Palatine tonsil neoplasms presenting as sleep disorders – report of two cases

Clinical Case

Authors

José Pedro Pais
Núcleo Académico e Clínico de Otorrinolaringologia CUF Tejo, Portugal

Ana Helena Campos
Núcleo Académico e Clínico de Otorrinolaringologia CUF Tejo, Portugal

Catarina Alves do Vale
Serviço de Anatomia Patológica CUF Descobertas, Portugal

Cristina Caroça
Núcleo Académico e Clínico de Otorrinolaringologia CUF Tejo, Portugal

Pedro Henriques
Núcleo Académico e Clínico de Otorrinolaringologia CUF Tejo, Portugal

João Paço
Núcleo Académico e Clínico de Otorrinolaringologia CUF Tejo, Portugal

Correspondence:
José Pedro Pais
jpcpais123@gmail.com
962360692
Rua Ilha do Pico n. 18 2790-362 Queijas

Article received on November 5, 2022.
Accepted for publication on March 4, 2023.

Abstract

We report two cases of malignant palatine tonsil tumors presenting with snoring and symptoms of obstructive sleep apnea (OSA). This presentation is rarely reported in the literature in patients with superior aerodigestive tract neoplasms. These paradigmatic cases highlight the importance of a systematic evaluation of the aerodigestive tract in patients with snoring and suspected OSA for the early detection or exclusion of malignancy. A multidisciplinary approach that includes otorhinolaryngologists is essential for the management of OSA.

Keywords: Obstructive sleep apnea; Snoring; Head and neck cancer; Tonsillar neoplasms; Case report.

Introduction

Sleep disorders encompass a wide range of disorders. Obstructive sleep disorders include obstructive sleep apnea syndrome (OSAS) and snoring. OSAS results from repeated episodes of collapse or narrowing of the upper airway during sleep, associated with breathing effort. Snoring is the sound produced by the vibration of the anatomic structures of the upper aerodigestive tract during sleep and may or may not be associated with OSAS.[1] It is often a clinical diagnosis, based on both the patient's anatomic characteristics that are potential risk factors as well as the presence of suggestive symptoms.[2] The diagnosis is confirmed by polysomnography, which quantifies the frequency and intensity of apnea/hypopnea episodes. The treatment should be individualized according to the disease-predisposing factors.[3]

The relationship between sleep disorders and head and neck neoplasms is controversial. Recent evidence suggests that the therapeutic or palliative strategies used for head and neck tumors, namely radiotherapy and surgery,

are risk factors for the development of OSAS, probably due to neuromuscular damage, xerostomia, and subsequent instability of the airway.[4,5,6,7]

However, the prevalence of snoring and sleep apnea in patients with neoplasms of the upper aerodigestive tract is not well known.[7] Reports of head and neck neoplasms presenting with snoring and OSAS are rare in the literature. Nevertheless, there has been a recent increase in the number of clinical case reports on this issue.

Clinical evaluation performed by an otorhinolaryngologist, with or without imaging methods, is often necessary to identify a tumor causing OSAS. Although polysomnography quantifies the severity of the disease, it does not aid in the identification of its etiology. Furthermore, an improvement in symptoms due to the initiation of ventilation therapy may contribute to a delay in the diagnosis.[8]

Here, we report the cases of two adult patients who attended the Snoring and Sleep Apnea clinic of Hospital CUF Tejo due to snoring and symptoms suggestive of OSAS and who were eventually diagnosed with palatine tonsil cancer (squamous cell carcinoma and follicular lymphoma).

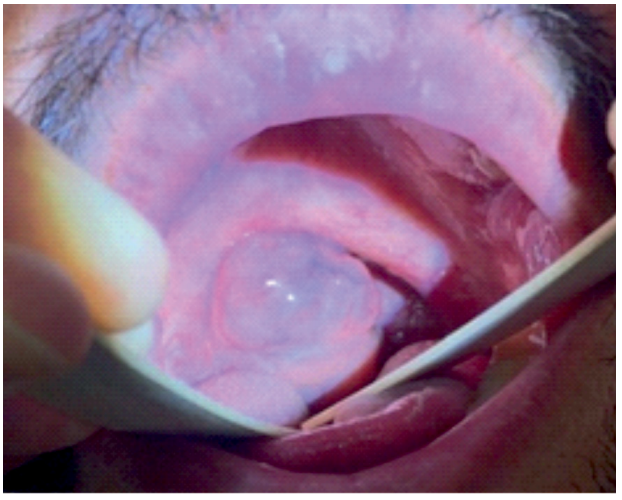
Description of the cases

Clinical case 1:

A 48 year-old man presented to the Snoring and Sleep Apnea clinic complaining of snoring for the last one month, which was gradually worsening, along with episodes of apnea and awakenings with gasping, witnessed by his spouse. He also reported daytime sleepiness and, more recently, globus sensation in the oropharynx.

