

A 22-Year-Old Woman With Hypertension and Hypokalemia Due to a Juxtaglomerular Cell Tumor

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Secondary hypertension is responsible for less than 10% of cases of hypertension. If associated with hypokalemia, it may be due to primary or secondary hyperaldosteronism, the latter being rarely caused by renin-secreting tumors. We present a 22-year-old woman with a history of hypertension and repeated hypokalemia, who was finally diagnosed with a small renin-secreting tumor after extensive paraclinical workup and imaging studies.

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INTRODUCTION

Secondary hypertension is responsible for less than 10% of cases of hypertension in the general population.¹ However, it can be challenging to approach and hard to control, especially in young patients. Here, we present a case of hypertension and hypokalemia in a young woman, which was finally diagnosed with a renin-secreting tumor after 6 years of follow-up.

CASE REPORT

A 22-year-old married woman presented our nephrology clinic with uncontrolled hypertension and proteinuria, first detected 4 years earlier during the assessment of recurrent headaches. She had repeated systolic blood pressure measurements hovering around 170 mm Hg to 180 mm Hg and diastolic pressure measurements between 130 mm Hg and 140 mm Hg. Proteinuria of 1+ to 2+ and hypokalemia were noticed in her laboratory tests (Table 1).

She had no family history of hypertension and was not receiving oral contraceptive pills. She had started on enalapril, 2.5 mg twice per day, and hydrochlorothiazide, 12.5 mg/d, since 2 days before the visit. Physical examinations, including upper and lower extremity pulses, were normal. Right- and left-arm blood pressures were 130/80 mm Hg and 130/85 mm Hg, respectively. No abdominal or flank bruits were detected. Renal ultrasonography did not detect any abnormality.

The initial laboratory results ruled out the presence of renal parenchymal disease (Table 1). High mineralocorticoid state (primary or secondary) was suspected because of repeated hypokalemia. Results of Doppler ultrasonography of the renal arteries and renal captopril-diethylene triamine pentaacetic acid renal scintigraphy were normal and hence ruled out the presence of renovascular hypertension. Serum plasma renin activity (PRA) and aldosterone levels were requested.

She returned 22 months later with a history

Laboratory Findings During the Follow-up

Parameter	4 Years Before	1 Year Before	First Visit	1.5 Year After	4 Years After
Blood urea, mg/dL	...	18	47	...	13
Serum creatinine, mg/dL	0.8	0.8	0.9	...	0.76
Serum sodium, mEq/L	...	135	140	140	140
Serum potassium, mEq/L	...	2.5	3.2	3.2	3.8
Hemoglobin, g/dL	...	14.3	11.5
Serum TSH, $\mu\text{mol/mL}$...	1.1
Plasma cholesterol, mg/dL	180
Plasma triglyceride, mg/dL	150
Plasma LDL cholesterol, mg/dL	80
Plasma HDL cholesterol, mg/dL	40
Aspartate aminotransferase, IU/L	22
Alanine aminotransferase, IU/L	20
Complement 3	0.52
Complement 4	0.26
CH50	95
ANA	Negative
ANCA	Negative
Urine sodium, mEq/L	130	20	...
Urine potassium, mEq/L	80	10	...
Spot urine protein	1+	2+
24-hour urine protein, mg/d	140
24-hour urine creatinine, mg/d	1000
Plasma aldosterone, ng/dL	128 (upright) (reference, 3 to 40)	(supine) (reference, 2 to 18)
Plasma renin activity, ng/mL/h	60 (upright) (reference, 1.9 to 6)	> 30 (supine) (reference, 0.5 to 1.9)

*TSH indicates thyroid-stimulating hormone; LDL, low-density lipoprotein; HDL, high density lipoprotein; ANA, antinuclear antibody; CH50, total complement activity; and ANCA, antineutrophil cytoplasmic antibody. Ellipses indicate not measured or not available.

of pregnancy termination at month 5 due to uncontrolled hypertension, laboratory tests indicating hypokalemia, metabolic alkalosis, elevated PRA and aldosterone and a normal abdominal magnetic resonance imaging (Table).

An abdominal computed tomography (CT) was requested; however, the patient returned after 2 years with a blood pressure of 190/110 mm Hg, while receiving enalapril, atenolol, spironolactone, and potassium chloride tablets. Supine PRA and aldosterone levels were tested again, which showed a high PRA and normal serum aldosterone level. Abdominal CT scan was first reported normal, but in a second radiology consult, a small tumor was detected on the dorsal midpole of the right kidney.

