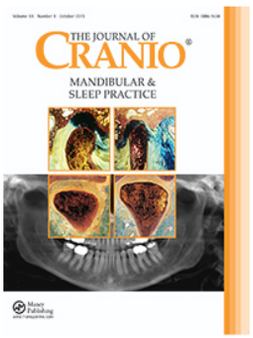

CRANIO®

The Journal of Craniomandibular & Sleep Practice

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ycra20

Obstructive sleep apnea caused by acromegaly: Case report

Ning Zhou , Jean-Pierre T.F. Ho , Nico De Vries & Jan De Lange

To cite this article: Ning Zhou , Jean-Pierre T.F. Ho , Nico De Vries & Jan De Lange (2020): Obstructive sleep apnea caused by acromegaly: Case report, CRANIO®, DOI: 10.1080/08869634.2020.1776530

To link to this article: https://doi.org/10.1080/08869634.2020.1776530

© 2020 The Author(s). Published with license by Taylor & Francis Group, LLC.

Published online: 02 Jun 2020.

Submit your article to this journal

Article views: 445

View related articles

View Crossmark data

Full Terms & Conditions of access and use can be found at https://www.tandfonline.com/action/journalInformation?journalCode=ycra20

CRANIO®: THE JOURNAL OF CRANIOMANDIBULAR & SLEEP PRACTICE
https://doi.org/10.1080/08869634.2020.1776530

Taylor & Francis
Taylor & Francis Group

CASE REPORT

OPEN ACCESS Check for updates

Obstructive sleep apnea caused by acromegaly: Case report

Ning Zhou MSD[a,b], Jean-Pierre T.F. Ho MD, DDS[a], Nico De Vries MD, PhD[b,c,d], and Jan De Lange MD, DDS, PhD[a]

[a]Department of Oral and Maxillofacial Surgery, Amsterdam UMC and Academic Center for Dentistry Amsterdam (ACTA), University of Amsterdam, Amsterdam, The Netherlands; [b]Department of Orofacial Pain and Dysfunction, Academic Center for Dentistry Amsterdam (ACTA), University of Amsterdam and VU University Amsterdam, The Netherlands; [c]Department of Otorhinolaryngology, Head and Neck Surgery, OLVG, Amsterdam, The Netherlands; [d]Department of Otorhinolaryngology, Head and Neck Surgery, Antwerp University Hospital (UZA), Antwerp, Belgium

ABSTRACT

Background: Acromegaly is an uncommon syndrome caused by growth hormone-producing pituitary adenoma or pituitary gland hypertrophy. Acromegaly is known to be characterized by progressive somatic disfigurement and a wide range of systematic manifestations. This case study describes a rare case of severe obstructive sleep apnea (OSA) caused by acromegaly.

Clinical Presentation: A female patient presented to the consultant clinic with the chief complaint of progressively worsening sleep and was diagnosed with severe OSA. Because of a peculiar facial appearance of the patient, acromegaly was suspected and confirmed by the findings of hormonal analysis and magnetic resonance imaging (MRI). After transsphenoidal resection of the pituitary adenoma, her OSA was almost cured, with residual AHI of 5.5.

Conclusion: This case highlights the importance of a comprehensive clinical examination of OSA patients. In every sleep-related breathing disorder case, sleep clinicians should be aware of alternate problems that could cause upper airway obstruction.

KEYWORDS
Obstructive sleep apnea; acromegaly; pituitary adenoma

Introduction

Acromegaly is a rare syndrome that affects both sexes equally, with an estimated annual incidence of three to four cases per million [1]. It is characterized by excessive secretion of growth hormone (GH) and insulin-like growth factor type 1 (IGF-1), largely owing to a hyperfunctioning pituitary adenoma [2]. It may present with a variety of clinical manifestations, the most common being acral and soft tissue overgrowth, diabetes mellitus, hypertension, and heart and respiratory comorbidities [3]. Currently, there is considerable evidence that acromegaly is associated with an increased risk of sleep apnea (SA), given that acromegaly alters the structure, elasticity, and function of the entire respiratory system [4].

This paper reports a rare case of severe obstructive sleep apnea (OSA) caused by acromegaly. The patient's OSA was almost cured following transsphenoidal resection of the pituitary adenoma.

Case presentation

In April 2013, a 50-year old woman who complained of poor sleep was diagnosed with moderately severe OSA at the Department of Otorhinolaryngology (ENT) and Head and Neck Surgery. Her polysomnogram (PSG) showed an apnea/hypopnea index (AHI) of 23.8 (Table 1). A mandibular advancement device (MAD) was prescribed. As shown in Table 1, a follow-up PSG 15 months later, performed with the MAD in situ, revealed a residual mild positional OSA with an AHI of 8.7 and an AHI supine of 14.3.

