CASE REPORT

RJME
Romanian Journal of Morphology & Embryology
http://www.rjme.ro/

Morphological and functional renovascular changes as cause of resistant arterial hypertension – case report and literature review

IRINA IULIANA COSTACHE[1,2)], CLAUDIA FLORIDA COSTEA[3,4)], VASILE FOTEA[5)], VICTOR LAURIAN RUSU[6)], VIVIANA AURSULESEI[1,2)], RAZAN AL NAMAT[1,2)], DAN ALEXANDRU COSTACHE[7)], NICOLETA DUMITRESCU[7)], CĂTĂLIN MIHAI BUZDUGĂ[8)], GABRIELA FLORENŢA DUMITRESCU[9)], ANCA SAVA[9,10)], CAMELIA MARGARETA BOGDĂNICI[3)]

[1)] *1st Medical Department, "Grigore T. Popa" University of Medicine and Pharmacy, Iaşi, Romania*

[2)] *Clinic of Cardiology, "St. Spiridon" Emergency Clinical Hospital, Iaşi, Romania*

[3)] *Discipline of Ophthalmology, Department of Surgery II, "Grigore T. Popa" University of Medicine and Pharmacy, Iaşi, Romania*

[4)] *2nd Ophthalmology Clinic, "Prof. Dr. Nicolae Oblu" Emergency Clinical Hospital, Iaşi, Romania*

[5)] *Department of Radiology, "Grigore T. Popa" University of Medicine and Pharmacy, Iaşi, Romania*

[6)] *Department of Neurology, "Grigore T. Popa" University of Medicine and Pharmacy, Iaşi, Romania*

[7)] *4th Year Student, Faculty of Medicine, "Grigore T. Popa" University of Medicine and Pharmacy, Iaşi, Romania*

[8)] *Department of Endocrinology, "Grigore T. Popa" University of Medicine and Pharmacy, Iaşi, Romania*

[9)] *Laboratory of Pathology, "Prof. Dr. Nicolae Oblu" Emergency Clinical Hospital, Iaşi, Romania*

[10)] *Department of Anatomy, "Grigore T. Popa" University of Medicine and Pharmacy, Iaşi, Romania*

Abstract

Resistant hypertension is defined by the inability to maintain within normal limits the blood pressure values of an individual, while he is under treatment with maximal tolerated doses of three antihypertensive agents. One of the most common types of resistant hypertension is renovascular hypertension (RVH), which is caused by the narrowing of the renal arteries, in the context of existing atherosclerotic plaques at that level. We are presenting the case of a hypertensive 56-year-old man admitted in the Clinic of Cardiology for a sudden rise of his blood pressure values, despite undergoing the scheduled treatment. The abdominal bruit discovered at the clinical examination and the hypokalemia, together with the mild impairment of the renal function raised the suspicion of an existing stenosis of the main renal blood vessels. Simple grey scale kidney ultrasound, Doppler ultrasound of the renal arteries, abdominal computed tomography and magnetic resonance angiography of the renal arteries, along with invasive renal angiography demonstrated a smaller right kidney, adrenal incidentalomas, reduced vascular diameter of renal arteries due to atheromatous lesions, thrombosis of the infrarenal segment of the abdominal aorta, and reduced vascular hemodynamics in the same territories. After the renal arteries revascularization and with minimal antihypertensive treatment, the patient had a favorable outcome, with normalization of blood pressure and renal function. Atherosclerotic disease causing renal artery stenosis is essential to be taken into consideration in the etiopathogenesis of resistant hypertension especially because RVH is a potentially curable disease.

Keywords: atherosclerotic renal artery stenosis, functional renovascular changes, angiography, resistant arterial hypertension.

Introduction

Arterial hypertension is an important modifiable risk factor for cardiovascular disease that affects approximately one billion people around the world [1]. It is considered that approximately 10–20% of the general hypertensive population (depending on the region) have resistant hypertension, which is defined by the international clinical guidelines as uncontrolled hypertension (blood pressure while seated >140/90 mmHg), despite the use of three antihypertensive drugs from different classes (one of which must be a diuretic) at the highest tolerated dose, or as blood pressure values maintained at target level with four or more antihypertensive drugs [1–3]. In both cases the patient has to be adherent to the regimen of prescribed drugs, because it has been stated that half of the events are actually due to the non-adherence to treatment [1, 2]. It is estimated that people with resistant hypertension have twice the risk of cardiovascular disease-related morbidity and mortality, which is an important leading risk factor regarding morbidity and deaths associated to stroke events [1].

