

Resistant hypertension, obstructive sleep apnea and chronic kidney disease: a menacing triangle

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Received: January 31, 2020, Accepted: March 7, 2020

Abstract

We present a case study of a 49-years-old male patient with type 2 diabetes mellitus, renal pathology (right kidney lithiasis, stage IIIA-chronic kidney disease) and resistant hypertension in spite of five anti-hypertensive drugs combination. In our attempt to further refine the diagnosis, we excluded causes of secondary hypertension such as renovascular and endocrine disorders. Because our patient was experiencing hypersomnia, prolonged asthenia and a higher-normal daytime sleepiness score (Epworth Sleepiness Scale = 6), we decided to perform a respiratory polygraphy which identified a severe form of obstructive sleep apnea. After all these findings we concluded that the obstructive sleep apnea was the aggravating setting for hypertension, so we added a nocturnal Continuous-Positive Airway Pressure (C-PAP) to the ambulatory treatment, with a significant improvement of patient's outcome (target values achieved, serum lactate decreased).

Keywords: resistant hypertension, obstructive sleep apnea, mild chronic kidney disease

Background

Resistant hypertension is defined as the failure to achieve a target blood pressure (BP) of <140/90 mmHg, despite the use of at least 3 antihypertensive drugs (including a diuretic) at tolerable doses [1]. From all outpatient medical visits about 15 to 20% of treated patients have resistant hypertension [2].

According to literature data, obstructive sleep apnea (OSA) may be an independent risk factor for

resistant hypertension in the general population [3, 4]. Unfortunately, research studies that investigated the connection between OSA and resistant hypertension have expressly excluded patients with mild to moderate chronic kidney disease (CKD) or included only few patients but with advanced CKD [5, 6].

Aim

We wanted to emphasize the link between severe OSA and resistant hypertension in the setting of mild chronic kidney disease (CKD), and also to raise awareness of the need to treat all underlying mechanisms in the attempt to improve patients' outcomes.

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Case report

We present the case of a 49-years-old male patient with resistant hypertension and stage IIIA-CKD, who was recently admitted in the Constanta County Hospital Internal Medicine Department in the attempt to further refine the diagnosis.

His medical history comprises type 2 diabetes mellitus diagnosed 2 years before, treated with metformin standard doses (with good metabolic control), and mild dyslipidemia (hypercholesterolemia with baseline LDL-cholesterol 121 mg/dl), well-controlled with statin therapy. As about renal pathology, our patient was diagnosed 5 years ago with right kidney lithiasis, treated with multiple sessions of shock wave lithotripsy, and also chronic pyelonephritis, stage IIIA-CKD - being since then under regular nephrology surveillance. He was diagnosed with grade II arterial hypertension (HTN) for about 3 years; at that moment biological investigations excluded possible secondary endocrine cause of HTN. He exhibited increasingly high values in the last year (with systolic BP values up to 210 mmHg), so being progressively added up to 5 antihypertensive agents (perindopril, indapamide, nebivolol, amlodipine and spironolactone) in maximal dosages.

From the anamnesis we excluded any potential offending drugs or habits, and also confirmed a good treatment adherence.

The clinical exam was normal, except the high values of BP inspite treatment (160/90 mmHg) and a body mass index of 28.73 kg/m² that shows an

overweight patient with predominantly abdominal fat tissue distribution.

The 12-lead electrocardiogram was normal. Standard transthoracic echocardiography revealed only mild left ventricle diastolic dysfunction (impaired relaxation), with all other parameters normal. Laboratory tests confirmed IIIA-CKD (eGFR 47 ml/min/1.73m²) and a good metabolic control.

We performed serial 24-hour Continuous Ambulatory Blood Pressure Monitoring (C-ABPM), in order to exclude white coat hypertension and to assess dipping status. Our patient revealed persistent nocturnal non-dipping BP profile.

Abdominal ultrasound revealed a slight difference between kidney long axis (the right one was 11 cm, the left one 12.5 cm); so, considering high creatinine and resistant HTN we decided to perform

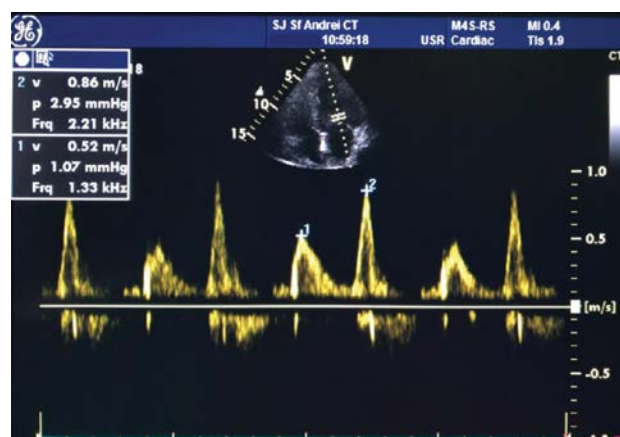


Figure 1 Transthoracic echocardiography - stage I diastolic dysfunction.

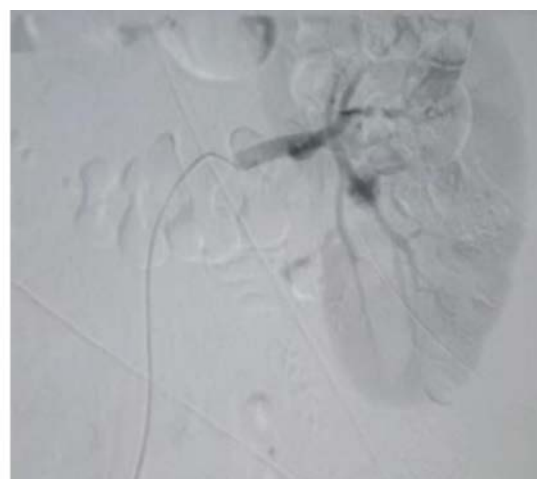


Figure 2 Renal angiography - normal calibrated renal arteries.

