

## Case Report

## Acromegaly and Sleep Apnea Syndrome

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**Abstract:** Acromegaly is a rare disease linked to an excessive secretion of growth hormone that causes cardiovascular, metabolic, articular, bone, neoplastic and respiratory disorders including sleep apnea syndrome. The prevalence of sleep apnea syndrome (SAS) during acromegaly is high. Becoming the latter is variable under treatment: improvement, stabilization or deterioration. His research must then be systematic. The objective is to specify the characteristics of SAS in an acromegalic population.

**Keywords:** Acromegaly; Pituitary adenoma; Sleep apnea syndrome; Continuous positive airway pressure.

### INTRODUCTION

Acromegaly is an acquired disease, rare (1 in 15,000 to 1 in 25,000), related to excessive secretion of growth hormone (GH); most often occurring between the ages of 30 and 40 and affecting as many women as men (Blanco. Pérez. J. *et al.*, 2004). This disease is characterized by a progressive onset of a dysmorphic syndrome when it appears after puberty and a gigantism when it occurs before, with a significant systemic impact.

The sleep apnea syndrome (SAS) is one of the most common complications of acromegaly (it affects 69% of acromegalic patients on average), which can aggravate hypertension, insulin resistance and blood disorders, carbohydrate metabolism and consequently increase cardio- and cerebrovascular morbidity with a repercussion on the quality of life, hence the interest of systematic research in these patients (Attal, P., & Chanson, P. 2010; Weiss, V. *et al.*, 2000)

Surgical or medical treatment (somatostatin analogs, growth hormone receptor antagonists) often improves SAS, but assisted ventilation or CPAP treatment remains the basic treatment for this syndrome.

### Sleep Apnea Syndrome

Sleep apnea syndrome is defined as the occurrence of more than 5 episodes of apnea-hypopnea per hour of sleep (apnea-hypopnea index [IAH]> 5)

associated with an increase in daytime sleepiness or at 2 following symptoms:

- A non-restorative sleep.
- A feeling of night choking, or repeated nighttime awakenings.
- Asthenia, disorders of alertness and concentration.

Apnea is defined by the disappearance of the naso-oral respiratory flow for more than 10 seconds. So, that a hypopnea is defined by the decrease in respiratory rate by at least 50% for at least 10 seconds.

Apnea-hypopneas lead to recurrent episodes of decreased arterial oxygen saturation (a decrease of at least 4% from the usual level), resulting in repeated micro-awakenings.

Recent studies have shown a frequency of SAS between 46% and 87.5% (Davi, M. V. *et al.*, 2008), (69% on average in acromegalic patients), without forgetting the syndrome of the legs without rest, found in more than 20% of these patients (Cannavo, S. *et al.*, 2011).

### Pathophysiology

During inspiration, the contraction of the diaphragm generates an intra-thoracic pressure that is negative and tends to occlude the airways; however, the tonicity of the wall of the oropharynx and the

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contraction of the dilator muscles of the upper airways are opposed to the normal state.

During acromegaly, there will be an imbalance between these two forces with (Isono, S. *et al.*, 1999):

- Narrowing of the upper airways, due to the presence of macroglossia.
- Hypertrophy of the laryngeal mucosa, with lengthening and thickening of the soft palate.
- Alteration of the passive mechanical properties of the velopharynx and oropharynx due to their infiltration (presence of glycosamino-glycans deposits and increase of collagen production with soft tissue edema secondary to the increase in the reabsorption of sodium through the distal convoluted tubule).
- Modifications of the skeleton, especially of the mandible, due to dorso-caudal development, cause a retroposition of the base of the tongue and subsequently a reduction of the pharyngeal air space (Dostalova, S. *et al.*, 2001; Hochban, W. *et al.*, 1999).

To all these factors is added: age, body mass index (BMI) and in particular, abdominal overweight (Rodrigues, M. P. *et al.*, 2008), making it very easy to collapse the airways and subsequently, the onset obstructive apnea and hypopnea in patients who have this disease.

**N.B:** The pathogenesis of central apnea remains less clear; some studies suggest the direct role of increasing plasma GH levels. In addition, patients with central apnea exhibit an abnormal ventilatory response to hypoxia in a hypercapnic situation.

#### Diagnosis of Sleep Apnea Syndrome:

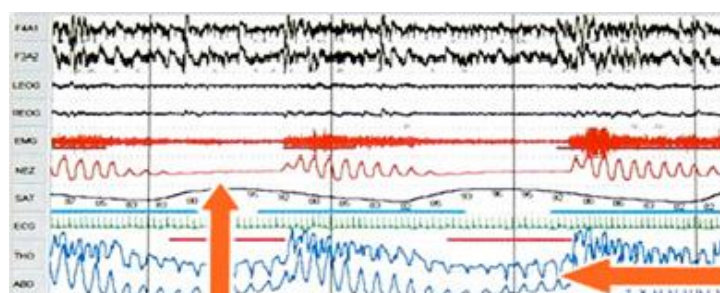


Fig-1: example of pathological polysomnography plot.

