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Case Report

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An uncommon cause of severe hypertension: unilateral renal hypoplasia

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Abstract

We present the case of a patient with severe hypertension caused by unilateral renal hypoplasia and review the theoretical aspects behind secondary hypertension with a particular emphasis on renovascular hypertension and renal hypoplasia.

A 43-year old hypertensive patient presented to our clinic with persistently elevated blood pressure values in spite of treatment with perindopril, nebivolol and indapamide. Secondary hypertension was suspected and the patient was switched to verapamil 240 mg in 3 divided doses for 2 weeks prior to blood sampling for endocrine causes. TSH, freeT4, cortisol, aldosterone-renin ratio (ARR), plasma and urinary metanephrine levels were within the normal range. However, there was a slightly elevated serum renin (48.7 µUI/mL, normal range: 4.4 – 46.1) with normal aldosterone.

As a renal duplex ultrasound could not be obtained due to poor acoustic window, CT angiography was performed and demonstrated a small but patent right renal artery supplying a small right kidney. The patient was started on a fixed combination of olmesartan/amlodipine and is currently asymptomatic, with optimal BP control.

Congenital anomalies of the kidney and urinary tract include renal hypoplasia and dysplasia and the final diagnosis is provided by renal histology. Hypoplastic kidneys are small but normo-functional, as opposed to dysplastic kidneys which function abnormally. While malformations of the urinary tract and corresponding vasculature may remain silent well into adulthood, they carry a risk of infection, hypertension and kidney stone formation.

Keywords: arterial hypertension, severe hypertension, secondary hypertension, renovascular hypertension, hypoplastic kidney, renal hypoplasia, urinary tract malformations, renal asymmetry, small renal artery, small kidney

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Case presentation

A 43-year old man, recently diagnosed with grade 3 arterial hypertension (BP: 200/140 mmHg) presented to our clinic with dizziness on standing up.

His medical history included recurrent renal colic; moreover, both his mother and sister had been diagnosed with HTN before age 40. The patient had been undergoing treatment with bisoprolol 5 mg o.d, perindopril 10 mg o.d. and indapamide 2.5 mg o.d. since the initial diagnosis, one month prior.

On examination, his temperature was 36.8°C, the heart rate 72 beats per minute, the sitting blood pressure 150/90 mmHg, without a difference in readings between arms, and with no drop in BP on standing up, the respiratory rate 16 breaths per minute and the oxygen saturation 99% with the patient breathing ambient air. He was overweight (BMI = 29 kg/m^2) and the remainder of the clinical examination was normal. Echocardiography revealed mild circumferential ventricular hypertrophy and an ejection fraction of 60%, without evidence of dynamic left ventricular outflow tract obstruction, valvular disease or aortic coarctation.

Secondary hypertension was suspected and the patient was switched to verapamil 240 mg in 3 divided doses for 2 weeks prior to blood sampling for endocrine causes. TSH, freeT4, cortisol, aldosterone-renin ratio (ARR), plasma and urinary metanephrine levels were within the normal range. However, the patient had a slightly elevated serum renin (48.7 µUI/mL, normal range: 4.4 – 46.1) and normal aldosterone.

Due to poor acoustic window, a renal duplex ultrasound could not be obtained; thus, the patient underwent CT angiography which demonstrated a normal aorta with a small but patent right renal artery supplying the small right kidney (Figure 1), and normal contralateral kidney and renal artery (Figure 2). There was no evidence of adrenal adenoma, significant stenoses or aneurysmal dilations of the renal arteries, nor of nephrogram abnormalities.

Verapamil failed to control BP values, so immediately after obtaining blood samples for hormonal testing, the patient was started on a fixed combination of olmesartan/amlodipine 20 mg/5 mg o.d. and nebivolol 5 mg o.d. Currently, the patient is completely asymptomatic and has achieved optimal BP control.

Theoretical considerations

1. Secondary hypertension

Secondary hypertension is defined as increased systemic blood pressure (BP) due to an identifiable cause [1]. The 2018 ESC Guideline for the management of arterial hypertension (HTN) reports a prevalence of secondary hypertension between 5 and 15% [2]. Guidelines also recommend testing for a secondary cause of HTN in the following patients [2]:

- under 40 years of age with grade 2 HTN
- HTN onset during childhood
- acute worsening HTN in patients with previously documented chronically stable normotension
- resistant HTN (SBP > 140 mmHg / DBP >90 mmHg under treatment with 3 or more drugs at optimal doses, including a diuretic [1, 2])
- severe HTN (BP >180/110 mmHg [1])