In November 2017, she presented to the Department of ENT and Head and Neck Surgery again, due to increasing complaints of poor sleep, snoring, apneas, choking, and not being refreshed after a night's rest, in spite of compliant use of the MAD. On physical examination, she weighed 71 kg, height was 168 cm, BMI was 25.2, and neck circumference was 34 cm. A PSG confirmed severe OSA (AHI = 74.1) (Table 1). A drug-induced sleep endoscopy (DISE) exhibited a total obstruction at velum and oropharynx levels, together with partial obstruction at tongue base and epiglottis levels. When the jaw thrust maneuver was applied, only the obstruction at tongue base level disappeared. Continuous positive airway pressure (CPAP) therapy was proposed and advocated by the ENT surgeon. However, the patient refused CPAP therapy.

The patient was referred to the Department of Oral and Maxillofacial Surgery (OMFS) for a maxillomandibular

CONTACT Ning Zhou ning.zhou115@gmail.com; n.zhou@amsterdamumc.nl Department of Oral and Maxillofacial Surgery, Amsterdam UMC, University of Amsterdam, Meibergdreef 9, Amsterdam 1105 AZ, The Netherlands

© 2020 The Author(s). Published with license by Taylor & Francis Group, LLC.
This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives License (http://creativecommons.org/licenses/by-nc-nd/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited, and is not altered, transformed, or built upon in any way.

Table 1. Results of polysomnogram.

	1st PSG	2nd PSG with MAD	3rd PSG	4th PSG
Parameters	April 2013	August 2014	February 2018	April 2019
AHI, events/h	23.8	8.7	74.1	5.5
AI, events/h	14.8	5.7	55.5	2.4
HI, events/h	9	2.9	18.6	3.2
AHI supine, events/h	43.5	14.3	62.2	5.4
AHI non-supine, events/h	17.6	3.5	81.6	5.9
Mean O^2 saturation, %	95	96	93	95
Minimum O^2 saturation, %	80	77	67	86
3% ODI, events/h	18.6	14.8	75.9	16
REM sleep rate, % TST	21.2	20.6	15.7	27.2

PSG: polysomnogram; MAD: mandibular advancement device; AHI: apnea-hypopnea index; AI: apnea index; HI: hypopnea index; ODI: oxygen desaturation index; REM: rapid eye movement; TST: total sleep time.

advancement (MMA). At this point, both the ENT surgeon and the maxillofacial surgeon noticed a peculiar facial appearance, e.g. thickened skin, widened nose, and pronounced chin. The patient was, therefore, also referred to the Department of Internal Medicine.

A thorough workup at the Department of Internal Medicine, including hormonal analysis and magnetic resonance imaging (MRI) (Figure 1), revealed the diagnosis of acromegaly, due to a pituitary macroadenoma. The patient was then referred to the Department of Neurosurgery for resection of the pituitary macroadenoma.

In September 2018, the patient underwent an endoscopic transsphenoidal resection of the pituitary macroadenoma. The histopathology confirmed a plurihormonal pituitary adenoma. The postoperative course was uneventful.

A follow-up PSG 7 months after surgery demonstrated a dramatic improvement of OSA (AHI = 5.5), as shown in Table 1. The patient reported significant improvement of sleep quality and did not show any symptoms of residual OSA. Her IGF-1 level remained normal in hormonal analysis at 13 months after surgery (81 nmol/L pre-surgery vs. 25 nmol/L post-surgery; reference range: 10–27 nmol/L).

However, 13 months after surgery, the clinical examination showed a malocclusion that had not been present at the initial consultation at the Department of OMFS. A cone beam computed tomography (CBCT) scan showed a significant condylar hyperplasia on the right side and a skeletal asymmetry. Different treatment options were discussed with the patient for creating an optimal occlusion and skeletal symmetry. However, the patient declined orthodontic treatment and/or orthognathic surgery because she did not want to have another operation. She was prescribed an Essix retainer to prevent further malocclusion, and she had regular checkups to evaluate possible further progression of asymmetry.

Discussion

Acromegaly is a rare disease that can lead to a multi-systemic disorder. Patients with acromegaly are at a high risk of developing SA, specifically OSA. In a review by Attal et al. [5], PSG-diagnosed OSA was found in an average of 69% of patients with active acromegaly in 11 studies (n = 239).

The pathophysiology of nocturnal airway obstruction in acromegaly is not yet understood, but it is thought to be multifactorial [4,6]. The persistent excessive GH and IGF-1 in acromegaly could cause anatomical changes, affecting the craniofacial bones and soft tissues, respiratory mucosa and cartilage, as well as the activity of the respiratory muscles, thus facilitating collapse or obstruction of the upper and middle oropharyngeal space during sleep.

This case, to the authors' knowledge, is the first reported acromegalic case where DISE was performed, by means of which dynamic evaluation of the upper airway during sleep was obtained. DISE revealed total obstruction during inspiration at the level of the soft palate and oropharynx with partial narrowing at the base of the tongue and epiglottis, which was similar to the outcome of the Muller maneuver in the study of Pelttari et al. [7]. In that study, significant narrowing during forced inspiration at the level of the soft palate was observed in 11 patients with acromegaly, while little if any narrowing occurred at the base of the tongue.