**The ventilation polygraphy:** feasible at home and can be offered as first-line therapy in case of clinical signs typical of sleep apnea syndrome.

It is used to record:

- The ventilatory flow.
- The respiratory efforts.
- The arterial oxygen saturation.
- The electrocardiogram (ECG).

#### The Usual Clinical Picture:

Several clinical signs can guide the diagnosis of sleep apnea syndrome:

- Non-restorative sleep, repeated night-time awakenings with sometimes a feeling of suffocation, or nocturnal polyuria.
- An increase in daytime sleepiness, evaluated by the Epworth scale (pathological if the score is greater than 10).
- Snoring or interruptions of breathing during sleep that may be reported by the spouse.
- Other symptoms, some of which are common with acromegaly, such as asthenia, headache, sweating, or even a decline in libido.

#### Confirmation of Diagnosis:

**Polysomnography:** is the reference exam whose realization most often requires hospitalization.

This technique makes it possible to quantify apneas or hypopneas, to verify their obstructive or non-obstructive nature and to document the sleep disruption characteristic of SAS (Fig-2)

It includes:

- The measurement of the ventilatory flow.
- The measurement of thoraco-abdominal movements or esophageal pressure.
- Achieving oximetry.
- The study of sleep with quantification of micro-arousals.

An AHI greater than 5 and an index of micro-arousals greater than 10 are considered pathological.

An AHI greater than 30 is enough to make the diagnosis of severe SAS. However, this study does not study sleep disorders, requiring the realization of a complementary polysomnography in order to measure the index of micro-arousals and to guide the therapeutic attitude.

**Night oximetry:** makes it possible to evoke an SAS if the index of oxygen desaturation (number of episodes of decrease in arterial oxygen saturation greater than

4% per hour of sleep) is greater than or equal to 10, or, for some, at 15.

### Consequences of sleep apnea syndrome in acromegaly:

**Metabolically** (Bradley, T. D., & Floras, J. S. 2009; Al Lawati, N. M. *et al.*, 2009 ; van Haute, F. R. *et al.*, 2008), the SAS increases the risk of:

- Metabolic syndrome.
- HTA, conduction disorders and heart rhythm.
- Coronary insufficiency and stroke.

**On the quality of life of patients**, the SAS causes:

- drop in vitality.
- Disorders of memory and concentration, with decreased intellectual performance.
- Mood disturbances.
- Relative risk of road accidents due to daytime sleepiness.

### The therapeutic management of sleep apnea syndrome during acromegaly (Epstein, L. J. 2009) is based on:

The treatment of hypersomatotropism, whether surgical or medical (Ip, M. S. M. *et al.*, 2001 ; Herrmann, B. L. *et al.*, 2004 ; Sze, L. 2007) (somatostatin analogs or GH receptor antagonist), can correct or improve SAS by decreasing infiltration and edema of soft tissues.

- Dietary management of an existing overweight.

- Elimination of sedative therapies and alcoholic drinks aggravating the hypotonia of the upper airways.

- Mechanical ventilation by continuous positive pressure (cPAP) is proposed from the outset to patients with severe SAS (IAH greater than 30 or if an IAH greater than 10 and associated with a micro-arousal index greater than 10) and whose the goal is to keep the upper airways open and to clear apneas and hypopneas and also snoring. However, this medication is most often subject to mask tolerance problems by the patient and his spouse.

- 2-level pressure ventilation is proposed when SAS is associated with obesity-hypoventilation syndrome.

Normalization of IAH is mainly observed in patients who initially had moderate SAS. However, SAS persists in more than 40% of cases of acromegaly treated, this illustrates the multifactorial nature of the pathophysiology of SAS in acromegaly (role of obesity) and is also probably the consequence of skeletal changes not reversible after correction of hypersomatotropism.

### Conclusion

Sleep Apnea Syndrome is a severe and frequent complication during acromegaly, which may increase the risk of cardiovascular and cerebrovascular morbidity and mortality.

It must be systematically researched and confirmed by performing a polysomnography, or even a polygraphy and whose treatment is based on cPAP from the outset during severe forms, not to mention the basic treatment (surgical and / or medical) whose purpose and reduce tumor size, hyper-somatotropism, complications of acromegaly and ultimately, improve the quality of life in these patients.