Several studies indicate that around 5–10% of patients diagnosed with resistant hypertension have underlying secondary causes, among them primary hyperaldosteronism being the most common [3]. Renal artery stenosis, chronic kidney disease, obstructive sleep apnea, pheochromocytoma, thyroid disease, Cushing's syndrome, coarctation of the aorta and intracranial tumors can also cause resistance to antihypertensive treatment [3, 4].

Renovascular hypertension (RVH) is one of the most

frequent types of secondary hypertension [5]. It is considered that the occlusion of the renal arteries reduces the blood flow to the kidneys, leading to the activation of the renin–angiotensin system (RAS) that will produce an increase in the systemic blood pressure. Endothelin release, activation of the sympathetic nervous system and oxidative stress are other renovascular mechanisms involved in the process [5]. Even if the most common causes of RVH are atherosclerotic renal artery disease (85–90% of cases) and fibromuscular dysplasia (in almost 10% of cases), other mechanisms such as acute renal artery occlusion (by thrombosis, embolism, or trauma), aortic dissection with renal artery involvement or Takayasu arteritis can also be the causes of this disease [5, 6].

The incidence of atherosclerotic renal artery disease is continuously increasing, either silently as an independent cardiovascular risk factor, or by leading to RVH and chronic kidney disease [6]. Therefore, a correct quick diagnosis of this condition and an adequate therapeutic approach are required.

Aim

We present a case of resistant hypertension due to bilateral atherosclerotic renal artery stenosis and emphasize on the morphological and functional renovascular changes identified on various imagistic investigations. Also, we highlight the fact that the revascularization of renal arteries transforms the RVH into a treatable disease.

Case presentation

A 56-year-old man came to his family physician for shortness of breath and chest pain, but also for the revaluation of his antihypertensive treatment as he had high blood pressure (maximal value of 200/130 mmHg) in the last three months, despite a treatment with three antihypertensive drugs taken for a few years.

Apart from arterial hypertension (diagnosed 15 years ago), he had a positive history for important cardiovascular risk factors, such as smoking and alcohol consumption. Approximately 10 years ago, he was also diagnosed with *angina pectoris*, but the coronary arteriography performed at that time did not emphasize any significant lesions. He also had a positive history for other pathologies, such as alcoholic fatty liver, chronic obstructive pulmonary disease, lower limb arteriopathy obliterans (diagnosed when the patient was 50 years old), with an arteriography showing thrombosis of the left primitive iliac artery and a relatively tight stenosis of the left popliteal artery, and degenerative changes of the aortic and mitral valves without major hemodynamic impact (as it was found at his last echocardiographic examination).

The "at-home" treatment consisted of beta-blocker, angiotensin-converting enzyme (ACE) inhibitor, diuretic, long-acting nitrate in maximal doses and also antiplatelet therapy, lipid lowering drug and vasodilators for the peripheral arterial disease.

The physical examination of the cardiovascular system revealed rhythmic heartbeats, without any extrasystoles, a new harsh systolic murmur with highest intensity in the aortic area, and bilateral carotid bruit (its intensity suggested the existence of significant carotid stenosis). Abdominal bruit and low femoral pulse pressure were also identified. The blood pressure was 200/130 mmHg, when the patient was in supine position and standing up.

The pre-existent hypertension was well tolerated for almost 15 years, until it worsened suddenly and became resistant to medication. The high values of diastolic blood pressure (>130 mmHg) associated with the abdominal bruit and the existing clinical signs made us consider the possibility of a RVH produced by the presence of an atheromatous plaque in one or both renal arteries, in the context of the existing risk factors.

