Secondary Hypertension Due To A Juxtaglomerular Cell Tumor

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SECONDARY HYPERTENSION DUE TO A JUXTAGLOMERULAR CELL TUMOR

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ABSTRACT

Juxtaglomerular cell tumors are rare, generally benign and they are one of the secondary surgically treatable causes of arterial hypertension. There are about 100 reported cases on literature and the diagnosis is usually made based on a high clinical suspicion index, mostly in patients with hypokalemia and arterial hypertension. The diagnosis involves blood tests and imaging studies, but it is only definite with histopathological exam after surgical treatment. We present a case of a 22-year-old woman with resistant arterial hypertension and renal and cardiovascular target-organ lesions. High plasmatic renin and a nodular renal mass on MRI were present. A tumorectomy was performed and the histological exam confirmed a reninoma. After surgery, blood pressure and serum renin values returned to normal without medication. This work focuses on the need to exclude rare secondary causes of hypertension in young patients with resistant forms of this disease.

KEYWORDS: hypertension, juxtaglomerular cell tumor, plasma renin activity, renin-secreting tumor
INTRODUCTION

Juxtaglomerular cell tumors also known as Reninomas, first described by Robertson in 1967, are neoplasms of the juxtaglomerular kidney cells\(^1\). They are usually benign and there are only about 100 cases described in the literature\(^2\). Clinically, patients may present with high blood pressure, headaches, palpitations and blurred vision. Blood and urine analysis may reveal hypokalemia and other abnormal values related to target-organ lesions, as proteinuria\(^2-4\). The diagnosis is based on clinical, laboratory, imaging and histological exams and tumorectomy is the curative management, generally with return of blood pressure to normal values after surgery. We present the case of a 22 year-old woman with resistant hypertension and established target organ lesions, whose diagnosis was suggested based on clinical, laboratory and imaging data, with subsequent histological confirmation after tumorectomy.
CASE REPORT

We describe the case of a 25 year-old caucasian woman, hotel receptionist, referred to our Hypertension (HT) Outpatient clinic two years before with the diagnosis of probable secondary HT. She had no relevant personal medical history till her nineteen-year-old when, in a school screening, asymptomatic hypertension was detected. Her father was diagnosed with hypertension in his forties controlled with only one drug. She was initially treated by general practitioner with Alisciren 300 mg/day, Diltiazem 300 mg/day, Spironolactone 100 mg/day with inadequate blood pressure (BP) control, 160/120 mmHg. There was no target organ damage at presentation. The Ambulatory Blood Pressure Monitoring (ABPM) revealed a dipper pattern with no other relevant data. Further investigation revealed normal catecholamine levels, hypokalemia and slightly elevated renin levels (234pg/mL) (Table 1).

Despite treatment improvement with optimal quadruple dose regimen (Valsartan 160 mg + HCTZ 25 mg/day, Amlodipine 10 mg/day, Spironolactone 100 mg 1x/dia, Nebivolol 5 mg 1x/dia) BP remained persistently high (Grafic 2). Target organ damage at this time included concentric left ventricular hypertrophy (Figure 1) and proteinuria (Table 1). A renal angio-computed tomography (CT) showed normal renal arteries (Figure 2) and a solid, well circumscribed nodule on the mid-section of the right kidney (2.6x2.4x2.2 cm) was noted on abdominal MRI (Figure 3).

The hypothesis of juxtaglomerular cell tumor was considered and the patient underwent successful laparoscopic tumorectomy with apparently clear surgical margins. Prior to surgery, she was treated with an alpha-blocker (phenoxybenzamine) followed by a beta-blocker (propranolol) in order to avoid surgical hypertensive crises or tachyarrhythmias. Pathological examination confirmed the presence of an encapsulated tumor, with sheet-like growth pattern (figure 4), composed of polygonal to spindle cells, with eosinophilic cytoplasm and central vesicular nuclei (figure 5). Tumor cells were immunoreactive for CD34, CD117, vimentin and smooth muscle actin, and negative for pan-cytokeratin AE1/AE3. Electron microscopy studies confirm the presence of angulated, rhomboid renin protogranules (figure 6).

