



Nephron-sparing surgery for treatment of reninoma: a rare renin secreting tumor causing secondary hypertension

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ABSTRACT

Main findings: A 25-year-old hypertensive female patient was referred to our institution. Initial workup exams demonstrated a 2.8 cm cortical lower pole tumor in the right kidney. She underwent laparoscopic partial nephrectomy without complications. Histopathologic examination revealed a rare juxtaglomerular cell tumor known as reninoma. After surgery, she recovered uneventfully and all medications were withdrawn.

Case hypothesis: Secondary arterial hypertension is a matter of great interest to urologists and nephrologists. Renovascular hypertension, primary hyperaldosteronism and pheochromocytoma are potential diagnosis that must not be forgotten and should be excluded. Although rare, chronic pyelonephritis and renal tumors as rennin-producing tumors, nephroblastoma, hypernephroma, and renal cell carcinoma might also induce hypertension and should be in the diagnostic list of clinicians.

Promising future implications: Approximately 5% of patients with high blood pressure have specific causes and medical investigation may usually identify such patients. Furthermore, these patients can be successfully treated and cured, most times by minimally invasive techniques. This interesting case might expand knowledge of physicians and aid better diagnostic care in future medical practice.

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INTRODUCTION

Approximately 5% of patients with hypertension have specific secondary causes, which may be identified after meticulous medical history, physical examination, laboratory tests, and image workup. Secondary hypertension might be caused by several conditions affecting the kidneys, heart, arteries, or the endocrine system. Proper treatment addresses the underlying condition and tends to normalize blood pressure, reducing the risk of severe heart, kidney and brain complications.

The purpose of this article is to report and illustrate an interesting case where radiological

investigation discovered a renal tumor as a possible cause of hypertension.

Cases hypothesis and rationale

A 25-year-old female patient was referred for examination at our institution because of severe hypertension. She presented with daily mild headache for one year. When she arrived to our office, she was already taking propranolol, hydrochlorothiazide and spironolactone for blood pressure control. Physical examination was essentially normal except for persistent high blood pressure (Systemic Blood Pressure = 150x100 mmHg). She had no family history of hypertension.

Laboratory screening included serum sodium, calcium, potassium, aldosterone, renin, cortisol, catecholamines, and urinary metanephrines. Initial work-up revealed mild hypokalemia (3.4 mEq/L) and increased renin levels (7.7 ng/mL/h) with normal aldosterone (22 ng/dL). Other hormone levels were within normality. Doppler ultrasound did not reveal any abnormality in renal vessels flow. However, a 2.5 cm hypoecogenic mass was found in the right kidney. Contrast-enhanced computed tomography of the abdomen demonstrated a 2.8 cm, well circumscribed, solid, hypoenhancing cortical lower pole lesion in the right kidney with 100 Hounsfield Units (Figure-1). The patient was counseled on options regarding radical nephrectomy and nephron-sparing surgery, as well as alternative for open or laparoscopic intervention. She decided for laparoscopic partial nephrectomy and the procedure was accomplished without intra-operative complications. Total surgical time was 120 minutes and renal hilum clamping time was 14 minutes. Bleeding was negligible. The patient had an uneventful recovery and was discharge home in postoperative day one. Histopathologic examination revealed a rare juxtaglomerular cell tumor known as reninoma

(Figure-2) after minucious immunohistochemical analysis, which was negative for Cytokeratin 35BH11, EMA, CD 34, CD 56, S-100, Chromogranin A, HMB-45, WT-1, and CD 31; and positive for AML (areas), vimentin (focally), ACTIN HHF35 (rare cels), and CD 117 (focally). Patient's blood pressure normalized within 2 months of surgery (Systemic Blood Pressure < 120x90 mmHg), allowing withdrawal of all medications.