Therefore, he was sent to the Clinic of Cardiology, "St. Spiridon" Emergency Clinical Hospital, Iaşi, Romania. Blood test results showed hypokalemia (serum K^+ 3 mmol/L), but normal natremia (serum Na^+ 139 mmol/L), metabolic alkalosis (alkaline reserve 30 mEq/l HCO_3^-), slightly elevated levels of serum urea (41 mg/dL) and creatinine (1.31 mg/dL), suggesting mild renal impairment with estimated glomerular filtration rate 18 mL/min/1.73 m^2, and mild dyslipidemia (serum cholesterol 206 mg/dL, serum triglycerides 190 mg/dL). The complete blood count and urine analysis were within normal limits.

As clinical clues were suggestive of RVH, we undertook imagistic diagnostic tests in order to establish if our patient could be a candidate for revascularization. Renal ultrasound and Doppler examination of the renal arteries revealed an obvious renal asymmetry and lower renal blood flow on the right side. The length of the right kidney (RK) was 91 mm and its parenchymal thickness was 8 mm. The length of the left kidney (LK) was 115 mm and its parenchymal thickness was 14 mm (Figure 1, a and b). Spectral Doppler ultrasound on the renal arteries showed reduced flow speed, especially on the right side, where the spectrograms had a "*parvus et tardus*" configuration (Figure 1, c and d).

The magnetic resonance angiography (MRA) of the kidneys demonstrated a smaller right kidney and bilateral renal artery stenosis (Figure 2, a and b). A morphological difference between the two kidneys was noticed (considering the longitudinal diameter of almost 10 mm for the RK and 12.7 mm for the LK) along with delayed nephrogram on the right side. Right renal artery stenosis affected more than 50% of its diameter on a 9 mm distance from its origin, and left renal artery stenosis was determined by a 13 mm atheromatous plaque that reduced the arterial lumen to less than 50% of its diameter. A thrombosis of the infrarenal segment of the aorta, which extended on the common and external iliac arteries on both sides could also be seen (Figure 2c). Because of the turbulent flow of the infrarenal aorta, it was difficult to quantify the level of bilateral renal artery stenosis produced by the atheromatous plaque, which was however more severe on the right side.

Computed tomography angiography (CTA) with prehydration was performed and confirmed bilateral renal artery stenosis (44% on the right side and 54% on the left) at their origin from the aorta. CTA also revealed an atrophic right kidney and identified the right suprarenal

gland with multiple well delimited nodules (with maximum diameter of 32.1 mm), with dynamics suggesting a benign lesion, and the left suprarenal gland with a well delimited nodule (with maximum diameter of 32.1 mm and with dynamics also suggestive for a benign lesion) (Figure 3, a and b).

A CTA three-dimensional reconstruction image clearly delineated vascular anatomy and the smaller dimensions of the RK (Figure 3c). A delayed scan (about 10 minutes after contrast agent administration) revealed asymmetrical signal intensity in collecting systems, being a reliable indicator of right renal hypoperfusion (Figure 3d).