She was operated on in the modified right flank position under general anesthesia. The tumor was not evident first and only a subtle bulge was noted on the dorsum of the right kidney, which was verified to be a tumor by intra-operative endocavitary ultrasonography. Thereafter, the patient has been off medication with normal

follow-up abdominal CT scans.

Pathologic examination reported a 20 × 18-mm encapsulated yellowish-brown mass surrounded by 5 mm to 6 mm of normal tissue margin. Microscopic study showed an encapsulated neoplastic tissue composed of sheets of homogenous spindle-shaped cells with distinct cell borders intermixed with some uniform round-to-oval cells with distinct margins (Figures 1 and 2). Numerous capillaries and branching blood vessels and sinusoids were noted. The stroma contained scattered lymphoplasmocytic infiltrate, with periodic acid-Schiff-positive cytoplasmic granules in a subset of cells (Figure 2). The diagnosis was juxtaglomerular cell tumor with free surgical margins.

DISCUSSION

The most common causes of hypertension and hypokalemia are primary aldosteronism, renovascular disease, and diuretic therapy.² The less common causes are Cushing syndrome, Liddle syndrome, certain types of congenital adrenal

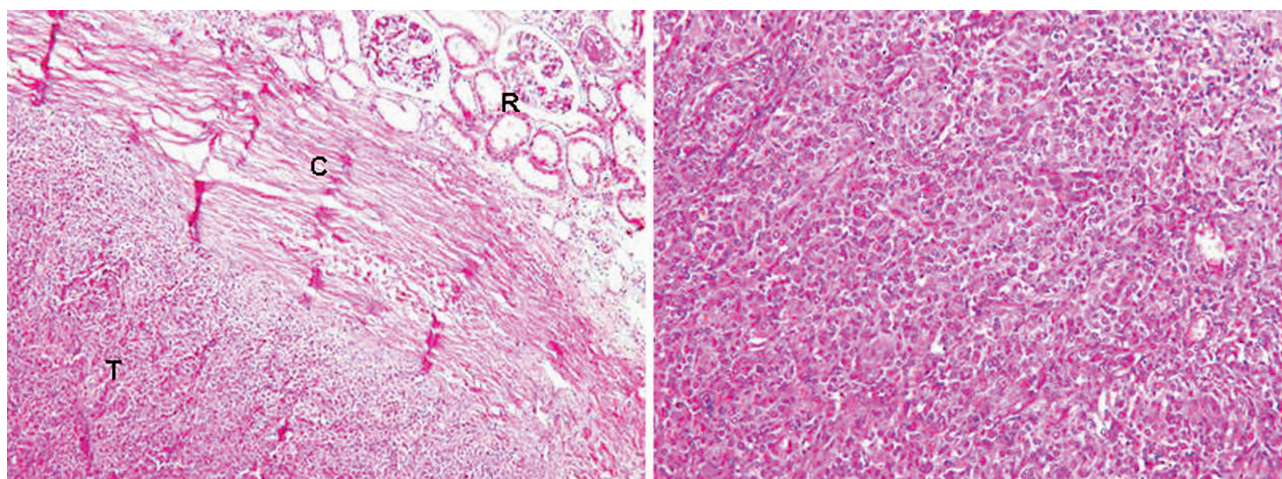


Figure 1. Left, Tumor with adjacent renal tissues and tumor capsule (hematoxylin-eosin, $\times 4$). Right, tumor tissue (hematoxylin-eosin, $\times 10$). T indicates tumor; R, renal tissue; and C, tumor capsule.

