CASE REPORT

Another Approach of Resistant Hypertension: What to Do When the Pharmacological Treatment Fails?

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Abstract

Background: Obstructive sleep apnea (OSA) is an important risk factor for elevated blood pressure (BP), especially in patients with resistant hypertension. Metaanalyses showed decrease of maximum 10 mmHg in BP after continuous positive airway pressure (CPAP). **Case Report:** A 42-year-old female patient, obese, presented for dyspnea with moderate exertion, daytime sleepiness, snoring, insomnia, tingling in the legs. She has a long history of hypertension (maximum known BP=220/100 mmHg), with progressive increase in medication; BP values are currently uncontrolled with 5 antihypertensive agents hypertension, some causes of resistant hypertension were excluded. The patient underwent polysomnography (PSG), which revealed fragmented sleep (sleep efficiency= 61%), severe OSA with apnea hypopnea index (AHI) of 45/h, minimum oxygen saturation ($minSaO_2$) of 65%, periodic leg movements during sleep index (PLMS) of 108/h. Ambulatory blood pressure monitoring (ABPM) report showed medium BP of 181/99/24h, non-dipper. Sleep architecture under CPAP treatment was restructured (sleep efficiency 78%), with correction of respiratory events at pressure of 11 cm H_2O (residual AHI=2.1/h, $minSaO_2$=93%), less ample periodic leg movements, PLMS index 80/h. The patient followed CPAP treatment for 1 year, with no changes in antihipertensive regimen or lifestyle. After 1 year of CPAP, patient reported none of the previous symptoms and ABPM report showed medium BP of 148/88/24h, dipper. **Conclusion:** CPAP not only controlled OSA and metabolic consequences, but also determined a significant drop in BP values after 1 year of compliant use.

Keywords: sleep apnea, insomnia, polysomnography, CPAP

Rezumat

Introducere: Sindromul de apnee în somn obstructiv este un factor de risc important pentru hipertensiunea arterială (HTA), mai ales în cazul pacienților cu hipertensiune rezistentă. Metaanalize au arătat scăderea TA cu maxim 10 mmHg după utilizarea de presiune pozitivă continuă în căile aeriene (CPAP). **Prezentare de caz:** Pacientă în vârstă de 42 de ani, obeză, se prezintă pentru: dispnee la efort moderat, somnolență diurnă, sforăit, insomnie, parestezii la nivelul picioarelor. Din antecedentele personale patologice, menționăm hipertensiune de grad 3 (maximul fiind de 220/100 mmHg), slab controlată, în ciuda tratamentului cu 5 agenți antihipertensivi. Pacienta a efectuat o polisomnografie (PSG), ce a evidențiat un somn fragmentat (eficiența somnului=61%), SASO sever cu indexul de apnee-hipopnee (IAH) de 45/h, saturația minimă de oxigen ($minSaO_2$) de 65%, indexul mișcării periodice a picioarelor în timpul somnului (PLMS) de 108/h. Monitorizarea Holter pe 24 ore a relevat o TA medie pe 24 ore de 181/99 mmHg, non-dipper. O PSG ulterioară sub CPAP de 11 cm H_2O a dovedit eficiența somnului de 78%, IAH rezidual de

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2,1/h, SaO_2 minimă de 93%, rare mișcări periodice, indexul PLMS de 80/h. La un an de la începerea tratamentului CPAP, pacienta avea același stil de viață și aceeași medicație antihipertensivă. Însă, ea nu a mai raportat niciunul dintre simptomele SASO, iar monitorizarea Holter a evidențiat o TA medie de 146/78/24h, dipper. **Concluzie:** CPAP nu doar că a controlat SASO și consecințele metabolice ale acestuia, dar a redus semnificativ TA după doar un an de utilizare compliantă.

Cuvinte cheie: apnee în somn, insomnie, polisomnografie, CPAP

BACKGROUND

Obstructive sleep apnea (OSA) is an important risk factor for elevated blood pressure (BP), especially in patients with resistant hypertension (RHT)[1]. HT physiopathology in OSA patients involves aspects such as secondary sympathetic hyper reactivity because of intermittent hypoxia, decreased barometric sensitivity, endothelial dysfunction. Obesity can significantly contribute to the HT mechanism in OSA. This pathology can affect organs such as the heart, blood vessels and kidneys and it plays a major cardiovascular role[2].