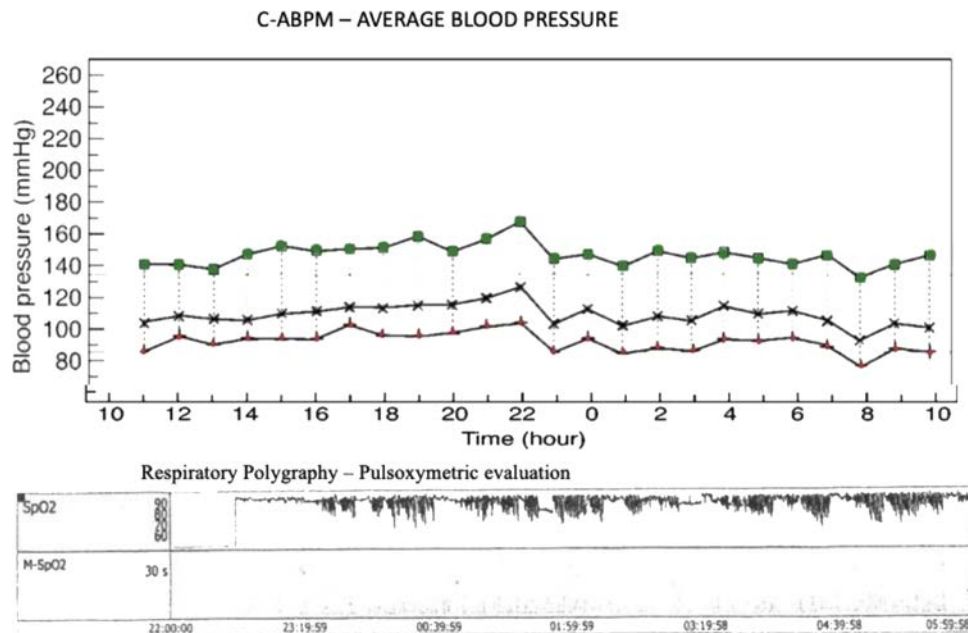


Figure 3 C-ABPM versus Respiratory Polygraphy.

a renal angiography to detect a potential renal artery stenosis. This investigation exposed a slightly tapered right renal artery, without intraluminal stenosis and a left renal artery of normal caliber, thus ruling out the suspicion of right renal stenosis.

Although the spirometry was normal, the arterial blood gas showed some discrepancies (upper limit blood pH, with normal levels of carbon dioxide and bicarbonate, but high values of lactic acid).

After a more accurate anamnesis that confirmed snoring, hypersomnia, and a higher-normal daytime sleepiness score (Epworth Sleepiness Scale = 6), we decided to perform respiratory polygraphy which identified a sleep-disorder breathing pattern very suggestive of severe obstructive sleep apnea (Apnea-Hypopnea Index-AHI was 34/h and Oxygen Desaturation Index ODI was 7).

After all these findings we conclude that OSA was the aggravating setting for hypertension, so we added nocturnal Continuous-Positive Airway Pressure (C-PAP) to the ambulatory medical treatment, with good adherence and with a significant improvement of patient's outcome (target BP values achieved).

Discussion

In this report we expose a very particular case: it is about a young male adult with an initial diagnosis

of renal lithiasis, chronic pyelonephritis and mild CKD. He progressively added multiple cardiovascular risk factors – such as overweight, diabetes mellitus, dyslipidemia (efficiently treated), moderate HTN (with an initial satisfactory response to therapy) and, of course, increasing age. His chronic conditions remained stable: no CKD aggravation, a good metabolic control regarding diabetes, but HTN became severe and resistant to gradually intensified treatment. Thinking out investigations we diagnosed severe obstructive sleep apnea, and applying C-PAP therapy led our patient to an important clinical improvement.

Previous studies in the general population have demonstrated a correlation between OSA and resistant HTN, particularly in 40-to 59-year-old overweight male, due to surges in systolic and diastolic pressure that keep mean BP levels elevated at night, but which can also remain elevated during daytime, when breathing is normal [3].

OSA is in close relations with resistant HTN and this co-morbid association may lead to accelerated target organ damage [7]. Especially in diabetic patients OSA proved to be an aggravating factor for renal function deterioration *via* increased proteinuria and blood pressure variation [8, 9].

High prevalence of sleep apnea is reported among patients with CKD, but these findings were emphasized by studies that either excluded patients

with mild to moderate CKD or did not mention participant's renal function [10]. Literature studies and reviews in distinct cohorts suggest OSA indeed negatively affects kidney function over time, but there are limitations and controversies regarding mild-moderate CKD patients [11, 12]. Therefore, the interactions between OSA, resistant HTN and CKD need to be more clarified by further dedicated trials.

Because of the differences between distinctive clinical phenotypes of OSA patients, the possible protective role of OSA treatment is still unpredictable [13]. The European experts on OSA recently confirmed this point of view and recommend that both symptoms and organ damage should be considered when choosing the opportune treatment for OSA [14].

Conclusion

A more accurate screening for OSA in patients with CKD is mandatory, even when all other cardiovascular risk factors are apparently well-controlled, as well as if CKD is classified as mild-to-moderate and especially when a patient develop an aggravated/resistant HTN.

Conflict of interest

The authors confirm that there are no conflicts of interest

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