

## Juxtaglomerular Cell Tumor: A Rare, Curable Cause of Hypertension in a Young Patient



Aleksandra Walasek, Sounak Gupta, Samson Fine, and Paul Russo

### CASE PRESENTATION

**A**n otherwise healthy 25-year-old woman diagnosed with a renal neoplasm on work-up of new onset hypertension was referred to Urology clinic for further evaluation and management. The patient initially presented to her primary care provider 3 weeks prior for a well visit and was diagnosed with stage 2 hypertension with a blood pressure of 172/117 mm Hg and heart rate of 87 beats per minute. She endorsed history of intermittent headaches, but denied palpitations, diaphoresis, anxiety, or visual changes. She also denied flank pain, hematuria, weight loss, or weakness. The patient had no family history of hypertension or genitourinary malignancy. She was started on 100 mg of labetalol 3 times daily; however, her blood pressure remained poorly-controlled. Renal ultrasound was obtained to assess for renovascular causes of hypertension and although it showed no evidence for renal artery stenosis, it demonstrated a right renal neoplasm measuring 3.5 × 3.2 cm.

At the initial urology clinic visit the patient's blood pressure remained elevated at 148/95 mm Hg. On physical examination peripheral pulses were equal in both arms and legs. There were no palpable masses, edema, or Cushingoid features present.

### DIFFERENTIAL DIAGNOSIS

Hypertension is prevalent among adults in the United States, with 7.3% of adults aged 18 to 39 and 33% of those aged 40-59 diagnosed with hypertension.<sup>1</sup> Essential hypertension is the most common diagnosis among older individuals, but is less common among younger hypertensive patients who often have secondary hypertension resulting from a reversible underlying cause. Secondary hypertension can have medical and surgical causes. Medical causes include hypothyroidism, hyperparathyroidism, renal

parenchymal disease, obstructive sleep apnea, substance abuse, and certain medications. Surgical causes include vascular pathology (such as renal artery stenosis or coarctation of aorta) and neoplastic causes (eg, pheochromocytoma, juxtaglomerular cell tumor [JGCT], and functional adrenal cortical tumors).

Although careful review of patient's history, laboratory tests, imaging studies, and pathology is required to accurately differentiate causes of secondary hypertension, new onset hypertension in a young female patient with a renal neoplasm makes a functional renal tumor a strong consideration.

### DIAGNOSTIC ASSESSMENT, MANAGEMENT, AND OUTCOMES

Diagnostic work-up included thorough endocrine evaluation. Initial laboratory findings revealed mild hypokalemia with serum potassium level of 3.2 mEq/L and metabolic alkalosis. Serum TSH, creatinine, sodium, calcium, and fasting glucose were normal. Urinalysis was normal and drug screen was negative for stimulants. Normal serum cortisol and plasma free metanephrines and normetanephrines ruled out a cortisol-producing tumor and pheochromocytoma, respectively. Plasma renin activity (11.40 ng/mL/h; normal range 0.25-5.82 ng/mL/hr) and aldosterone (111 ng/dl; normal range <31 ng/dl) were markedly elevated. To differentiate primary and secondary hyperaldosteronism, an aldosterone:renin ratio (ARR) was calculated and was found to be within normal limits (9.73 ng/dl per ng/ml/h) consistent with secondary hyperaldosteronism due to excess renin. With a renal Doppler ultrasound demonstrating no evidence of renal artery stenosis, which can also cause elevated renin secretion, these results were consistent with the diagnosis of a JGCT.

Magnetic resonance imaging with intravenous contrast was obtained to further characterize the neoplasm, demonstrating a heterogeneous mixed cystic and solid endophytic mass measuring 2.9 × 3.6 × 3.2 cm located in the interpolar region of the right kidney and extending to renal sinus without invasion (Fig. 1).

