Refractory Hypertension and Obstructive Sleep Apnea

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ABSTRACT

Obstructive sleep apnea syndrome (OSAS) plays an important role in cardiovascular morbidity and mortality. Several mechanisms have been suggested to explain the morbid association between OSAS and cardiovascular disease, especially with hypertension (HT). About half of the patients with OSAS have hypertension, and the prevalence of OSAS is greater in hypertensive patients than in general population.
The current case report describes a patient with hypertension refractory to pharmacological treatment which presented favorable outcomes after OSAS was diagnosed and properly treated.

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Key words > Obstructive Sleep Apnea Syndrome - Hypertension

Abbreviations >

LA	Left atrium	**AHI**	Apnea-hypopnea index
CPAP	Continuous positive airway pressure	**AMI**	Acute myocardial infarction
Type 2 NIDDM	Type 2 non-insulin dependent diabetes mellitus	**BMI**	Body mass index
		APBM	Ambulatory blood pressure monitoring
ECG	Electrocardiogram	**O_2**	Oxygen
VPBs	Ventricular premature beats	**PCO_2**	Partial pressure of carbon dioxide
HR	Heart rate	**OSAS**	Obstructive sleep apnea syndrome
AF	Atrial flutter	**BP**	Blood pressure
HT	Hypertension	**LV**	Left ventricle

BACKGROUND

Several clinical and epidemiological data support the idea that patients with obstructive sleep apnea syndrome (OSAS) have increased cardiovascular risk. (1)This theory has been sustained by a few studies that have demonstrated the role OSAS plays on cardiovascular morbidity and mortality, even in presence of a limited number of episodes of nocturnal apnea. Several mechanisms have been suggested to explain the morbid association between OSAS and cardiovascular disease, with especially hypertension. Cardiovascular responses to apneas are acute, following each respiratory episode, and chronic. (2)

About half of the patients with OSAS suffer from hypertension, and the prevalence of OSAS among hypertensive patients is greater than in the general population. (3)

A significant association has also been demonstrated between OSAS and myocardial infarction irrespective of age, body mass index, hypertension, smoking habits and blood cholesterol levels, and the risk of myocardial infarction increases with the rise in the value of the apnea-hypopnea index. (4)

The current case report describes a patient with hypertension refractory to pharmacological treatment which presented favorable outcomes after OSAS was diagnosed and properly treated.

CASE REPORT

The patient was a 53-year old man with a history of mixed dyslipemia, hyperuricemia, fatty liver, ex-smoker (he gave up smoking 12 years ago), extracorporeal shock wave lithotripsy due to kidney stones, gastritis and gastroesophageal reflux, paroxysmal atrial flutter (AF) in 1999 and sexual dysfunction.

Family history: father: HT, type 2 NIDDM, AMI at the age of 54; mother: HT, breast cancer; younger sibling: HT.

Clinical manifestations: HT and chest pain.

Personal history: the patient had a history HT since the last 5 years and was currently receiving an-

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tihypertensive drugs with poor response to treatment; during the previous 10 days he started complaining of chest oppression unrelated to efforts but associated with HT (190/110 mm Hg). He consulted to the emergency room. The ECG showed ventricular bigeminy. TnT was normal and a perfusion imaging scan was normal with an ejection fraction of 67%.

Habitual medication: losartan 100 mg/day, amlodipine 10 mg/day, carvedilol 50 mg/day.

After the administration of diuretics blood pressure decreased to 160/90 mm Hg; the patient was referred to the outpatient clinic for subsequent evaluation. He was discharged from the ER with an additional daily dose of 50 mg of clortalidone.

Physical examination: weight: 123 kg; height: 181 cm; BMI: 32.26; waist circumference: 132 cm; BP: 160/100 mm Hg in both arms; HR: 70 bpm, with premature beats. Head and neck: absence of goiter and of carotid bruits.

Cardiovascular exam: the point of maximum impulse (PMI) was neither seen nor felt; a S4 was present with normal S1and S2. Peripheral pulses were symmetrical. Lung auscultation: RR: 15 bpm, normal and clear lung sounds. Abdominal exam: rounded abdomen; absence of visceromegalies.

Neurological examination: normal.

