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Case report

A 63–year–old female with bilateral renal artery stenosis – highlights on diagnosis and optimal medical treatment

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Abstract: Renal artery stenosis is responsible for approximately 75% of secondary hypertensive cases. A 63-year-old female patient with uncontrolled hypertension and other comorbidities including type 2 diabetes mellitus and knee osteoarthritis presented with drastically raised systolic blood pressure in this case report (220 mmHg). Bilateral abdominal bruits were detected upon of physical examination. Imaging investigation showed significant bilateral atherosclerotic renal artery stenosis. An optimal combination of antihypertensive agents mainly with an angiotensin converting enzyme inhibitor, other than interventional revascularization, was applied and resulted in controlled blood pressure.

Keywords: Bilateral renal artery stenosis; arteriosclerosis; renovascular hypertension; abdominal bruits; angiotensin converting enzyme inhibitors; angiotensin receptor blocker.

1. INTRODUCTION

Hypertension is one of the most leading causes of mortality in Vietnam and all over the world. About 80-95% patients are primary hypertension. It is, however, essential for clinicians to consider a secondary cause of hypertension in those at risk [1]. The prevalence of renal artery stenosis is 6.8% in people over 65 years old and 14% in those at risk and it is attributable for approximately 75% of secondary hypertension cases [2-4]. Renovascular hypertension is caused primarily by atherosclerotic renal artery stenosis and fibromuscular dysplasia, the former largely occurring more frequently in elderly adults with atherosclerosis risk factors [5]. It is controversial whether to initiate renal vascular intervention early in these patients. In this clinical case, a female patient was admitted to the hospital due to a hypertensive crisis on the background of uncontrolled blood pressure and comorbidities. The findings were consistent with bilateral renal artery stenosis ascribed to atherosclerosis. The blood pressure was then well controlled by optimizing medications mainly with an angiotensin converting enzyme (ACE) inhibitor without further invasive approach.

2. CASE DESCRIPTION

A 63-year-old female presented to the emergency department (ED) with a hypertensive crisis. At home, her blood pressure was 220/100 mmHg and reached 250/100 mmHg on admission without other symptoms. She was diagnosed with primary hypertension and type 2 diabetes mellitus 5 years earlier. She reported that her home systolic blood pressure was never lower than 140 mmHg and had admitted to the ED due to hypertensive crisis three times previously. The patient was prescribed with enalapril (10 mg qd), amlodipine (5 mg qd), indapamide (2.5 mg qd), bisoprolol (2.5 mg qd) and rosuvastatin (10 mg qd). Her glycemia was poorly controlled with insulin. The patient had taken meloxicam (7.5 mg qd) for her knee osteoarthritis but stopped several days before this admission.

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On physical examination, abdominal bruits were detected in the epigastric region and radiated bilaterally to upper quadrants which was louder on the right side. The bruit was holosystolic, high-pitched, and of grade III intensity. No significant acute target organ damage due to hypertension was detected.

In laboratory results, uncontrolled diabetes (glucose 26.8 mmol/L, HbA1c 11.7%), normal renal function (creatinine 85.4 μmol/L, eGFR 62.01 mL/min/1.73 m^2), normal complete blood count and normal lipid profile were observed. Echocardiography demonstrated left ventricular ejection fraction of 73% with no enlarged chambers. The ECG manifested sinus rate 75 bpm with poor R wave progression from V1–V3 and negative T waves on multiple leads.