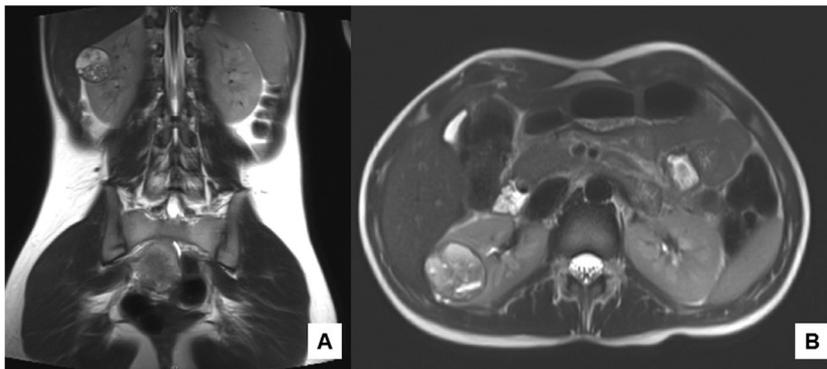
Surgical resection of the renal neoplasm using a nephron-sparing approach was recommended. After counseling

From the SUNY Downstate Medical Center, College of Medicine, Brooklyn, NY; the Memorial Sloan Kettering Cancer Center, Urology Service, Department of Surgery, New York, NY; and the Memorial Sloan Kettering Cancer Center, Department of Pathology, New York, NY

Address correspondence to: Aleksandra Walasek, BA, SUNY Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, NY 11203.

E-mail: [aleksandra.walasek@downstate.edu](mailto:aleksandra.walasek@downstate.edu)

Submitted: June 9, 2019, accepted (with revisions): June 11, 2019



**Figure 1.** (A) Coronal T2-weighted MR image showing a 3.5 cm enhancing mass in the interpolar region of the right kidney. (B) Axial T2-weighted MR image showing the same mass.

and a discussion of risks, benefits, and alternatives, the patient elected to proceed with partial nephrectomy. An open partial nephrectomy was performed through a mini-flank incision, with 27 minutes cold ischemia time and 50 mL estimated blood loss. The patient had an uneventful post-operative course. Her blood pressure normalized after surgery and her antihypertensive medication was discontinued. She was discharged home on postoperative day 2. At 1 month and again at 1 year postoperative follow-up, the patient remained normotensive and asymptomatic, with resolution of her intermittent headaches. Renal function and renal ultrasound at 1 year follow-up were normal.

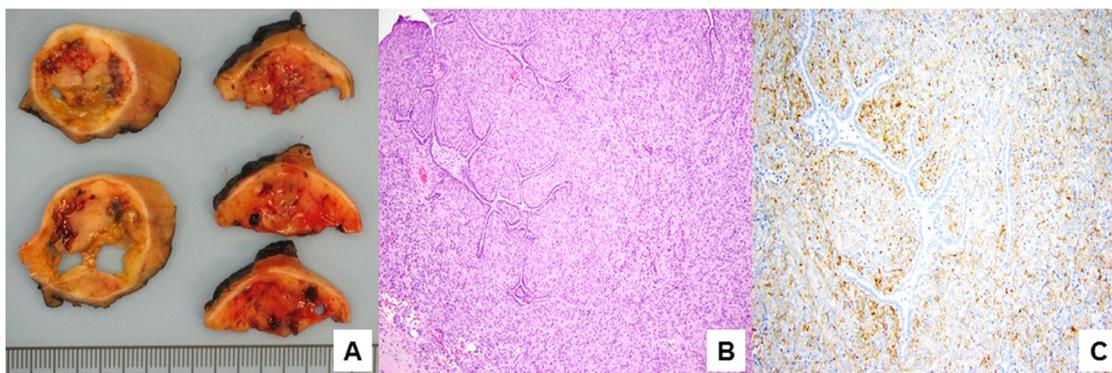
Surgical pathology demonstrated a 3.5 cm encapsulated, well-circumscribed tumor confined to the kidney without involvement of the perinephric or sinus fat. The tumor showed predominantly solid proliferation of spindle cells with areas of cystic degeneration, dilated and entrapped renal tubules, lymphocyte-predominant inflammatory infiltrate, and scattered regions with prominent and irregular vasculature. Immunohistochemical stains showed the tumor cells to be positive for CD34 (Fig. 2). Renin immunostain can also be used to confirm the diagnosis; however, this was not available at our institution. Although, the immunoprofile of the tumor was

nonspecific, the clinical presentation and morphology were highly suspicious for juxtaglomerular cell tumor.