A septoplasty performed in 2005 stood out in his medical history. On objective physical examination, he had a body mass index (BMI) of 28.1 kg/m^2 and marked tonsillar asymmetry. The right tonsil extended across the midline and exhibited a smooth, shiny, and pinkish surface with prominent superficial vessels and an elastic consistency, without apparent

Figure 1
Preoperative examination of the oropharynx shows asymmetry of the palatine tonsils, with an enlarged right tonsil. Note: the right anterior tonsil pillar was retracted posteriorly to the upper pole of the tonsil for better exposure



fixation to the pharyngeal wall. The left tonsil was classified as Friedman grade I. Nasopharyngolaryngoscopy did not show any other lesions in the upper aerodigestive tract. Computed tomography (CT) of the neck showed a tumor originating in the palatine tonsil with a transverse diameter of 30 mm and antero-posterior diameter of 22 mm, without changes in the permeability of the parapharyngeal space or presence of cervical adenopathy (Figure 2).

Diagnostic unilateral tonsillectomy using the LigaSure® (BiZact™) technique was performed. Intraoperatively, there was no macroscopic evidence of extracapsular involvement (Figure 3).

Histopathological analysis showed a B-cell lymphoma, namely grade 3B follicular lymphoma (WHO 2017)/follicular large cell lymphoma (WHO 2022) (Figure 4).

After the surgery, there was complete resolution of the sleep-related symptoms. The patient was then referred to the hematology clinic where he underwent evaluation with positron emission tomography, upper gastrointestinal endoscopy, and bone marrow analysis, which excluded systemic involvement. He started chemotherapy with rituximab, cyclophosphamide, doxorubicin,

Figure 2
Cervical computed tomography (CT) with contrast (A –axial plane and B – reconstruction in the coronal plane) shows a neoformation in the right tonsil causing reduced airway permeability.

