



## Juxtaglomerular cell tumor (reninoma) as a cause of arterial hypertension in adolescents. A case report

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### ABSTRACT

Severe arterial hypertension (HTN) in pediatrics is mainly due to secondary causes.

Here we describe the case of a 14-year-old female adolescent with severe HTN, metabolic alkalosis, and hypokalemia, secondary to a renin-secreting juxtaglomerular cell tumor diagnosed after 2 years of HTN progression.

**Key words:** renovascular hypertension; hypokalemia; juxtaglomerular apparatus; kidney neoplasms; renin.

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## INTRODUCTION

Severe arterial hypertension (HTN) in children and adolescents is defined as blood pressure (BP) above the 95<sup>th</sup> percentile (P) + 12 mmHg based on age, sex, and height, and entails investigating potential secondary causes.<sup>1,2</sup> A rare cause of secondary HTN is juxtaglomerular cell tumor of the kidney or reninoma, a benign neoplasm first described in 1967 by Robertson et al.<sup>3</sup> It is characterized by excessive renin secretion, secondary hyperaldosteronism with hypokalemia and severe HTN.<sup>4</sup> Its treatment consists of total or partial nephrectomy so it is a potentially curable cause of HTN; its early diagnosis and appropriate treatment is important.<sup>4,5</sup>

Here we describe the case of a 14-year-old female adolescent with severe HTN secondary to reninoma, with 2 years of HTN progression and target organ damage.

## CASE REPORT

Female, 14-year-old patient with normal body weight: 63 kg (P90) and a height of 169 cm (P97), 2 years of HTN progression, followed-up for hypothyroidism, managed with levothyroxine. She had a history of isolated elevated BP recordings in health checkups for 2 years.

At the outpatient clinic, her systolic BP was 160 mmHg and diastolic BP was 114 mmHg (P > 95 + 12 mmHg), confirmed by 24-hour ambulatory blood pressure monitoring.

A search for target organ damage was performed. The echocardiogram showed left ventricular hypertrophy, pathological fundus oculi,

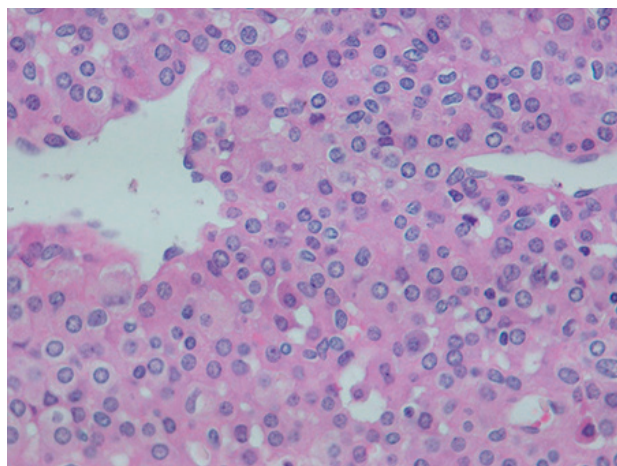
and microalbumin/creatinine ratio of 72 mg/g (normal value: < 30 mg/g), which confirmed long-standing HTN.

