Obstructive sleep apnea following treatment of head and neck cancer

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Abstract
A growing body of literature is suggesting that there is a link between head and neck cancer treated with radiation therapy and the development of obstructive sleep apnea/hypopnea syndrome (OSAHS). We describe the case of a 54-year-old man with a history of head and neck cancer whose OSAHS had gone undiagnosed for 3 years. After the diagnosis was made on the basis of sleep study data, we determined that the OSAHS was a long-term complication of cervical radiation therapy that had been delivered to treat the patient's laryngeal squamous cell carcinoma 3 years earlier. We also review the literature regarding the association between head and neck cancer and the development of OSAHS.

Introduction
Obstructive sleep apnea/hypopnea syndrome (OSAHS) is characterized by repetitive airway collapse during sleep. The site of airway collapse extends from the velopharynx to the hypopharynx; in some patients, more than one site of obstruction is involved. Weight gain, which narrows the upper airway secondary to the deposition of adipose in the parapharyngeal space, is the most common risk factor for OSAHS. In nonobese individuals, airway abnormalities and craniofacial abnormalities that narrow the airway may predispose to the development of respiratory disturbances during sleep.

Because these sequelae of untreated OSAHS are significant, prompt diagnosis and treatment are crucial. Unfortunately, most cases of OSAHS are undiagnosed, and patients with atypical symptoms may go unrecognized. Awareness of the risk factors for the development of OSAHS makes it possible to determine which patients should be screened for this condition. We describe a case of OSAHS that occurred as a result of cervical radiation therapy for laryngeal squamous cell carcinoma. We also review the literature regarding the association between head and neck cancer and the development of OSAHS.

Case report
A 54-year-old man with T1N2bM0 squamous cell carcinoma of the right pharyngoepiglottic fold (status post right modified neck dissection and subsequent radiation therapy 3 years earlier) was referred to our sleep center with complaints of poor sleep, somnambulism (sleepwalking), and somniloquy (sleep talking). His symptoms had begun shortly after the completion of his radiation therapy. Prior to referral, he had been treated for depression and insomnia, but no changes in his sleep symptoms had occurred.

A further sleep history obtained from the patient and his wife revealed that the man frequently awoke during the night, choking and gasping. He also snored, and his wife had witnessed some apneas. His wife reported that the patient was very active (“constantly jerking”) during sleep. She said he would talk and make purposeful gestures as if he were trying to build something. The patient reported sleepwalking, often waking to find himself sitting on the floor. He did not feel refreshed after sleep. In fact, he was very sleepy during the day and had stopped working as a result. His Epworth sleepiness scale score was 23 out of a possible 24 (a score >10 suggests pathologic sleepiness). A review of symptoms revealed chronic hoarseness and dysphagia with solids. The patient denied morning headaches.

On physical examination, the patient’s body mass index was 21.3 (within the normal range). He had a left nasal septal deviation and scarring of the right side of the neck in the area of his previous surgery and radiation. His oropharynx was graded as Mallampati class III (only the soft palate and tongue were visible upon opening of the oropharynx and extension of the tongue), and no stridor was heard over his trachea.

A 19-channel overnight polysomnography that included full seizure-montage electroencephalography and video recording was performed. The polysomnogram revealed extremely severe obstructive sleep apnea, and the patient’s apnea/hypopnea index (AHI) was 94 events per hour; he experienced 561 apneas over a 6-hour period of sleep.
Accompanying this finding was a marked degree of oxygen desaturation into the 60th and 70th percentile range during rapid-eye-movement (REM) sleep. No seizure activity was noted, although the patient was observed to have thrashed about during his sleep because of his breathing difficulty.

The patient was prescribed noninvasive ventilation. However, even with bilevel pressure support settings of 20/16 cm H$_2$O with a 3-L/min oxygen bleed, the patient continued to experience significant respiratory disturbances with desaturations. Therefore, a volume-cycled ventilator was used with a full-face mask interface. On a volume-cycled ventilator in an assist-control mode with 2 L/min of oxygen, the patient was able to achieve satisfactory oxygen saturation and adequate control of his sleep apnea. He was kept on noninvasive ventilation at home, and his symptoms diminished but did not completely resolve.