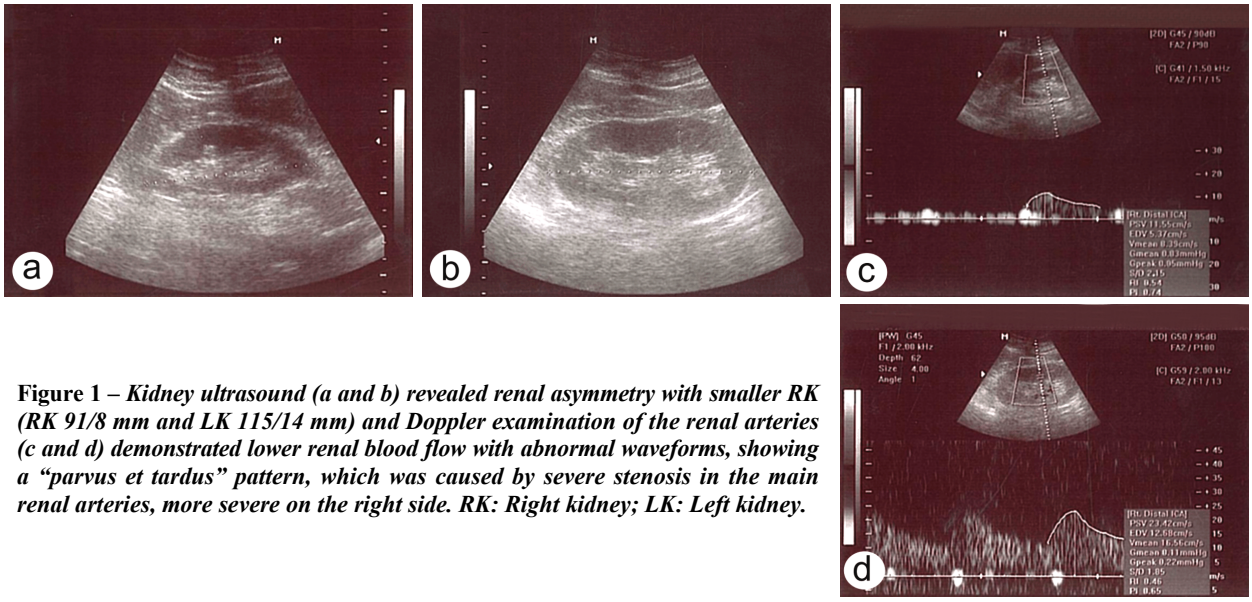

Figure 1 – ***Kidney ultrasound (a and b) revealed renal asymmetry with smaller RK (RK 91/8 mm and LK 115/14 mm) and Doppler examination of the renal arteries (c and d) demonstrated lower renal blood flow with abnormal waveforms, showing a "parvus et tardus" pattern, which was caused by severe stenosis in the main renal arteries, more severe on the right side. RK: Right kidney; LK: Left kidney.***

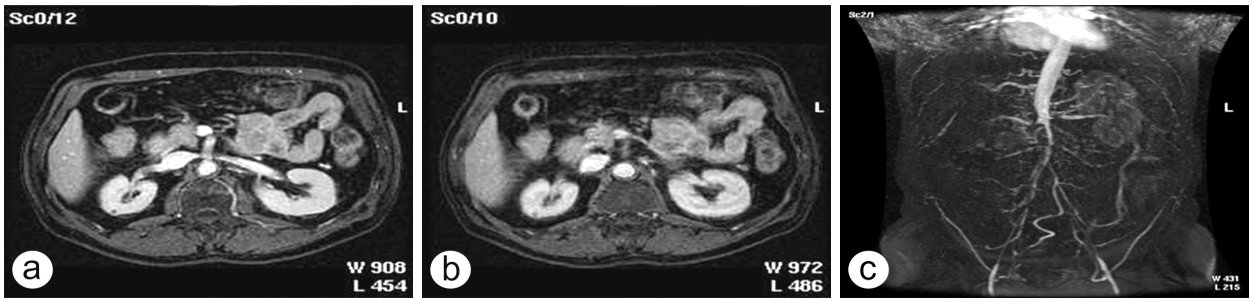

Figure 2 – ***Contrast-enhanced magnetic resonance angiography: transverse image demonstrated smaller right kidney and bilateral renal artery stenosis (a and b); coronal image showed renal artery stenosis, more significant on the right side and an extensive thrombosis of the infrarenal segment of the abdominal aorta which extended on the common and external iliac arteries on both sides (c).***

