Renal artery bilateral arteriosclerosis cause of resistant hypertension in hemodialysed patients

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Abstract
We present the case of a 57-year-old hemodialysed male patient known with severe hypertension resistant to six classes of hypotensive medication, in maximal doses, correlated with increased ultrafiltration during the hemodialysis session. In this case, bilateral nephrectomy was performed as final treatment option for malignant hypertension, and histopathological examination of both kidneys emphasized arteriosclerosis lesions. The results consisted in better hypertension management, with a reduction in both the number and doses of antihypertensive drugs.

Keywords: malignant hypertension, hemodialysis, nephrectomy, outcome.

Introduction
Malignant arterial hypertension (MHT) is a severe disease that produces retinopathy stage three or four (retinal exudates and hemorrhages ± papilledema), resistant to three or more hypotensive classes of drugs in maximal doses [1, 2]. It is a disease with a high risk of cardiovascular events (stroke, myocardial infarction) with a higher rate of mortality in the absence of a fast and proper treatment [3–5]. One of the main causes of secondary renal MHT is atherosclerotic renal artery stenosis, especially when the lesions are severe – over 70% obstruction [2, 5, 6]. Between 10–45% of patients with MHT are estimated to have renal artery stenosis [5, 7, 8]. In general, male population over 45-year-old is more affected [5]. The stenosis produces renal hypoperfusion with hyperactivation of rennin–angiotensin–aldosterone system (RAAS), consequently leading to hydrosaline retention with elevated arterial pressure [5, 9]. About 23% of MHT cases are associated with chronic kidney disease (CKD), in which hypertension has a multifactorial pathogenesis: usually is volume dependent, but also hyperstimulation of RAAS, and nervous sympathetic system, nitric oxide deficiency or high level of endothelin and oxidative stress are implicated [5, 10–15]. In general, patients with MHT and CKD must be submitted to investigation for the presence of renal artery stenosis. Duplex ultrasonography, computed tomographic angiography (CTA) and magnetic resonance angiography (MRA) are the most commonly used screening tests; plasma renin activity is no longer used; but arteriography remains the “gold standard” for the diagnosis of renal artery stenosis [5, 16–18]. For the treatment of resistant arterial hypertension is recommended to associate up to three or more classes of hypotensive drugs with different action mechanisms (e.g., diuretics) along with controlling the other risk factors [5, 19–22]. When medication is no longer effective, it is necessary to perform revascularization surgery (percutaneous transluminal angioplasty, stent or by-pass) or transcatheter renal denervation with radiofrequency of the adventitial renal artery sympathetic nerves [5]. Bilateral nephrectomy is required in case of bilateral stenosis associated with CKD (with other etiology than ischemia) and repeated episodes of pulmonary edema that are potentially life threatening.

The aim of the present case report was to emphasize the need of bilateral nephrectomy on the management of malignant arterial hypertension due to bilateral renal artery stenosis in chronic hemodialysed patients.

Case presentation
A 57-year-old male patient known with autosomal dominant polycystic kidney disease and on chronic hemodialysis program for four years presented the following symptomatology for three months: intense headache, vertigo, impaired vision and constantly very high values of arterial pressure (systolic blood pressure 280/130 mmHg), resistant to medical treatment and high ultrafiltration. Serum analysis results emphasized creatinine 13.3 mg/dL,
Hb (hemoglobin) 12.7 g/dL, Ht (hematocrit) 36.6%. Renal ultrasound highlighted both kidneys about 120 mm length with disorganized structure, and multiple transonic formations with different diameters, well delimited. Signs of stage four-hypertensive angiopathy according to Keith–Wagener classification were noticed at funduscopic test. The echocardiography exam revealed the following pathological features: left ventricle’s wall concentric hypertrophy with diastolic dysfunction (septum more hypertrophied in the third basal – 22 mm), the mitral and aortic valve thicker but mobile, and an ejection fraction of 50%, without pericardial fluid. Before hospital admission, the patient’s therapy included an association of four classes of antihypertensive drugs, without effect in decreasing blood pressure. During hospitalization, an association of six classes of hypotensive drugs was used (Metoprolol 200 mg/day, Nifedipine 90 mg/day, Clonidine 1.2 mg/day, Furosemide 80 mg/day, Candesartan 32 mg/day and intravenous Nitroglycerine), according to hypertensive guidelines, in maximal allowed doses, together with intravenous Nitroglycerine, lipid lowering and antiplatelet medication, but also without any benefit. In order to exclude an endocrine cause of MHT, hormonal determinations were made – TSH (thyroid-stimulating hormone), free T4 (free thyroxine), cortisol, plasmatic aldosterone – that were in normal limits. An arteriography was performed that showed 60% stenosis after origin on right renal artery and 80–90% serial stenosis on the segmentary branches, as well as 80% stenosis after origin on the left renal artery with 90% serial stenosis on the segmentary branches (Figure 1).

