Case Report

Secondary Hypertension due to a Renin-secreting Juxtaglomerular Cell Tumor

Shih-Yi Lin, Wayne-Young Liu, Wen-Chi Chen, Rong-Hsing Chen*

A juxtaglomerular cell tumor (JCT) is a rare, renin-secreting tumor of the kidney and can cause hypertension. JCT is pathologically benign, and resection of the tumor is curative for hypertension. We report the case of a 17-year-old girl who had hypertension and hypokalemia for 1 year. Laboratory studies showed increased basal plasma renin activity, but normal serum aldosterone level. Abdominal computed tomography disclosed a 2 cm solid mass in the left kidney. However, renal vein sampling and captopril test results were equivocal. Partial nephrectomy was performed and histologic examination demonstrated typical features of JCT. Hypertension and hypokalemia completely resolved postoperatively. JCT should be considered when investigating hypertensive individuals with high plasma renin activity.

Key Words: hypertension, juxtaglomerular cell, plasma renin activity, renin-secreting tumor

Since the first case described in 1967 by Robertson et al, renin-secreting juxtaglomerular cell tumor (JCT) of the kidney has appeared to be a rare, but curable cause of hypertension. The clinical manifestations of JCT syndrome are clearly established and comprise hypertension, hyper-reninemia, and secondary aldosteronism. Nonetheless, the diagnosis of such tumors remains challenging because there are considerable ambiguities while interpreting laboratory and radiological studies. We report a patient with JCT whose serum aldosterone level remained normal despite the existence of typically high plasma renin activity (PRA). Furthermore, the response of PRA to a renin-angiotensin system-blocking agent, renal arteriography, and renal venous sampling all failed to present the typical features of JCT. We also discuss some diagnostic difficulties, which could be encountered during investigation of individuals with suspected JCT.

Case Report

A 17-year-old girl was referred to our hospital due to severe hypertension for 1 year. A family history of hypertension was present and her hypertension was first noted during a routine health examination 1 year prior to this hospitalization. She was previously well and did not receive any diagnostic examination or treatment for her hypertension.
Palpitations and pulsating headaches occasionally accompanied her hypertension. She had no polydipsia, nocturia, flushing, sweating, visual disturbance, or any neurological symptoms.

She was 161 cm in height and 74.5 kg in weight. On admission, her blood pressure was 163/102 mmHg. Physical examination revealed intact eye fundi and no evidence of cardiac abnormalities, coarctation of the aorta, abdominal bruits, or abdominal masses. There was also no Cushingoid appearance. Renal function, as judged by serum creatinine, blood urea nitrogen, and urine analyses, was not compromised. Electrocardiography and chest roentgenography were normal. The results of a complete blood count and plasma levels of fasting glucose, cholesterol, sodium, calcium, and phosphorus were unremarkable, except for hypokalemia (3.2 mmol/L). The 24-hour urine sodium and potassium output were, respectively, 115.6 mmol (normal, 50–250 mmol) and 44.2 mmol (normal, 25–150 mmol).

A random PRA was markedly increased (11.3 ng/mL/hr; normal, 1.9–3.7 ng/mL/hr), but serum aldosterone level was normal (134 pg/mL; normal, 37–240 pg/mL). The diurnal rhythm of serum cortisol was preserved, with a level of 16.9 μg/dL at 8 a.m. and 5.6 μg/dL at 4 p.m. The 24-hour urinary vanillylmandelic acid was 2.8 mg (normal, 1–7.5 mg). The effects of posture change and oral captopril (50 mg) on the PRA and serum aldosterone levels yielded conflicting results. The PRA and serum aldosterone levels were, respectively, 11.2 ng/mL/hr and 215 pg/mL (aldosterone normal, 38–307 pg/mL) in the upright posture, 5.09 ng/mL/hr and 222 pg/mL (aldosterone normal, 29–159 pg/mL) in the supine position, 8.03 ng/mL/hr and 146 pg/mL before oral captopril intake, and 4.99 ng/mL/hr and 266 pg/mL after captopril intake.

Intravenous pyelography and renal arteriography revealed no evidence of collecting system distortion or renal artery stenosis, whereas computed tomography of the abdomen disclosed a small round nodule (17 mm in diameter) in the middle region of the left kidney (Figure 1). Bilateral renal venous sampling showed no definitive lateralization of PRA (left side, 11.4 ng/mL/hr; right side, 8.7 ng/mL/hr; left to right ratio: 1.3). A renin-secreting tumor originating in her left kidney was highly suspected.

We performed partial resection of the patient’s left kidney on Day 12 after admission and resected a well-defined nodule measuring 2.0 × 2.0 × 1.4 cm in size. Microscopically, the tumor, which was circumscribed by a thick fibrous capsule, consisted of polygonal tumor cells with abundant eosinophilic cytoplasm arranged in an organoid pattern within vascular stroma (Figure 2A). Immunohistochemically, the tumor stained positively for CD34 (Figure 2B) and negatively for CD117, cytokeratins, desmin, S100 protein, and HMB-45, which is typical for a JCT.