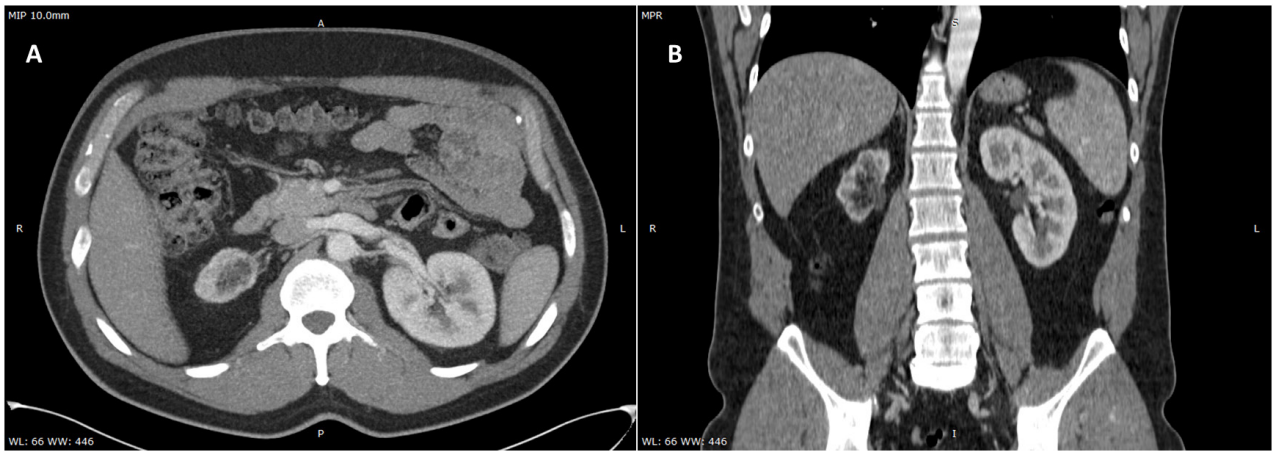

Figure 1. Panel A – Transverse section of CT angiogram demonstrating right kidney and renal artery hypoplasia. Panel B - Sagittal section of CT angiogram demonstrating right kidney hypoplasia.

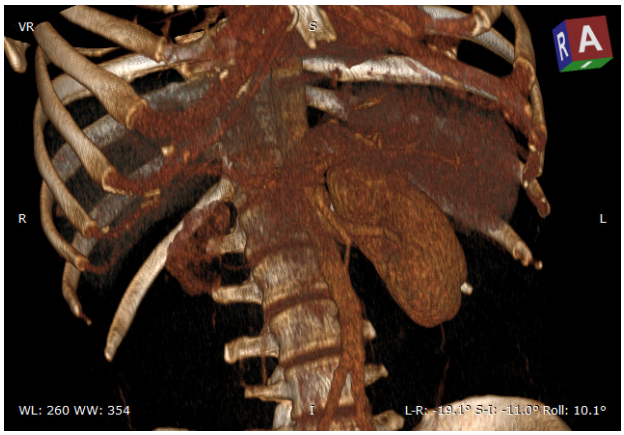

Figure 2. 3D reconstruction of the renal arteries using CTA showing right kidney and renal artery hypoplasia

- a hypertension emergency at presentation
- extensive hypertension-mediated organ damage (either asymptomatic or established renal and cardiovascular disease)
- clinical or biochemical features suggestive of endocrine causes of HTN; family history of pheochromocytoma
- clinical features suggestive of obstructive sleep apnea

The prevalence of secondary hypertension varies with age and is more common in younger patients; the figure is close to 30% in those 18 to 40 years of age [3]. In adults (19 - 65 years) causes of secondary hypertension include [1, 2]:

- renovascular disease
- renal parenchymal disease
- endocrine disease: primary aldosteronism, Cushing's disease, pheochromocytoma, thyroid disease, hyperparathyroidism
- obstructive sleep apnea

Testing for endocrine causes of hypertension (particularly primary aldosteronism and pheochromocytoma) requires avoidance of certain substance before blood sampling in order to avoid false-positive results. A 2-week discontinuation of beta-blockers, anti-inflammatory drugs, clonidine, ACEi, ARBs, potassium wasting or sparing diuretics, aliskiren or alpha-methyldopa is required prior to aldosterone and renin testing. Moreover, patients should have a diet without sodium restriction and have normal serum potassium at the time of evaluation [2, 4]. In the case of pheochromocytoma, caffeine and drugs that interfere with catecholamine metabolism are to be avoided at least 24 hours before testing [5]. According to present guidelines, if possible, hypertensive treatment should be replaced with verapamil slow-release (90–120 mg b.d.) hydralazine (10–12.5 mg b.d.) or doxazosin (2–8 mg o.d) before testing for primary aldosteronism or pheochromocytoma [1].

2. Renovascular disease

Renovascular hypertension (RVH) entails the presence of an obstructive lesion of one or both renal arteries and accounts for 10 - 45% of severe or malignant hypertension cases [6]. RVH may remain asymptomatic or produce a wide range of effects including mild to severe hypertension, circulatory congestion leading to pulmonary edema and various degrees of renal failure [7].