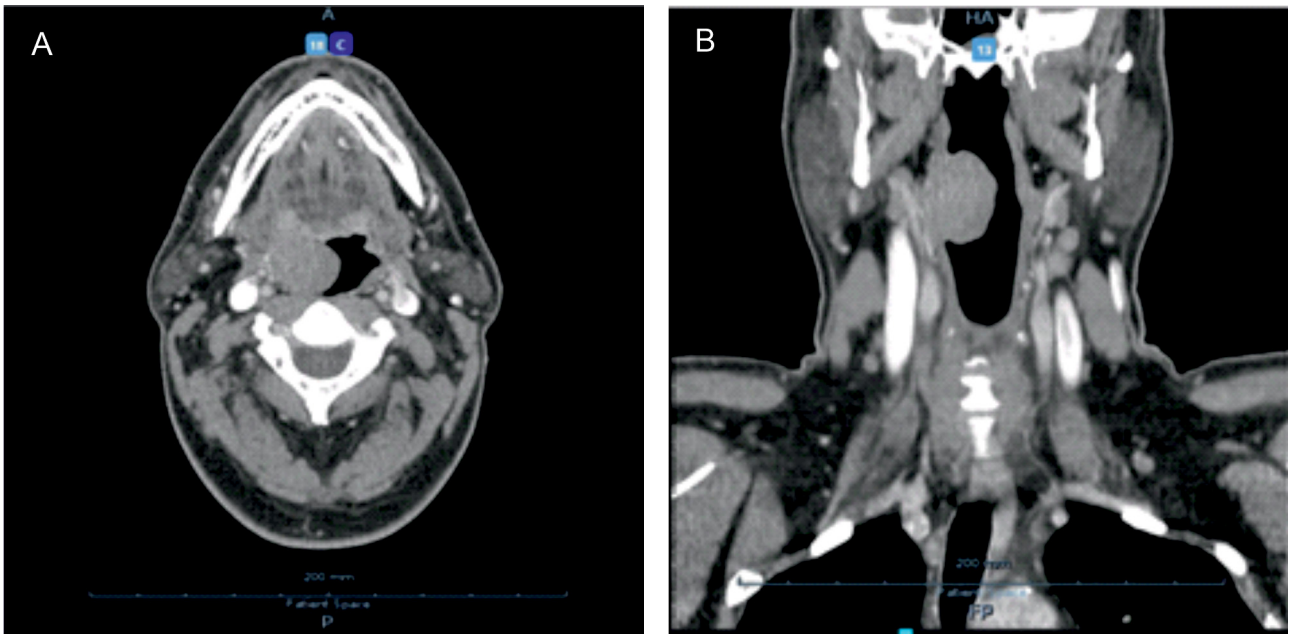
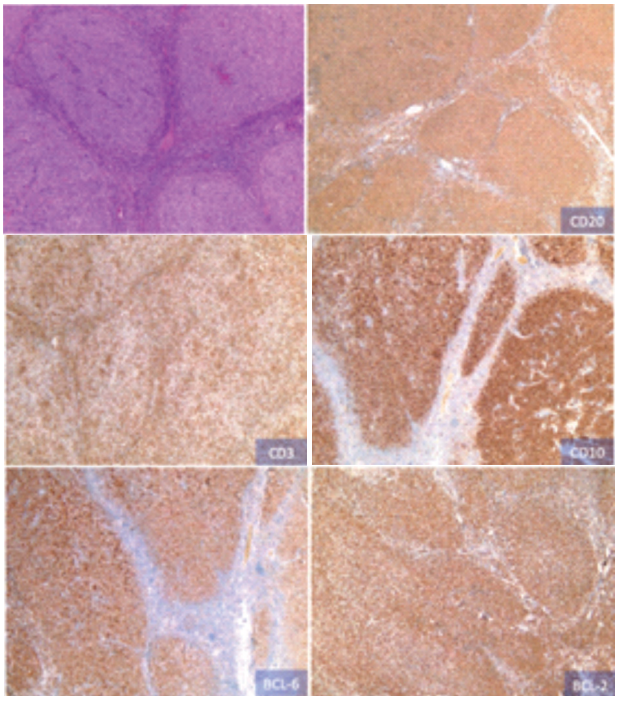


Figure 3
Surgical specimen of the diagnostic tonsillectomy

and prednisone. There was no evidence of disease recurrence or progression during the 6-month follow-up period at our hospital (the patient chose to undergo systemic treatment in another institution).

Figure 4
Histological images of B-cell lymphoma/grade 3B follicular lymphoma, (WHO 2017)/follicular large cell lymphoma (WHO 2022) showing lymphoid proliferation with nodular pattern, without diffuse areas, and with many centroblasts; immunohistochemical staining is positive for CD20, CD10 (with cells in the interfollicular region), BCL-6, and BCL-2, and negative for CD3.



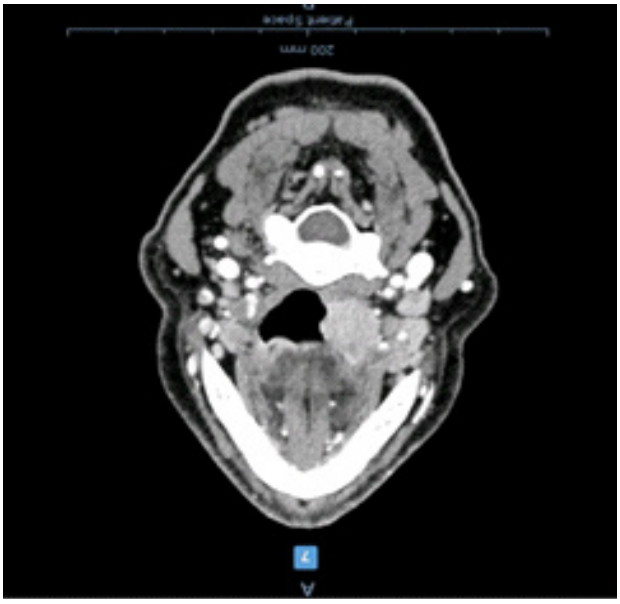
Clinical case 2:

A 67 year-old man attended the Snoring and Sleep Apnea clinic with complaints of snoring, episodes of sleep apnea, and nasal obstruction for the last two months, which had worsened rapidly in the three weeks before the visit.