The effect of treated acromegaly on OSA is inconsistent. Tasbakan et al. [6] found that OSA commonly persisted in

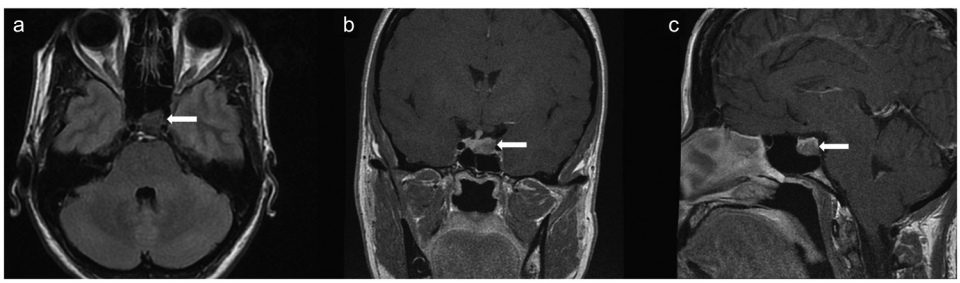

Figure 1. Preoperative magnetic resonance imaging in the axial (a), coronal (b), and sagittal (c) planes shows the large pituitary mass (indicated by arrows).

well-controlled acromegaly patients, despite normal levels of IGF-1 and GH after adenomectomy. In another study, it was demonstrated that surgical treatment of acromegaly had no significant effect on OSA [8]. In contrast, Buyse et al. [9] reported the cases of three acromegalic patients with severe OSA, who demonstrated a manifest improvement in apnea after treatment of acromegaly.

In this case, after adenomectomy, severe OSA was dramatically reduced, as was proven by the postoperative PSG. Therefore, the cure or control of acromegaly could be associated with alleviation of OSA, although further studies are needed to investigate this relationship. Swelling of soft tissue, owing to direct stimulation of the epithelial sodium channel by the high GH and IGF-1 levels, is considered to play a major role in the onset of OSA for patients with acromegaly. Therefore, the reduction of soft tissue swelling after the treatment of acromegaly, possibly leading to better upper airway patency, may be the main explanation for the patient's relief from OSA [5,10].

The patient in the current report was satisfied with the final treatment outcome and believed that all her concerns about sleep quality and daily energy had been addressed. She did not want any further orthodontic and/or orthognathic treatment for her facial asymmetry and malocclusion. Long-time follow-up is therefore needed to monitor the possible progression of her facial abnormalities and malocclusion, together with her OSA status.

Conclusion

Acromegaly, as a rare risk factor for OSA, is often detected late, owing to its insidious onset and slow progression. This case highlights the importance of clinical examination and diagnostic suspicion in OSA. Given the complex interplay of multiple etiologies in OSA, the assessment of patients with suspected OSA should take into consideration all the possible risk factors.

Disclosure statement

The authors declare no conflicts of interest.

Funding

No funding was received for this study.

ORCID

Ning Zhou MSD http://orcid.org/0000-0002-1927-3784

References

[1] Alexander L, Appleton D, Hall R, et al. Epidemiology of acromegaly in the Newcastle region. Clin Endocrinol. 1980;12:71–79.

[2] Ben-Shlomo A, Melmed S. Acromegaly. Endocrinol Metab Clin North Am. 2008;37(1):101–122.

[3] AlDallal S. Acromegaly: a challenging condition to diagnose. Int J Gen Med. 2018;11:337–343.

[4] Colao A, Ferone D, Marzullo P, et al. Systemic complications of acromegaly: epidemiology, pathogenesis, and management. Endocr Rev. 2004;25:102–152.

[5] Attal P, Chanson P. Endocrine aspects of obstructive sleep apnea. J Clin Endocrinol Metab. 2010;95 (2):483–495.

[6] Taşbakan MS, Kaçmaz Başoğlu Ö, Yıldırım Şimşir I, et al. Obstructive sleep apnea characteristics in patients with well-controlled acromegaly and their compliance with positive airway pressure therapy. Turk J Med Sci. 2017;47(5):1348–1353. DOI:10.3906/sag-1612-139.

[7] Pelttari L, Polo O, Rauhala E, et al. Nocturnal breathing abnormalities in acromegaly after adenomectomy. Clin Endocrinol (Oxf). 1995;43(2):175–182. DOI:10.1111/j.1365-2265.1995.tb01912.x.

[8] Chemla D, Attal P, Maione L, et al. Impact of successful treatment of acromegaly on overnight heart rate variability and sleep apnea. J Clin Endocrinol Metab. 2014;99 (8):2925–2931. DOI:10.1210/jc.2013-4288.

[9] Buyse B, Michiels E, Bouillon R, et al. Relief of sleep apnoea after treatment of acromegaly: report of three cases and review of the literature. Eur Respir J. 1997;10 (6):1401–1404. DOI:10.1183/09031936.97.10061401.

[10] Imbert-Teboul M, Doucet A, Chanson P, et al. Epithelial sodium channel is a key mediator of growth hormone-induced sodium retention in acromegaly. Endocrinology. 2008;149:3294–3305.