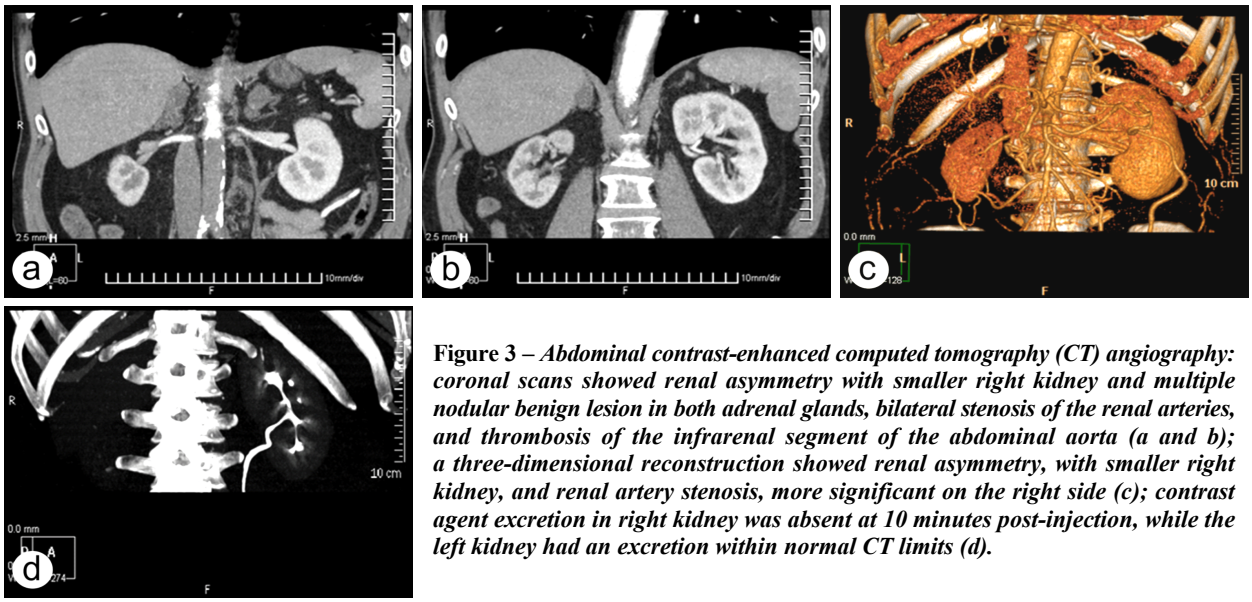

Figure 3 – ***Abdominal contrast-enhanced computed tomography (CT) angiography: coronal scans showed renal asymmetry with smaller right kidney and multiple nodular benign lesion in both adrenal glands, bilateral stenosis of the renal arteries, and thrombosis of the infrarenal segment of the abdominal aorta (a and b); a three-dimensional reconstruction showed renal asymmetry, with smaller right kidney, and renal artery stenosis, more significant on the right side (c); contrast agent excretion in right kidney was absent at 10 minutes post-injection, while the left kidney had an excretion within normal CT limits (d).***

Due to the presence of nodular lesions in both adrenal glands, we investigated the laboratory values of urinary vanillylmandelic acid (VMA) and metanephrine, and plasma aldosterone and cortisol levels, which showed negative results.

The resting electrocardiography (ECG) showed sinus rhythm and left ventricular hypertrophy. The echocardiography described left ventricular hypertrophy without dilatation, normal systolic function, diastolic dysfunction (delayed relaxation), calcification of the mitral valve's ring, and aortic atheromatosis. The mitral valve was echo-dense, with small calcifications and motion within normal limits. The aortic valve was also echo-dense, calcified, with limited opening (14 mm) and mean aortic valve pressure gradient of 30 mmHg. The chest X-ray was normal (cardiothoracic ratio of 0.39, with no other changes). The ophthalmoscopic examination revealed hypertensive retinopathy grade II (Gunn crossing sign was present).

After establishing the diagnosis of a RVH, ACE inhibitors were replaced with calcium channel blockers and the patient was referred to the Service of Cardiovascular Surgery for carotid angiography examination and coronarography. The latter investigation revealed severe coronary disease. The left main coronary (LC) artery had at its bifurcation a calcified atheromatous plaque. Left anterior descending (LAD) artery had a severe stenosis (95%) due to a calcified atheromatous plaque in its first segment and diffuse and non-significant stenosis in its distal segments, while the left circumflex artery (LCx) and the right coronary artery (RCA) had no lesions. Carotid angiography was performed but did not show any lesions.

Non-selective renal arteriography revealed that the right renal artery had a severe stenosis (95%) in its proximal third part. Left renal artery showed a severe stenosis (80%) in its proximal third part, too. Aortography demonstrated occlusion of the abdominal aorta just under the origin of the renal arteries, without visualization of the distal arterial bed.