The relevant clinical history included smoking (60 pack-years). On objective physical examination, he had a BMI of 26.5 kg/m^2 and marked tonsil asymmetry, with an enlarged right palatine tonsil due to an infiltrative lesion with ulcerated areas, without apparent extension to the anterior and posterior pillars or the glossotonsillar sulcus. Nasopharyngolaryngoscopy showed a reduction in the velpharyngeal space because of the enlarged right tonsil and excluded other lesions at the level of the upper aerodigestive tract.

Cervical CT confirmed the presence of a neoformation at the level of the right tonsil with a transverse diameter of 35 mm and involvement of the tonsillar pillars was not excluded. There was no apparent extension to the nasopharynx or the masticator, parapharyngeal, and carotid spaces. There was no cervical adenopathy (Figure 5). Chest, abdomen, and pelvis CT did not show adenopathies or signs of metastasis.

Figure 5
Cervical computed tomography (CT) with contrast (axial plane) shows a neoformation in the right tonsil.



The patient underwent diagnostic tonsillectomy using the LigaSure® (BiZact™) technique 15 days after the first visit. Intraoperatively, a slight increase in the size of the lesion was noted relative to the first observation, with involvement of the anterior tonsil pillar, which was also partially excised (Figure 6).

Histological analysis showed squamous cell carcinoma of the palatine tonsil, with focal involvement of the deep margin (R1). The neoplastic cells showed diffuse positivity for p16, which is strongly associated with human papillomavirus (HPV) infection (Figure 7).

Considering the histological and imaging findings, the tumor was staged as pT2N0M0R1.

Figure 6
A – Surgical specimen of the diagnostic tonsillectomy (exterior surface).
B – Tonsillectomy specimen (cross section) showing a white and elastic nodular area of size 32 mm, adjacent to the deep margin.

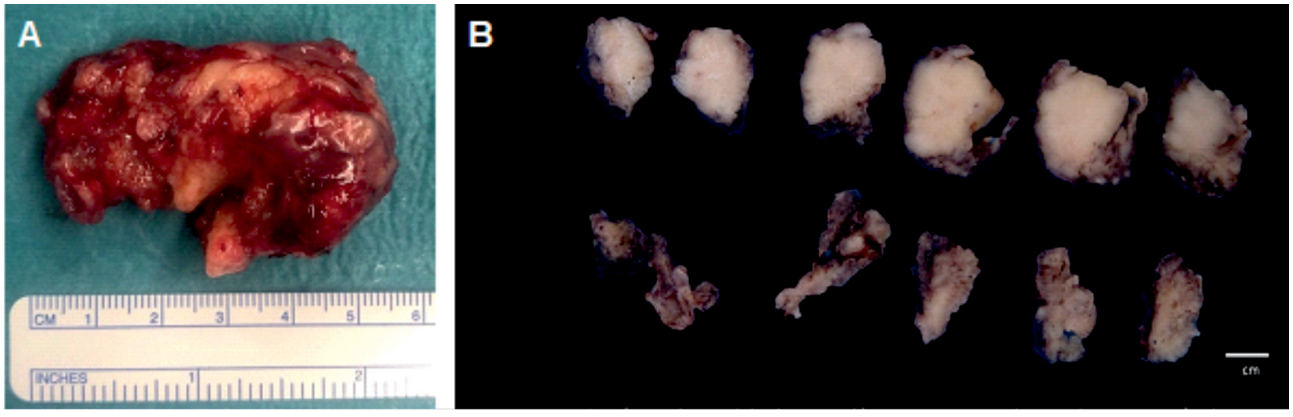
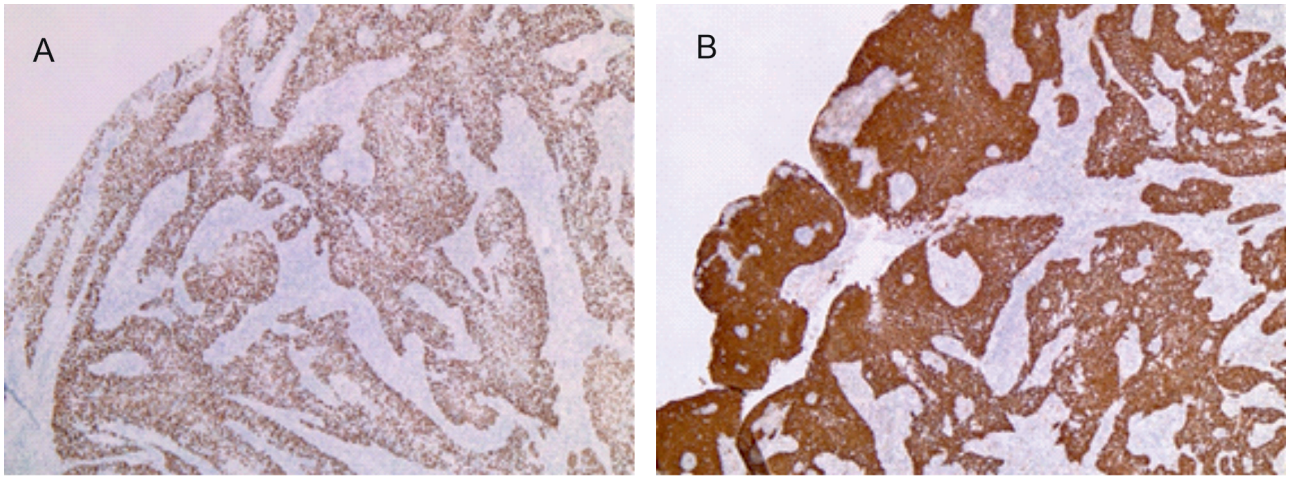