CASE PRESENTATION

42-year-old female patient, obese, presents at „Marius Nasta" Pneumophtisiology Institute emergency room, accusing the following: long evolution dyspnea with moderate exertion, aggravated in the last months, daytime sleepiness, snoring, insomnia (for already 4 years), tingling in the legs.

Her medical history revealed stage 3 hypertension (maximum known 220/100 mmHg), poorly controlled (average values at home: 170/70 mmHg) despite correct treatment and dedicated cardiologist. Actual treatment: Indapamide 1,5 mg/day, Zofenopril Calcium/ Hydrochlorothiazide 30 mg/day, Betaxolol 10 mg/day, Amlodipine 20 mg/day, Rilmenidine 1 cp/day. The patient was already tested for other causes of secondary hypertension, all of them having negative results: chronic kidney disease, primary hyperaldosteronism, renovascular disease, Cushing syndrome, pheochromocytoma, coarctation of the aorta, Conn syndrome, thyroid or parathyroid pathology.

Physical examination revealed a patient with class I obesity (BMI= 32 kg/m^2), good general condition, increased anteroposterior diameter of the chest because of adipose tissue mass, decreased global sonority, without crackles, oxygen saturation (SaO_2) at rest of 94%, rhythmic heart sounds, pulse of 80 bpm, regularly, moderate edema of the lower limbs, blood pressure (BP) at rest of 190/90 mmHg, without left to right arm differences. According to Epworth Sleepiness Scale, the patient has a score of 12, which is suggestive for sleep apnea.

Investigations

Paraclinical investigations:

Electrocardiography: normal, present sinus rhythm, heart rate of 83 bpm, QRS complex at +60 degrees, without repolarization disorders.

Blood tests revealed non-specific inflammatory syndrome and mixed dyslipidemia (Table 1).

Chest X-ray: reticulo micronodular and nodular opacities, bilaterally spread, subpleural basal predominance.

Spirometry: restrictive ventilatory dysfunction with 38.5% forced vital capacity (FVC) reduction (Table 2).

The presumptive diagnosis at this moment consists of: resistant, possible secondary hypertension, metabolic syndrome, suspicion of OSA, suspicion of obesity-hypoventilation syndrome (OHS) (giving the restrictive dysfunction), restless legs syndrome (RLS), insomnia.

Arterial gasometry, polysomnography and ambulatory blood pressure monitoring (ABPM) were performed in order to verify the suspected diagnoses.

Table 1. Blood tests

Condition	Data
Non-specific inflammatory syndrome	ESR=58/1h CRP >6 mg/L
Mixed dyslipidemia	Cholesterol=284 mg/dL Triglycerides=622 mg/d: HDL-Cholesterol=37 mg/dL LDL-Cholesterol=123 mg/dL

Table 2. Spirometry results

	Value (L)	Percentage
FVC	2	61.5
FEV1	1.72	61.5
FEV1/FVC		84.3
PEF	5	68.3
MEF50	2.09	51.2

Mild hypoxemia was detected at the arterial gasometry. Without hypercapnia, OHS was invalidated (Table 3).

Table 3. Awake arterial blood gases

pH	pO_2 (mmHg)	pCO_2 (mmHg)
7,43	69,9	32,9

pO_2: partial pressure of oxygen; pCO_2: partial pressure of carbon dioxide

Polysomnography (PSG) confirmed severe obstructive sleep apnea syndrome diagnosis, with a sleep efficiency of 61%, an apnea-hypopnea index (AHI) of 45/h, minimum SaO_2 of 65%, PLMS (periodic leg movements during sleep index) of 108/h (Table 4, Fig. 1).

Ambulatory blood pressure monitoring (ABPM) report revealed an average BP of 181/99/24h, with a maximum of 236/126 mmHg and non-dipper profile (Fig. 2).

The final positive diagnosis was: stage 3 arterial hypertension, severe OSA, sleep-maintenance and sleep-onset insomnia, RLS, metabolic syndrome.

Table 4. Polysomnography parameters

Event	Number
Obstructive apneas	14/h
Central apneas	1
Mixed apneas	2
Hypopneas	28/h

Treatment

The patient follows continuous positive airway pressure (CPAP) titration which points out the 11 cm H_2O value as an optimal one for controlling respiratory events. A further polysomnography under 11 cm H_2O CPAP showed a sleep efficiency of 78%, a residual apnea-hypopnea index (AHI) of 2.1/h, minimum SaO_2 of 93%, desaturation index of 6/h, PLMS of 80/h (Fig. 3).

