Letter to the Editor

A case of pediatric secondary hypertension caused by juxtaglomerular cell tumor

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Introduction

Juxtaglomerular cell tumor (JGCT), first reported by Robertson *et al.* in 1967 (1), is a rare benign tumor with renin-secreting features, which can cause symptoms related to hypertension, high renin, high aldosterone, and hypokalemia. In this article, we report the clinical and imaging features of typical JGCT to raise readers' awareness as well as promote the diagnostic accuracy of the disease, which can ultimately shorten the time interval between a clear diagnosis and the administration of suitable medical treatment.

Case presentation

All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was provided by the patient's parents for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

A 12-year-old female who presented with recurrent chest tightness over the previous 3 months was found to have the following manifestations: blood pressure (152/93 mmHg; reference range =140/90 mmHg) that had remained at a high level for 3 days; plasma renin activity (standing position) >17.48 ng/mL/h (reference range =0.25–5.82 ng/mL/h); hypokalemia (2.96 mm/L; reference range =3.5–5.5 mm/L); high aldosterone level (69.70 ng/dL; reference range ≤28 ng/dL). Unilateral venous blood sampling showed that renin activity was higher on the right renal vein (far beyond the laboratory detection limit) than on the left (>20.52 ng/mL/h), and the value of the right to left renal vein renin ratio was far greater than 1.5.

The patient underwent mid-abdominal tomographic examination including computed tomography (CT) and magnetic resonance imaging (MRI). The lesion showed an abnormal nodule in the middle of the right kidney on tomographic images (*Figure 1*). Combined with the clinical manifestations, the case was diagnosed as JGCT.

The patient underwent enucleation of the renal tumor with a postoperative pathology (*Figure 2*). According to the morphological and immunohistochemical findings, the diagnosis was confirmed as JGCT.

The aldosterone and renin levels of the patient returned to normal 3 days after surgery, and blood pressure and serum potassium returned to normal 1 week after surgery. No recurrence occurred within a follow-up of 50 months.

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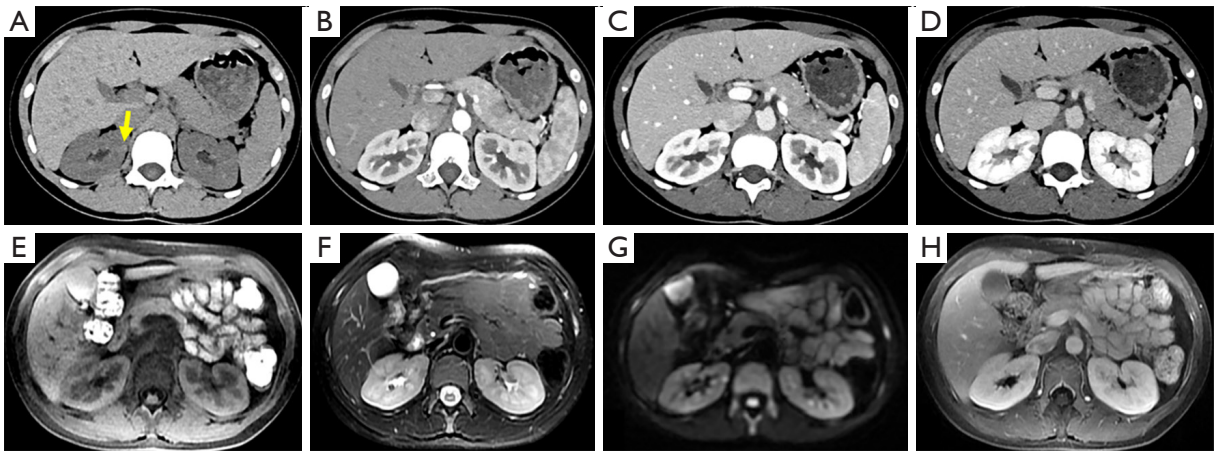

Figure 1 Female, 12 years old, right renal tumor. (A) CT: a slightly high-density nodule in the cortex of the inner edge of the middle pole of the right kidney (46 Hu) (yellow arrow), with uneven density. (B) The nodule of the middle pole of the right kidney showed moderate enhancement in the cortical phase, and the degree of enhancement was significantly weaker than that of the cortex and medulla, with CT values of 72 Hu. (C) The nodule of the middle pole of the right kidney showed moderate enhancement in the corticomedullary phase, and the degree of enhancement was significantly weaker than that of the cortex and medulla, with CT values of 92 Hu. (D) The nodule of the middle pole of the right kidney showed moderate enhancement in the excretory phase, and the degree of enhancement was significantly weaker than that of the cortex and medulla, with CT values of 92 Hu. (E) The lesion, in the inner cortex of the middle pole of the right kidney, showed a hypointense nodule on T1WI. (F) The lesion, in the inner cortex of the middle pole of the right kidney, showed a hyperintense nodule on T2WI. (G) The lesion, in the inner cortex of the middle pole of the right kidney, showed a hyperintense nodule on DWI. (H) In the parenchymal phase, there was a moderate enhancement in the extreme nodule of the right kidney, which was weaker than that of the cortex and medulla. CT, computed tomography; Hu, Hounsfield units; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; DWI, diffusion-weighted imaging.