ECG: sinus rhythm. HR: 70 bpm. Electric axis of the heart: -15º. Frequent VPBs. LA enlargement. LV hypertrophy.

Lab exams: HCT: 41%; WBCC: 6.100; platelet count: 236.000; PT: 80%; APTT: 30"; BUN: 28 mg/dl; blood creatinine: 0.7 mg/dl; Na^+: 142 mEq/L; K^+: 3,8 mEq/L; uric acid: 7.9 mg/dl; fasting glucose: 117 mg/dl; postprandial glucose (2 hours): 132 mg/dl; total cholesterol level: 226 mg/dl; HDL cholesterol: 40 mg/dl; LDL cholesterol: 146 mg/dl; triglycerides: 174 mg/dl; ultrasensitive CRP: 2; Microalbuminuria: 46 mg/24 hours; TSH: normal.

Echocardiogram: LA enlargement, LV concentric hypertrophy. Preserved systolic function. Mitral inflow: impaired relaxation pattern.

Abdominal ultrasound: fatty liver. Aorta with normal diameter and calcified plaques. Kidneys normal in size and shape; normal urinary tracts.

Radionuclide renography: normal

Fundoscopy: grade I.

24 hour-Holter monitoring: permanent sinus rhythm. Frequent monomorphic VPB with episodes of bigeminy. Normal ST-T segment.

Evolution

Two months after the first consultation losartan was replaced by irbesartan 300mg/day and spironolactone (25 mg/day) was prescribed. Nevertheless, despite of having lost weight (113 kg) two weeks later the patient persisted with HT both outside and inside the consulting room (up to 190/100 mm Hg); for this reason an ambulatory blood pressure monitoring (ABPM) was performed.

ABPM: mean daytime blood pressure was163/98 mm Hg, and mean nocturnal blood pressure was 161/93 mm Hg, with a non-dipper pattern.

A polysomnography was performed due to the clinical suspicion of OSAS.

Polysomnography: Figures 1 and 2 show nocturnal polysomnography with continuous control of nasal and oral air flow, thoracic and abdominal respiratory movements, pulse oximetry, electroencephalogram, electroculograhy, chin electromiogram and electrocardiogram.

Patient cooperation was good and the quality of the record was acceptable.

The result showed the presence of obstructive apneas with a mean duration of 20 seconds. The apnea-hypopnea index was 32 and coexisted with intense snoring.

The ECG showed supraventricular and ventricular premature beats.

The sleep phases were disorganized with fragmentation of sleep, predominance of the superficial phases of sleep (I and II), and reduction of deep sleep (phases III and IV) and REM phase.

The episodes of obstructive apnea coincided with periods of pronounced oxygen desaturation (up to 60%).

Therefore, the presumptive diagnosis was hypertension associated with sleep obstructive apnea syndrome.

The patient started therapy with nocturnal CPAP (8 cm H_2O) for 5 hours. Two weeks later, blood pressure showed a gradual and important reduction with a concomitant improvement of symptoms. Spironolactone was discontinued.

One month after starting therapy with CPAP, a new ABPM showed mean daytime blood pressure of 138/86 mm Hg and mean nocturnal blood pressure of 124/82 mm Hg, with a dipper pattern.

Blood pressure remained within normal limits in ambulatory and office controls. Carvedilol and amlodipine were discontinued and the patient continued treatment with irbesartan 300 mg/day. The patient is currently stable with normal blood pressure controls and free of cardiovascular events.

DISCUSION

OSAS is a frequent disease affecting 5% of the population, preferentially men. The clinical picture includes four main symptoms: *daytime sleepiness, frequent nocturnal microarousals, morning asthenia with or without headache, and severe snoring*. (Table 1). (5)