Daily 11 cm H_2O CPAP administration is recommended to the patient, with a minimum use of 5h/day during sleep time, medication maintenance, losing weight and a healthy lifestyle.

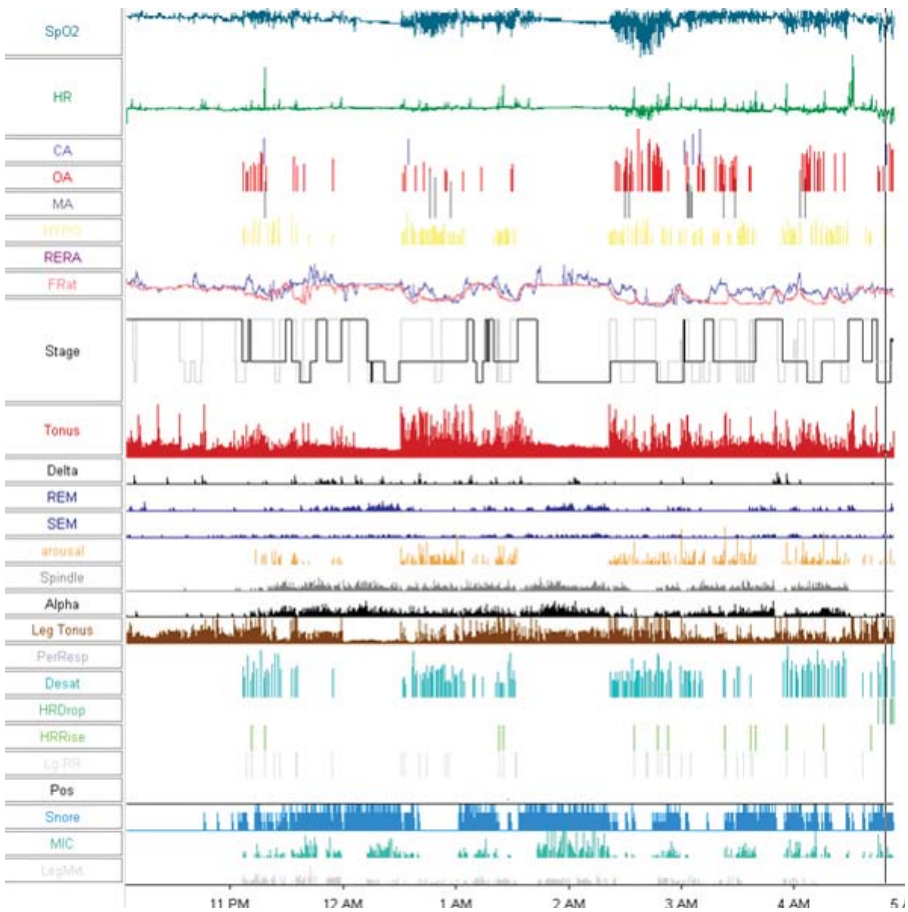

Figure 1. Polysomnography.

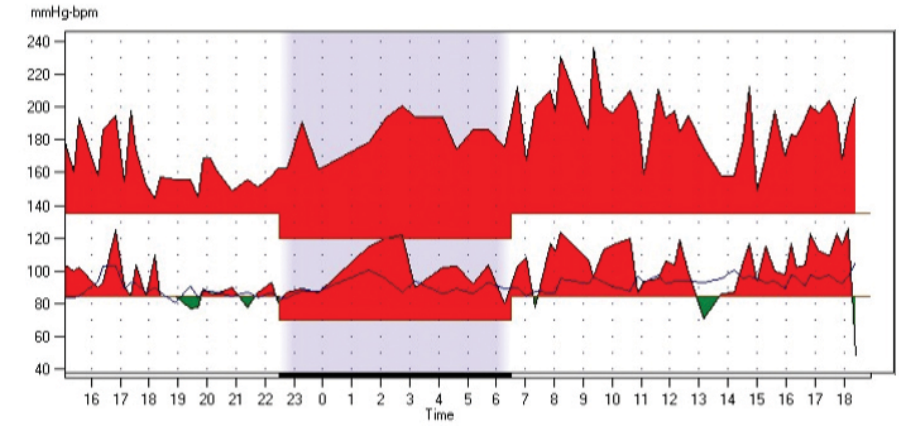

Figure 2. ABPM.

