

## CASE REPORTS

# An Unusual Cause of CPAP Intolerance

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Continuous positive airway pressure (CPAP) is a first-line treatment for obstructive sleep apnea (OSA). However, the adherence to CPAP can be difficult for patients due to several reasons. In this case report we describe a patient with severe OSA who initially was treated successfully with CPAP, but after a few months adherence problems developed because of macroglossia. This was caused by amyloidosis due to multiple myeloma. During treatment with chemotherapy and stem cell transplantation, the size of the patient's tongue decreased and he could successfully use his CPAP device again.

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## INTRODUCTION

Continuous positive airway pressure (CPAP) is a first-line treatment for obstructive sleep apnea (OSA). However, the adherence to CPAP can be difficult for patients for several reasons, including psychological factors, nose complaints and a dry mouth.<sup>1</sup> In this case report we describe an unusual cause of CPAP intolerance.

## REPORT OF CASE

Severe OSA was diagnosed in a 62-year-old man who had an apnea-hypopnea index (AHI) of 68 events/h (supine 89 events/h, nonsupine 68 events/h). He started with CPAP treatment with a pressure of 8 cmH<sub>2</sub>O, which resulted in a clear reduction of symptoms of sleepiness and tiredness. The patient stated that he “never felt better.” The AHI decreased to 4 events/h. After a few months, the patient complained of facial swelling and a swollen tongue. Angioedema was considered, although no clear relation between angioedema and CPAP is known. The patient did have an allergy for an angiotensin-converting enzyme inhibitor in the past. The patient was referred to the internist, who did not find any other allergies or a C1 esterase deficiency. The complaints of a swollen tongue persisted after withdrawal of angiotensin-converting enzyme inhibitor but the facial swelling decreased.

The patient was referred to our clinic because of his difficulties using CPAP and to evaluate alternative therapeutic options. The patient told us that he had difficulties with swallowing and talking because of his swollen tongue. The complaints increased during the day and seemed to aggravate when he used his CPAP device. Although the patient had very disturbing complaints he continued to use his CPAP device because of the positive effect on his sleepiness. Different CPAP masks were tried but did not make a difference. No alternative

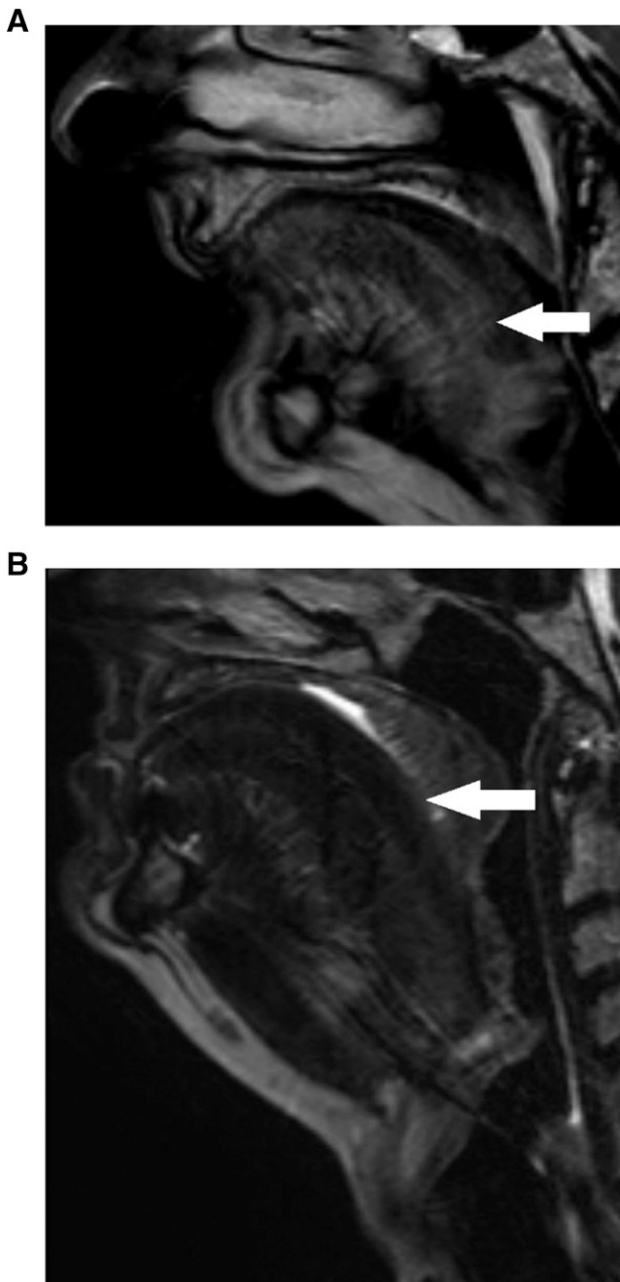
causes were found for his sleep disturbance; for example, the patient did not report increased stress levels, more caffeine use, or increased weight. He was very motivated to use his CPAP because this treatment previously alleviated his complaints. There were no indications of cardiovascular disease that might cause central sleep apnea. On physical examination an enlarged tongue was observed. The patient had a distinct slurred speech. Laboratory tests were normal. A CPAP titration report did not show central apneas, the AHI was <5 events/h. No new sleep study was performed. A cervical MRI showed macroglossia (**Figure 1B** shows the MRI of our patient, **Figure 1A** shows an MRI with a normal tongue for reference). Acquired macroglossia has a broad differential diagnosis, which is shown in **Table 1**.<sup>2,3</sup> Other than macroglossia, the MRI showed no abnormalities of the upper and lower airway.

