CLINICAL CASE

Sleep obstructive apnea and extranodal NK/T-cell lymphoma of the nasal type

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KEY WORDS
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Abstract The extranodal T/NK-cell nasal type occurs in middle-aged men, and often compromises the aerodigestive tract with nonspecific initial symptoms such as rhinorrhea, nasal obstruction and epistaxis. We report the case of a 43-year-old male with snoring, apneas, drowsiness and impaired concentration, nasal obstruction and rhinorrhea. The cardiorespiratory polygraphy confirmed severe obstructive sleep apnea syndrome. Flexible nasofibroscopy showed an irregular tumor in nasopharynx; while the tomography also concluded with the presence of lymphadenopathy in level I, III and III. Nasopharyngeal biopsy showed extranodal T/NK-cell nasal type, continuing with chemotherapy and radiotherapy. (creativecommons.org/licenses/by-nc-nd/4.0/).
INTRODUCTION

Extranodal NK/T-cell lymphoma of the nasal type is more common in middle-aged men, and in 80% of cases it compromises the aerodigestive tract, including the nose and paranasal sinuses\(^1\). Symptoms are unspecific and include rhinorrhea, nasal obstruction and epistaxis\(^2\), and thus these cases are initially seen at the otorhinolaryngology department. The diagnosis is often delayed due to multiple biopsies with insufficient sample or areas of necrosis, and treatment includes radiotherapy and chemotherapy\(^2,3\).

CASE PRESENTATION

The case is presented of a 43-year old male patient with a history of controlled hypertension and tonsillectomy at 42 years (as a result of chronic tonsillitis). His presenting complaint was snoring, nocturnal respiratory pauses and nocturia, and he referred having fallen asleep while driving, as well as concentration and memory alterations, with decreased working performance. In addition, he had bilateral nasal obstruction, rhinorrhea and aural fullness. Epworth scale score was 24 and physical exam findings included a body mass index of 36.89, neck circumference of 52 cm, deviated nasal septum, hypertrophic and pale turbinates, grade 0 tonsils, Mallampati III and Friedman Tongue Position III. The cardiorespiratory polygraphy revealed an apnea-hypopnea index (AHI) of 102, oxygen desaturation index of 68%, saturation < 90%: 60%, with diagnosis of severe obstructive sleep apnea syndrome (OSAS).

An irregular mass of friable appearance, obstructing both Eustachian tubes, was found in the nasopharynx on flexible nasofibroscopy. A computed tomography (CT) scan of the pharyngeal cavum revealed a concentric mucosal thickening with air bubbles dependent of the nasopharynx posterior wall, which obstructed the nasopharynx and the posterior third of both nostrils, as well as the left maxillary sinus with mucosal content and smaller than 4 cm adenopathetic conglomerates at left level I, II and III, and smaller in size at right level I and II, the largest of 2.8 cm (Fig. 1). During evolution, he developed a 6 x 4 cm left cervical solid mass, painful on palpation and not adhered to deep planes.

A nasopharyngeal biopsy taken in the operating room demonstrated a T-cell lymphoproliferative process with high degree of malignancy, with cytomorphologic appearance of neoplastic cells and angiocentric pattern suggestive of extranodal NK/T-cell lymphoma of the nasal type. Immunohistochemistry further examination was positive for CD3, CD20, Ki67 with 80% and granzyme B, and negative for panCK, CD30 and CD56 (Fig. 2).

Chemotherapy was started with vincristine, L-asparaginase and prednisolone, with associated radiotherapy. Currently, the patient is on treatment with favorable response and improvement of nocturnal symptoms.

DISCUSSION

In our case, the patient presented with initial symptoms of OSAS, which is characterized by repeated episodes of obstruction/partial or total collapse of the upper airway at night, with a prevalence of 5 to 20%, depending on the study population\(^1\). Males are at 2-3-fold higher risk of developing OSAS, and main symptoms include daytime somnolence, fatigue, nocturia, memory and cognitive alterations, headache and decreased libido. The diagnosis is established by means of polysomnography; however, its elevated cost and implementation difficulties have led to the use of other types of sleep studies, such as cardiorespiratory polygraphy, which is indicated in patients without significant comorbidities and high suspicion of OSAS, as it was the case of our patient\(^1\). Complications associated with this condition are: cardiovascular disease, including high blood pressure, coronary artery disease and stroke. It also increases mortality of motor vehicle accidents, type 2 diabetes and postoperative complications, and deteriorates quality of life in general\(^1\).

Obstructive sleep apnea has also been postulated to be able to cause cancer or its progression, possibly through intermittent hypoxia. The Wisconsin cohort trial concluded that patients with AHI > 30 have 4.8-fold higher risk of cancer-related mortality than those without OSAS, and saturation percentage < 90% (TSat90) is significantly associated with cancer mortality\(^1\). A multicenter cohort study in Spain reported that patients with OSAS have higher incidence of cancer, which increased 1.07-fold for every TSat90 10%
increase. However, this was only valid for male patients younger than 45 years\textsuperscript{7}. Another study with 5,894 patients found no significant correlation between daytime symptoms and cancer. However, when grouped by ages, patients younger than 50 years with significant daytime somnolence had 4.09 times more incidence of cancer than the control group. In addition, the incidence of viral/immune tumors (for example, leukemia and melanoma) and alcohol-related tumors (for example, liver and intestinal tumors) in patients with daytime somnolence was 2.73 and 4.92-fold higher than in the control group\textsuperscript{8}. These trials demonstrate an association between cancer and OSAS, but do not prove causality.

The possible mechanisms by means of which OSAS promotes the development and progression of cancer are not clear. Intermittent hypoxia followed by post-hypoxic re-oxygenation is postulated to produce oxygen free radicals and to increase oxidative stress, which damages the DNA, and it is thought to be an important factor in tumorigenesis. In addition, intermittent hypoxia promotes hypoxia-inducible factor overexpression, which plays an important role in tumor angiogenesis and is highly expressed in many solid tumors\textsuperscript{9,10}.

In the presented case, a male patient younger than 45 years had highly elevated AHI and TSat90, which is consistent with cancer-associated risk factors in patients with OSAS. Although the symptoms and initial physical examination suggested OSAS, polygraphy with an extreme AHI led to suspect a concomitant neoplasm, with the ultimate finding of extranodal NK/T-cell lymphoma of the nasal type, an entity that is not that infrequent in our setting. This report highlights the need to consider OSAS as a presentation of aerodigestive tract tumors, mainly non-Hodgkin lymphomas, according to the clinical cases reported in the literature\textsuperscript{11-13}, as well as to perform a comprehensive workup that includes a nasofibroscopy and a CT scan.

**CONFLICT OF INTERESTS**

The authors declare not having any conflicts of interests.

**REFERENCES**