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SLEEP MEDICINE PEARLS

A case of treatment-emergent central sleep apnea?

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A 47-year-old woman with a history of hypertension, diabetes mellitus, and obesity was referred to the sleep clinic for snoring and witnessed apneas. She reported daytime sleepiness with an Epworth Sleepiness Scale score of 16 out of 24. On examination Mallampati score was 4, neck circumference was 17 inches, and BMI was 44.92 kg/m^2. Medications included lisinopril, hydrochlorothiazide, and metformin.

Split-night polysomnography (PSG) was performed. During the titration portion of the study, the patient was titrated from continuous positive airway pressure (CPAP) onto bilevel positive airway pressure (BPAP) with a backup rate up for treatment-emergent central sleep apnea (TE-CSA). Pertinent results are shown in **Table 1** and **Table 2**. An event representative of the central apneas during the titration is shown in **Figure 1A** and **Figure 1B**.

QUESTION: Does this patient have treatment-emergent central sleep apnea? What type of respiratory event is present in Figure 1A and Figure 1B?

ANSWER: This patient does not have TE-CSA, but rather this is a case of obstructive sleep apnea (OSA) masquerading as TE-CSA. Figure 1A shows an obstructive apnea with reduced gain in the respiratory inductance plethysmography (RIP) belts. When the gain is increased in Figure 1B, clear respiratory effort in the RIP belts can be seen.

DISCUSSION

In complex sleep apnea, central apneas occur on positive airway pressure after which predominantly obstructive events have been shown during a diagnostic study. TE-CSA is a subset of complex sleep apnea, with the other subsets being CSA with Cheyne-Stokes breathing and CSA due to drugs or medications. Risk factors for TE-CSA include non-rapid eye movement sleep (stages N1 and N2) versus rapid eye movement (REM), supine position versus non-supine position, men versus women, high AHI, central apneas during the diagnostic study, split-night study versus separate night for titration, high CPAP (overtitration), and BPAP without a backup rate. In TE-CSA, central apneas "emerge" on treatment due to a sleeping pCO_2 that is close to their apneic threshold. With positive airway pressure (PAP), increased ventilation blows pCO_2 below the apneic threshold and a central apnea occurs.[1]

Table 1—Split-night polysomnography data.

	Diagnostic	Treatment
Total sleep time (minutes)	152	311
Apnea-hypopnea index (events/h)	24.9	11.9
Obstructive apneas (no.)	38	2
Mixed apneas (no.)	0	0
Central apneas (no.)	0	36
Hypopneas (no.)	25	24

The International Classification of Sleep Disorders, Third Edition (ICSD-3) specifies that for TE-CSA, the diagnostic PSG (here, the diagnostic portion of the study) must show five or more obstructive respiratory events per hour of sleep. During a PAP titration without a backup rate, there must then be significant resolution of obstructive events and emergence or persistence of central apnea or hypopnea with a central apnea-hypopnea index (AHI) ≥ 5 events/h. The number of central apneas and central hypopneas must be ≥ 50% of the total number of apneas and hypopneas. Finally, in TE-CSA the central apneas cannot be better explained by another CSA disorder.[2]