Figure 7
Histological diagnosis was squamous cell carcinoma of the palatine tonsil. A – Positive immunochemical staining for p63 confirms the squamous nature of the lesion. B – p16 positivity suggests association with the human papillomavirus (HPV)



After discussion in a multidisciplinary meeting, the patient was started on definitive chemotherapy and radiotherapy. Complete resolution of the sleep-related symptoms was achieved after the surgery. The patient was monitored and showed no signs of tumor recurrence during six months of follow-up.

Discussion

Herein, we have described two clinical cases of malignancy of the palatine tonsil, who presented with symptoms of snoring and obstructive sleep apnea. In these two cases, the anatomic cause of the symptoms was easily identified by an objective examination of the oropharynx.

During sleep, because of the decubitus position and relaxation of the neck muscles, there is a narrowing of the airway, which facilitates its collapse and vibration. The reduction in the diameter of the airway further promotes this collapse.[9] Thus, tumor growth in any part of the upper aerodigestive tract can cause snoring and obstructive apnea due to a reduction in its diameter. It is expected that a significant percentage of patients with upper airway tumors will develop these symptoms (of varying degrees) before receiving a cancer diagnosis. However, these symptoms are rarely reported in the literature. This may be due to several reasons, such as the absence of sleep-related symptoms until the very advanced stages of the disease; diagnosis of the tumor because of the presence of other earlier signs and symptoms; the patient and/or sleep partner downplaying or not detecting the symptoms; and disregard of symptoms or inadequate clinical guidance by health professionals.

In 2021, Moore et al. conducted a review of the literature that included 79 patients with head and neck tumo rs who presented with OSAS.[8] The symptoms of OSAS occurred in isolation in 28 cases and appeared, on an average, 29.2 months before the definitive diagnosis of cancer. The most frequently reported accompanying symptoms were dysphagia (18.9%), dysphonia (12.6%), and pharyngeal globus (8.8%). Lipomatous tumors of the parapharyngeal and retropharyngeal spaces were the most common (18.9%), although tumors of the oropharynx, larynx, nasopharynx, deep neck spaces, and oral and nasal cavities were also reported. Lymphoma was the most frequently identified cancer, with most cases being diffuse large B cell lymphoma (n=3/11). Only one patient had squamous cell carcinoma of the tonsil as the cause of OSAS. Malignancy was suspected during nasopharyngolaryngoscopy in all cases and by direct observation of the mouth and oropharynx in half of the patients. By the time

of the diagnosis, 55 patients had undergone polysomnography and 22 patients were receiving treatment with continuous positive airway pressure (CPAP).[8]

These two clinical cases are paradigmatic examples of this issue. In the first case, the patient had been experiencing snoring and apnea for one month, as witnessed by his spouse, with recent worsening. Pharyngeal globus was also reported during the consultation. The final diagnosis was follicular lymphoma of the tonsil. Palatine tonsil lymphomas are the malignant neoplasms that present the most frequently with OSAS.[8] This fact may be related to tumor growth often being limited by the tonsillar capsule, which leads to airway narrowing that is similar to that seen in benign tonsillar hypertrophy.[10] In this case, the tumor was classified as high-grade follicular lymphoma (3B), which grows faster than most lymphomas , thus explaining the relatively rapid worsening of the symptoms. Moreover, local or additional systemic symptoms are often absent in the initial stages of indolent lymphomas (including follicular lymphoma).[11] Fatigue is a frequently reported symptom in hematological diseases; however, the immediate improvement in the patient's complaints after surgery favors a causal relationship with the presence of OSAS.