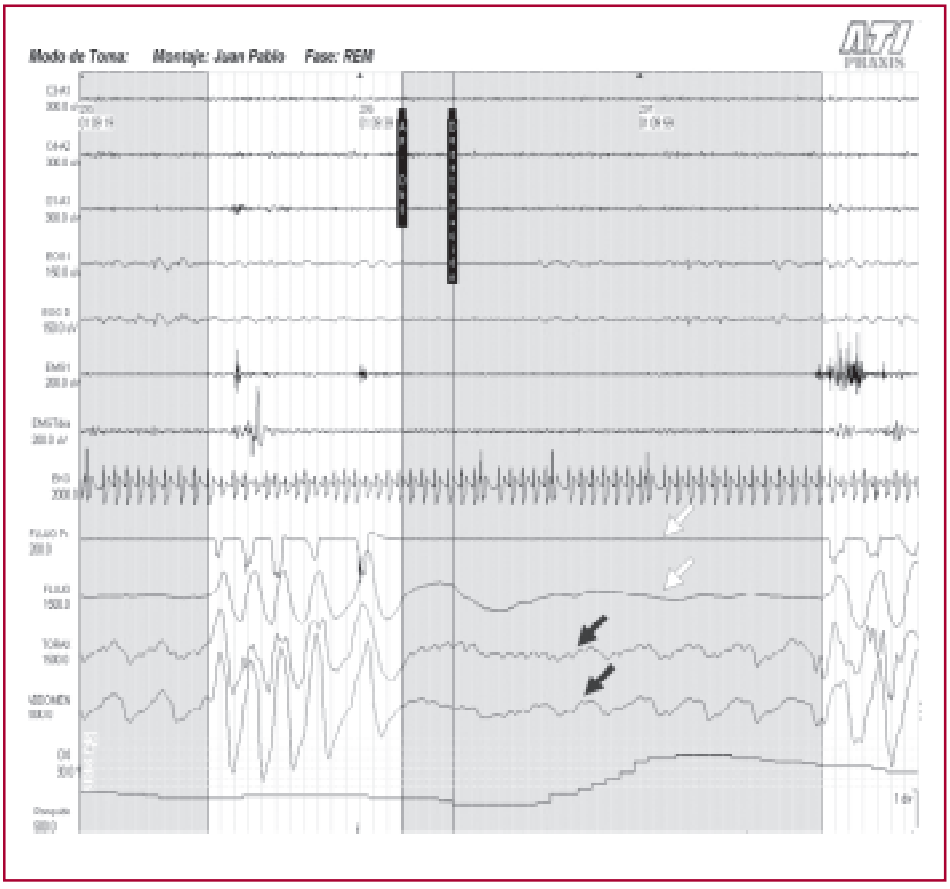

Fig. 1. Polysomnography. Interruption of the air flow (*red arrows*) in concordance with a reduction in thoracic and abdominal movements (*blue arrows*). This corresponds to periods of obstructive apneas.

Table 1. Symptoms associated with OSAS

Daytime symptoms
- Daytime sleepiness (90% of patients)
- Motor incoordination and fatigability
- Morning headache
- Irritability
- Dryness in the mouth and pharynx
- Memory loss
- Sexual dysfunction
Nocturnal symptoms
- Apneas or pauses in breath
- Snoring or gasping
- Interruption of sleep. Restless sleep
- Somniloquy

The apnea-hypopnea index (AHI) – the number of apneas during sleep time - defines the severity of the condition (Table 2). (5)

Table 2. Apnea-hypopnea index (AHI)

Severity	AHI
Mild	5-15
Moderate	15-30
Severe	> 30

Nevertheless, the classical symptoms were not present in our patient; morbid obesity was his most important risk factor and he suffered from hypertension refractory to optimal medical treatment with target organ damage and sexual dysfunction.

The interaction between OSAS and the cardiovascular system is displayed with permanent oscillations in the hemodynamic parameters during the night. The variations in BP occur under the influence of four predominant stimuli: oxygen desaturation, increase in PCO_2, increased respiratory effort, and microarousal at the end of the apnea. (6) Repetition of these stimuli every night leads to chronic changes in the cardiovas-

