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## Nocturnal Diaphoresis Secondary to Mild Obstructive Sleep Apnea in a Patient with a History of Two Malignancies

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Numerous medical disorders, including obstructive sleep apnea, may cause nocturnal diaphoresis. Previous work has associated severe obstructive sleep apnea with nocturnal diaphoresis. This case report is of import as our patient with severe nocturnal diaphoresis manifested only mild sleep apnea, and, for years, his nocturnal diaphoresis was ascribed to other causes, i.e., first prostate cancer and then follicular B-cell lymphoma. Additionally, it was the nocturnal diaphoresis and not more common symp-

toms of obstructive sleep apnea, such as snoring, that led to the definitive diagnosis of his sleep apnea and then to treatment with a gratifying resolution of his onerous symptom.

**Keywords:** Diaphoresis, sleep apnea

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Diverse medical disorders including malignancies, infections, and endocrine abnormalities have been associated with nocturnal diaphoresis.<sup>1</sup> Nocturnal diaphoresis may occur in obstructive sleep apnea syndrome (OSAS).<sup>2</sup> Nevertheless, research has been limited and findings mixed.<sup>3,4</sup> One study found night sweats to be associated with snoring and sleepiness but not apnea-hypopnea index (AHI).<sup>3</sup> Excessive nocturnal sweating occurred in 34% of patients with severe OSAS ([AHI] = 52).<sup>4</sup> Our case is instructive as our patient's severe nocturnal diaphoresis occurred with mild OSAS and was not clearly connected to his two malignancies.

### REPORT OF CASE

A 67-year-old male first manifested diaphoresis in 2002 following a radical prostatectomy for T2N0MX prostate cancer. His clinicians reassured him that diaphoresis, common after surgery, should resolve.

It worsened; the patient often soaked through clothing and slept on a towel. Endocrine evaluation was negative. A negative QFT Gold Test for tuberculosis, negative HIV test, normal erythrocyte sedimentation rate test (1), and normal testosterone level (444) were obtained in 2010. However, follicular B-cell lymphoma was diagnosed (1/2011) and thought the likely cause of profuse, almost nightly sweats. The Rituximab treatment for lymphoma (3/2011) did not improve his diaphoresis. The patient's oncologist recommended sleep medicine consultation.

The patient presented 6/2011 to sleep medicine with a chief complaint of "severe night sweats that have gotten progressively worse over the last 12 months." Sweating was most apparent 02:30 until 04:00. His registered nurse wife noted infrequent snoring and pauses in respiration. He denied restless sleep. Epworth Sleepiness Scale score was normal (5), though he felt tired upon arising after 7-8 hours in bed. He used minimal alco-

hol and no caffeine. He ceased smoking cigarettes in 1975 and reported a comfortable bedroom temperature.

Past medical history: Prostate cancer history (treated first with surgery, then with radiation therapy in 2006 for micrometastatic disease), follicular B-cell lymphoma, radiation cystitis, coronary heart disease, supraventricular and ventricular dysrhythmias (dronedrone previously stopped given concerns it contributed to diaphoresis), pacemaker implantation, adenomatous colon polyps with dysplasia, pneumonia, previous left upper extremity thrombophlebitis, gastroesophageal reflux disease (GERD), Barrett's esophagus, and distant tonsillectomy history.

Medications (at time of initial sleep center visit) included clopidogrel, niacin, atorvastatin, aspirin, flecainide, pantoprazole, lubiprostone, glucosamine/chondroitin, and fish oil.

Review of systems demonstrated no recent change in weight, no history of diabetes mellitus or thyroid disease, and some difficulties with memory and concentration.

Exam demonstrated a tall, slender male with normal respiratory rate and pulse. Upper airway exam revealed no frank anterior septal deviation. He had a large tongue, borderline class III malocclusion, Mallampati IV, retrognathia, and 15-inch neck circumference. Neck exam revealed normal thyroid, and no cervical, supraclavicular, or axillary adenopathy. Cardiopulmonary exam: normal lung sounds and heart tones, and a pacemaker. There was no cyanosis, clubbing, or edema.

The patient's diagnostic and continuous positive airway pressure (CPAP) polysomnographic data are presented in **Table 1**. By numeric indices, the patient's diagnostic study manifested mild apnea that was more pronounced in stage R sleep. Pre and post blood pressures were normal at 109/67 and 104/64, respectively. Esophageal pressure monitoring and ambulatory blood pressure monitoring were not done as part of the patient's clinical evaluation.

**Table 1**—Summary of polysomnographic data

Study Date	Max. CPAP	AHI <sup>a</sup>	REM AHI	Supine AHI	Low O <sub>2</sub> %	Length (s)	Max Length (s)	Arousal Index	Total Sleep (min)	Sleep Efficiency %	Min REM	PLMS/h	BMI (kg/m <sup>2</sup> )
06/09/11	0	7	27	7	89	21	52	8	381	93	53	0	22.7
06/22/11	9 <sup>b</sup>	1	0	1	94	26	29	14	326	78	29	0	23.1

<sup>a</sup>Hypopneas defined as:  $\geq 30\%$  decline in tidal volume for  $\geq 10$  seconds associated with  $\geq 4\%$  oxygen desaturation. <sup>b</sup>The AHI on the CPAP titration study of 6/22/11 is averaged over all CPAP pressures.