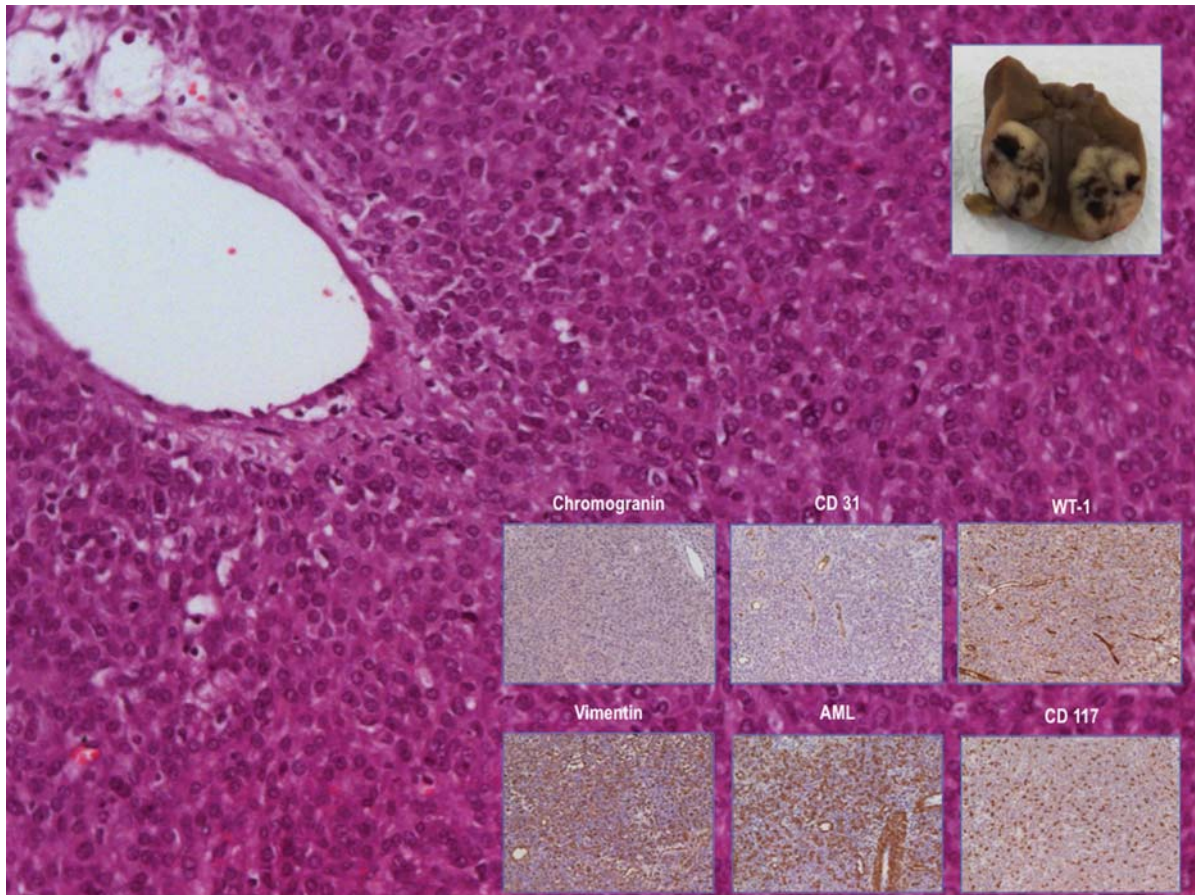
DISCUSSION AND FUTURE PERSPECTIVES

Secondary hypertension is a topic of particular interest for urologists worldwide, mainly because it has potential causes that may be recognized and definitively treated by their specialty. Patients with severe or refractory hypertension, sudden onset of hypertension, high blood pressure before 20 year-old or after 50 year-old, spontaneous hypokalemia, and unexplained renal dysfunction are situations in which complete workup for secondary hypertension and its related pathologies should be performed. Renovascular hypertension, primary hyperaldosteronism, and pheochromocytoma are among those causes and should always be ruled out (1-4). Although

Figure 1 - Contrast-enhanced computed tomography reveals a 2.8 cm, well circumscribed, solid, hypoenhancing cortical lower pole mass in the right kidney with 100 Hounsfield Units (axial and coronal view).