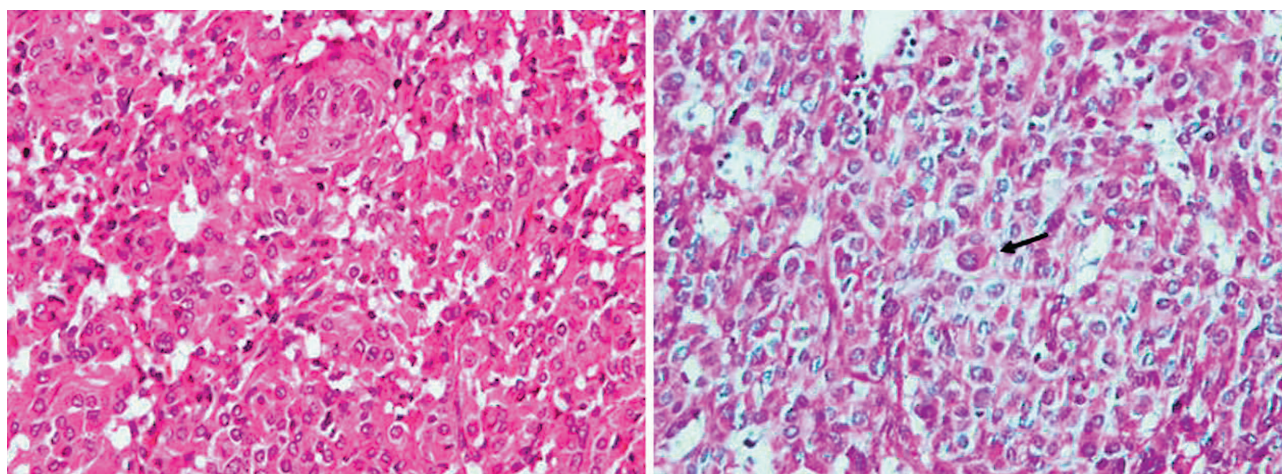


Figure 2. Left, tumor tissue (hematoxylin-eosin, $\times 40$). Right, Periodic acid-Schiff-positive intracytoplasmic renin granules, shown by arrow (periodic acid-Schiff, $\times 40$).

hyperplasia, licorice ingestion, benign adrenal cysts, and rarely renin secreting tumors.^{3,4} Robertson and colleagues first described a renin-secreting tumor in 1967, and subsequently, Kihara and colleagues named it “juxtaglomerular cell tumor.”^{5,6} Since then, less than 50 cases of renin-secreting tumors have been reported.⁷ Haab and colleagues reported 8 cases of renin-secreting juxtaglomerular cell tumors among 30 000 hypertensive patients during a 15-year period.⁸ Clinical characteristics included severe poorly medically controlled hypertension in young patients (mean age, 22.3 years) and severe hypokalemia (mean serum potassium, 2.83 mmol/L). Computerized tomography showed the tumor in all cases. The mean tumor size was 24 mm. Surgical removal of the tumor cured the disease.

In our patient, repeated episodes of hypokalemia,

even in periods that the patient was not receiving any diuretics, together with normal Doppler ultrasonography and captopril-diethylene triamine pentaacetic acid scan of the kidneys and lack of any clinical features of Cushing syndrome led us to the possibility of either primary aldosteronism or a renin-secreting tumor. High PRA and plasma aldosterone level raised the suspicion of reninoma, although being an extremely rare disease. In the first magnetic resonance imaging, no tumor was detected, and in repeat laboratory examination, aldosterone level was normal in spite of high PRA. We explained this with the high dose of enalapril, which could have blocked the aldosterone-increasing effect of renin and searched for the tumor by CT. We were not convinced by the first normal report of CT, further assessment

of which proved to show a small tumor behind the right kidney in a second radiology consult. Even intra-operatively, the tumor was hard to find and intracavitary ultrasonography could help the surgeon to locate the tumor.

In addition to reporting another case of reninoma, as a rare disease entity to the literature, we emphasize the possible indolent clinical course of renin-secreting tumors, which may not be easily detectable and need a high level of suspicion and endeavor to reach the final diagnosis.

CONFLICT OF INTEREST

None declared.

REFERENCES

1. Acelajado MC, Calhoun DA. Resistant hypertension, secondary hypertension, and hypertensive crises: diagnostic evaluation and treatment. *Cardiol Clin.* 2010;28:639-54.
2. Young WF, Jr., Hogan MJ. Renin-Independent hypermineralocorticoidism. *Trends Endocrinol Metab.* 1994;5:97-106.
3. Botero-Velez M, Curtis JJ, Warnock DG. Brief report: Liddle's syndrome revisited--a disorder of sodium reabsorption in the distal tubule. *N Engl J Med.* 1994;330:178-81.
4. Basiri A, Salim NS, Shadpour P. Hypertension secondary to an adrenal pseudocyst cured by laparoscopic partial adrenalectomy. *J Endourol.* 2002;16:689-91.
5. 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;43:963-76.
6. 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.
7. Rubenstein JN, Eggener SE, Pins MR, Rosner K, Chugh S, Campbell SC. Juxtaglomerular apparatus tumor: a rare, surgically correctable cause of hypertension. *Rev Urol.* 2002;4:192-5.
8. Haab F, Duclos JM, Guyenne T, Plouin PF, Corvol P. Renin secreting tumors: diagnosis, conservative surgical approach and long-term results. *J Urol.* 1995;153:1781-4.

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