### DISCUSSION BY PAUL RUSSO, MD

JGCT also known as reninoma is a rare, benign neoplasm of myoendocrine cell origin first described by Robertson et al in 1967 and named by Kihara et al 1 year later.<sup>2,3</sup> To date there are about 100 cases reported in literature. JGCT is most commonly seen in the second to third decade of life and exhibits a 2:1 female predominance. Half of patients with JGCT report headache as the only symptom with some also experiencing double vision, dizziness, nausea, vomiting, and polyuria.<sup>4,5</sup> As symptoms are nonspecific, there is often a delay in diagnosis of young patients with reninoma.

Work up of JGCT requires a high index of suspicion based on the patient's history and presentation and a thorough work-up including endocrine evaluation and renal imaging. When assessing a patient with hypertension, hypokalemia, and metabolic alkalosis one must differentiate between primary versus secondary hyperaldosteronism. This is done by measuring plasma renin activity and aldosterone with calculation of ARR. Primary hyperaldosteronism is characterized by high ARR due to negative



**Figure 2.** (A) Gross specimen with cystic and hemorrhagic areas. (B) H&E Image at 100x magnification showing juxtaglomerular cell tumor with entrapped renal tubules. (C) Immunohistochemistry: CD34 at 200x magnification showing CD34 expression in tumor cells, but not in entrapped renal tubules. (Color version available online.)

feedback in renin-angiotensin-angiotensinogen system whereas secondary hyperaldosteronism (eg, due to renin-secreting tumor) presents with normal ARR. In our patient's case the ARR was normal which is more consistent with JGCT as a cause of her hypertension. Although JGCTs classically present with hypokalemia, there are also atypical and nonfunctioning variants.<sup>6</sup> The atypical variant is less common and is characterized by hypertension without hypokalemia. The nonfunctioning variant is the least common and presents as a renal neoplasm in the absence of hypertension or metabolic derangement.<sup>6</sup>

Radiographic imaging has been successfully used in the past to anatomically localize and diagnose JGCT as well as to rule out other potential causes of secondary hypertension. Renal ultrasound is important in detection of renal masses as well as in assessing renovascular causes of hypertension. Computed tomography and magnetic resonance imaging can be used for further characterization of renal tumors. JGCTs typically show similar attenuation to adjacent normal parenchyma without enhancement; however, radiographic findings are nonspecific for this tumor type.

Renal vein sampling can be used to lateralize excessive renin production and is useful in select cases of diagnostic uncertainty for example when the tumor is small or no tumor can be identified on imaging studies.<sup>7</sup> A lateralizing ratio of 1.5 or more has sensitivity of 56% and specificity of 94% and was previously reported to be the most useful in diagnosis of JGCT.<sup>8</sup> Considering the invasive nature of this procedure and diagnostic certainty based on our work-up, renal vein sampling was not pursued in this case.

Ultimately histopathological analysis is necessary for diagnosis of JGCT.<sup>9</sup> Reninomas are typically solitary, well circumscribed tumors surrounded by an incomplete fibrous capsule. They have a yellow-grey surface and can have hemorrhagic and cystic changes<sup>9</sup> as was observed in our patient. The tumors are generally comprised of neoplastic cells that have a spindle to polygonal morphology and the majority of these tumors range between 3.0 and 5.0 cm in size. Some architectural features that have been described include solid to papillary patterns of growth, entrapment of renal tubules and prominent vasculature ranging from delicate thin-walled vessels to thick hyalinized vessels. Due to the rarity of cases with documented metastatic behavior, features associated with malignant behavior have not been clearly established. These tumors have been described to express CD34 and renin and both markers are commonly employed in clinical practice to support this diagnosis. Other characteristic features include the documentation of rhomboid renin granules on ultrastructural studies.<sup>10</sup>