Figure 2 - Histological examination showing microscopic characteristics of juxtaglomerular tumor cells (Eosin and Hematoxylin): tumor cells with mild nuclear atypia, inconspicuous nucleoli and pale ill-defined cytoplasm; Immunohistochemical study negative for Chromogranin A, WT-1, and CD 31; positive for AML (areas), vimentin (focally), and CD 117 (focally).



rare, chronic pyelonephritis and renal tumors as renin-producing tumors, nephroblastoma, hypernephroma, and renal cell carcinoma might also induce hypertension by different mechanisms and should be a part of the clinician diagnostic list. The purpose of this article was to report and illustrate an interesting case where radiological investigation discovered a renal tumor as a possible cause of hypertension. Partial nephrectomy and pathological examination confirmed a juxtaglomerular cell tumor known as reninoma. The rationale is to provide the better care for patients with reversible causes of hypertension, diminishing their need for medications and cardiovascular risks.

In our case, a young female patient presented with severe hypertension. The above-mentioned diagnoses must be remembered so that appropriate investigation can be started. Renovascular hypertension is a condition in which patients have unilateral or bilateral renal artery stenosis and become normotensive when the vessel constriction is treated by angioplasty or surgery (1). The two main etiologies are fibromuscular dysplasia and atherosclerotic plaque. Doppler ultrasound is the most cost-effective study to screen renal artery stenosis, but it is dependent on the operator. The following option is nuclear magnetic angiography or computed tomography angiography. Atherosclerotic disease is more common in older patients

and has worse outcomes than fibromuscular dysplasia when treated by angioplasty (5).

This case was very illustrative to remind us that approximately 5% of patients with hypertension have reversible secondary causes (6). Here, we presented a patient with reninoma, an unusual cause of hypertension that mainly affects young individuals (7-9). The patient was successfully treated by minimally invasive laparoscopic nephron-sparing surgery, reducing the risk of loss of renal function and shorting hospital stay. Gottardo et al (8) reported the case of a 16-year-old hypertensive boy who presented with severe hypokalemia and markedly increased plasma renin activity. Abdominal ultrasonography and contrast-enhanced computed tomography revealed a 2 cm well-circumscribed, solid, hypoenhancing cortical lesion in the lower pole of the left kidney. The patient underwent open nephron-sparing surgery. Histopathologic examination revealed a juxtaglomerular cell tumor. In our case, immunohistochemical (IHC) study comprised vascular markers (CD31 and Vimentin), neuroendocrine tumor marker (Cromogranin), Mesothelioma marker (WT1), and hematopoietic markers (CD117 and AML). All were negative or focally positive (Vimentin, CD117) and were used to exclude others rare renal tumors. Cases like reninoma do not have a specific pattern and IHC findings are inconsistent in the literature. Our diagnosis was based on microscopic characteristics such as tumor cells with mild nuclear atypia, inconspicuous nucleoli and pale ill-defined cytoplasm (8, 10).

Mete et al (7) reported a similar case in which a 14-year-old boy with hypertension and preoperative diagnosis of reninoma underwent open nephron-sparing surgery for a 2 cm mass in right kidney. The patient became normotensive postoperatively and follow-up intravenous urography showed bilateral normally functioning kidneys. Although image exams may find renal masses that could be associated to secondary arterial hypertension, there are other methods to prove such association. Wong et al (9) demonstrated the utility of both appropriate imaging studies and selective venous catheterization following provocative administration of an ACE-I for diagnosis of reninoma. We do not perform selective venous sampling routinely since it

is a more invasive technique. Nevertheless, it may help in cases where all other diagnostic modalities have been performed and doubt regarding the specific cause of secondary hypertension persists.

General physicians, urologists and nephrologists are probably the most prone to seeing these patients in an office basis. We hope that our case may help these and other physicians in their future practice. Laboratory testing and image workup may identify the cause of secondary hypertension and guide therapeutic options as in our case. Untreated secondary hypertension culminates in complications such as heart failure, kidney failure and stroke. The detection of a secondary cause provides an opportunity to convert an incurable disease into a potentially curable one. Moreover, even when cure cannot be achieved, early recognition and management may prevent target organ damage, reduce socioeconomic burden and improve quality of life (11).

CONFLICT OF INTEREST

None declared.

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