Based on a resistant hypertension, in the presence of the bilateral stenosis of renal arteries, we decided to proceed to surgical intervention for revascularization. Percutaneous transluminal angioplasty of the renal artery and stenting were performed in both kidneys. Also, the patient underwent artery bypass grafting, with internal mammary artery graft, aortobifemoral bypass surgery with Hemashield patch and endarterectomy with removal of the thrombus from the abdominal aorta.

In the postoperative period, the recovery process was good, with the decreasing of serum creatinine levels and the normalization of blood pressure values under minimal antihypertensive medication.

Discussions

Up to 15% of the patients diagnosed with hypertension develop a resistant form of the disease, with values that are not controlled with proper medication [2]. The cardiovascular risk is definitely higher in patients with resistant hypertension than in those having a hypertensive disease that is responsive to drugs meant to control it [2, 7]. Also, renal artery stenosis is one of the most common causes of chronic kidney disease in the elderly [8]. Therefore, the meticulous follow-up is essential for an adequate approach of the condition and for the secondary prevention of stroke and other cardiovascular events.

This case report emphasizes the need for monitoring the patient with hypertension and other cardiovascular risk factors, such as atherosclerosis, smoking and dyslipidemia. It is of great importance to do a complete physical examination of the patient, including the auscultation of the renal arteries for the early discovery of a renal bruit that would suggest a significant stenosis at that level.

Taken into consideration the case of our male patient, who had multiple risk factors, we highlight the fact that his secondary RVH was caused by the atherosclerotic renal artery disease, and overlapped an existing essential hypertension.

As those two suspicious adrenal masses identified in our patient were smaller than 4 cm, imaging suggested they are benign and the hormonal assessment was negative (urinary VMA and metanephrine, plasmatic aldosterone, and cortisol having normal values), we considered them as being incidentalomas and decided to follow them. However, approximately 75% of them are nonfunctional adenomas [9].

In our case, the fact that blood tension values and renal function got normalized after surgical intervention on renal artery stenosis and minimal antihypertensive treatment was a strong argument for the renovascular cause of the resistant hypertension and demonstrated that there was no causal link between patient's hypertension and his adrenal incidentalomas.

A particular aspect of this case was represented by the absence of a major renal impairment in a patient treated with ACE inhibitors and bilateral stenosis of renal arteries, despite the fact that his blood tests showed hypokalemia, raised alkaline reserve and a mild increase of serum urea and serum creatinine levels. Some studies also evaluated the plasma renin activity measured in a blood sample from the renal vein, in order to determine whether the renal artery stenosis activates the RAS, increasing the plasma level of renin [8]. However, for the presented case this blood investigation was not performed.

In the case of a resistant hypertension, the morphology of kidneys and renal arteries as well as their function should be evaluated by various imaging methods.

The imaging techniques (Doppler ultrasound, MRA, CTA, and renal angiography), currently used in the evaluation of RVH, are the best tools for the assessment of renal function, arterial perfusion, and morphology of the kidneys.

Kidney ultrasound and Doppler examination, which are non-invasive techniques, can be used in patients with moderate-to-severe renal function impairment. Doppler ultrasound allows diagnosis and grading of renal artery stenosis in atherosclerotic disease and can indirectly

measure the hemodynamic impact of renal artery stenosis on the homolateral kidney, by virtue of the stenosis-related decrease in pulse pressure [10].

CTA (which requires small amounts of contrast agent) and MRA of the renal arteries are also useful to detect the kidneys morphology and function, and the narrowing of the renal arteries, especially when renal failure is present [6]. Both modalities have high specificity, but low sensitivity [11].

In our case, CTA lack of contrast agent excretion at 10 minutes post-contrast injection was a reliable indicator of right renal hypoperfusion because a renal retention of the radiopharmaceutical appeared due to decreased urinary output secondary to reduced glomerular filtration rate (GFR). Also, the image was suggestive for marked renal artery stenosis on the right side.

However, gadolinium-enhanced MRA had the additional advantage of not having radiation exposure, and a limited nephrotoxicity.