### REFERENCES

1. Blanco Pérez JJ, Blanco-Ramos MA, Zamarrón Sanz C, Souto Fernández A, Mato Mato A, Lamela López J.( 2004). Acromegaly and sleep apnea. *Arch Bronconeumol*,40(3),55-9.
2. Attal, P., & Chanson, P. (2010). Endocrine aspects of obstructive sleep apnea. *The Journal of Clinical Endocrinology & Metabolism*, 95(2), 483-495.
3. Weiss, V., Šonka, K., Pretl, M., Dostalova, S., Klozar, J., Rambousek, P., ... & Haas, T. (2000). Prevalence of the sleep apnea syndrome in acromegaly population. *Journal of endocrinological investigation*, 23(8), 515-519.
4. Davi, M. V., Dalle Carbonare, L., Giustina, A., Ferrari, M., Frigo, A., Cascio, V. L., & Francia, G. (2008). Sleep apnoea syndrome is highly prevalent in acromegaly and only partially reversible after biochemical control of the disease. *European journal of endocrinology*, 159(5), 533-540.
5. Cannavo, S., Condurso, R., Ragonese, M., Ferrau, F., Alibrandi, A., Arico, I., ... & Silvestri, R. (2011). Increased prevalence of restless legs syndrome in patients with acromegaly and effects on quality of life assessed by Acro-QoL. *Pituitary*, 14(4), 328-334.
6. Isono, S., Saeki, N., Tanaka, A., & Nishino, T. (1999). Collapsibility of passive pharynx in patients with acromegaly. *American journal of respiratory and critical care medicine*, 160(1), 64-68.
7. Dostalova, S., Šonka, K., Smahel, Z., Weiss, V., Marek, J., & Horinek, D. (2001). Craniofacial abnormalities and their relevance for sleep apnoea syndrome aetiopathogenesis in acromegaly. *European journal of endocrinology*, 144(5), 491-497.
8. Hochban, W., Ehlenz, K., Conrath, R., & Brandenburg, U. (1999). Obstructive sleep apnoea in acromegaly: the role of craniofacial changes. *European Respiratory Journal*, 14(1), 196-202.
9. Rodrigues, M. P., Naves, L. A., Casulari, L. A., Silva, C. M., Paula, W. D., Cabral, M. T., ... & Viegas, C. A. (2008). Craniofacial abnormalities, obesity, and hormonal alterations have similar

- effects in magnitude on the development of nocturnal hypoxemia in patients with acromegaly. *Journal of endocrinological investigation*, 31(12), 1052-1057.
10. Epstein, L. J., Kristo, D., Strollo, P. J., Friedman, N., Malhotra, A., Patil, S. P., ... & Weinstein, M. D. (2009). Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *Journal of clinical sleep medicine*, 5(03), 263-276.
  11. Bradley, T. D., & Floras, J. S. (2009). Obstructive sleep apnoea and its cardiovascular consequences. *The Lancet*, 373(9657), 82-93.
  12. Al Lawati, N. M., Patel, S. R., & Ayas, N. T. (2009). Epidemiology, risk factors, and consequences of obstructive sleep apnea and short sleep duration. *Progress in cardiovascular diseases*, 51(4), 285-293.
  13. van Haute, F. R., Taboada, G. F., Corrêa, L. L., Lima, G. A., Fontes, R., Riello, A. P., ... & Gadelha, M. R. (2008). Prevalence of sleep apnea and metabolic abnormalities in patients with acromegaly and analysis of cephalometric parameters by magnetic resonance imaging. *European journal of endocrinology*, 158(4), 459-465.
  14. Ip, M. S. M., Tan, K. C. B., Peh, W. C. G., & Lam, K. S. L. (2001). Effect of Sandostatin® LAR® on sleep apnoea in acromegaly: correlation with computerized tomographic cephalometry and hormonal activity. *Clinical endocrinology*, 55(4), 477-483.
  15. Herrmann, B. L., Wessendorf, T. E., Ajaj, W., Kahlke, S., Teschler, H., & Mann, K. (2004). Effects of octreotide on sleep apnoea and tongue volume (magnetic resonance imaging) in patients with acromegaly. *European journal of endocrinology*, 151(3), 309-315.
  16. Sze, L., Schmid, C., Bloch, K. E., Bernays, R., & Brändle, M. (2007). Effect of transsphenoidal surgery on sleep apnoea in acromegaly. *European Journal of Endocrinology*, 156(3), 321-329.
  17. Berg, C., Wessendorf, T. E., Mortsch, F., Forsting, M., Teschler, H., Weischer, T., ... & Herrmann, B. L. (2009). Influence of disease control with pegvisomant on sleep apnoea and tongue volume in patients with active acromegaly. *European journal of endocrinology*, 161(6), 829-835.