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Sleep Apnea-Hypopnea Syndrome at the Onset of Acromegaly Due to Ectopic Secretion by a Pancreatic Neuroendocrine Tumor

Síndrome de apneas-hipoapneas durante el sueño como forma de inicio de acromegalia por secreción ectópica a tumor neuroendocrino pancreático

To the Editor:

Sleep apnea-hypopnea syndrome (SAHS) is common in patients with acromegaly and both conditions are independently associated with hypertension and insulin resistance, conditions which increase morbidity and mortality.¹ Acromegaly caused by ectopic oversecretion of growth hormone is unusual (with an incidence of <1%²) and has not been reported in association with SAHS. We describe a case in which SAHS was the first sign of ectopic acromegaly secondary to a pancreatic neuroendocrine tumor metastasized to the liver.

The patient was a 40-year-old man referred to our sleep clinic for snoring, witnessed apneas, and a 6-month history of mild daytime sleepiness. Twenty-one months earlier, asymptomatic hypertension (220/140 mm Hg) was detected. A pseudonodular lesion at the head of the pancreas and 20 nodular lesions on the liver were also identified; after resection, the lesions were diagnosed as a pancreatic neuroendocrine tumor and hepatic metastases. Three months before coming to the sleep clinic, the patient had begun treatment with lanreotide in gel form at a dosage of 120 mg/mo after he was diagnosed with acromegaly secondary to ectopic secretion by the tumor of 811 µg/L of type 1 insulin-like growth factor, 2.7 µg/L of growth hormone after an oral glucose tolerance test, and 1273 pg/mL of growth-hormone releasing factor. Noteworthy findings of physical examination included a score of 9 on the Epworth sleepiness scale, blood pressure of 140/90 mm Hg, a body mass index of 28.4 kg/m², a neck circumference of 43 cm, a Mallampati class III score, upper airway narrowing due to soft palate hypertrophy, and mild prognathism. Nighttime polysomnography demonstrated sleep efficiency of 86%, abnormal sleep architecture with a reduced percentage of rapid eye movement sleep (2.3%) and a high percentage of superficial sleep stages (stage 1-2, 64%; stage 3-4, 33.7%), apnea-hypopnea index of 30 events/h due to obstructive apneas, an arousals at a rate of 28/h, arterial oxygen saturation of 92% with 16 desaturations/h, and 0.6% of sleep time with oxygen saturation less than 90%. Continuous positive airway pressure (CPAP) was adjusted in incremental steps during the second part of the night, until most events were corrected with a flow of 7 cmH₂O (Figure). With a diagnosis of SAHS related to acromegaly due to ectopic secretion by a metastatic neuroendocrine tumor, nighttime CPAP treatment through a nasal canula was started. Tolerance and adherence were good. A year later, under controlled conditions, treatment with analogs was withdrawn and polysomnographic

abnormalities were once again demonstrated. Four years after the initial diagnosis, the patient was alive and continued to use CPAP, even though hepatic metastases were persistent.

The prevalence of SAHS in patients with acromegaly is approximately 60%, with rates ranging from 19% to 93% in different series.³ Most patients with acromegaly and SAHS have obstructive apneas, although central apneas have been described in a third of cases and are possibly attributable to a direct effect on respiratory drive of elevated growth hormone, or insulin-like growth factor, or somatostatin levels.⁴ Patients with central apneas and acromegaly also have a more marked response to hypercapnic hypoxia.⁴ Acromegaly leads to important structural changes in para- and retropharyngeal soft tissues and these can disrupt the balance of forces during inspiration, enhancing pharyngeal collapsibility during sleep.⁵ The relationships between craniofacial changes, hormone activity in acromegaly, and treatment with somatostatin analogs, and the presence and severity of apneas are disputed.^{3,6,7} The treatment of acromegaly (surgery, radiotherapy, or somatostatin analogs) improves but rarely cures SAHS, which persists if growth hormone secretion is not halted, possibly because structural changes in the soft tissue and bony structures of the upper airway are irreversible.³ Sleep studies are therefore needed in order to start treatment as soon as possible, as prognosis may be affected even though mortality has not been shown to decrease.⁵ SAHS in association with ectopic acromegaly has not been described in the literature, possibly because the incidence is low and survival as in our patient's case may be exceptional. We emphasize the presence of symptoms of SAHS as the initial manifestation of ectopic acromegaly even before SAHS was diagnosed, and also the fact that the patient continues to require CPAP treatment in spite of therapeutic control of the underlying disease. The explanation may be the metastases that were not removed or the presence of irreversible changes in craniofacial structures and soft tissues caused by ectopic secretion of growth hormone.

