

Chronic total occlusion of renal artery in symptomatic young patient with resistant hypertension: is a revascularization necessary or redundant?

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Renal artery stenosis (RAS) can be described as a narrowed vessel lumen at least 60% which hemodynamic significance may be subsequently confirmed by the pressure gradient measuring with endovascular methods. Frequency with which a disease appears in a population is 5–10% and its dominant cause is the occurrence of atherosclerotic plaque. Infrequent causes include fibromuscular dysplasia and vasculitis such as Takayasu arteritis. Diagnostic gold standard of RAS is digital subtraction angiography (DSA) with pressure measurements. Nevertheless, Doppler ultrasonography (DUS), magnetic resonance angiography (MRA) and computed tomography angiography (CTA) may also play a key role during diagnostics process. Revascularization of narrowed or occluded vessel consists of percutaneous transluminal angioplasty (PTA) with balloon, drug-coated balloon or stent implantation. Surgical procedures are rare and dedicated only to treatment-resistant cases.

We reported a 19-year-old patient with resistant arterial hypertension, left ventricular hypertrophy and stenosis of the proximal segment of the right renal artery, confirmed in angio-CT examination. Subsequent follow-up endovascular diagnostic procedure after 12 months revealed complete occlusion of renal artery with angiographic features of chronic total occlusion (CTO). Additionally, laboratory tests showed increase of creatinine level, with an estimated eGFR of 32.9 ml/min/1.73 m². Considering the whole case – history of fibromuscular dysplasia, deterioration of renal function and the presence of resistant hypertension in a young patient – the invasive treatment was decided. Revascularization with paclitaxel-coated balloon was performed leading to renal perfusion improvement and normalization of the creatinine level. The patient was discharged from hospital with significantly reduced doses of antihypertensive drugs.

There are few publications on opening CTOs of renal arteries. The method is rarely used and research in this field should be extended. While routine revascularization is not recommended, in some cases, we should take under consideration that early restoration of normal renal perfusion can bring benefits to the patient both clinical and related to the number of drugs taken and quality of life.

Keywords: chronic total occlusion, renal artery, resistant hypertension

Abbreviations: ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensinreceptor blocker; CTA, computed tomography angiography; CTO, chronic total occlusion; DCB, drug-coated balloon; DSA, digital subtraction angiography; DUS, Doppler ultrasonography; FMD, Fibromuscular dysplasia; MRA, magnetic resonance angiography; PTA, percutaneous transluminal angioplasty; RAAS, renin-angiotensin-aldosterone system; RAS, renal artery stenosis

INTRODUCTION

Renal artery stenosis (RAS) refers to the presence of a lesion that narrows the vessel lumen by at least 60%, the hemodynamic significance of which can be further confirmed by determining the pressure gradient with endovascular methods [1]. It can occur in up to 5–10% of the general population, and its main cause is the presence of atherosclerotic plaque. Thus, the prevalence of the disease increases with age and correlates with the presence of cardiovascular risk factors: hypertension, dyslipidemia, smoking, male sex, diabetes, chronic kidney disease or a family history. In 20%, it occurs bilaterally or involves the single functioning kidney. Rarer causes include fibromuscular dysplasia (FMD), a history of or active vasculitis including the presence of Takayasu arteritis (type 3, 4 or 5 disease). FMD occurs in a younger population, is nine

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times more common in women and is more common in people without cardiovascular risk factors, except for smoking, which contributes to its occurrence. It develops in less than 1% of the general population and is usually diagnosed in the fifth decade of life, often incidentally during diagnostic imaging performed for other clinical indications, but cases diagnosed in childhood have also been described. The pathogenesis of FMD is not fully understood. There are suggestions that it is related to the presence of genetic and environmental factors, smoking and estrogens [1,2]. In 10%, the disease occurs in a family member. FMD takes the form of narrowing or widening (ectasias, aneurysms) of medium-sized arteries, and the sudden dissection of the vessel at the site of the primary lesion may occur. The condition most often affects the arteries of the central nervous system and renal arteries, less often other locations in the abdomen and vessels of the extremities. RAS, regardless of the cause, can lead to a number of adverse consequences. Reducing the flow behind the stenosis results in increased secretion of renin in the affected kidney, which leads to the activation of the renin-angiotensin-aldosterone system (RAAS) and the sympathetic nervous system and consequently the development of secondary hypertension and increased cardiovascular risk. RAS is the most common form of renovascular hypertension and one of the most common (5–28%) of secondary hypertension in general [3]. Progressive renal ischemia may contribute to the deterioration of its excretory function and lead to chronic kidney disease and, in advanced cases, to loss of function and atrophy of the organ. During RAS, there may also be recurrent pulmonary oedema with abrupt onset (flash pulmonary edema), and in those cases, exclusion of structural disease in the heart suggests the presence of RAS. Other conditions that raise suspicion of renal artery disease include onset of hypertension less than 30 years of age, rapid acceleration of previously well controlled blood pressure, onset of resistant hypertension, hypertensive crisis (acute heart failure, hypertensive encephalopathy), unexplained renal atrophy or disproportion in kidney size, unexplained kidney failure, worsening of kidney function after starting an angiotensin-converting enzyme inhibitor (ACEi) or an angiotensin-receptor blocker (ARB).

