
APAP	Automatic positive airway pressure
ASV	Adaptive Servo Ventilation
BiPAP-S	Bilevel positive airway pressure - Spontaneous Timed
CHF	Congestive heart failure
CO2 Carbon dioxide	
CompSAS	Complex Sleep apnea Syndrome
CPAP	Continuous positive airway pressure
CSA	Central sleep apnea
CSAS	Central sleep apnea syndrome
CSR	Cheyne-Stokes Respiration
ESS	Epworth Sleepiness Scale
LVEF	Left ventricular ejection fraction
MWT	Maintenance of Wakeful Test
NSAIDs	Nonsteroidal anti-inflammatory drugs
NOT	Nocturnal oxygen therapy
OSA	Obstructive sleep apnea
PAP	Positive airway pressure
P_{CO2}	Carbon dioxide tension
PCSA	Positional central sleep apneas
PLMS	Periodic limb movements during sleep
PSA	Positional sleep apnea
PSG	Polysomnography
PtcCO2 Transcutaneous CO2 Pressure	
SBD	Sleep-disordered breathing
SPT	Sleep positional therapy

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