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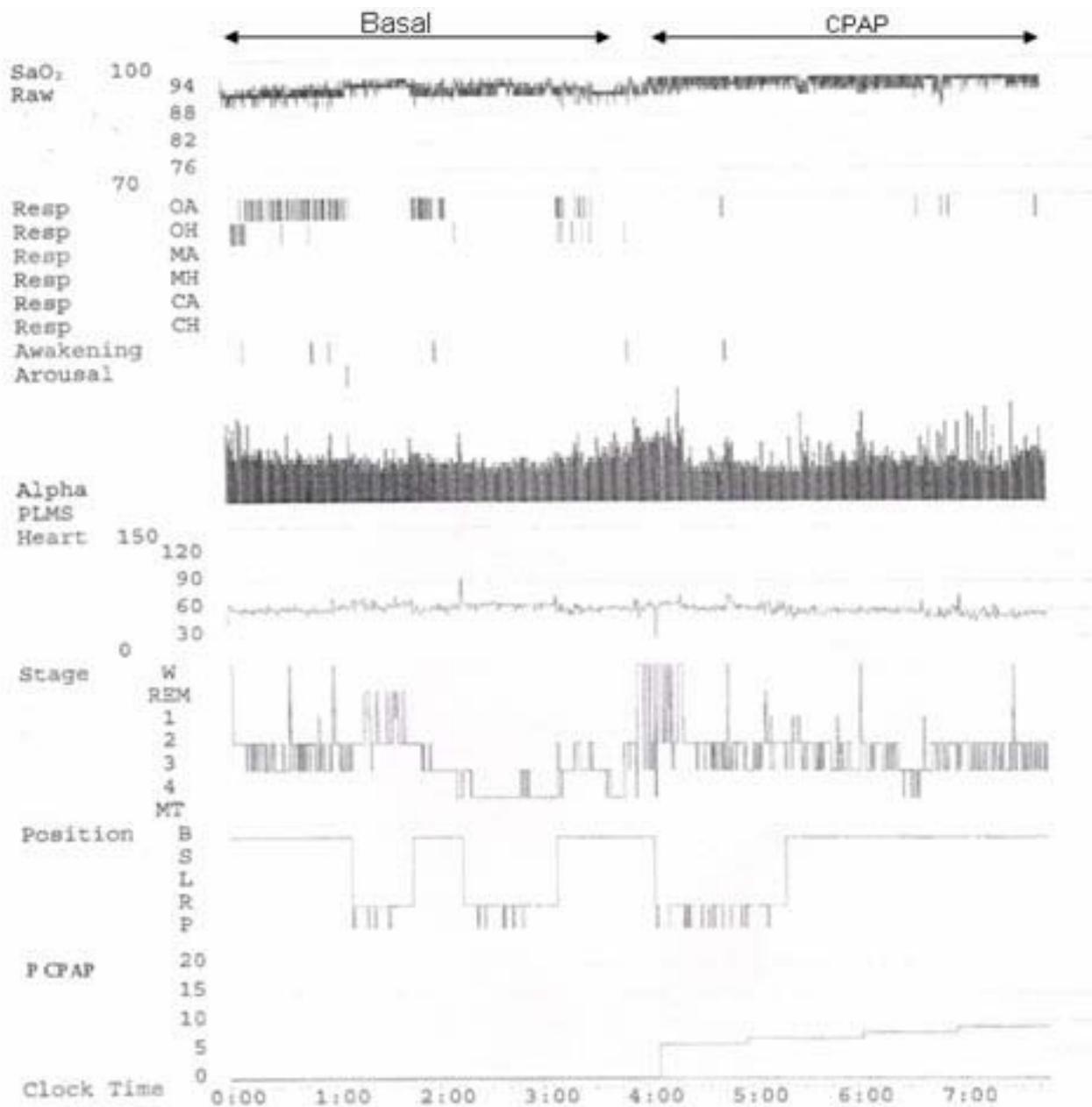


Figure. Split-night polysomnography findings for a patient with acromegaly due to ectopic secretion of growth hormone related to a pancreatic tumor and hepatic metastasis. The findings indicate severe sleep apnea-hypopnea syndrome, with normalization of the apnea-hypopnea index with continuous positive airway pressure (CPAP) during the second part of the night. Basal indicates baseline; SaO₂, oxygen saturation; Resp, breathing; PLMS, periodic limb movements in sleep; W, awake; REM, rapid eye movement; MT, time in movement; B, body; S, supine; L, left; R, right; P, prone; and PCPAP, level of CPAP pressure.

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