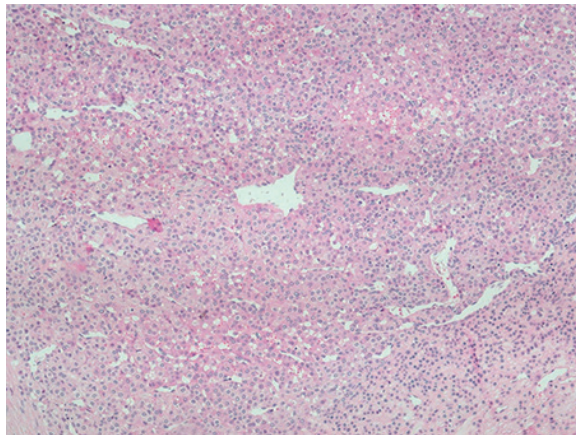
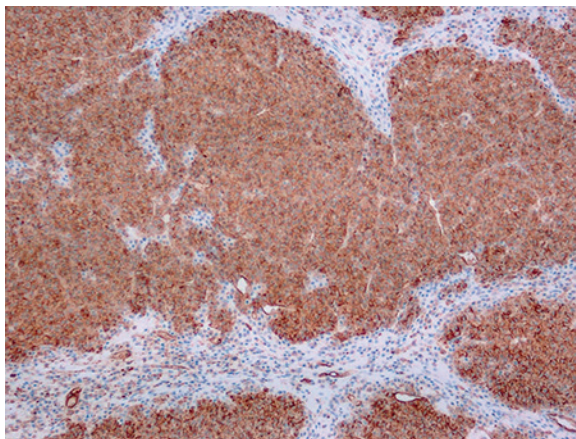
Treatment was started with amlodipine 5 mg/day and tests were done to search for secondary causes. A kidney ultrasound with renal artery Doppler was performed. Serum lab tests showed metabolic alkalosis and hypokalemia. Plasma renin activity (PRA): 21.6 ng/mL/hour (normal value: < 6 ng/mL/hour) and plasma aldosterone (PA): 858.1 pg/mL (normal value: < 40 pg/mL). Spironolactone 50 mg/day was added.

The abdominal computed tomography angiography (CTA) showed a rounded, homogeneous image with solid density in the right kidney at the level of the anterior valve of the lower pole (*Figures 1 and 2*), so the diuretic agent was discontinued and the patient continued receiving amlodipine and ramipril 5 mg/day. A new kidney ultrasound was performed, which showed a rounded subcapsular isodense image with renal parenchyma (*Figure 3*).

Surgical resection of a solid lesion measuring 1.7 × 1.7 × 1.9 cm with well-defined borders was performed. Upon sectioning, it had a yellowish brown, multinodular appearance. Upon microscopic examination, proliferation of polygonal neoplastic cells with large, eosinophilic cytoplasm and well-defined borders arranged in nests or strands or in a hemangiopericytic pattern was observed. These cells were diffusely positive for CD34 and vimentin, multifocally positive with actin (HMF35), and showed a proliferative index of

**FIGURE 1. H&E stain, 100X, presence of polygonal cell strands with broad eosinophilic cytoplasm, well-defined borders, central, round, and uniform nuclei**



**FIGURE 2. H&E stain, 40X, prominent small vessel component arranged in a hemangiopericytic pattern****FIGURE 3. Immunohistochemistry: diffusely positive for CD34**

10–15% with Ki67. The diagnosis corresponded to a juxtaglomerular cell tumor (*Figures 1–4*).

During the postoperative follow-up, the patient's laboratory values and BP returned to normal. The antihypertensive medication was discontinued.

A clinical and BP control was performed monthly during the first 6 months and then every 3 months during the following 12 months postoperatively; BP values were normal.

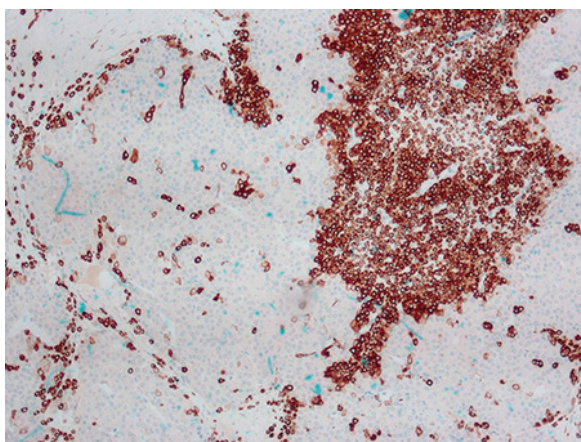
Follow-up included a cardiac control with a normal echocardiogram and negative 24-hour urine proteinuria at 6 and 12 months. The kidney ultrasound was normal 3 months after surgery. At 18 years of age, the patient was referred to an adult care facility.