A biopsy of the tongue showed depositions of amyloid. The hematologist confirmed the diagnosis of amyloid light-chain amyloidosis associated with a multiple myeloma. Total-body CT scan did not show other localization of amyloidosis. The cardiologist did not find indications of cardiac amyloidosis, the echocardiogram showed the ventricular septum was of normal size, and systolic and diastolic function were normal.

The patient was treated with chemotherapy and autologous stem cell transplantation. During this treatment, the size of his tongue decreased substantially and the patient was able to better tolerate his CPAP device again.

## DISCUSSION

Different mechanisms can cause CPAP intolerance. For instance, dry mouth or nose discomfort are common complaints. In our patient, complaints developed after a period of successful CPAP use. Different factors can influence CPAP adherence; not only physiological aspects are important. Also,

**Figure 1**—Cervical MRI.

(A) Cervical MRI showing a normal tongue. (B) Cervical MRI T1 weighted scan showing macroglossia in our patient.

psychological factors and social context can play an important role in CPAP use.<sup>4</sup>

A recent study showed that 47% of patients with amyloid light-chain amyloidosis experienced moderate to high distress.<sup>5</sup> Trouble sleeping was a specific problem associated with distress.<sup>5</sup>

Our patient did have symptoms of distress; however, he felt much better when the size of his tongue decreased and he could use his CPAP device without problems. There were no clear social factors that appeared to cause his CPAP intolerance. On the contrary, the patient and his wife were very motivated to

**Table 1**—Etiology of an acquired macroglossia.

Cause	Example
Neoplasm	Lymphoma, epidermoid carcinoma, neurofibromatosis
Systemic	Angioedema
Endocrine disorder	Acromegaly, hypothyroidism
Infection	Echinococcus, actinomyces, tuberculosis, syphilis
Trauma	tongue biting, maxillofacial trauma
Autoimmune disorder	Pemphigus
Metabolic disorder	Amyloidosis

use the CPAP device and the patient did not want to discontinue its use to evaluate the effect.

We believe that the sleep problems our patient experienced were mainly caused by his macroglossia because when the size of his tongue decreased after treatment, he could use his CPAP device again without difficulty talking and swallowing.

An acquired macroglossia is a very rare cause of CPAP intolerance. A pilot study in 2017 showed that nocturnal oxygen desaturations, which are suggestive for sleep-disordered breathing disturbances, are common in patients with amyloidosis that is localized in the oropharyngeal tract.<sup>6,7</sup>

Physiologic causes of sleep disturbances in amyloidosis are deposition of amyloid in the upper airway, neuropathy, or central sleep apnea in cardiac amyloidosis. Our patient did not have complaints of neuropathy and there was no central sleep apnea.

When patients have complaints of a swollen tongue, imaging and biopsy should be considered. Of course, acquired macroglossia is a rare cause of CPAP intolerance but it can have important consequences.

## ABBREVIATIONS

AHI, apnea-hypopnea index

CPAP, continuous positive airway pressure

OSA, obstructive sleep apnea

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## DISCLOSURE STATEMENT

Both authors have seen and approved the manuscript. Work for this study was performed at St. Antonius Ziekenhuis, Utrecht, The Netherlands. The authors report no conflicts of interest.