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ORIGINAL ARTICLE

Severe sleep apnea–hypopnea syndrome is related to left ventricle dysfunction and hypertrophy in acromegalic patients

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KEYWORDS
Acromegaly;
Cardiomyopathy;
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Sleep-disordered breathing

Abstract
Objective: To assess whether sleep apnea-hypopnea syndrome (SAHS) is a risk factor for development of acromegalic cardiomyopathy.
Methods: A descriptive, cross-sectional study of 32 patients with acromegaly (15 categorized as non-controlled-NCA and 17 as controlled-CA) compared to 20 matched controls (by sex, age, and BMI) referred to the pulmonology department for suspected SAHS. Polysomnography, echocardiography (M-mode, 2-dimensional, and Doppler), and 12-lead electrocardiography were performed in all participants. Development of cardiac morbidity (ischemia heart disease or heart failure) was evaluated after 7 years.
Results: SAHS was diagnosed in 81.3% of patients with acromegaly and 85% of controls. Mild SAHS was more common in CA than in NCA patients (31.3% vs. 0%, $p = 0.048$). There was a trend to greater prevalence of left ventricular diastolic dysfunction (LVDD) in acromegalic patients as compared to controls (58.1% vs. 30%, $p = 0.05$). Presence of severe SAHS in patients with acromegaly was related to greater risk of LVDD (90.9% vs. 40%, $p = 0.008$; OR 2.3 [1.3–4.0]), LV hypertrophy (55.6% vs. 10.5%, $p = 0.02$; OR 5.3 [1.3–22.2]), and cardiac events (87.5% vs. 35.6%; $p = 0.01$; OR 7.53 [1.07–53.24]).
Conclusion: SAHS is highly prevalent in patients with acromegaly. Only in these patients was severe SAHS associated to hypertrophy, LV diastolic dysfunction, and cardiac events.

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PALABRAS CLAVE
Acromegalia;
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Síndrome de apnea-hipopnea del sueño;
Transtorno respiratorio del sueño

El síndrome de apnea-hipoventilación del sueño grave se asocia a disfunción del ventrículo izquierdo e hipertrofía cardíaca en pacientes acromegálicos

Resumen
Antecedentes y objetivo: La acromegalia se asocia con el síndrome de apnea-hipopnea del sueño (SAHS) y cambios a nivel cardíaco. Nuestro objetivo es evaluar si la presencia de SAHS es un factor de riesgo de desarrollo de cardiomiopatía acromegálica.
Material y método: Estudio transversal descriptivo de 32 pacientes acromegálicos (15 clasificados como no-controlados−NCA- y 17 como controlados-CA-) comparados con 20 controles pareados (en sexo, edad e IMC) derivados al Servicio de Neumología por sospecha de SAHS. Se realizó polisomnografía, ecocardiografía (M-modo, 2-dimensiones, y Doppler) y electrocardiograma de 12-derivaciones a todos los participantes. Tras 7 años, se evaluó el desarrollo de morbilidad cardiológica (isquemia o insuficiencia cardíacas reportadas).
Resultados: 81,3% pacientes acromegálicos y 85% controles se diagnosticaron de SAHS. SAHS leve fue más frecuente en CA que NCA (31,3% vs. 0%, p = 0,048). Existía una tendencia a mayor prevalencia de disfunción diastólica del ventrículo izquierdo (DDVI) en los pacientes acromegálicos comparados con los controles (58,1% vs. 30%, p = 0,05). La presencia de SAHS grave en los pacientes acromegálicos se relacionó con mayor riesgo de DDVI (90,9% vs. 40%, p = 0,008; OR 2,3 [1,3−4,0]), hipertrofia del VI (55,6% vs. 10,5%, p = 0,02; OR 5,3 [1,3−22,2]) y eventos cardíacos (87,5% vs. 35,6%; p = 0.01; OR 7.53 [1.07−53.24]).
Conclusiones: SAHS es muy frecuente en los pacientes acromegálicos. Sólo en pacientes acromegálicos, el SAHS grave se asoció con hipertrofia, disfunción diastólica del VI y eventos cardíacos.

Introduction

Sleep apnea−hypopnea syndrome (SAHS) is characterized by episodes of interruption of respiration associated with fragmented sleep and hypoxia. It can be divided into obstructive sleep apnea (OSA), defined by recurrent episodes of either partial or complete upper airway obstruction during sleep, and central sleep apnea (CSA), with reductions in central respiratory drive.[1] SAHS is frequently associated with cardiovascular diseases in general population. It has been described that 40% of patients with hypertrophic cardiomyopathy also have SAHS and it is related to left atrial and aortic enlargement.[2] It is also a frequent association between SAHS and heart failure. The negative intrathoracic pressure produced during obstructive apneas increases left ventricular (LV) after load, reduces cardiac output, and may promote the progression of heart failure. Moreover, intermittent hypoxia and reoxygenation cause vascular endothelial damage and could be associated with coronary artery disease and ischemic cardiomyopathy.[3] Indeed, it has been proven that SAHS, in particular central sleep apnea, is an independent predictor of readmission in hospitalized patients with systolic heart failure.[4] Furthermore several investigations reported an increasing frequency of cardiac arrhythmias among SAHS patients as consequence structural myocardial changes induced by recurrent hypoxemias and an increased sympathetic activity.[2,5]

Acromegaly is a rare disease, with an estimated prevalence around 69 cases per million inhabitants, characterized by an excess of growth hormone that causes important morbidity affecting cardiac and respiratory systems among others.[1] Acromegaly induces myocardial hypertrophy and fibrosis of left ventricle, causing diastolic and more rarely systolic dysfunction and arrhythmias.[6] It is known that cardiac involvement is the major determinant of the shortened life expectancy in these patients.[7] There has been described a prevalence around 36−58% of left ventricle diastolic dysfunction (LVDD).[7,8] On the other hand, SAHS affects 67−75% of acromegalic patients, although higher prevalence has been described.[1] In acromegaly, OSA is more frequent than CSA due to craniofacial deformations, hypertrophy of pharyngeal soft tissue, macroglossia and thickening of upper airway. CSA is caused by central inhibition of breathing center by elevated levels of GH/IGF-1 serum levels.[9]

Some studies have explored the association between SAHS and cardiovascular outcomes in general population,[2–5] but there are few data referred to acromegaly. Our purpose was to evaluate if SAHS is a risk factor to myocardiopathy on acromegalic patients.

Materials and methods

It was designed a prospective observational descriptive study of 32 acromegalic patients (14 men, 50.3 ± 11.4 years, $29.4 \pm 4.8\,kg/m^2$) treated in the Endocrinology Department of Hospital General Universitario de Alicante. The study was offered to all acromegalic patients without known SAHS that visited our department in 2007. The diagnosis of acromegaly was made based on elevated age-adjusted IGF-1 levels and lack of suppression of GH to less than 1 ng/mL after oral glucose testing. Patients were classified as non-controlled acromegaly (15 patients, NCA) or controlled acromegaly