Moreover, as in our case, when serum creatinine indicates only a mild impairment of the kidney function, invasive renal angiography could also be used to confirm and evaluate the bilateral renal artery stenosis, before the surgical intervention took place. Even if it is an older technique, non-selective renal arteriography provides direct, definitive demonstration of anatomic lesions that may be responsible for RVH. In addition to identifying arterial stenoses and providing data which permit estimation of the degree of stenosis, arteriographic findings are often sufficiently specific for diagnosis of the underlying disease [12].

Some other reports on RVH investigated the microscopic changes that developed in kidney due to this medical condition. Histopathological exam made after nephrectomy revealed nephroangiosclerosis as the cause of malignant hypertension [13]. However, once the atherosclerotic cause of a RVH is confirmed, early management and appropriate treatment of the case must be established [14].

Many studies, including CORAL (*Cardiovascular Outcomes for Renal Atherosclerotic Lesions*), did not succeed in showing the benefits of renal revascularization over the use of intensive drug therapy, at least on the short term [14, 15]. Others argue that surgery has an important impact on the management of congestive heart failure, but it is also considered to reduce the hospitalization period and the decline in renal function [8].

Our patient underwent percutaneous transluminal angioplasty of the renal artery and stenting in both kidneys, along with aorto-coronarian bypass surgery and aorto-bifemoral bypass surgery with Hemashield patch. Also, the thrombus located in the abdominal aorta was removed by endarterectomy. The interventional treatment improved our patient's quality of life because he received only a minimum dose of antihypertensive medication at the moment of his discharge. An antiplatelet drug and a lipid lowering-agent (statin) were also part of the recommended at-home treatment along with the need to change his lifestyle, as indicated by the *European Society of Hypertension*/*European Society of Cardiology* (ESH/ESC) Guidelines for the management of arterial hypertension [16, 17].

Conclusions

In an ageing society, it is extremely important to suspect a RVH, which in the presence of atherosclerotic renal artery disease is a medical condition that is more accurately diagnosed nowadays, due to the modernization of imaging techniques and a better management of the patients suffering from resistant hypertension. The early diagnosis of bilateral renal artery stenosis and an immediate therapeutic approach of the case (surgery and the appropriate use of antihypertensive drugs) are essential towards a better cardiovascular outcome and a lower risk of undesirable events.

Conflict of interests

The authors declare that they have no conflict of interests.

References

[1] Sinnott SJ, Smeeth L, Williamson E, Douglas IJ. Trends for prevalence and incidence of resistant hypertension: population based cohort study in the UK 1995–2015. BMJ, 2017, 358:j3984.

[2] Judd E, Calhoun DA. Apparent and true resistant hypertension: definition, prevalence and outcomes. J Hum Hypertens, 2014, 28(8):463–468.

[3] Myat A, Redwood SR, Spertus JA, Williams B. Resistant hypertension. BMJ, 2012, 345:e7473.

[4] Doroszko A, Janus A, Szahidewicz-Krupska E, Mazur G, Derkacz A. Resistant hypertension. Adv Clin Exp Med, 2016, 25(1):173–183.

[5] Labidi J, Touat D, Abdelghanim K, Ajili F, Ariba YB, Abdelhafidh NB, Louzir B, Othmani S. Renovascular hypertension: a report of 21 cases. Saudi J Kidney Dis Transpl, 2014, 25(1):96–100.

[6] Baumgartner I, Lerman LO. Renovascular hypertension: screening and modern management. Eur Heart J, 2011, 32(13):1590–1598.

[7] Plouin PF, Bax L. Diagnosis and treatment of renal artery stenosis. Nat Rev Nephrol, 2010, 6(3):151–159.

[8] Ando K, Takahashi K, Shibata S, Matsui H, Fujita M, Shibagaki Y, Shimosawa T, Isshiki M, Fujita T. Two cases of renovascular hypertension and ischemic renal dysfunction: reliable choice of examinations and treatments. Hypertens Res, 2004, 27(12):985–992.

[9] Song JH, Chaudhry FS, Mayo-Smith WW. The incidental adrenal mass on CT: prevalence of adrenal disease in 1,049 consecutive adrenal masses in patients with no known malignancy. AJR Am J Roentgenol, 2008, 190(5):1163–1168.

