CASE REPORT

# A Case of Obstructive Sleep Apnea Syndrome in Acromegaly

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*Received on:* 10 August 2023; *Accepted on:* 25 October 2023; *Published on:* 23 November 2023

## Abstract

A 78-year-old male patient was referred with a history of snoring and excessive daytime sleepiness for 3 years. The patient was diagnosed case of Acromegaly due to pituitary microadenoma. He was evaluated with polysomnography, which confirmed severe obstructive sleep apnea syndrome (OSAS). Acromegaly is an endocrine disorder resulting from excessive secretion of growth hormone in adults. They have a high prevalence of OSAS which often goes undiagnosed. We report one such case of OSAS in a diagnosed case of Acromegaly.

**Keywords:** Acromegaly, Coronavirus disease-2019, Guidelines, Obstructive sleep apnea syndrome, Pituitary microadenoma, Sleep practice.

*Indian Journal of Sleep Medicine* (2023): 10.5005/jp-journals-10069-0121

## Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized by recurring episodes of collapse of the upper respiratory tract. The obstruction during sleep leads to arousal from sleep with or without oxygen desaturation. Obstructive sleep apnea syndrome is a common disease, detected in patients with definite comorbidities and risk factors.[1] In acromegaly patients, upper airway obstruction may develop due to enlarged tongue and thickened laryngeal tissues. Acromegaly cases are commonly diagnosed with OSAS.[2]

## Case Description

A 78-year-old man was referred for polysomnography (PSG) given complaints of dyspnea on exertion Grade I of modified Medical Research Council (mMRC) grading, snoring, excessive daytime sleepiness and irritability for 3 years. He also had a history of pulmonary tuberculosis 14 years back which was treated adequately. The patient was diagnosed case of Acromegaly due to pituitary microadenoma and was receiving the tablet cabergoline 0.5 mg once a week. He was also a known case of chronic kidney disease (CKD) on conservative medical management without dialysis including oral sodium bicarbonate, angiotensin-converting enzyme inhibitor drug, and diabetes mellitus treated with injection insulin. On physical examination features like frontal bossing, widening of nasal bridge, thick lips, macroglossia and widening of fingers and toes were present (Figs 1 and 2). The patient's body mass index (BMI) was 28.2 kg/m$^2$. Sleep evaluation revealed unrefreshing sleep and excessive daytime sleepiness. His Epworth sleepiness score (ESS) was 16. The pretest probability scores for OSAS including the sleep apnea clinical score (SACS) and STOP BANG indicated a high pretest probability for OSAS. High-resolution computed tomography (HRCT) thorax revealed diffuse fibro bronchiectatic changes in the left upper lobe with compensatory hyperinflation of the right upper lobe and retrosternal herniation (Fig. 3). A two-dimensional echocardiography revealed mild right atrium and right ventricle hypertrophy with moderate pulmonary hypertension. Evaluation of acromegaly was available. The serum IGF-1 (insulin-like growth factor-1) level was 432 µg/L (normal values: 81–220 µg/L). Magnetic resonance imaging (MRI) brain showed asymmetrical enlargement of the right half of the pituitary measuring 8 mm in maximum length with few cystic changes (Fig. 4). Spirometry showed moderate obstructive abnormality with a forced expiratory volume in 1 second (FEV1) to forced vital

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**How to cite this article:** Najeeb N, Bhalerao SS, Chintalwar VM, *et al*. A Case of Obstructive Sleep Apnea Syndrome in Acromegaly. Indian J Sleep Med 2023;18(3):50–52.