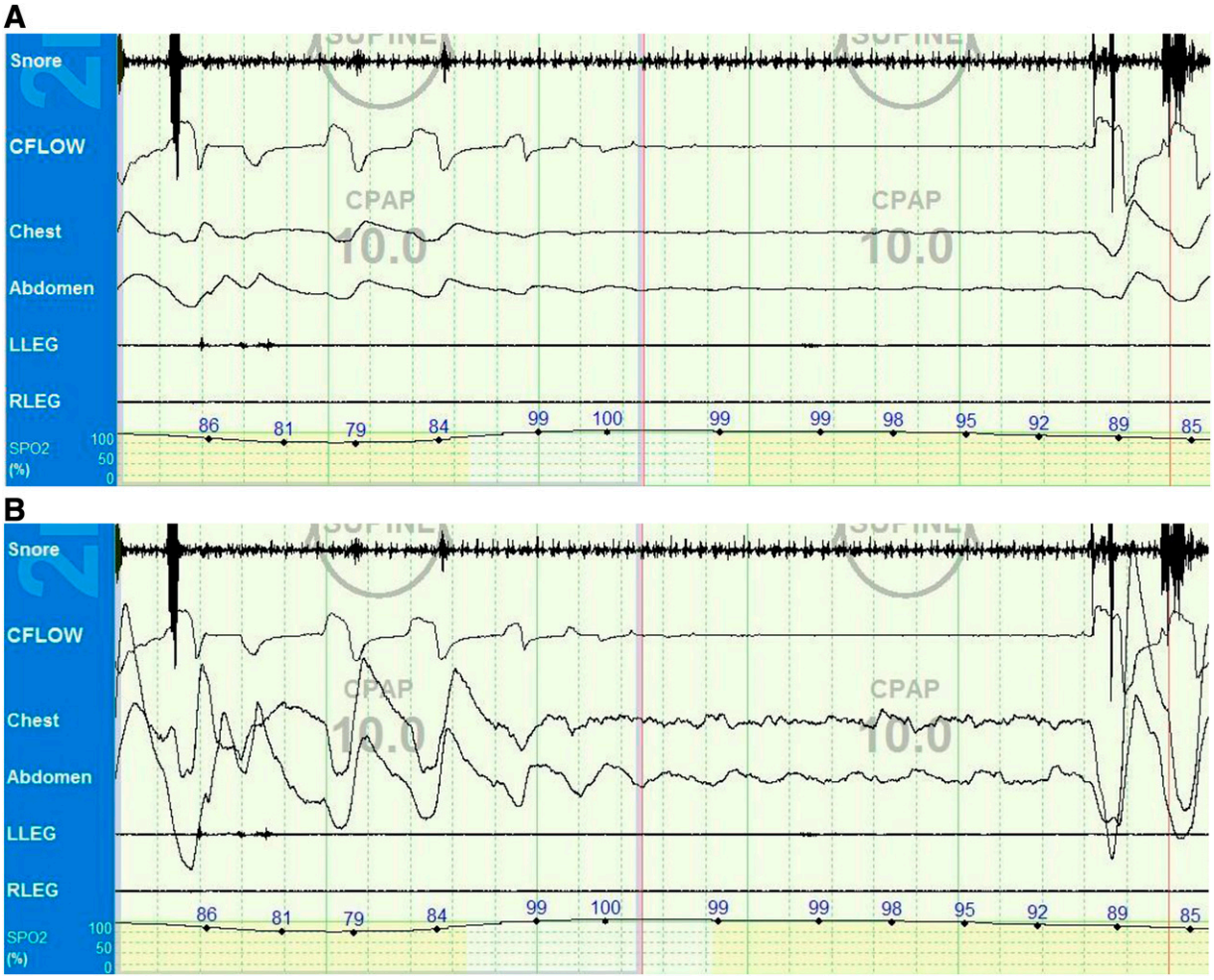
Initially, this case appears to meet the ICSD-3 criteria for TE-CSA. **Table 1** shows an AHI of 24.9 events/h in the diagnostic portion of the study with no central apneas, and the titration shows a significant number of central apneas. **Table 2** shows that during the titration at CPAP 9 cm H_2O the AHI was < 5 events/h and obstructive events resolved. Beginning at a pressure of 10 cm H_2O there is an increase in central apneas and ≥ 50% of the remaining apneas and hypopneas are central from this point forward. CPAP was decreased to 9 cm H_2O, but central apneas persisted and the patient was titrated onto BPAP with a backup rate. The respiratory event in **Figure 1A** and **Figure 1B**, however, is the key to this case. Increasing the gain in **Figure 1B** demonstrates that respiratory effort is present in the RIP belts and these "central" apneas are actually *obstructive* in type. An explanation for the sudden occurrence of so many respiratory events can be gleaned from close review of **Table 2**. Once the "central" apneas occurred at 10 cm H_2O the pressure was decreased to 9 cm H_2O, however, they persisted. When the pressure was decreased, REM sleep occurred for a period of time during which many respiratory events occurred. The backup rate was set to 10. However, the backup rate did *not* fire in the treatment portion and the spontaneous respiratory rate was approximately 14. The backup rate trigger type used was Auto-Trak (Philips Respironics, Murrysville, Pennsylvania). In summary, on this study what appeared to be many central apneas emerging from treatment was actually multiple *obstructive* apneas occurring while in supine REM sleep. Increasing the gain on the central apneas in the

Table 2—Positive airway pressure treatment.