Hypertension secondary to renovascular disease should be suspected in patients with [6]:

- serum creatinine increase ≥ 50% within one week of ACEi/ ARB initiation
- severe HTN + kidney asymmetry (difference in kidney size greater than 1.5 cm)
- recurrent flash pulmonary edema

The most common causes of RVH are: atherosclerotic renal artery stenosis (plaque build-up due to flow turbulence, usually at the site of emergence, occurring in elder patients with other cardiovascular risk factors) [3, 8, 9] and fibromuscular dysplasia (FMD – non-inflammatory, non-atherosclerotic arteriopathy, frequently associated with aneurysmal dilation occurring in the mid-portion of the vessel, in young women) [10]. However, other causes have been cited: Takayashu arteritis [11, 12], acute or chronic renal artery dissection [13, 14], renal artery thrombosis [15], extrinsic compression by diaphragmatic crus entrapment [16, 17] or adjacent tumors [15], malformations of the urinary tract with subsequent vascular abnormalities [18-21].

Diagnosis methods for renovascular disease include noninvasive screening tests – Doppler ultrasonography, computed tomography angiography (CTA), magnetic resonance angiography (MRA) [3] - with lower accuracy and the invasive, "gold standard" method for diagnosis: digital subtraction angiography [6, 7]. Unfortunately, techniques that require the use of contrast material also carry the risk of nephropathy (angiography / CTA) or

nephrogenic systemic fibrosis (MRA with gadolinium) [7] and should not be used as first-line tests [6]. Additionally, the required eGFR for CTA and MRA is ≥ 60 and ≥ 30 mL/min, which may prove problematic in a clinical setting [22].

Studies have shown that a 10-20 mmHg decrease in renal perfusion pressure, equivalent to a luminal narrowing in excess of 70%, is necessary to stimulate renin secretion and produce a significant rise in BP [7]. Though renovascular disease may remain clinically silent, the contralateral kidney may become hyperperfused and hyperfiltering secondary to the activation of renin-angiotensin-aldosterone axis. This ultimately leads to accelerated atherosclerosis and proteinuria as an expression of progressive parenchymal injury [7].

Consequently, ACEi and ARBs, by RAA system inhibition reduce hyperfiltration and proteinuria and should be included in the treatment of patients with RVH [23] as they lower the risk of heart failure, dialysis initiation and mortality [6, 7, 24] and may be introduced in the treatment of bilateral renal artery stenosis or renal artery stenosis of a single functioning kidney [22]. A rise in serum creatinine exceeding 30% from baseline at least 4 weeks into ACEi treatment should prompt regimen reevaluation [7, 25]. Percutaneous renal artery angioplasty is another therapeutic modality, though more appropriate in FMD patients who are generally younger and less likely to have long-standing hypertension [7, 26].

3. Renal hypoplasia

A small kidney is defined as one with a mass below two standard deviations of that of age-matched normal individuals' or a combined kidney mass of less than half normal for the patient's age [20]. Small kidney size may occur in the setting of renal tract malformations (arrest in the normal development of the kidney including parenchyma, renal pelvis and ureter), ischemia (renal artery [15, 27] or vein [28] thrombosis or renal artery stenosis [3, 8, 9]), recurrent infection or urinary tract obstruction [29] and the definitive diagnosis is established based on histology [30].

Congenital anomalies of the kidney and urinary tract include renal hypoplasia (nephron deficit in a completely formed kidney [20]) and dysplasia (abnormal, incomplete development [20]). However, renal histology is seldom available and the clinical diagnosis is oriented by the size and remaining excretory function of the kidney. While a hypoplastic kidney is small but retains its function, a dysplastic kidney may be either small or deformed by multiple cysts, has loss of cortico-medullary differentiation and impaired function [20, 30]. Conversely, renal artery hypoplasia leads to functional impairment and is characterized by a regular, elongated and tubular narrowing without focal stenoses [31].

While malformations of the urinary tract may remain silent in asymptomatic patients well into adulthood, hypodysplastic kidneys are also prone to infection and nephrolithiasis [29] and may lead to urosepsis [18], hypertension [18, 19], proteinuria [21] or renal impairment at any age [20, 32].

Conclusions

We present the case of a patient with severe hypertension who, after screening for secondary causes of hypertension, was diagnosed with renal hypoplasia on account of renal asymmetry and the small caliber of the patent right renal artery but without focal stenose. Renal hypoplasia is a relatively uncommon cause of renovascular hypertension and seems to respond well to treatment with blockers of the renin-angiotensin-aldosterone system in adult patients.

Conflict of interests (financial or non-financial)

The authors declare that there are no conflicts of interest.

List of abbreviations used (optional)

ACEi – angiotensin converting enzyme inhibitor
ARBs – angiotensin receptor blockers
ARR – aldosterone-renin ratio
b.d – two times per day
BP – blood pressure
CT(A) – computed tomography (angiography)
DBP – diastolic blood pressure

ESC – European Society of Cardiology
FMD – fibromuscular dysplasia
HTN – arterial hypertension
MRA – magnetic resonance angiography
o.d. – once daily
RVH – renovascular hypertension
TSH – thryoid stimulating hormone

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