Looking beyond in Sleep Medicine Practice: Effect of OSA Management in Floppy Eyelid Syndrome – A Case Report

Helya Bolouki-Azari[1,2] Arman Soleimani[1,2] Arezu Najafi[2,3] Hamed Amirifard[4]

[1] School of Medicine, Tehran University of Medical Sciences, Tehran, Tehran, Iran
[2] Occupational Sleep Research Center, Baharloo Hospital, Tehran University of Medical Sciences, Tehran, Iran
[3] Sleep-Disordered Breathing Research Center, Tehran University of Medical Sciences, Tehran, Tehran, Iran

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Address for correspondence Arezu Najafi, MD, Assistant Professor, Occupational Sleep Research Center, Baharloo Hospital, Tehran University of Medical Sciences, Tehran, Iran (email: najafeeaz@gmail.com).

[4] Department of Neurology, The Iranian Center of Neurological Research, Department of Neurology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran

Abstract

Obstructive Sleep Apnea Syndrome (OSA) is a common sleep disorder characterized by recurrent episodes of partial or complete upper airway obstruction during sleep. Floppy Eye Syndrome (FES) is a condition in which the upper eyelids easily evert with upward traction due to underlying tarsal plate laxity and is associated with chronic, reactive papillary conjunctivitis; this causes the eye to be vulnerable to discomfort and visual symptoms. A 49-year-old man with an 8-year history of snoring, sleep fragmentation, and daytime sleepiness was admitted as an outpatient in our sleep clinic. The patient had complied ocular symptoms such as burning eyes, redness, and irritative ocular symptoms in the past five years, arising upon waking up. The symptoms did not regress with the use of artificial tears and proper ointment. The patient was diagnosed with OSA and began using continuous positive airway pressure (CPAP). CPAP therapy significantly corrected the symptoms of FES associated with OSA . This would help to sensibilize ocular findings in patients with OSA and identify hidden sleeping diseases needing a more appropriate investigation and possible treatment. We must look beyond our approach to sleep clinic patients and avoid being kept to the common symptoms patients represent.

Keywords

- Obstructive sleep apnea syndrome
- OSA
- Floppy eyelid syndrome
- FES
- sleep
- CPAP

Introduction

Obstructive sleep apnea syndrome (OSA) is a common sleep disorder characterized by recurrent episodes of partial or complete upper airway obstruction during sleep. It causes arterial oxygen desaturation, sleep fragmentation, and daytime sleepiness.[1] It has been hypothesized[2] that frequent arousals, deoxygenation, and reoxygenation result in the activation of the sympathetic nervous system, causing oxidative stress, an acute increase in blood pressure, and systemic inflammation.

Due to the systemic inflammation, OSA could cause changes in the microvasculature,[3] abnormal vascular reactivity in the cerebral circulation,[4,5] stroke,[6,7] cardiovascular

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events such as hypertension[8,9] and coronary artery disease,[10] and even death. Obstructive sleep apnea syndrome can have a similar effect on the eyes; the ocular manifestations of OSA derive from its mechanical and vascular effects, and they include central retinopathy, retinal vein occlusion, glaucoma, papilledema, corneal abnormalities, nonarteritic anterior ischemic optic neuropathy (NAION),[11] and floppy eyelid syndrome (FES). Kadyan et al.[12] observed that eye rubbing, gritty sensation, mucoid discharge, and photophobia were significantly frequent in patients with OSA; FES is known to be one of the more common eye diseases associated with OSA.[13]

First described in 1981 in obese middle-aged men by two ophthalmologists, Culbertson and Ostler,[14] FES is a condition in which the upper eyelids easily evert with upward traction[15] due to underlying tarsal plate laxity; it is associated with chronic reactive papillary conjunctivitis, which causes the eye to be vulnerable to discomfort and visual symptoms. The prevalence of FES in the adult population ranges from 3.8% to 15.8%, although this is likely an underestimation.[16]