Partial nephrectomy is curative in the majority of cases and should be a strong consideration in patients with JGCT, who tend to be young and are thus most likely to benefit from nephron-preservation long-term. In cases of large or deep, centrally located tumors in which nephron-sparing surgery is not feasible, radical nephrectomy may be necessary. In one study of 83 patients with JGCT who

underwent surgical resection, 9 (11%) reported persistent hypertension at 10 months follow-up.<sup>11</sup>

This case highlights the importance of investigating secondary causes of hypertension in young adults. Since only 5%-10%<sup>12</sup> of adults diagnosed with hypertension have an underlying, potentially treatable cause of hypertension, a high index of suspicion is required to promptly diagnose and manage the underlying cause of hypertension in these patients. The necessary work up of patients with secondary hypertension and a retroperitoneal mass includes laboratory studies to assess for electrolyte abnormalities or acid-base disturbance as well as hormonal studies, especially in the setting of an adrenal neoplasm. Imaging studies are needed to rule out renovascular cause of hypertension and to further characterize the neoplasm. In preparation for surgery in patients harboring a JGCT, perioperative blood pressure control with an angiotensin-converting enzyme inhibitor or angiotensin receptor blocker may be considered, however it should not be given to patients being evaluated with renal vein sampling as it can interfere with renin/aldosterone sampling.<sup>7</sup> Patients who undergo surgery for JGCT have excellent outcomes after surgery and often do not require any additional treatment.<sup>13</sup>

## References

1. Zhang Y, Moran AE. Trends in the prevalence, awareness, treatment, and control of hypertension among young adults in the United States, 1999 to 2014. *Hypertension (Dallas, Tex.: 1979)*. 2017;70:736–742.
2. Robertson PW, Klidjian A, Harding LK, Walters G, Lee MR, Robb-Smith AH. Hypertension due to a renin-secreting renal tumour. *Am J Med*. 1967;43:963–976.
3. Kihara I, Kitamura S, Hoshino T, Seida H, Watanabe T. A hitherto unreported vascular tumor of the kidney: a proposal of "juxtaglomerular cell tumor". *Acta Pathol Jpn*. 1968;18:197–206.
4. McVicar M, Carman C, Chandra M, Abbi RJ, Teichberg S, Kahn E. Hypertension secondary to renin-secreting juxtaglomerular cell tumor: case report and review of 38 cases. *Pediatr Nephrol*. 1993; 7:404–412.
5. Agrawal R, Jafri SZ, Gibson DP, Bis KG, Ali R. Juxtaglomerular cell tumor: MR findings. *J Comput Assist Tomogr*. 1995;19:140–142.
6. Dong D, Li H, Yan W, Xu W. Juxtaglomerular cell tumor of the kidney—a new classification scheme. *Urol Oncol*. 2010;28:34–38.
7. Trnka P, Orellana L, Walsh M, Pool L, Borzi P. Reninoma: an uncommon cause of renin-mediated hypertension. *Front Pediatr*. 2014;2: 89–89.
8. Warsaw BL, Anand SK, Olson DL, Grushkin CM, Heuser ET, Lieberman E. Hypertension secondary to a renin-producing juxtaglomerular cell tumor. *J Pediatr*. 1979;94:247–250.
9. Kuroda N, Gotoda H, Ohe C, et al. Review of juxtaglomerular cell tumor with focus on pathobiological aspect. *Diagn Pathol*. 2011; 6:80.
10. Martin SA, Mynderse LA, Lager DJ, Chevillie JC. Juxtaglomerular cell tumor: a clinicopathologic study of four cases and review of the literature. *Am J Clin Pathol*. 2001;116:854–863.
11. Wong L, Hsu TH, Perlroth MG, Hofmann LV, Haynes CM, Katznelson L. Reninoma: case report and literature review. *J Hypertens*. 2008;26:368–373.
12. Rudnick KV, Sackett DL, Hirst S, Holmes C. Hypertension in a family practice. *Can Med Assoc J*. 1977;117:492–497.
13. Liu K, Wang B, Ma X, et al. Minimally invasive surgery-based multidisciplinary clinical management of reninoma: a single-center study. *Med Sci Monit*. 2019;25:1600–1610.