## DISCUSSION

A reninoma or juxtaglomerular cell tumor is a rare cause of renin-mediated HTN. It starts in the modified smooth muscle cells of the afferent arteriole of the juxtaglomerular apparatus.<sup>3,4,6</sup>

Since it was first reported by Robertson et al. in 1967, approximately 100 cases have been published; it is more common among adolescents and young adults, with a slight female predominance.<sup>3,7</sup>

Patients diagnosed with reninoma usually have a history of nonspecific symptoms suggestive of severe HTN, such as headache, polyuria with nocturia, polydipsia, and general malaise, which result in a diagnostic delay or confusion.<sup>6–8</sup> During our patient's routine health checkups, she had long-lasting headache, which

**FIGURE 4. 40X, multifocally positive in smooth muscle actin immunohistochemical staining**

is consistent with reported cases.<sup>8,9</sup>

The clinical consequences of the activation of the renin-angiotensin-aldosterone system (RAAS) are peripheral vasoconstriction with water and sodium retention, and the consequent increase in BP. Elevated aldosterone stimulates sodium-potassium exchange at the level of the main cells of the collecting tubule causing excessive urinary potassium loss, resulting in hypokalemia and metabolic alkalosis. Such pathophysiological changes are present in all causes of renin-mediated HTN.<sup>10</sup> Our patient had nocturia with metabolic alkalosis and hypokalemia.

In the presence of suspected renin-mediated HTN, the most physiological treatment option is RAAS blockade, which may be done at different levels of the axis.<sup>11</sup> It is worth noting that, in patients with no established cause of HTN, the use of angiotensin-converting enzyme (ACE) inhibitors may mask hypokalemia and the detection of elevated blood renin levels. For this reason, we started treatment with a calcium channel blocker (amlodipine 5 mg/day). The association of hypertension, hypokalemia, and metabolic alkalosis guides to the diagnosis of hyperaldosteronism. High PRA and BP values allow to make a differential diagnosis between primary and secondary hyperaldosteronism.<sup>11,12</sup>

In the presence of hyperaldosteronism, elevated blood renin levels, and HTN, a differential diagnosis among renal artery stenosis, coarctation of the aorta, and renin-secreting tumor should be made.<sup>12</sup>

Renin and aldosterone production may be affected by many factors.<sup>13</sup> The levels of these hormones may fluctuate over time, but an

increase above the upper limit of the range is usually sustained.<sup>13</sup> In our patient, PRA and BP levels were significantly high, which confirmed the activation of the RAAS, suggestive of a renal cause of HTN.

Diagnostic imaging tests are critical in the assessment of secondary HTN. The CTA is considered the gold standard in the assessment of renin-mediated HTN and is highly sensitive for the diagnosis of reninoma.<sup>6-8</sup>

In our patient, at first, the kidney ultrasound was normal. Given the suspicion of renovascular HTN, a CTA was done in our patient, which revealed the image in the right kidney. It is known that an ultrasound is an operator-dependent method and some images, due to their size and/or location, may not be visible.<sup>14</sup> After observing the CTA image, the abdominal ultrasound was repeated in our patient and the tumor was visualized. This is why, in the presence of a high diagnostic suspicion, even with a normal ultrasound, other imaging studies should be requested, such as CTA or magnetic resonance imaging (MRI). According to Faucon et al,<sup>14</sup> very small tumors may go unnoticed or be mistaken for a cyst due to their isodensity in the CTA without contrast and their hypodensity in the CTA with contrast, especially if the density is not accurately measured. This was the main reason for the use of MRI techniques in the diagnosis.

Once there was a diagnostic suspicion, it was decided to add an ACE inhibitor (ramipril 5 mg/day), which resulted in a progressive normalization of clinical and laboratory parameters, disappearance of polyuria and nocturia, and BP control return to acceptable

values. The surgical resection is curative and normalizes BP in most cases, as in the case of our patient.<sup>5,7,8</sup>

For this type of tumor, nephron-sparing surgery in the form of partial nephrectomy, wedge excision, or tumor enucleation are possible alternatives to complete nephrectomy. The procedure may be open or laparoscopic.<sup>5,6,8</sup> In our patient, a laparoscopic wedge excision was performed with adequate tolerance and renal function preservation.