Studies[11,16,17] in the literature have found a statistically significant association between FES and OSA. Several studies have reported[11,17,20] a nearly 100% prevalence of OSA among FES patients, while other authors[16] have presented more conservative estimates. Although the prevalence of OSA is high among FES patients, some studies[11,17] suggest that only 2% to 5% of OSA patients present simultaneously with FES. Chambe et al.,[13] in a prospective study with 127 patients, observed FES in 22.8% of their OSA population and higher FES prevalence in severe OSA cases. Controversial findings are reported about the relationship between FES and OSA; however, why patients with OSA are at risk for FES is not known.[18] There is some histologic evidence that suggests mechanisms linking FES and OSA. The pharyngeal collapse in OSA occurs due to connective tissue compromise against increased neck thickness, and FES histology reveals decreased elastin content and increased matrix metalloproteinase activity in the eyelid's connective tissue, which presents similar weakness.[15]

The association between FES and OSA has both diagnostic and therapeutic implications. The current case report shows how an appropriate OSA treatment with continuous positive airway pressure (CPAP) results in the improvement of FES-related symptoms.

Case Report

A 49-year-old man with hypothyroidism, hyperlipidemia, gastroesophageal reflux disease (GERD), and mild obesity (body mass index [BMI]: 34 Kg/m^2), with an 8-year history of snoring, sleep fragmentation, and daytime sleepiness, was admitted as an outpatient to our sleep clinic. He also complained of nocturnal groaning (catathrenia), restless legs syndrome before sleep, sweating, and palpitation. The diurnal symptoms were excessive daytime sleepiness, sleep attacks, a recent history of aggression, depressed mood, and asthenia (which caused a decrease in performance in his job as medical equipment salesman), and his score on the Epworth Sleepiness Scale (ESS) was of 13/24. Despite his daytime sleepiness, narcolepsy was excluded due to lack of sleep paralysis, hypnagogic hallucinations, and cataplexy. The medication he was taking included pantoprazole, domperidone, atorvastatin, and levothyroxine. History of family diseases included diabetes mellitus, hypertension, and hyperlipidemia on the mother's side. His habitual history included heavy smoking and opioid abuse.

Furthermore, the patient had experienced ocular symptoms such as burning eyes, redness, and irritation for 5 years, which were felt upon waking up. Xerophthalmia in the presence of burning and pain, palpebral laxity, conjunctival hyperemia and irritation, puffy eyes, poor vision, and strabismus were also present. The ocular symptoms started in the right eye and then spread to the left (the symptoms in the right eye have been more severe), and they did not improve with artificial tears or proper ointments.

On the upper airway examination, the patient's presented a Mallampati score of 4, and the tonsil grade was 1. Venus blood gas analysis showed pH of 7.434, partial pressure of oxygen (PaO_2) of 45.4 mmHg, and partial pressure of carbon dioxide ($PaCO_2$) of 39 mmHg. The patient underwent polysomnography, which showed severe OSA that worsened in the supine position. The total sleep time measured was of 276 minutes. The patient had 301 apneas and hypopneas (192 obstructive apneas [41.7%], 17 mixed apneas [3.7%], 61 central apneas [13.3%], and 31 hypopneas [6.7%]), which resulted in a total apnea/hypopnea index (AHI) of 65.4. The patient was referred for a cardiologic consultation, and the pulmonary artery wedge pressure in the echocardiogram was of 35 mmHg.

A positive airway titration study was recommended. After an in-laboratory positive airway pressure (PAP) titration study, CPAP of 12 cmH_2O resolved the respiratory events and snoring. Accordingly, the patient started undergoing CPAP with a pressure of 12 cmH_2O. Escitalopram 10 mg was prescribed daily to control anxiety. Orofacial myofunctional therapy and weight loss were also recommended, but the patient did not adhere to them.

At the follow-up visit, the rate of adherence of the patient to the CPAP therapy was of 81%, and he reported improvement in eye symptoms, snoring, and anxiety, although the burning in the eyes was still present occasionally. He felt uncomfortable with the Amara mask, so we recommended the use of a full-face mask to cover his nose bridge. The treatment efficacy was confirmed by a further respiratory assessment that showed a significant reduction in the AHI to 0 events/hour (−100% compared to the versus baseline index). The obstructive apnea index, central apnea index, obstructive hypopnea index, and central hypopnea index were also of 0 events/hour. Nocturnal oximetry data significantly improved: Sleep efficacy was improved (from 58.9% to 77.4%) in the PAP titration study. Other OSA symptoms were significantly reduced.