PAP Level	Backup Rate	O_2 Vol	TST (minutes)	REM (minutes)	TST (sup)	AHI	AHI REM	OA (no.)	MA (no.)	CA (no.)	HYP (no.)
5	0	0	9	0	0	6.7	0	0	0	0	1
6	0	0	47	8	0	3.8	7.5	0	0	1	2
7	0	0	40	0	4	15.0	0	1	0	2	7
8	0	0	12	0	12	4.8	0	1	0	0	0
9	0	0	31	0	31	3.8	0	0	0	1	1
10	0	0	4	0	4	37.5	0	0	0	4	1
9	0	0	5	4	5	84.0	80	0	0	7	0
12/7	10	0	11	11	11	70.9	70.9	0	0	7	6
13/8	10	0	30	3	28	13.8	68.6	0	0	4	3
14/8	10	0	108	25	0	1.7	0	0	0	0	3

Pressure is in cm H_2O. AHI = apnea-hypopnea index, CA = central apnea, HYP = hypopnea, MA = mixed apnea, OA = obstructive apnea, PAP = positive airway pressure, REM = rapid eye movement, sup = supine, TST = total sleep time, Vol = volume.

Figure 1—Tracing.



(A) A section from a 120-second tracing showing a respiratory event from the titration portion of the study scored as a central apnea. CFLOW, pressure flow signal. Chest and abdomen, respiratory inductance plethysmography effort belts. LLEG = left leg lead, RLEG = right leg lead. **(B)** A section from the same tracing as panel A, with the gain increased.

titration portion revealed respiratory effort that had not been noted during initial scoring. Because the apneas in the titration were actually obstructive in type, it follows that as the pressure on the titration was increased from 12/7 to 13/8 to 14/8 these apneas improved without the backup rate kicking in. If a backup rate is applied but does not fire this can be a clue to the interpreter that it was not needed. The stage in which central apneas occur should be considered—if occurring in REM sleep a second look for respiratory effort is warranted as obstructive apneas are more common in REM sleep due to decreased muscle tone, and TE-CSA occurs more often in non-rapid eye movement sleep.

Obstructive apneas can be misclassified as central when respiratory effort is present but is not detected or the deflections not seen. Obstructive apneas in REM sleep may be more difficult to appreciate because of smaller chest wall and abdominal excursions in RIP belts. Autoscale gain is often used on PSG software to minimize the appearance of signal deflections into adjacent channels. This can result in small amplitude deflections that give the appearance that the chest and abdomen are not moving. By manually increasing the gain, evidence of respiratory effort can be discovered if present. Improper placement of RIP belts (ie, not tightening them enough or not placing the belts at places of maximum movement during respiration) may also lead to misclassification.[1]

In our case, the patient was put on automatic PAP 9 to 14 cm H_2O with resolution of symptoms and normalization of the residual AHI on download at follow up. The 90% pressure was 11.4 cm H_2O.

SLEEP MEDICINE PEARLS

1. The occurrence of a central apnea in REM sleep should cue a second look to ensure that respiratory effort has not been missed. Central apneas are less common in REM sleep. Due to decreased muscle tone during REM sleep, obstructive apneas are more common and chest wall and abdominal excursions may be small.

2. Complex SA occurs when central apneas occur on PAP and predominantly obstructive events were shown on a diagnostic study. Complex sleep apnea includes three subsets: TE-CSA, CSA-Cheyne-Stokes breathing, and CSA due to drugs or medications. Apnea morphology and patient history help distinguish between these types.
3. Risk factors for TE-CSA include non-rapid eye movement sleep (stages N1 and N2) versus REM sleep, supine position versus nonsupine position, men versus women, high AHI, central apneas during the diagnostic study, split-night study versus separate night for titration, high CPAP (overtitration), and BPAP without a backup rate. In TE-CSA the sleeping pCO_2 is close to the AT and central apneas occur on PAP when the pCO_2 drops below the AT.

CITATION

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