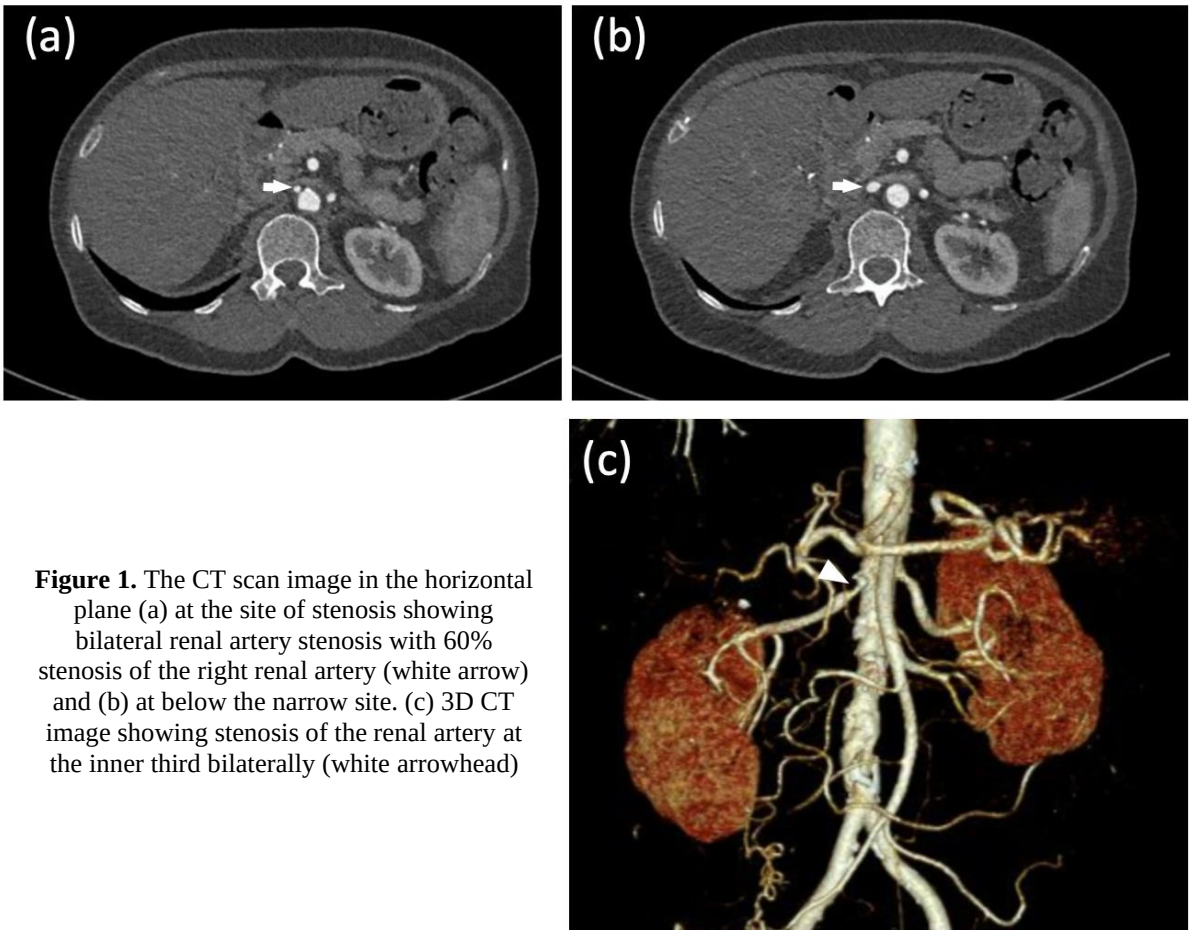

Figure 1. The CT scan image in the horizontal plane (a) at the site of stenosis showing bilateral renal artery stenosis with 60% stenosis of the right renal artery (white arrow) and (b) at below the narrow site. (c) 3D CT image showing stenosis of the renal artery at the inner third bilaterally (white arrowhead)

From physical examination signs, computed tomography renal artery angiography was indicated next. The results showed bilateral renal artery stenosis with uniform contrast filling. The atherosclerotic plaque caused 60% narrowing the vascular lumen on the right side and 50% on the other. No extrarenal collateral circulation was observed (figure 1).

The etiology of uncontrolled hypertension was established by bilateral renal artery stenosis identifiable on physical examination and on imaging investigation. The patient was then advised to withdraw NSAIDs and treated with a fixed-dose combination regimen of peridopril and amlodipine (Coveram® 10/10 mg) and bisoprolol 5 mg.