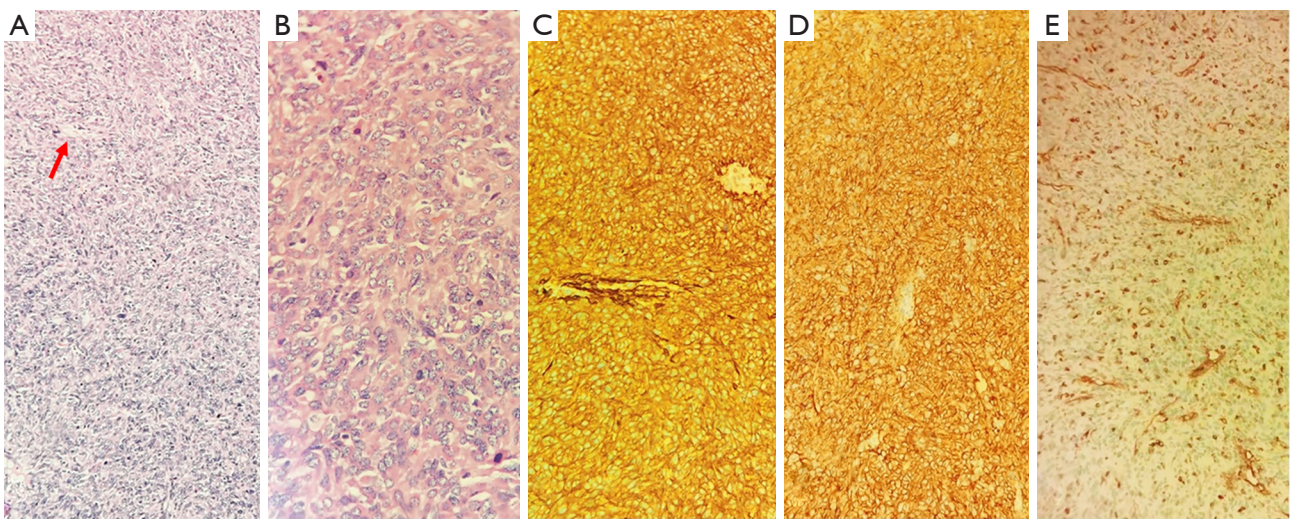

Figure 2 Histopathology of the same patient, including HE staining and IHC staining. (A) Morphological features of JGCT. The tumor was tightly packed with polygonal cells, and the cytoplasm was pale and eosinophilic. There were large amounts of blood vessels within the tumor (red arrow) (HE, ×100). (B) Tumor cells nucleus was presented as a round or oval bubble shape, but the nucleolus was not obvious, and there were no signs of nuclear division (HE, ×400). (C) IHC features of JGCT. The tumor cells were obviously positive for SMA (IHC, ×200). (D) IHC features of JGCT. The tumor cells were obviously positive for CD34 (IHC ×200). (E) IHC features of JGCT. The tumor cells were obviously positive for VIM (IHC, ×200). JGCT, juxtaglomerular cell tumor; HE, hematoxylin-eosin; SMA, smooth muscle actin; IHC, immunohistochemical; CD34, cluster of differentiation 34; VIM, vimentin.

Discussion

JGCT (or reninoma) was first described in 1967 and was also reported by Kihara (2) the following year. It is also known as renin-secreting tumor and Robertson–Kihara syndrome, which involves a rare kidney tumor arising from the differentiation of glomerular vascular smooth muscle into glomerular arterioles. JGCT occurs mostly in young females, with a peak onset age of 15–25 years (3). It can cause severe hypertension and hypokalemia by activating the renin-angiotensin-aldosterone system through secreting an excess of renin, with clinical symptoms of "three high and one low', namely hypertension, high plasma renin activity, secondary aldosteronism, and hypokalemia (4). Patients often have hypertension as the first symptom, and blood pressure is well controlled with angiotensin-converting enzyme inhibitors or angiotensin II receptor antagonists.

In the case of JGCT, laboratory tests will show significantly increased plasma renin activity and aldosterone levels alongside decreased blood potassium levels. Plasma renin activity may be further elevated in the orthostatic position. At the same time, the fractional plasma renin activity ratio has a diagnostic value (5): if the plasma renin activity ratio between the affected side and the healthy side is over 1.5, it can support the diagnosis of JGCT.