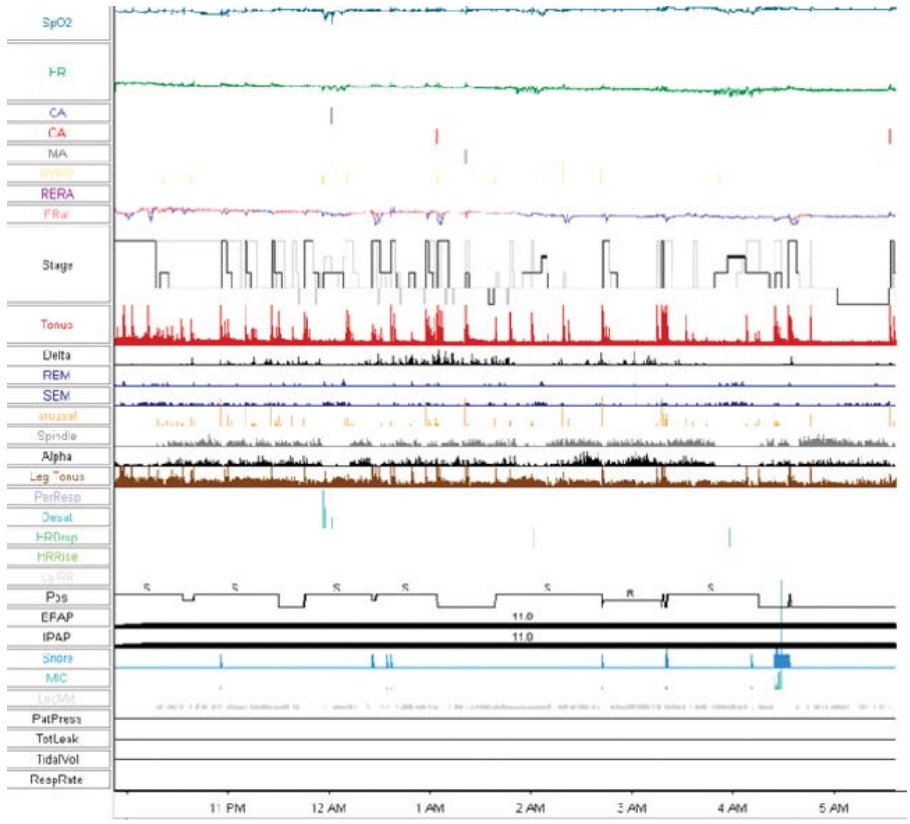

Figure 3. Therapeutic PSG under 11 cm H_2O CPAP titration.

Outcome and follow-up

The evolution under this treatment was favorable, the symptoms decreased and the patient had a very good compliance to the CPAP therapy, using it 96.6% of the time, with an average of 7h/day.

At only one year after treatment initiation, the patient had the same lifestyle, weight and medication. Nevertheless, she didn't report any of the previous OSA symptoms that she used to have and Epworth score was 6.

ABPM report emphasized the significant decrease in BP values, with an average BP of 146/78/24h, a maximum of 183/100 mmHg and dipper profile (Fig. 4). The changes between the two ABPM reports can be seen in Table 5.

DISCUSSIONS

We presented the case of a young patient, known with uncontrolled elevated blood pressure, without reported

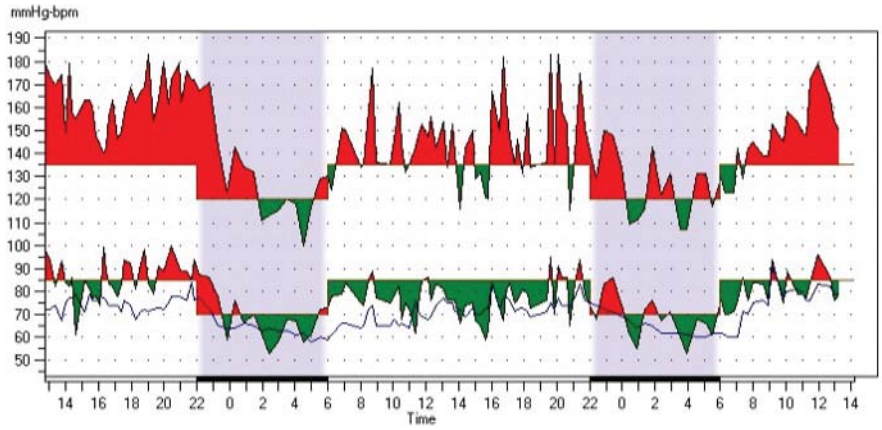

Figure 4. ABPM report one year after CPAP use.