In view of the severity of the patient’s sleep apnea in the context of his medical history, an upper airway fiberoptic examination was performed by the ENT service. This investigation revealed the presence of significant fibrotic tissue in the supraglottic larynx with airway narrowing, as well as edema of the false vocal folds. No evidence of tumor recurrence was noted. Computed tomography (CT) of the neck was ordered to better evaluate the patient’s airway. CT demonstrated a marked narrowing of the airway in the area of the larynx but no definite soft-tissue abnormality (Figure). These findings were interpreted to represent mucosal edema without evidence of cancer recurrence.

A tracheostomy was recommended, and the patient agreed. Following tracheostomy with placement of a permanent tube, his nocturnal oxygen saturation level increased dramatically and all of his sleep-related symptoms resolved completely.

Discussion

Friedman et al described a high rate of OSAHS in a series of 24 patients treated for head and neck cancer. All 24 patients had an AHI greater than 5, and 67% of them met the criteria for the consensus definition of clinically significant OSAHS. This rate is significantly higher than the often-cited rate of 2 to 4% in middle-aged adults overall. Moreover, obesity was absent in this group (mean BMI: 22). Numerous hypotheses were offered to explain the high rate of OSAHS in this population, including anatomic airway modification caused by surgery or tumor burden, a loss of pharyngeal muscle function following surgery, and the effects of radiation therapy. It is interesting that all 10 patients in this series who had undergone radiation therapy had polysomnographic evidence of sleep-disordered breathing, compared with only 79% (11/14) of those who were not treated with radiation. This suggests that radiotherapy may play a significant role in the development of OSAHS in patients with head and neck cancer.
sleep apnea,\textsuperscript{11-13} but it should be kept in mind that central sleep apnea may also occur, as Udwadia et al noted in a report detailing radiation necrosis of the medulla with resultant central apneas.\textsuperscript{14}

The typical symptoms of OSAHS are excessive daytime sleepiness, insomnia, loud snoring, morning headaches, and dry mouth upon awakening. Because some of these symptoms are nonspecific and may be seen in a variety of disease states, including malignancy and depression, it is not uncommon for patients with sleep apnea to be treated for other diagnoses for years before the correct diagnosis is made.\textsuperscript{15} In fact, this situation occurred in the case described herein, as our patient had been treated for insomnia and depression during the 3 years preceding his diagnosis of OSAHS. Clinicians who care for patients who fit into a high-risk profile for OSAHS should aggressively screen for this condition. Patients with head and neck cancer, especially those who undergo radiotherapy, should be included in this high-risk group. Otolaryngologists also need to recognize that not all patients with OSAHS fit the classic profile—that is, an obese, loud snorer who is unable to maintain wakefulness. Atypical symptoms, such as abnormal behaviors during sleep, may be the first clue to the presence of OSAHS, and they warrant further evaluation.

The standard treatment for OSAHS—noninvasive ventilation—may not be adequate for patients with radiation-induced OSAHS. In our patient, the airflow obstruction was attributable to a relatively fixed airway abnormality, and thus noninvasive ventilation was only marginally effective. Some other treatment modalities for OSAHS—among them weight loss, dental appliances, and mandibular surgery—would not be expected to be effective because they do not address the underlying pathology. Treatments that are not typically considered for OSAHS—for example, CO\textsubscript{2} laser vaporization targeting laryngeal edema—may be worth considering, depending on the specific patient's airway anatomy.\textsuperscript{16} Tracheostomy, the only definitive therapy for sleep apnea, can be performed if standard ventilation therapy fails or if the clinical situation requires it. Because the site of airway obstruction following treatment of head and neck cancer is typically at the level of the larynx and not at the level of the soft palate or the base of the tongue,\textsuperscript{17} diagnostic modalities such as CT of the neck should be considered for patients who are found to have OSAHS. This may help to determine the optimal therapeutic approach for a given patient.

Clinicians who care for patients with a history of head and neck cancer, especially those who have received radiation therapy, need to have a high index of suspicion for OSAHS. Polysomnography should be ordered for patients who complain of excessive daytime sleepiness or insomnia.

References