JGCT is divided into typical, atypical, and nonfunctional types according to blood pressure and serum potassium. Typical JGCT clinically involves hypertension and hypokalemia, and the imaging manifestations of JGCT have certain characteristics; most tumors located within the renal cortex are small. On non-contrast enhanced computed tomography (NECT), JGCT shows low-density or isodense nodules within the renal cortex, and a few are high-density with clear boundaries, but the interior of the mass is heterogeneous. On contrast-enhanced computed tomography (CECT), JGCT is significantly intensified, with less enhancement than the renal parenchyma in the cortical period, yet the venous and delayed periods are still obviously intensified. On MRI, JGCT shows a hypointense or isointense lesion on T1-weighted imaging (T1WI), hyperintense lesion on T2-weighted imaging (T2WI) (6), and hyperintensity with a restricted apparent diffusion coefficient on diffusion-weighted imaging (DWI), and reinforcement characteristics similar to that of CECT. This case had a definite preoperative diagnosis of JGCT owing to the typically clinical and imaging findings, which was consistent with the literature reports. Atypical JGCT (with hypertension or hypokalemia) and nonfunctional JGCT (without hypertension and hypokalemia) are often misdiagnosed as other benign or malignant tumors of the kidney.

Clinically, JGCT needs to be differentiated from other vascular diseases and similar clinical diseases that lead to elevated plasma renin activity levels: (I) renal vascular hypertension, such as renal artery stenosis: in patients with unilateral or bilateral renal artery stenosis, due to insufficient renal perfusion, the secretion of renin increases, resulting in increased aldosterone and hypokalemia. Blood vascular murmur can be heard in the abdomen; based on these, renal angiography or renal artery computed tomography angiography (CTA) provides a definite diagnosis. (II) Primary aldosteronism: clinical findings show the following symptoms of hypertension, hyperaldosteronemia, and hypokalaemia, but renin activity is lower than normal. There is 1 or more mass-occupying lesions in the adrenal glands on imaging examination, most of which are Conn's syndrome-type adenoma. The density of Conn's adenoma is lower than that of muscles on NECT, which is present as the edge or capsule contrast enhancement on CECT, but few show obvious and heterogeneous contrast enhancement on CECT. On MRI, comparing in-phase with out-of-phase, the signal of the lesion is attenuated on out-of-phase. (III) Renal parenchymal hypertension, such as accelerated hypertension: accelerated hypertension with persistent diastolic blood pressure of no less than 130 mmHg, which can also lead to increased renin secretion due to fibrinoid necrosis of renal arterioles and relative renal ischemia, characterized by high renin hypertension. The progression is rapid, the prognosis is poor, and patients often die from severe target organ damage, but symptoms of high renin levels are relieved by effective antihypertensive therapy. (IV) Segmental renal hypoplasia, also called as Ask-Upmark Kidney, was first reported by Ask-Upmark in 1929. The etiology of segmental renal hypoplasia is congenital, which may be due to congenital reflux that damages a ureteral bud branch affecting the development of the local renal lobe. Segmental dysplasia can occur unilaterally or bilaterally, the incidence of which in females is significantly higher than that in males (7). Segmental renal dysplasia can cause hyper-renin hypertension. On the tomograph images, segmental renal dysplasia usually presents as a small kidney with an uneven surface and transverse groove deep to the collecting system. Surgical resection of the focus can immediately cure some patients' hypertension symptoms. In addition, JGCT needs to be differentiated from epithelioid angiomyolipoma, metanephric adenoma, embryoma of the kidney (Wilm's

tumor), and renal cell carcinoma.

The clinical diagnosis of typical JGCT is usually only based on clinical manifestations and renal imaging abnormalities. The diagnosis of atypical JGCT and nonfunctional JGCT are often based on pathological diagnosis. The pathologic differential diagnosis of JGCT includes glomus tumor and epithelioid angiomyolipoma. (I) Glomus tumor is composed of round cells with the same shape, which are distributed between the blood vessels in a sheet shape or around the blood vessels in a ring shape. The cell boundary is clear, and the morphology is similar to that of parabulbar cell tumor. However, parabulbar cell tumors often have mast cells and thick-walled, transparent, denatured blood vessels. Immunohistochemically, glomus tumor occasionally expresses cluster of differentiation 34 (CD34) and does not express renin. (II) Epithelioid angiomyolipoma: When the tumor tissue is mainly composed of epithelioid smooth muscle and thick-walled vessels, and the fat content is relatively small, it may be misdiagnosed as JGCT. They can be differentiated by immunohistochemistry. Epithelioid angiomyolipoma shows biphasic differentiation of smooth muscle and pigment cells, and expresses smooth muscle actin (SMA) and pigment markers (HMB45, MelanA); some cases could express CD117. Although JGCT expresses SMA and CD117, it also expresses vascular markers CD34 and renin.

Surgical resection is the mainstay of treatment for JGCT (8). MRI can perform better in the detection and characterization of kidney lesions than CT (9). DWI contributes to the finding of the small lesion within the cortex, which usually appears as a hyperintensity with a restricted apparent diffusion coefficient. From the tomographic imaging, we can identify the lesion's location and size to guide the clinical selection of surgical procedures such as tumor enucleation, partial nephrectomy, or radical nephrectomy. Most of those cases are benign, with a good prognosis. A case of malignant JGCT has been reported outside of China (10).

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-22-1222/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was provided by the patient's parents for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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