In the screening diagnosis of RAS, Doppler ultrasonography (DUS) is of primary importance. The performance and interpretation of the result requires a great deal of experience, and the difficulties in the examination are encountered in overweight patients. It is worth remembering that DUS may overestimate the degree of stenosis in relation to the reference test, which is digital subtraction angiography (DSA) with pressure measurements. The latter one is performed especially in situations of inconclusive noninvasive findings or when revascularization is being considered. The significance of stenosis is confirmed by a systolic pressure gradient more than 20 mmHg or a ratio of pressure behind the lesion to pressure before the lesion of less than 0.9 [4]. Magnetic resonance angiography (MRA) or computed tomography angiography (CTA) also play an important role in the diagnosis.

The mere finding of RAS does not imply the need for treatment, especially endovascular one. The basis is the

elimination of cardiovascular risk factors, treatment with a statin and acetylsalicylic acid in atherosclerotic cause. The occurrence of hypertension requires taking steps in accordance with the relevant guidelines, with ACEi, or ARBs as first-line pharmacotherapy, because they improve the prognosis in this group of patients, including mortality reduction. The exception is when the stenosis is bilateral or involves a single kidney, in which case these medicines may lead to a significant reduction in glomerular filtration. Therapy with ACEi and ARBs in this subgroup of patients can be used exceptionally, but it should only be performed under strict monitoring [5,6]. In addition, diuretics, beta-blockers and calcium antagonists are effective.

Revascularization consists of percutaneous transluminal angioplasty (PTA) with only balloon or with stent implantation; recently, an attractive option has been the use of a drug-coated balloon (DCB). Surgery is undertaken only in exceptional or refractory cases. The discussion on the effectiveness and benefits from invasive procedures has been going on for years. Currently, the authors of the guidelines do not recommend routine revascularization since there are no benefits of such management over conservative treatment have been demonstrated, apart from a slight reduction in the number of antihypertensive drugs used (2.96 vs. 3.18 drugs) [1,7–10]. Studies, including the randomized CORAL and ASTRAL trials, have not confirmed the benefit of revascularization in terms of renal function [10,11]. However, it should be remembered that only patients with atherosclerotic cause of stenosis were included in these studies. Thus, European guidelines do not recommend routine revascularization for RAS (recommendation class III) and allow endovascular treatment in specific causes or clinical situations, such as stenosis due to FMD, renal artery disease with sudden pulmonary edema or congestive heart failure and in renal artery disease with acute renal failure with oliguria or anuria [1]. In the case of FMD, it should be undertaken only in symptomatic patients with organ ischemia, and balloon angioplasty is the treatment of choice, with stent implantation only in case of arterial dissection or balloon angioplasty failure (class of recommendations IIa).

CASE PRESENTATION

Dilemmas related to indications for invasive treatment were reflected in the case of a 19-year-old patient with arterial hypertension for several years, currently on therapy with four antihypertensive drugs in full doses, including a thiazide-like diuretic (chlorthalidone), meeting the criteria for resistant hypertension. The patient with left ventricular hypertrophy diagnosed in echocardiography and stenosis of the proximal segment of the right renal artery found in duplex Doppler examination, subsequently confirmed in angio-CT, was admitted for arteriography and assessment of the indications for revascularization. The length of both kidneys was equal and amounted to 10.5 cm. In an invasive examination (DSA), which the patient underwent 12 months after angio-CT imaging, complete arterial occlusion with angiographic features of chronic total occlusion (CTO) was found (Fig. 1). In the parenchymal phase, delayed contrasting of the right kidney by the collateral

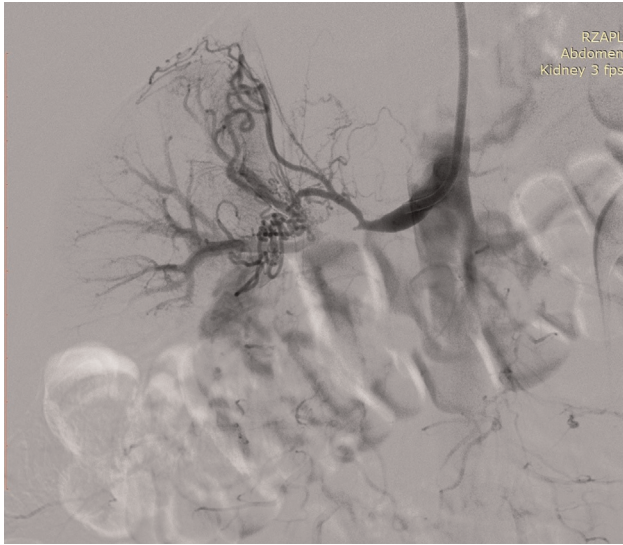


FIGURE 1 Complete arterial occlusion with angiographic features of chronic total occlusion.

circulation from the adrenal arteries was revealed, with clearly worse visualization of the lower pole of the kidney (Fig. 2). Since BOLD MRI was available only in a few centers and the information obtained from DUS and CT was satisfactory, MRI was not performed in this patient.