[10] Boddi M. Renal ultrasound (and Doppler sonography) in hypertension: an update. In: Islam MS (ed). Hypertension: from basic research to clinical practice. Vol. 2, Series "Advances in Internal Medicine", "Advances in Experimental Medicine and Biology" – vol. 956, Springer International Publishing, Switzerland, 2017, 191–208.

[11] Vasbinder GB, Nelemans PJ, Kessels AG, Kroon AA, Maki JH, Leiner T, Beek FJ, Korst MB, Flobbe K, de Haan MW, van Zwam WH, Postma CT, Hunink MG, de Leeuw PW, van Engelshoven JM; Renal Artery Diagnostic Imaging Study in Hypertension (RADISH) Study Group. Accuracy of computed tomographic angiography and magnetic resonance angiography for diagnosing renal artery stenosis. Ann Intern Med, 2004, 141(9):674–682; discussion 682.

[12] Black HR, Glickman MG, Schiff M Jr, Pingoud EG. Renovascular hypertension: pathophysiology, diagnosis, and treatment. Yale J Biol Med, 1978, 51(6):635–654.

[13] Niculae A, Peride I, Marinescu-Paninopol A, Vrabie CD, Ginghină O, Jecan CR, Bratu OG. Renal artery bilateral arteriosclerosis cause of resistant hypertension in hemodialysed patients. Rom J Morphol Embryol, 2016, 57(2):591–594.

[14] Textor SC. Secondary hypertension: renovascular hypertension. J Am Soc Hypertens, 2014, 8(12):943–945.

[15] Mark PB, Schiffrin EL, Jennings GL, Dominiczak AF, Wang JG, De Buyzere M, Staessen JA. Renovascular hypertension: to stent or not to stent? Hypertension, 2014, 64(6):1165–1168.

[16] Costache II, Cozma A, Aursulesei V. Hipertensiunea arterială secundară. În: Aursulesei V, Bădilă E, Bartoş D (eds). Hipertensiunea arterială. De la practică la teorie, de la pacienţi la ghiduri. Ed. Niculescu, Bucureşti, 2017, 209–230.
[17] Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, Christiaens T, Cifkova R, De Backer G, Dominiczak A, Galderisi M, Grobbee DE, Jaarsma T, Kirchhof P, Kjeldsen SE, Laurent S, Manolis AJ, Nilsson PM, Ruilope LM, Schmieder RE, Sirnes PA, Sleight P, Viigimaa M, Waeber B, Zannad F, Redon J, Dominiczak A, Narkiewicz K, Nilsson PM, Burnier M, Viigimaa M, Ambrosioni E, Caufield M, Coca A, Olsen MH, Schmieder RE, Tsioufis C, van de Borne P, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Clement DL, Coca A, Gillebert TC, Tendera M, Rosei EA, Ambrosioni E, Anker SD, Bauersachs J, Hitij JB, Caulfield M, De Buyzere M, De Geest S, Derumeaux GA, Erdine S, Farsang C, Funck-Brentano C, Gerc V, Germano G, Gielen S, Haller H, Hoes AW, Jordan J, Kahan T, Komajda M, Lovic D, Mahrholdt H, Olsen MH, Ostergren J, Parati G, Perk J, Polonia J, Popescu BA, Reiner Z, Rydén L, Sirenko Y, Stanton A, Struijker-Boudier H, Tsioufis C, van de Borne P, Vlachopoulos C, Volpe M, Wood DA. 2013 ESH/ESC guidelines for the management of arterial hypertension: the Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J, 2013, 34(28):2159–2219.

Corresponding authors

Claudia Florida Costea, Assistant Professor, MD, PhD, Discipline of Ophthalmology, Department of Surgery II, "Grigore T. Popa" University of Medicine and Pharmacy, 16 Universităţii Street, 700083 Iaşi, Romania; Phone +40744–972 648, e-mail: costea10@yahoo.com

Victor Laurian Rusu, MD, Clinic of Rehabilitation – Neurology, Rehabilitation Teaching Hospital, 14 Pantelimon Halippa Street, 700661 Iaşi, Romania; Phone +40754–301 337, e-mail: rusu.victorl@gmail.com

Received: September 9, 2017

Accepted: May 5, 2018