**Source of support:** Nil

**Conflict of interest:** None

**Fig. 1:** Acromegaly patient with frontal bossing, widening of nasal bridge, thick lips, macroglossia

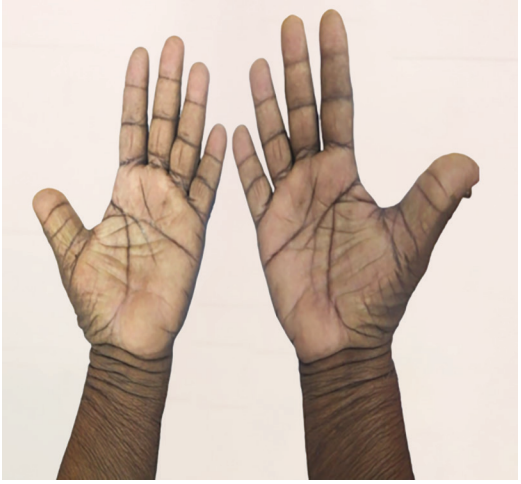

**Fig. 2:** Acromegaly patient with widening of fingers and toes

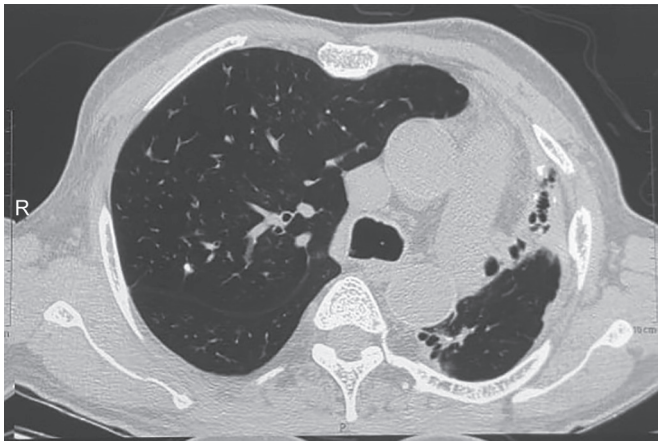


**Fig. 3:** High resolution computed tomography thorax showing diffuse fibrobronchiectatic changes in the left upper lobe with compensatory hyperinflation of right upper lobe and retrosternal herniation

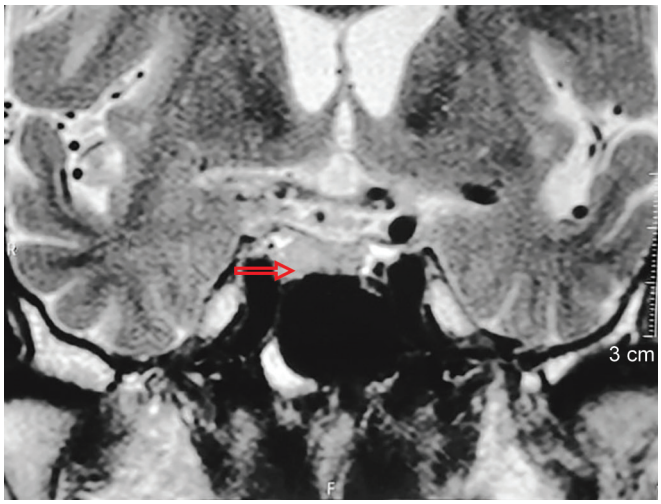


**Fig. 4:** MRI brain showing asymmetrical enlargement of right half of pituitary measuring 8 mm in maximum length with few cystic changes

capacity (FVC) ratio of less than 0.7 and FEV1 of 1.07 liters (51% predicted) without post bronchodilator reversibility (PBDR) of 1% and 20 mL. A level 3 polysomnography (PSG) was performed. It measured an apnea-hypopnea index (AHI) of 31.5/h suggestive of severe OSAS, oxygen desaturation index (ODI) of 16.4/h, average saturation of oxygen of 94%, and minimum saturation of oxygen during sleep of 82%. On continuous positive airway pressure (CPAP) titration, the AHI was corrected to 4.1/h with a mean pressure of 11.6 cm $H_2O$. The final diagnosis of overlap syndrome (post-infectious obliterative bronchiolitis due to past treated pulmonary tuberculosis with OSAS) with acromegaly with diabetes mellitus and CKD was made. The patient was prescribed CPAP therapy for OSA. In addition, inhaled corticosteroids along with long-acting beta 2 agonists were added due to a history of multiple exacerbations were prescribed. The previous treatment of Cabergoline 0.5 mg once a week for acromegaly, insulin for diabetes mellitus, and conservative medical management without dialysis for CKD was continued. The patient was doing well with good response with management of all the coexisting comorbidities.