After 5 days of treatment, the patient's blood pressure remained above 140/90 mmHg measured by sphygmomanometer three times a day. Indapamide 1.5 mg once daily was then added and resulted in lowering the blood pressure to 130-140/90 mmHg. The patient was kept in hospital 5 days after new treatment applied to ensure the blood pressure was controlled prior to discharge. During the admission, she showed no adverse effects of the antihypertensive drugs.

On discharge, the prescribed drugs included fixed-dose combination regimen of peridopril and amlodipine (Coveram® 10/10 mg), bisoprolol (5 mg qd), indapamide (1.5 mg qd) for her hypertension. Her diabetes mellitus and chronic coronary syndrome were managed with Novomix® 30 Flexpen (25 units ac breakfast, 20 units ac dinner), metformin (500 mg bid), atorvastatin (40 mg qd) and clopidogrel (75 mg qd).

Throughout 3 months of follow up, the patient was advised to use home blood pressure and glycemia monitoring diary twice a day. The following check-ups showed controlled home and office blood pressure, and normal renal kidney function. Regarding blood glucose, her fasting values were better in range of 7.2-7.7 mmol/L under the follow-up of an endocrinologist.

3. DISCUSSION

Renovascular hypertension accounts for 75% of secondary hypertension [3]. The underlying mechanism involves decreased renal perfusion and increased activation of the Renin-Angiotensin-Aldosterone System (RAAS) [4]. An experimental study had shown a dramatically increase in plasma renin activity over a threshold of 58% renal artery stenosis [6]. It is important to recognize any condition such as fibromuscular dysplasia, Takayasu arteritis, renal artery aneurysm, renal atherosclerotic artery, etc. that causes decreased blood flow to the kidney may lead to renovascular hypertension [7]. The latter is far more prevalent among them that cause renovascular hypertension. Clinical clues for renovascular hypertension are listed in Table 1 [8]. In this patient, the stenosis was remarkable with narrowing 60% of the vascular lumen.

Table 1. Clinical clues for Renovascular Hypertension [3]

1.	Other vascular beds with significant atherosclerosis
2.	Hypertension begins before the age of 30 or beyond the age of 55
3.	Abdominal bruit
4.	Hypertension that was previously under control is worsening
5.	"Accelerated/malignant hypertension" or refractory hypertension
6.	Unilateral atrophic kidney on kidney ultrasound
7.	Kidney function rapidly deteriorates (spontaneous or in response to RAAS inhibitors)
8.	Hypertensive individuals with intact left ventricular ejection function may experience recurrent congestive heart failure or flash pulmonary edema
9.	Keith-Wegener-Barker grade III or IV on fundoscopy
10.	Angina in hypertensive individuals without severe coronary artery damage

Abdominal bruits have been documented in a substantial percentage of healthy individuals and are typically characterized by a low- to mid- pitch systolic bruit, heard between the epigastrium and the umbilicus and rarely bilaterally. In contrast, the presence of a holosystolic, high-pitched bruit heard in the epigastric region in the setting of hypertension helped to rule in renovascular hypertension with a likelihood ratio of 39 [9].

Various imaging investigations are available to evaluate renal artery stenosis. Renal artery Doppler ultrasonography, computed tomography renal artery angiography (CTA), and magnetic resonance angiography (MRA) are noninvasive imaging techniques for diagnosing renal artery disease (IB). Though renal angiography (DSA) remains the "gold standard", such invasive and expensive, time-consuming evaluation can lead to complications such as renal artery dissection or embolism. Therefore, it is recommended as second choice when noninvasive imaging evaluation is inconclusive (IIB-C) [10].

Medical treatment and revascularization are used to treat hypertension caused by atherosclerotic renal artery stenosis. Medical treatment is the first-line therapy, according to current guidelines [11]. ACE inhibitors and ARBs are considered fundamental treatment (IA, ACC/AHA) because RAAS activation is thought to be the main mechanism of renalvascular hypertension. They have proven effectiveness in lowering mortality in people with renal artery disease [5]. Nevertheless, these drugs, which dilate efferent arterioles may cause a decline in glomerular capillary hydrostatic pressure sufficiently leading to a transient decrease in glomerular filtration rate and increase in serum creatinine [5]. It is mandatory for close monitoring in patients who are prescribed with these medications (IIB-B).