Discussion

Floppy eyelid syndrome is a condition in which the eyelids easily evert with upward traction,[15] causing the eye to be vulnerable to discomfort and visual symptoms. Several studies have reported[11,16,17] a statistically significant association between FES and OSA: FES may be a presenting symptom in patients with undiagnosed OSA; in addition, the treatment of obesity and OSA may have a favorable effect on the course of FES. This association (with an odds ratio of 12.5) persists even when controlled for obesity and other confounding factors.[19]

Muniesa et al.[20] tried to determine the correlation between OSA and FES bidirectionally. They studied OSA patients – among whom they determined the prevalence of palpebral hyperlaxity – and patients already diagnosed with FES – in whom they performed polysomnography studies, and they found a considerably higher incidence of eyelid hyperlaxity in OSA than in non-OSA patients ($p = 0.004$). A total of 38 of the 45 patients with FES were diagnosed with OSA (85%), and 65% had severe OSA. They[20] concluded that OSA might be an independent risk factor for eyelid hyperlaxity, and severe OSA is common in patients with FES.

Histologic evidence suggests mechanisms linking FES and OSA. Connective tissue compromise against increased neck thickness is the cause of the pharyngeal collapse in OSA, and FES histology shows reduced elastin content and increased matrix metalloproteinase activity in the eyelid's connective tissue, which presents similar weakness.[15] Analogous to the increased neck thickness in OSA, FES patients display tissue redundancy in the lateral canthal tendon.[15] Patients with FES often experience symptoms on the side on which they sleep, verifying the theory of mechanical stress as the cause of the syndrome.

Eyelid histology in FES also shows chronic inflammation with no tissue atrophy,[15] which suggests a second sleep apnea theory for the development of FES: pressure from sleeping on a particular side induces transient ischemia in eyelid tissue, which is aggravated by hypoxia during apneic events. With the resumption of normal breathing, reperfusion oxidation injury may cause continuous eyelid inflammation.[15] The FES observed in OSA patients is related to chronic inflammation and underlying connective tissue weakness. Histopathology alterations and the relationship between FES and OSA seem to support the hypothesis that both processes could be different manifestations of the same condition.

The treatment for FES is ophthalmological, with frequent instillation of artificial tears and ocular lubricants. To date, few studies[11,12,18,21] have reported effect of the CPAP treatment on reversing FES-related symptoms on the eye and ocular surface. Furthermore, a limited number of sleep medicine and ophthalmology healthcare professionals are aware of the association between these entities.

Vieira et al.[22] conducted a prospective study with 47 patients with newly-diagnosed OSA who underwent objective diagnostic testing for FES to analyze the effect of CPAP on FES before and after 6 months of the therapy. Patients with nonreversible FES presented more severe OSA and worse airway access according to the Mallampati score. A higher AHI in the supine position might predict FES. After CPAP therapy, FES is resolved in 53.8% of the patients. They[22] concluded that CPAP therapy might reverse FES symptoms.

In the case herein reported, CPAP therapy significantly corrected apnea/hypopnea, oxygen nocturnal desaturation, and improved the quality of the sleep pattern and daytime symptoms. The present report highlights the considerable effect of CPAP treatment on signs and symptoms of FES associated with OSA. This would help raise awareness regarding the ocular findings in patients with OSA and contribute to the identification of hidden sleeping diseases needing a more appropriate investigation and possible treatment. Sleep medicine specialists and ophthalmologists should pay greater attention to the ocular symptoms of the patients and consider a deeper collaboration.

Ethical Considerations

Informed consent was obtained from the patient for the inclusion in the study.

Authors' Contributions

HBA: literature review, data collection, and writing and editing of the manuscript draft; AS: literature review, data collection, and writing of the manuscript draft; HA: patient management and follow-up, and review and editing of the manuscript. AN patient visit, management, and follow-up, and writing, review, and editing of the manuscript draft.

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Conflict of Interests

The authors have no conflict of interests to declare.

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