The CPAP titration study revealed control of the patient's apnea and improved oxygen nadir. Blood pressures pre and post study, respectively, were again normal at 101/63 and 99/57. In neither study was there evidence for other sleep pathology such as periodic limb movements of sleep.

The patient began CPAP at 9 cwp. At 1-month follow-up, he noted near-disappearance of nocturnal diaphoresis. Diaphoresis had taken a few days after CPAP initiation to dissipate. Medications including niacin remained unchanged. A CPAP download revealed that during the first month (7/12/11-8/10/11), the patient used the machine 5 h 45 min per night, with 87% of the time  $\geq 4$  h and with an AHI of 2.9 on 9 cwp. His daily records for the preceding month indicated no night sweats save for "moist" neck area and armpits on 3 nights.

Endocrinology work up (8/2011), requested by the patient's oncologist, revealed normal renal, hepatic, and glucose levels. The overall thyroid panel suggested "borderline low" thyroid function, yet TSH was normal (2.94).

His last visit (8/2012) revealed continued control of his diaphoresis with CPAP therapy. He noted some diaphoresis and snoring with CPAP interface slippage.

A CPAP download from 7/8/11-8/1/12 revealed that the patient used his CPAP machine an average of 5 h 8 min per night, with 77% of the time  $\geq 4$  h and with an AHI of 1.6 on 9 cwp.

At one and a half years post CPAP initiation, on phone communication, the patient believed his diaphoresis was still dramatically improved. The patient stated that if he stopped CPAP that the first night he would sweat only modestly. With CPAP discontinuation for a few days, he noted that increasingly severe diaphoresis ensued.

## DISCUSSION

Firstly, this report illustrates the importance of not excluding OSAS from the differential diagnosis of nocturnal diaphoresis, despite other more obvious potential etiologies. Secondly, this case indicates that even *mild* OSAS may result in *severe* diaphoresis, extending findings regarding its presence in severe OSAS.<sup>4</sup> Thirdly, CPAP both treated mild OSAS and resolved the troubling night sweats. This case emphasizes the onerous nature of diaphoresis in OSAS, even when unaccompanied by more typical symptoms, such as prolific snoring and sleepiness. In this case, severe nocturnal diaphoresis was our primary clue to the presence of OSAS.

It is possible that the AHI underestimated the patient's degree of respiratory instability and that the patient may have had concomitant respiratory event related arousals (RERAs). However, a careful review of the raw data did not reveal evidence

for RERAs. For example, the patient's breathing was usually in-phase, and the intercostal electromyogram signals were almost exclusively quiet. We did not see subtle out-of-phase breathing terminating in arousals. The normal arousal index also argued against our missing subtle upper airway events.

Sleep stages have been associated with different predispositions to diaphoresis. For that reason, we looked for changes in stage N3 sleep (the stage with greatest diaphoresis) and stage R sleep (the stage ostensibly with the least) that might have explained his diaphoresis and response to therapy. We found no explanation in our review of the sleep architecture (please see minutes of stage R for each study in **Table 1**. The patient had no stage N3 on either study).

We did not analyze heart rate variability (HRV), a measure of autonomic function. With only one night in each condition, selecting samples for analysis while controlling for proximity of apnea events, proximity of arousals, sleep stage, and time of night was beyond our capability.

The severe night sweats in this patient with mild OSAS were noteworthy. Few studies<sup>3,4</sup> have investigated diaphoresis in OSAS. Electrodermal activity has also been utilized to probe this relationship in patients with severe apnea (AHI = 45.3).<sup>5</sup> These findings, however, may not be generalizable to our patient, who had much milder apnea. Future studies aimed at assessing the prevalence of diaphoresis in *mild* OSAS and clarifying its pathophysiological basis may be warranted. Perhaps this severe diaphoresis reflects individual variability, just as some patients with mild OSAS by numeric indices may have severe sleepiness. The patient's sympathetic nervous system may have been more sensitive to the impact of OSAS, and the sweating may have reflected heightened autonomic activity. The association of autonomic dysfunction with mild OSAS was previously reported in 2004,<sup>6</sup> and, in 2008, systolic non-dipping of blood pressure was reported to be associated with sleep apnea, even mild apnea.<sup>7</sup>

Finally, this patient had a history of GERD. GERD has itself been reported to cause nocturnal sweats,<sup>8</sup> to be comorbid with OSAS, and improved by CPAP.<sup>9</sup> While the improvement of diaphoresis by CPAP may have been due to GERD reduction, the patient presented to the sleep center with diaphoresis notwithstanding use of a proton pump inhibitor. Thus, CPAP treatment of OSAS was likely primarily responsible for the gratifying response described herein.

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## DISCLOSURE STATEMENT

This was not an industry supported study. The authors have indicated no financial conflicts of interest.