Despite bilateral renal artery stenosis, the patient's renal function remained normal during maximum dose of ACE inhibitor. This can be explained that stenosis is sufficient for secondary hypertension but not critical for post-RAAS inhibition dysautoregulation leading to kidney injury. Safety and tolerability of ACE inhibitor/receptor in atherosclerotic renal artery stenosis were reexamined in recent study which showed that ACEI/ARB-based therapy was well tolerated without causing acute kidney injury or hyperkalemia in those with bilateral stenosis [12]. Notably, in this patient, CT scan of the renal artery did not show extrarenal collateral circulation. An experimental study had shown that collateral circulation develops in cases of significant renal artery stenosis and proportionally relates to the severity of stenosis as well as renal dysfunction [13].

Blood pressure control usually requires a mix of medications: calcium channel blocker, thiazide diuretic, and beta blocker have all been demonstrated to be useful in the treatment of renal artery stenosis (IC) [10]. In addition, statins are associated with improved survival rate, delayed progression of atherosclerotic lesions and reduced risk of restenosis after stenting in patients with atherosclerotic etiology [5].

Reperfusion therapy is of controversial benefit over medical management in individuals with atherosclerotic renal artery stenosis [5]. Three recent large studies including ASTRAL, CORAL and STAR did not show a difference in the antihypertensive effect and number of antihypertensive drugs needed (2.96 versus 3.18) as well as benefit in improving mortality rate, end-stage renal disease and major cardiovascular events when comparing post-reperfusion versus medical therapy [14-16].

It has been shown that following stenting, around a third of patients with severe renal artery stenosis and reduced renal function improve [5]. The remainders showed no advancement or even worsening in renal function whose hypothesis is a consequence of atheroembolization post-intervention [17]. As a result, routine reperfusion therapy in individuals with atherosclerotic renal artery stenosis is no longer indicated (IIIA). The low level of evidence for the efficacy of reperfusion intervention compared with medical management suggests that renal reperfusion should only be considered in the following patients: (1) fibromuscular dysplasia, (2) flash pulmonary edema or congestive heart failure with preserved ejection fraction in addition to renal

artery disease and (3) acute kidney injury with renal artery stenosis [10].

In the reported case, before this admission, the patient's blood pressure was not on target and there had been hospitalizations for hypertensive crisis. Bisoprolol 2.5mg dose was not effective in lowering blood pressure. Moreover, enalapril and amlodipine adjustment was not optimal [18]. The use of NSAIDs might be a temporary factor that contributed to the difficulty to control blood pressure. A high-pitched holosystolic abdominal bruit in combination with the results of computed tomography investigation provided clinical clues for important cause of uncontrolled hypertension that is renal stenosis.

There was no evidence for indicating interventional reperfusion despite bilateral stenosis. An optimal medical management was initiated in this patient. Four classes of antihypertensive drugs are used including an ACE inhibitor, a calcium channel blocker, a thiazide-like diuretic, and a beta blocker to help control blood pressure. Nonetheless, the blood pressure target that should be attained in patients with renovascular hypertension remains a source of debate. Some concepts imply that in individuals with significant renal artery stenosis, ideal blood pressure should be greater to maintain adequate renal perfusion; however, there is also data that contradicts such viewpoint [5]. In order to minimize further hypertension-mediated organ damage, we aimed for a blood pressure of 130–140/70–80 mmHg in this patient, as recommended by the European Society of Cardiology (2018) and the Vietnam National Heart Association (2018), which are based on age and co-morbidities [18, 19].

Conclusion

Renovascular hypertension is most frequently caused by atherosclerotic renal artery stenosis. The preferred treatment is optimal medical management mainly with an ACE inhibitor/ARB as a cornerstone often in combination with other antihypertensive agents even in bilateral stenosis. Other cardiovascular risk factors should also be well managed to minimize the progression of atherosclerotic renal stenosis. The benefits and risks of revascularization are always carefully considered since there is no proved evidence to support invasive approach.

CONFLICT OF INTEREST

None declared.

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