pulmonary pathology associated. Causes of secondary hypertension were taken into consideration, giving the patient's age and the refractory hypertension; adding the symptomatology (daily sleepiness, snoring), we suspected OSAS diagnosis. Hypertension guidelines recommend OSAS testing in these patients[3].

Ambulatory blood pressure monitoring is relevant for following the control in BP values and for assessing OSAS risk. Non-dipper profile is frequently found in these patients[1]. Hypertension in OSAS patients is regularly associated with metabolic changes, thus increasing the prevalence of metabolic syndrome[4].

According to *American Academy of Sleep Medicine* OSAS diagnosis criteria[5], the patient has a severe form. One of OSAS comorbidities in obese patients is OHS[6]. The restrictive syndrome detected at spirometry was an additional argument for this diagnosis. Therefore, arterial gasometry became a mandatory investigation to establish a possible OHS. This diagnosis was invalidated based on the absence of hypercapnia. Thus, the spirometry changes were probably caused by obesity and by an insufficient respiratory effort, evaluated by the flow-volume and time-volume loops (insufficient 3 seconds exhale).

There was demonstrated in the last years that periodic leg movement during sleep is associated with arterial hypertension, cardiovascular and cerebrovascular risk. The movements involves flexion of toes, malleoli, knees, and hip. Each movement lasts between 0.5-10 seconds with a periodicity of 20-40 seconds[7]. Furthermore, RLS represents a particularity in our patient, especially because its evolution was favorable under CPAP, in this way contributing to the decrease in BP values.

CPAP is the reference treatment for OSAS patients, preventing respiratory events and restoring sleep quality, diminishing daytime sleepiness, decreasing the sympathetic activity, thus the cardiovascular risk[3]. The literature demonstrates a more important decrease in the asleep values than in the awake ones[8], aspect observed in our patient as well (see Table 5).

Nevertheless, there is conflicting information regarding CPAP effect in AHT. Favorable results were only reported in compliant patients, who followed CPAP treatment for at least 4-5 hours/day. In these patients, CPAP use revealed a decrease of 5 mmHg in BP values[9]. Results are similar regarding RHT, a decrease of approximately 4 mmHg in BP being noticed[10]. Even if there is no major decrease, it is of great importance if we take into consideration the other CPAP effects: avoiding the asleep hypoxemia, and thus the inflammatory cascade and the oxygen free radicals and hormones which play a role in increasing OSAS- associated BP values[2].

Table 5. Diagnostic ABPM and 1 year after 11 cm H_2O CPAP therapy

Parameter	Diagnosis (mean +/- SD)	Follow-up 1 year (mean +/- SD)
Mean systolic (mmHg)	181 +/- 21.0	146 +/- 19.6
Mean systolic awake (mmHg)	181 +/- 22.4	152 +/- 16.9
Mean systolic asleep (mmHg)	183 +/- 12.6	127 +/- 17.0
Mean diastolic (mmHg)	99 +/- 15.4	78 +/- 10.5
Mean diastolic awake (mmHg)	99 +/- 15.8	81 +/- 8.9
Mean diastolic asleep (mmHg)	99 +/- 14.0	68 +/- 9.6
Dipper systolic (%)	-1.3	15.9
Dipper diastolic (%)	0	15.6

Take home messages

In this case, CPAP not only controlled OSAS and its metabolic consequences, but it also significantly decreased BP values in only one year of compliant use, especially since there were no lifestyle changes. Even a decrease of a couple mm in BP values can trigger an important reduction of cardiovascular risk[1]. CPAP treatment in OSAS produces a major decrease of BP in patients with resistant hypertension. Its effect depends mainly on the number of hours of use. Patients who suffer from resistant hypertension should be evaluated for OSAS, which is a changeable risk factor.

Compliance with ethics requirements:

The authors declare no conflict of interest regarding this article.

The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study

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