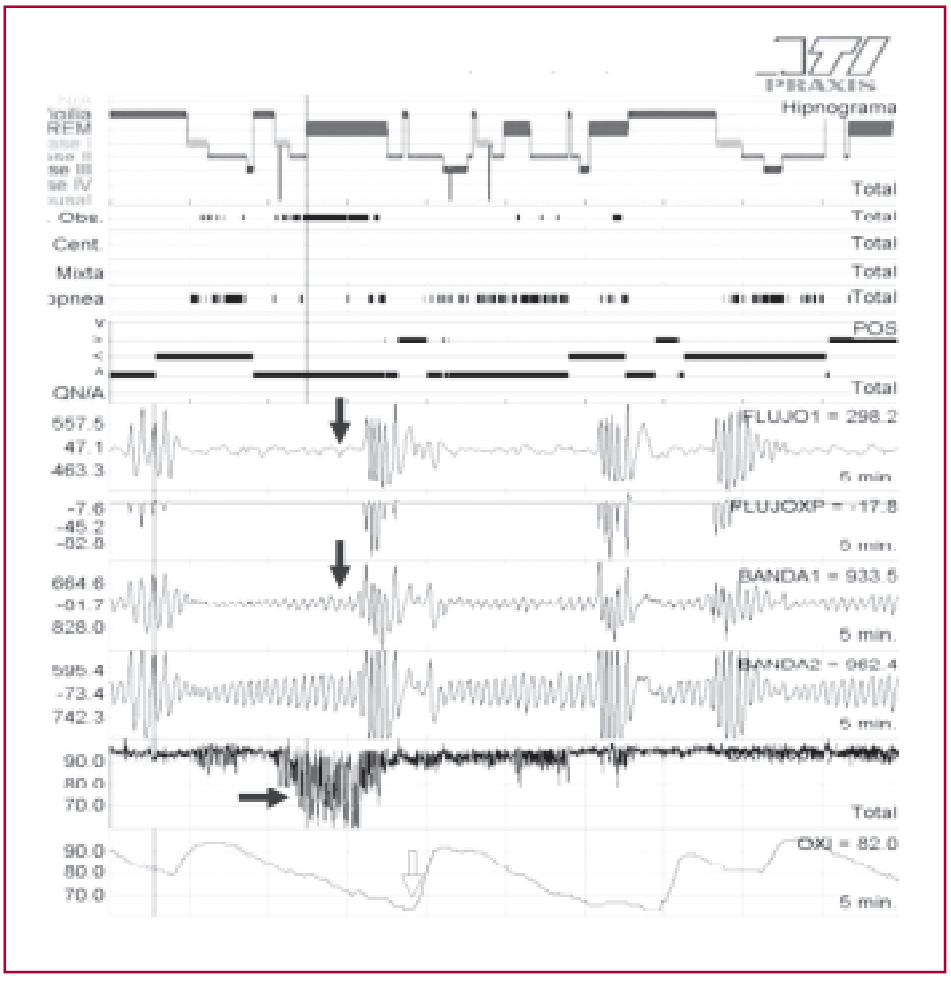

Fig. 2. Polysomnography. Pronounced oxygen desaturation, up to 60% (*green arrow*) during the periods of intense snoring and apnea (*violet arrows*).

cular system response and structural modifications. All these stimuli are a source of sympathetic stimulation which is responsible of the high incidence of cardiovascular events (angina, myocardial infarction, heart failure, arrhythmias and cerebrovascular events) particularly in patients with an AHI greater than 20. (7) Our patient did not present any of these hard events after 5 years of follow-up despite an AHI of 32.

OSAS treatment also includes therapeutic strategies such as postural changes, weight loss, avoiding alcohol abuse and hypnotic drugs. The use of CPAP at night prevents the collapse of the pharynx during the inspiratory efforts, thus reducing sympathetic activity and improving blood pressure levels. (8, 9) After a short period of treatment with CPAP, daytime as well as nocturnal levels of BP reduce, (10) especially in patients with HT refractory to pharmacology treatment (10) as our patient; he was able to discontinue part of the antihypertensive therapy after a short while, is still with normal values of BP and has not presented any cardiovascular event.

RESUMEN

Hipertensón arterial refractaria y apnea del sueño

El síndrome de apnea obstructiva del sueño (SAOS) tiene un papel importante en la morbimortalidad cardiovascular. Se han sugerido muchos mecanismos para explicar la asociación mórbida entre el SAOS y la enfermedad cardiovascular, especialmente la hipertensión arterial (HTA). Alrededor de la mitad de los pacientes con SAOS padecen hipertensión arterial y la prevalencia de SAOS en pacientes hipertensos es mayor que la existente en la población general.

En el presente caso se describe a un paciente con HTA refractaria al tratamiento farmacológico que evolucionó favorablemente luego del diagnóstico y el tratamiento del SAOS.

Palabras clave > Apnea obstructiva del sueño - Hipertensión arterial

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