The histological examination confirms the diagnosis, since other renal tumors may also secrete renin, such as Wilms tumor, carcinoid tumors, and renal cell carcinoma. Reninomas are usually small, well-circumscribed, encapsulated and benign subcapsular tumors; however, very rare cases of vascular invasion, recurrence, and metastasis have been described.<sup>7,8,15</sup>

The diagnosis is based on a combination of gross appearance, microscopy findings, immunohistochemical staining, and the search for intracellular renin deposits. Most of the cells are diffusely positive for CD34 (vascular marker).<sup>6-8,15</sup> Our patient was CD34 diffusely positive; vimentin: diffusely positive; actin (HMF35): multifocally positive; Ki67: 10–15% positive.

## CONCLUSIONS

The diagnosis of reninoma or juxtaglomerular cell tumor should be taken into consideration in patients with severe secondary HTN, with elevated blood renin levels, secondary hyperaldosteronism, hypokalemia, and metabolic alkalosis in whom parenchymal and renovascular disease have been excluded.

CTA is the main study in the assessment of renin-mediated HTN. The measurement of PRA and BP prior to treatment with RAAS blockade is recommended. Surgical resection is the treatment of choice and leads to BP normalization. ■

## REFERENCES

1. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. *Pediatrics*. 2017; 140(3):e20171904.
2. Lurbe E, Agabiti-Roseic E, Cruickshank JK, Dominiczak A, et al. 2016 European Society of Hypertension guidelines for the management of high blood pressure in children and adolescents. *J Hypertens*. 2016; 34(10):1887-920.
3. Robertson PW, Klidjian A, Harding LK, Walters G, et al. Hypertension due to a renin-secreting renal tumor. *Am J Med*. 1967; 43(6):963-76.
4. Venkateswaran R, Hamide A, Dorairajan LN, Basu D. Reninoma: a rare cause of curable hypertension. *BMJ Case Rep*. 2013; 2013:bcr2012008367.
5. Tessi C, Szklarz MT, Vásquez M, López Imizcoz F, et al. Laparoscopic Nephro-Sparing Surgery of a Reninoma Tumor in a Pediatric Patient. *Urology*. 2020; 143:261.
6. Gu WJ, Zhang LX, Jin N, Ba JM, et al. Rare and curable renin-mediated hypertension: a series of six cases and a literature review. *J Pediatr Endocrinol Metab*. 2016; 29(2):209-16.
7. Sierra J, Rigo D, Arancibia A, Mukdsi J, et al. Tumor de células yuxtaglomerulares como causa de hipertensión curable: presentación de un caso. *Nefrología Madr*. 2015; 35(1):110-4.
8. Trnka P, Orellana L, Walsh M, Pool L, Borzi P. Reninoma: an uncommon cause of renin-mediated hypertension. *Front Pediatr*. 2014; 2:89.
9. Mao J, Wang Z, Wu X, Dai W, Tong A. Recurrent hypertensive cerebral hemorrhages in a boy caused by a reninoma: rare manifestations and distinctive electron microscopy findings. *J Clin Hypertens (Greenwich)*. 2012; 14(11):802-5.
10. Gennari FJ. Pathophysiology of metabolic alkalosis: a new classification based on the centrality of stimulated collecting duct ion transport. *Am J Kidney Dis*. 2011; 58(4): 626-36.
11. Rajagopalan S, Bakris GL, Abraham WT, Pitt B, Brook RD. Complete renin-angiotensin-aldosterone system (RAAS) blockade in high-risk patients: recent insights from renin blockade studies. *Hypertension*. 2013; 62(3):444-9.
12. Gupta V. Mineralocorticoid hypertension. *Indian J Endocrinol Metab*. 2011; 15(Suppl 4):s298-312.
13. Gordon RD, Wolfe LK, Island DP, Liddle GW. A diurnal rhythm in plasma renin activity in man. *J Clin Invest*. 1966; 45(10):1587-92.
14. Faucon AL, Bourillon C, Grataloup C, Baron S, et al. Usefulness of Magnetic Resonance Imaging in the Diagnosis of Juxtaglomerular Cell Tumors: A Report of 10 Cases and Review of the Literature. *Am J Kidney Dis*. 2019; 73(4):566-71.
15. Gottardo F, Cesari M, Morra A, Gardiman M, et al. A kidney tumor in an adolescent with severe hypertension and hypokalemia: an uncommon case—Case report and review of the literature on reninoma. *Urol Int*. 2010; 85(1):121-4.