Case Report

A 51-year-old obese male was referred to sleep clinic with complaints of loud snoring, frequent snore arousals and daytime fatigue progressively worsening over three years. He woke up feeling exhausted in the morning after sleeping 6-8 hours a night. He used caffeinated drinks to improve alertness in the morning and sustain him throughout the day. The Epworth Sleepiness Scale (ESS) score was elevated at 15/24 (normal <9). He denied nodding off while driving or having motor vehicle accidents related to altered consciousness. Overnight polysomnogram showed severe obstructive sleep apnea with an apnea hypopnea index (AHI) of 111/hr and oxygen desaturation as low as 59% with obstructions lasting up to 63 seconds in duration. No central apneas were documented on the initial split night polysomnogram. Continuous Positive Airway Pressure (CPAP) at 15 cm H2O corrected the patient's obstruction and normalized oxygen saturation back to 92-96%. He had no other significant medical history, including cardiac disease. His social history was significant for smoking marijuana daily and weekly alcohol use. He was prescribed CPAP 15 cm H2O. The snoring resolved, but he continued to feel fatigued. The CPAP data card showed the AHI was improved, but remained elevated at 26/hr with a central apnea index of 22/hr.

The patient underwent repeat polysomnogram with PAP titration. On CPAP therapy, the patient had persistent central sleep apnea after obstruction of the airway was corrected. Adaptive servoventilation (ASV) titration was performed with Respironics BiPAP Auto SV. He tolerated the ASV titration well and subsequently was started on ASV therapy at home. At one month follow up visit in clinic, the patient reported improved energy and sharper mental focus. The AHI on the data card decreased AHI to 4/hr. Repeat ESS score normalized to 6/24.

Discussion

Complex sleep apnea syndrome (CompSAS), also referred to as treatment-emergent central apnea, is relatively new terminology used to describe the appearance of central sleep apnea in patients with obstructive sleep apnea in whom airway patency has been restored with CPAP therapy. The existence of complex apnea syndrome as a distinct disorder had been debated in the sleep community for the past several years. The term was first used by Morgenthaler in 2006 in his article "Complex sleep apnea syndrome: Is it a unique clinical syndrome?"1 The phenomenon of cessation of respiratory effort with relief of airway obstruction was not a new observation. Guilleminault et al first documented central apneas developing in post-tracheostomy patients for treatment of severe OSA in 19822. Subsequent case reports of CSA following mandibular advancement device application and maxillofacial surgeries for treatment of OSA are scattered in the medical literature3,4,5. Since CPAP therapy is the main stay of treatment that was performed under the watchful eye of the sleep technician, it is to be expected that the syndrome is most commonly associated with CPAP therapy.

CompSAS patients have both reduced upper airway tone and unstable central ventilatory control. Decreased upper airway tone leads to increased airway resistance and obstruction during sleep. Increased respiratory effort is made by the patients to maintain airway patency and flow. Obstruction and cessation of flow are often worse in the supine position and during REM sleep, which occurs more frequently during the latter half of the night. Non-hypercarbic central apneas involving periodic breathing or mixed apneas are seen in complex apnea6. Central apnea occurs when the patient's ventilatory effort ceases due to several possible reasons including, high loop gain (exaggerated hyperventilatory response to hypercarbia resulting in hypocapnea below the apnea threshold), low arousal threshold, or apnea threshold close to awake PCO2. CSA is worse during NREM sleep regardless of body position and increases in frequency in the first half of the night.
The prevalence of CompSAS in patients with OSA studied in a sleep laboratory is approximately 15%6. The literature reports prevalence ranging from 1.6% in the esthoff study from Germany (excluded patients with BNP l<100 pg/ml), to 25% in Pusalaivyadasagar's retrospective review which included patients with comorbid CHF7,8. There were no statistically significant differences between simple OSA patients and Comp SAS patients in their clinical characteristics and polysomnography data. The only significant differences found between the two populations were treated CompSAS patients reported more CPAP removal during sleep and dyspnea or air hunger at follow up.

The clinical presentation of CompSAS patients is indistinguishable from simple OSA patients. They complain of excessive snoring, nonrestorative sleep, nocturnal arousals and daytime hypersomnolence. They are only identified after CPAP therapy is initiated, either in the sleep laboratory or on subsequent follow up. Persistent symptoms of sleepiness or an elevated AHI on the CPAP data card suggest the development of CompSAS, as was the case with our patient.

Consequences of untreated CSA, like OSA results in adverse cardiovascular outcomes. As with all the patients with sleep related breathing disorder, treatment begins with good sleep hygiene, positional therapy and weight loss if indicated. Opiate medications should be avoided since they worsen central apnea and may increase airway obstruction. Sedative hypnotics medications worsen airway obstruction with increased airway instability, but may also decrease arousal threshold and improve central apnea3. Oxygen therapy may also stabilize respiratory control and reduce loop gain in the patients who are not CO2 retainers. PAP therapy remains the mainstay of treatment for most of the patients with CompSAS. CompSAS is a dynamic disease. With continued CPAP therapy, there is reduction in airway edema with decreased obstruction, reduced arousals and improved central chemosensitivity. A majority of these patients will have resolution of CSA over time on CPAP therapy10,11. In the retrospective review by Pusalaivyadasagar et al, CPAP was an effective treatment in 88% of the patients with CompSAS5. In the CPAP-unresponsive subgroup of the patients, adaptive servo-ventilation was superior to other biPAP modes in its ability to reduce AHI in multiple small retrospective studies. The American Academy of Sleep Medicine currently makes no formal recommendations for treatment of CompSAS due to insufficient evidence available in published literature.

**Conclusion**

CompSAS is a newly recognized sleep related breathing disorder that may complicate treatment course of patients with obstructive sleep apnea. As clinicians, we should be alert to its potential presence, especially when the patients are not responding appropriately to standard treatment as expected. CPAP therapy with or without oxygen supplementation will be effective in majority of the patients with CompSAS. A subpopulation of these patients will benefit from adaptive servo-ventilation to provide correction for their respiratory deficiency during sleep.

**REFERENCES**

10. Kuźniar TJ, Pusalaivyadasagar S, Gay PC, Morgenthaler TI. Natural course of complex sleep apnea—a retrospective