The laboratory tests showed a creatinine level of 2.68 mg/dl, with an estimated eGFR of 32.9 ml/min/1.73 m², which was the patient's first abnormal result compared to normal baseline values 1 year earlier and has been uncontrolled since then by the patient. Given the overall clinical picture – stenosis due to FMD, deterioration of renal function and the presence of resistant hypertension in a young patient – it was decided that revascularization was necessary. A procedure was performed to open the chronically total occluded renal artery. After crossing the occlusion with ASAHI wire, the lesions were dilated with balloons of increasing diameter, and finally, prolonged



FIGURE 2 Delayed contrasting with worse visualization of the lower pole of the kidney.

inflation of a 5.0 x 40 mm paclitaxel-coated balloon was performed. An exceptionally good angiographic result was obtained, with a clear improvement in the perfusion of the entire renal parenchyma (Fig. 3).

After hydration, the creatinine level normalized and the patient was discharged home with reduced doses of anti-hypertensive drugs. Control duplex Doppler examinations of the renal arteries after 3 and 6 months showed a sustained good result of the procedure. Creatinine levels remained normal, and the procedure itself allowed to maintain the treatment with three drugs at doses half the baseline. It was unable to achieve normal blood pressure without antihypertensive treatment. The patient remains under observation with the recommendation of strict monitoring of blood pressure and periodic creatinine level, as the progression of the lesion in the renal artery was mildly symptomatic, and one of its markers was the deterioration of kidney function.

DISCUSSION

In the authors' opinion, the presented case perfectly illustrates that RAS is a disease of heterogeneous cause, and in the qualification for revascularization not only the underlying cause of the lesion should be taken into account, but also the full clinical picture together with the possible consequences of abandoning this form of therapy. In contrast, CTO of the renal artery is a much less common disease. There are almost no studies on revascularization in renal artery CTO, and they usually refer to single case reports, treated both with endovascular and surgical methods. Several randomized clinical trials, including STAR, CORAL and ASTRAL, have not clearly demonstrated the benefits of revascularization in patients with renal dysfunction and uncontrolled blood pressure [12]. Manohar *et al.* [12] prove that there is still a cohort of patients who may benefit significantly from angioplasty of chronic arterial occlusion renal. Oskin *et al.* [13], who compared nephrectomy and revascularization in a cohort of patients with chronic total renal artery occlusion, demonstrated improved renal function after revascularization, which was significantly and independently associated with improved survival. The authors of clinical trials postulate that the progressive deterioration of kidney function as a result of abandonment of revascularization leads to a situation where, after a temporary asymptomatic worsening of renal blood supply, at the stage of renal artery occlusion, prolonged hypoxia of the renal cortex activates the inflammation, triggers the cytokines release which results in infiltration of the kidney parenchyma and finally leads to fibrotic transformation. Clinically, this is manifested by deterioration of renal function, which at that stage may be irreversible, even after successful revascularization [12,14–16]. This gives rise to careful control of the patient with RAS, monitoring of clinical and laboratory parameters and, in some cases re-evaluation, the indications for revascularization before irreversible changes occur.

CONCLUSION

It should also be remembered that many of the high-risk patients with chronic renal artery occlusion after sudden pulmonary edema, with a rapid deterioration of kidney



FIGURE 3 Good angiographic result with an improvement of perfusion of renal parenchyma.

function, or an immediate acceleration of hypertension, were not included in the large studies mentioned above. This means that the optimal treatment for most burdened patients is not fully known. On the other hand, in patients disqualified from revascularization or waiting for the procedure, treatment with a statin is obligatory due to its impact on the progression of atherosclerotic changes in the renal artery and the inhibition of fibrosis in the ischemic kidney [16]. It is exceedingly difficult to indicate a group of patients who will clearly benefit from the unblocking of chronic renal artery occlusion. Each case should be discussed individually with a multidisciplinary team consisting of a cardiologist, interventional cardiologist/radiologist and a nephrologist. Both the European and AHA guidelines on FMD state that catheter angiography with hemodynamic evaluation is warranted to determine the need for angioplasty and to assess postangioplasty gradient effacement. The guidelines do not recommend routine revascularization, but their authors most often take the position that early restoration of normal renal perfusion in such a situation may bring benefits to the patient: restore normal kidney function, reduce the number of medicines and improve the quality of life [12,17]. Finally, a meta-analysis of many studies in the group of patients with RAS and FMD proved that angioplasty or surgical revascularization brought moderate benefits for patients [18]. The presented case confirms this thesis, especially considering the significant deterioration of kidney function which occurred, and which was permanently improved after successful endovascular treatment.

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This case report was in adherence with the Declaration of Helsinki. The authors declared that written informed consent was obtained from the patient for publication of this case report and accompanying images.

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the manuscript draft. Mateusz Wiśniowski edited the manuscript. Piotr Wańczura and David Aebisher contributed to data analysis, interpretation and intellectual content of critical importance to the work described. All authors had the opportunity to revise the manuscript.

The patient was regularly followed up, and the clinical data are traceable. The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of interest

The authors declare that they have no relevant financial interests.

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