## Discussion

Acromegaly is an uncommon condition, associated with elevated growth hormone (GH) and Insulin-like growth factor 1 (IGF-1), mostly due to a pituitary adenoma (PA). Adequate treatment restores it to normal and mortality increases where the disease is not controlled.[3] It is a slowly progressive disease and there is a delay in diagnosis which adversely affects the prognosis. The prevalence is approximately 2.8–13.7 cases per lakh and the annual incidence rates between 0.2 and 1.1 per lakh population.[4] A sporadic growth hormone-secreting tumor is the most common cause of acromegaly. However, acromegaly can be due to inherited causes in association with other endocrine abnormalities (Multiple endocrine neoplasia type 1, Carney complex, and McCune–Albright syndrome) or as an isolated disorder. Pathogenesis of sporadic cases is well known. Ectopic GH production from ectopic PA and extrapituitary tumors of the pancreas, ovary, and lung is very rare. Growth Hormone-secreting pituitary adenoma is classified into two histological subtypes densely granulated (DG) and sparsely granulated (SG). The later subtype is more aggressive and occurs in young and poorly responds to somatostatin analogs. The most commonly occurring symptoms are somatic changes (jaw protrusion, prominent forehead, and enlargement of extremities), joint pain, osteoarthritis, systemic hypertension, cardiac dysrhythmias, diabetes mellitus, colon polyps, sleep apnea, upper airway obstruction, etc. The disease development is insidious; hence, the patients present late when they have developed specific complications. The common comorbidities are sleep apnea, systemic hypertension, and diabetes mellitus.[5] There is an increased death risk in Acromegaly patients mostly due to cardiovascular and respiratory comorbidities.[6,7] The common respiratory complications are as respiratory failure and OSAS in acromegaly patients.[8] In OSAS there is abnormal ventilation during sleep. Obstructive sleep apnea syndrome is defined as excessive daytime somnolence with any two of the following symptoms, i.e., snoring, apneas, unrefreshed sleep, poor concentration, and fatigue with a sleep study documenting an AHI of more than 5 events per hour. The risk factors for OSAS are male gender, old age, obesity, craniofacial deformities, smoking, alcohol consumption, and certain medications.[9,10] Our case had the risk factors of diabetes mellitus, CKD, COPD along acromegaly.

Obstructive sleep apnea syndrome is observed from 20 to 80% of acromegaly due to changes in the craniofacial bones and soft tissue swelling. Older age and higher neck circumference increase the risk of OSA in acromegaly.[8] Excess GH and IGF-1 may impair brain control of respiration causing central sleep apneas. As per the guidelines, it is necessary to conduct a screening test and IGF-1 levels especially when multiple medical comorbidities are present such as OSA.[11] As per recommendations, it is necessary to complete both ESS and sleep studies at diagnosis and follow-up.[12] Taşbakan et al. found that despite normal levels of GH and IGF-1 after surgery, OSAS was persistent in their cases of acromegaly.[13] Another study reported that surgery for acromegaly had no significant effect on OSAS.[14] In contrast, Buyse et al.[15] reported improvement in three acromegaly patients with severe OSAS after surgery. This was difficult to comment on in our case as our patient had not undergone surgery for pituitary microadenoma. He was managed on oral Cabergoline and had other risk factors along with acromegaly like DM, CKD, and COPD. Various treatment modalities are now available for the treatment of OSAS. Continuous positive airway pressure (CPAP) is the gold standard management in OSAS. Mandibular advancement devices can be used in mild to moderate OSA and can be considered as an alternate therapy in patients who are unable to tolerate CPAP. Uvulopalatopharyngoplasty is a surgical procedure considered rare if CPAP is contraindicated. Maxillary and mandibular correction surgeries can be attempted for craniofacial abnormalities.[16] Dopamine agonists, somatostatin analogs, and GH receptor antagonists are a medical line of management for acromegaly. Surgery for the tumor is best preferred in pituitary micro-and macro-adenomas.[11] Radiotherapy is a less preferred choice. Treatment of underlying acromegaly does improve OSAS, but in most cases requires simultaneous therapy with CPAP as in our case.

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