On the first postoperative day, the PRA decreased to 0.34 ng/mL/hr. By contrast, the blood pressure fluctuated, with a descending trend postoperatively, and then attained stable normotension after the 5th postoperative day, without medication. At outpatient follow-up, 1 month after discharge from hospital, her blood pressure was 120/70 mmHg, plasma potassium level was 4.0 mmol/L, and random PRA was 1.16 ng/mL/hr.

**Discussion**

JCT, a rare renal neoplasm, was first described in 1967 by Robertson et al. The incidence of this
tumor is very low, with only 95 cases reported in the published literature to date. The occurrence of JCT has a peak incidence in the 2nd and 3rd decades of life, and is rarely included in the causes of hypertension in children. All of the reported JCT cases were benign in nature, except for that of one patient who had an ischemic bowel due to malignant hypertension. The diagnosis of JCT is clinically imperative because of the possible long-term risk of cardiovascular and renal diseases caused by its accompanying hypertension.

JCT presents with a clinical triad of hypertension, hypokalemia, and an elevated plasma renin level (or activity). Although there is obesity and a family history of hypertension associated with this patient, other factors, such as the age of onset, severity of hypertension, and the accompanying hypokalemia, all raise concerns of secondary hypertension. The causes of secondary hypertension in adolescents include renal parenchymal/vascular diseases, endocrine disorders, and coarctation of the aorta. Because the patient had a high level of PRA, we believed that she was most likely to have renovascular disease, a renin-secreting tumor, or pheochromocytoma, which was considered because of its possible co-occurrence with renal artery stenosis.

Several diagnostic ambiguities were encountered for this case. First, acute inhibition by captopril caused an unexpected decrease of PRA and an unexpected increase of serum aldosterone level. A response to captopril challenge among individuals with JCT is usually not present due to the loss of the negative feedback control mechanism. However, some investigators do not agree with this theory. Corvol et al observed an increase of PRA after captopril intake in four patients, but a decrease in two. By contrast, unlike the paradoxical response to a pharmacological challenge, our patient had the typical increase of PRA in response to postural change. This variability of PRA response to different procedures could be attributed to the fact that the renin secretion in JCT is affected by different factors, such as sympathetic drive, posture, sodium balance, and angiotensin II negative feedback.

Unlike typical cases of JCT, our patient had normal serum aldosterone levels despite excess production of renin. Impaired elevation of serum aldosterone level in hyper-reninism is observed in several clinical conditions, such as aldosterone synthase deficiency, critical liver cirrhosis, plasma exchange, and metastatic carcinoma of the adrenal gland. Our patient’s healthy history and current physical status were not suggestive of these conditions. Since aldosterone secretion is primarily regulated by the renin-angiotensin system and serum potassium, we presumed that the stimulating effect of renin on aldosterone secretion was weaker than the inhibiting effect of hypokalemia. We suspected that hypokalemia of long duration led to direct inhibition of aldosterone secretion in our patient.

Figure 2. (A) The tumor developed with a characteristic hemangiopericytic pattern (black arrow; hematoxylin & eosin; original magnification, 100×). (B) Juxtaglomerular tumor cells are diffusely and strongly immunoreactive for CD34 (white arrowhead, original magnification, 200×).
Computed tomography is the most useful tool to document the presence of a renal mass, with a sensitivity approaching 100%. Magnetic resonance imaging and magnetic resonance angiography also provide useful initial data. We emphasize that the images derived from these non-invasive studies are purely descriptive, since any mass found must be proven by renal vein sampling or surgical pathology to determine if the observed renal mass is relevant to the overproduction of renin.

The positive observation of PRA upon renal venous sampling is also low and is reported in only 64% of patients with JCT. For our patient, PRA sampling also revealed absence of lateralization of PRA. This could be attributed to peripheral tumor localization, with venous drainage to the pericapsular vein instead of the main renal vein, or to the high levels of angiotensin II in the artioles of the tumor.

The microscopic studies of our patient's tumor are consistent with recent immunohistochemical findings for the majority of JCTs which show positive staining for CD34 but not for cytokeratins, desmin, S100 protein, or HMB-45. Such histologic appearance is typical and helps to clearly differentiate JCT from other renal tumors, such as renal cell carcinoma (positive cytokeratin staining), angiomyolipoma (positive HMB-45 staining) and hemangiopericytoma (negative CD34 staining). CD117 has also been proposed as another marker for JCT. Nevertheless, Ren et al reported negative findings of CD117 immunostaining of JCTs. Studies for CD117 expression are necessary to further evaluate the diagnostic utility of CD117 in conjunction with CD34 as an indicator of JCT.

In conclusion, JCT-related hypertension is rare but curable. After excluding the possibility of renal artery stenosis, the clinician must consider the existence of JCT in individuals with high levels of PRA. Diagnostic imaging studies using computed tomography, magnetic resonance imaging, or magnetic resonance angiography are imperative to define and localize the tumor mass. Prompt removal of JCTs yields good prognoses.

References