Considering the results, bilateral nephrectomy was considered as the only viable treatment option and the surgical associated risks were presented to the patient that gave his consent to the procedure. After the intervention, the patient recovered quickly without any post-surgical complications. Although the blood pressure values decreased, the patient still required the administration of three classes of hypotensive drugs (beta-blocker, calcium channels blocker and angiotensin receptors blocker) associated with lipid lowering and antiplatelet medication.

Furthermore, after the surgical intervention, both kidneys were sent to the Department of Pathology of our Hospital, where the examination emphasized arteriosclerosis lesions, proving once again the cause of malignant hypertension (Figure 2).

Discussion

MHT represents a major problem of diagnosis and treatment because increases the risk of cardiovascular events with high mortality rate if not treated properly and quickly [2–5]. The presence of MHT is suspected when blood pressure is constantly on high values despite the administration of more than three hypotensive drugs, one of which is a diuretic [2], and funduscopic exam shows exudates and hemorrhages with or without papilledema [1, 2, 5, 23].

Figure 1 – (A) Abdominal aorta – global arteriography; (B) Abdominal aorta arteriography with visualization of renal arteries emerging; (C) Left renal artery arteriography showing serial stenosis on the renal artery and its segmentary branches; (D) Right renal artery arteriography showing serial stenosis on the renal artery and its segmentary branches.
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Severe hypertension is usually secondary to endocrine (primary hyperaldosteronism, pheochromocytoma, hyper-/hypothyroidism) or renal causes. In our patient, the hormonal analysis as plasmatic aldosterone, cortisol and thyroidal hormones were in normal limits. CKD is frequently associated with high-pressure values, resistant to treatment, contributing primarily to fluid retention and then increased activity of sympathetic nervous system and RAAS, together with nitric oxide deficiency [5, 20, 24, 25]. In many cases, renal secondary hypertension is caused by atherosclerotic renal artery stenosis, especially with over 70% obstruction [5–7]. These atherosclerotic deposits are located in the proximal segment of renal arteries or at the ostium. Duplex ultrasonography, CTA and MRA are the most commonly used screening tests, but arteriography still remains the “gold standard” for diagnosis of arterial stenosis [5, 17, 18]. Stenosis produces renal hypoperfusion with hyper-reactivity of RAAS, which determines hydrosaline retention with concomitant interstitial tubular injury and fibrosis, increasing blood pressure [5, 9, 18]. These patients may have repeated episodes of pulmonary edema with high risk of cardiovascular events [5, 7]. Although the patient’s prognosis has improved in the last years due to the new classes of hypotensive drugs, there are situations when pharmacotherapy alone is not enough, and revascularization methods as angioplasty and by-pass, transcatether denervation or nephrectomy are required [5]. Especially in advanced long-term CKD, atherosclerotic renal artery stenosis MHT may often be refractory to medication or revascularization (CORAL study), and another therapeutic approach is recommended [26]. The mineralocorticoid receptor antagonists such as Spironolactone or Eplerenone – associated with a central blocker hypotensor and a loop diuretic – demonstrated to have a good effect in controlling blood pressure [19], but in our hemodialysed patient it was contraindicated because of the hyperkalemia produced by aldosterone antagonists (also, his plasma aldosterone was in normal limits). After hospital admission, the patient received a combination of six classes of hypotensive drugs (Metoprolol 200 mg/day, Nifedipine 90 mg/day, Clonidine 1.2 mg/day, Furosemide 80 mg/day, Candesartan 32 mg/day, in maximal allowed doses (according to European Guidelines for Management of Arterial Hypertension [19]) and intravenous Nitroglycerine with no results in lowering blood pressure. Although radiofrequency transcatether renal denervation at adventitial arterial wall is a minimal invasion method for resistant hypertension, it was not applicable to our patient, because his glomerular filtration rate (GFR <45 mL/min./1.73 m² represents contraindication [24]). Therefore, there are necessary radical intervention measures as bilateral nephrectomy in hemodialysed patients presenting resistant hypertension because of multifactorial mechanisms (hydrosaline retention, hyperactivity of RAAS, hyperactivity of sympathetic nervous system, nitric oxide deficiency, oxidative stress), concomitant with atherosclerotic renal artery stenosis injury and other associated cardiovascular risk factors (e.g., smoking, male sex, dyslipidemia) [5, 13, 14, 27–30]. Bilateral nephrectomy was performed in this patient, because of bilateral stenosis both in the proximal and deep segments of the renal arteries. Angioplasty or by-pass revascularization was futile. Furthermore, histopathological exam highlighted the presence of arteriolosclerosis lesions in both kidneys. Post-intervention, the evolution was favorable, with gradual decrease in blood pressure, but still requiring a combination of three antihypertensive drugs.
Conclusions

In hemodialysed patients with resistant hypertension, secondary to bilateral atherosclerotic renal stenosis, with no solution of revascularization or denervation, bilateral nephrectomy is the first treatment option.

Conflict of interests

The authors declare that they have no conflict of interests.

References


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