In the second clinical case, the final diagnosis was squamous cell carcinoma of the tonsil, which is more frequently of an infiltrative nature than lymphoma.[10] In this patient, fast macroscopic growth of the lesion was observed during the period between diagnostic suspicion and surgery, which suggested strong local aggressiveness, leading to a quick diagnosis.

None of the patients reported previous episodes of snoring or sleep apnea and both experienced a relatively rapid and progressive worsening of OSAS. With the exception of excessive weight, no other risk factors for OSAS were identified. Because there was complete resolution of the symptoms after tonsillectomy, polysomnography was not performed as it would add to the costs with no benefits and cause anxiety to the patient.

Considering these two clinical cases and the literature review, some clinical scenarios should raise suspicion of neoplastic disease as the cause of snoring and sleep apnea and lead to an evaluation or re-evaluation of the aerodigestive tract, namely: recent symptoms in a patient with no risk factors; worsening of symptoms without apparent cause; no improvement or worsening of symptoms in patients undergoing ventilation therapy; and symptoms suggestive of a neoplasm of the aerodigestive tract, namely dysphagia, dysphonia, pharyngeal globus, and weight loss.

Role of the otorhinolaryngologist

The clinical cases and literature review presented herein support the need to review the existing approach to obstructive sleep disorders. Head and neck tumors are rarely considered as a differential diagnosis of snoring and OSAS because the prevalence of these symptoms has not been studied in patients with head and neck tumors.

With sleep disorders being recognized by the scientific community and patients themselves, it is expected that these symptoms will be increasingly acknowledged and, consequently, a larger number of associated diseases will be identified. An adequate diagnostic approach to sleep disorders can facilitate the identification of prevalent etiologies and exclude serious associated diseases, including neoplastic diseases.

Assessment by sleep surgeons, including otorhinolaryngologists, is only "recommended" by the American Academy of Sleep Medicine for adults with OSAS and BMI < 30 who are intolerant or do not accept or adhere to treatment with CPAP, and is "suggested" for patients with a major anatomic variation of the airway.[12] This approach may be insufficient and exclude patients who would benefit from observation by an otorhinolaryngologist.

Polysomnography allows a formal diagnosis of OSAS and is becoming increasingly accessible. The efficacy and availability of

CPAP treatment has minimized the significant impact of OSAS, but the lack of treatment adherence remains a limiting factor.[13] Many patients with OSAS initiate CPAP therapy without an adequate evaluation of the upper aerodigestive tract. Thus, the prescription of this treatment should be considered on a case by case basis, after gathering a thorough clinical history and identifying the risk factors for OSAS. An incorrect use of these diagnostic and therapeutic resources may lead to a delay in the identification of serious diseases that require early and targeted treatment.

We think that the evaluation of all patients with obstructive sleep disorders by an otorhinolaryngologist is beneficial. In these disorders, the upper aerodigestive tract is simultaneously the area of study and intervention. However, its direct or indirect observation is often neglected. Although this assessment results in added costs to the initial management of patients with OSAS, evaluation by an otorhinolaryngologist has evident clinical benefits that translate into health gains by avoiding delays and errors in the diagnosis and, consequently, inadequate interventions. Nasopharyngolaryngoscopy performed in this context is an accessible and safe examination that helps in excluding serious diseases, characterizing the airway, and identifying potentially correctable anatomic factors during the treatment and/or adaptation to CPAP. It is thus essential to acknowledge the beneficial role of the otorhinolaryngologist in a multidisciplinary team, both in the diagnostic approach to this disorder and its surgical treatment.