During the post-operative period, a rapid decline in BP was observed. At 4-month follow-up, renin levels steadily declined (40pg/mL) and the patient remains normotensive in the absence of any treatment. Furthermore, there was a significant left ventricular wall thickness reduction and no proteinuria. Another abdominal CT was done and tumor recurrence was excluded.
DISCUSSION

Tumors of the juxta-glomerular kidney cells are rare neoplasms, mostly benign, with only one case of metastatic spread described. There are also reports of reninomas detected during pregnancy, some of which result in miscarriage or stillbirth and kidney involvement with focal and segmental glomerular sclerosis. They generally are found in young adults, in the second or third life decades, with a slight female predominance (1.9:1). These tumors can have various clinical and laboratory presentations: typical (most tumors), presenting with high serum renin and aldosterone levels, hypertension and hypokalemia; atypical (hypertension with normal potassium levels) and non-functioning (without hypertension and normal potassium levels).

Reported symptoms include headaches, blurred vision, dizziness, nausea and vomiting, mostly due to high blood pressure values. There is also a great variability pattern in respect of blood pressure values: some patients have persistently high blood pressure with weak response to medication, some of them with malignant hypertension, whereas others have only mild hypertension without target-organ lesions. These differences are independent of tumor size.

With respect to target-organ lesions, these patients have a similar behavior than any other hypertensive patient. However, it is important to focus on the recovery of these lesions after tumor resection.

The definite diagnosis is based on histologic examination: microscopically with polygonal cells, sometimes with nuclear atypia and immunohistochemically with positivity to renin, vimentin and CD34. However, when a young patient presents with hypertension and hypokalemia, this diagnosis should be considered together with hyperaldosteronism and a renal CT scan followed by a MRI planned.

Specific pharmacological treatment with renin antagonists seems a logical option, however, there are only two reports of patients treated with aliskiren, but even those underwent surgery because they seemed to be resistant to aliskiren after 5-6 months therapy.

After identification of the tumor, surgery is generally conservative in order to preserve the surrounding renal tissue. The approach can be laparotomic or laparoscopic and tumorectomy, partial or total nephrectomy can be done, depending on tumor size.
Our case is a paradigmatic example of this tumor: the patient was a young adult female with resistant hypertension, target-organ lesions, namely left ventricular hyper trophy. She had a nodular renal mass on CT, confirmed with MRI. Due to elevated renin levels, the diagnosis of reninoma was considered and a tumorectomy was performed. Morphology and immunohistochemical profile were compatible with the diagnosis of juxtaglomerular cell tumor, ultimately confirmed through electron microscopy, by the presence of rhomboid renin protogranules. During follow-up, there was a significant improvement in left ventricular wall thickness, blood pressure remains controlled without medication and renin values are normal.

Finally, it is important to early recognize the signs and symptoms that can point to this diagnosis, because this is a potential curable form of secondary hypertension with important benefits on target-organ lesions improvement.
### TABLES

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<th>ANALYSIS</th>
<th>Pre-operative blood tests</th>
<th>REF. VALUES</th>
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<tr>
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<td>Urinary metanephrines (µg/24h)</td>
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<tr>
<td>Albuminuria (mg/dL/24h urine collection)</td>
<td>253</td>
<td>52</td>
</tr>
</tbody>
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**Table 1**: blood analysis
Average 24h blood pressure: 131/97mmHg

Graphic 1 – Renin values

Graphic 2 - Ambulatory Blood Pressure Monitoring (ABPM)
Figure 1: Echocardiogram showing left ventricular hypertrophy

Figure 2: Renal angio-CT excluding renal artery stenosis
Figure 3: Abdominal MRI showing right renal nodular mass.

Figure 4: (Hematoxylin and eosin, 20x) Histological examination, highlights the presence of a capsule (arrow).
Figure 5: (Hematoxylin and eosin, 400x)

Figure 5: (Electron microscopy) Rhomboid renin protogranules (arrow).
REFERENCES


Highlights from this article

- Juxtaglomerular cell tumores are a rare cause of secondary hypertension
- They are a surgically treatable cause of secondary hypertension
- It is important to exclude rare causes of hypertension in young patients with resistance to the standard treatment