Conclusion

Neoplasms of the palatine tonsil are a rare cause of snoring and OSAS. This disorder should be diagnosed early and its treatment should be individualized. Adequate evaluation of the upper aerodigestive tract by an otorhinolaryngologist has multiple benefits, including the exclusion of cancer as the cause of OSAS, and should be integrated in the multidisciplinary approach. Polysomnography and/or improvement in the symptoms with the introduction of CPAP should not delay this evaluation, when indicated.

Conflict of Interest

The authors declare no conflict of interest regarding this article.

Data confidentiality

The authors declare that they followed the protocols in use at their working center regarding the publication of the patients' data.

Human and animal protection

The authors declare that the followed procedures were according to the regulations established by the Ethics and Clinical Research Committee and the Helsinki Declaration of the World Medical Association.

Privacy policy, informed consent, and approval by the ethics committee

The authors declare that they obtained written informed consent for the use of the patients' photographs in this article.

Funding

The present study was conducted in the absence of any contribution, funding, or grant.

Availability of scientific data

There are no publicly available datasets related to this study.

Bibliographic references

1. Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K. et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American academy of sleep medicine clinical practice guideline. J Clin Sleep Med. 2017 Mar 15;13(3):479-504. doi: 10.5664/jcsm.6506.

2. Deary V, Ellis JG, Wilson JA, Coulter C, Barclay NL. Simple snoring: not quite so simple after all? Sleep Med Rev. 2014 Dec;18(6):453-62. doi: 10.1016/j.smrv.2014.04.006.

3. Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of adult obstructive sleep apnea with positive airway pressure: an American academy of sleep medicine clinical practice guideline. J Clin Sleep Med. 2019 Feb 15;15(2):335-343. doi: 10.5664/jcsm.7640.

4. Saesen K, van der Veen J, Buyse B, Nuyts S. Obstructive sleep apnea in head and neck cancer survivors. Support Care Cancer. 2021 Jan;29(1):279-287. doi: 10.1007/s00520-

020-05428-7
5.Zhou J, Jolly S. Obstructive sleep apnea and fatigue in head and neck cancer patients. Am J Clin Oncol. 2015 Aug;38(4):411-4. doi: 10.1097/01.coc.0000436086.61460.cb.
6. Huyett P, Kim S, Johnson JT, Soose RJ. Obstructive sleep apnea in the irradiated head and neck cancer patient. Laryngoscope. 2017 Nov;127(11):2673-2677. doi: 10.1002/lary.26674.
7. Gavidia R, Dunietz GL, O'Brien L, Shannon C, Schuetz S, Spector M. et al. Obstructive sleep apnea in patients with head and neck cancer: a systematic review. J Clin Sleep Med. 2021 May 1;17(5):1109-1116. doi: 10.5664/jcsm.9134.
8. Moore P, Cardemil F, Hayward NJ, Flatman S. Scoping review of head and neck neoplasms presenting with obstructive sleep apnoea: the importance of flexible nasendoscopy. ANZ J Surg. 2021 Jan;91(1-2):55-61. doi: 10.1111/ans.16090.
9. Lee JJ, Sundar KM. Evaluation and management of adults with obstructive sleep apnea syndrome. Lung. 2021 Apr;199(2):87-101. doi: 10.1007/s00408-021-00426-w
10. Dong C, Zheng YM, Li J, Wu ZJ, Yang ZT, Li XL. et al. A CT-based radiomics nomogram for differentiation of squamous cell carcinoma and non-Hodgkin's lymphoma of the palatine tonsil. Eur Radiol. 2022 Jan;32(1):243-253. doi: 10.1007/s00330-021-08153-9.
11. Storck K, Brandstetter M, Keller U, Knopf A. Clinical presentation and characteristics of lymphoma in the head and neck region. Head Face Med. 2019 Jan 3;15(1):1. doi: 10.1186/s13005-018-0186-0.
12. Kent D, Stanley J, Aurora RN, Levine CG, Gottlieb DJ, Spann MD. et al. Referral of adults with obstructive sleep apnea for surgical consultation: an American academy of sleep medicine systematic review, meta-analysis, and GRADE assessment. J Clin Sleep Med. 2021 Dec 1;17(12):2507-2531. doi: 10.5664/jcsm.9594.
13. Salman LA, Shulman R, Cohen JB. Obstructive sleep apnea, hypertension, and cardiovascular risk: epidemiology, pathophysiology, and management. Curr Cardiol Rep. 2020 Jan 18;22(2):6. doi: 10.1007/s11886-020-1257-y.