CT and MRI Characteristic Findings of Sporadic Renal Hemangioblastoma: Two Case Reports and Review of the Literature

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Case report

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Abstract

Background

Hemangioblastoma in the kidney is rare. Although a few renal hemangioblastoma cases have been reported, the content of these articles mainly focused on clinical and pathological research, with minimal descriptions of radiologic findings. Moreover, there are no descriptions of magnetic resonance imaging with enhancement for this condition. We herein report two cases of renal hemangioblastoma with computed tomography and magnetic resonance imaging findings.

Case presentation

Two patients presented to our institution due to dull pain of the left abdomen, and a mass in the left kidney was found by ultrasound examination in each case. They had no special family history. Physical examination revealed no obvious tenderness or percussion pain in the renal region and ureteral walking area, and there was no obvious mass. Routine blood and urine tests were normal, and serum tumor markers were negative. No obvious lesions were found on imaging of other body parts. Similar radiologic findings were observed in both cases and mimicked those of cavernous hemangiomas of the liver, including peripheral nodular enhancement in the corticomedullary phase, progressive centripetal enhancement in the nephrographic and delayed phases, and occasional complete “filling in” in the delayed phase. Given the suspicion for renal cell carcinoma, both patients underwent partial nephrectomy. The pathological results showed renal hemangioblastoma.

Conclusions

Renal hemangioblastoma is a rare benign tumor that is easily misdiagnosed as clear cell carcinoma. Characteristic computed tomography and magnetic resonance imaging manifestations may improve preoperative diagnostic accuracy to avoid surgery or indicate nephron-sparing surgery.

Background

Hemangioblastomas are vascular tumors that often occur in the central nervous system (CNS), especially the cerebellum. Most cases are sporadic, and about 20-38% of patients also have Von-Hippel-Lindau (VHL) disease, which is an autosomal dominant genetic condition with an incidence of 1/27,300–1/45,000[1-3]. The VHL gene located on chromosome 3p25-26 and is an important tumor suppressor gene that contains 3 exons[4, 5]. The VHL gene is transcribed to a 4.5-kb-long mRNA that encodes a VHL protein (PVHL) containing 213 amino acids. The loss, mutation, or methylation inactivation of the VHL gene disturbs PVHL synthesis, which is an important molecular basis for VHL disease. VHL-related tumors include hemangioblastomas that are usually located in the CNS, fewer renal and pancreatic cystic tumors, neuroendocrine tumors of the pancreas, renal clear cell carcinoma, endolymphatic sac tumors, pheochromocytomas, and paragangliomas[2, 6].

Beyond the CNS, hemangioblastomas can also occur in the peripheral nervous system[7, 8], retroperitoneum[9, 10], pelvic cavity[11], soft tissue[12], bone[13], adrenal glands[14], lung, and liver[15]. The PubMed database was searched for literature using the keywords “hemangioblastoma” and “kidney or renal.” After screening all the articles in the database, the first case report of renal hemangioblastoma (RH) was by Nonaka et al. in 2007[16]. RH is rare, and no more than 30 cases have been reported, but the content of these articles mainly focused on clinical and pathological research with limited descriptions of radiologic findings[17-27]. Moreover, there are no descriptions of enhanced magnetic resonance imaging (MRI) findings of RHs.

We report two cases of patients with RH confirmed by surgery and pathology with complete clinical, pathological, and imaging data collected in our hospital. Neither patient had VHL disease and were diagnosed with sporadic RH.

Case Presentation

Case 1

In November 2015, a 45-year-old male patient presented to our institution with a dull pain in the left abdomen that had been present for 2 weeks. The patient had never undergone surgery and had an unremarkable family history. The respiratory frequency of the patient was 18 times per minute, with body temperature 36.7°, pulse rate 76 times per minute, and blood pressure 110/76 mmHg. Physical examination revealed no obvious tenderness or percussion pain in the renal region or ureteral walking area, and there was no palpable mass. Routine blood and urine tests were normal, and serum carbohydrate antigen 199, carbohydrate antigen 125, alpha-fetoprotein, carcinoembryonic antigen, and prostate-specific antigen were negative. No obvious lesions were found on chest X-ray; head computed tomography (CT); or ultrasonography of the liver, gallbladder, pancreas, and spleen.

Ultrasonography (Fig. 1A) did reveal a 37×42 mm heterogeneous echo mass inside the lower pole of the left kidney that had an irregular shape and distinct margin. There was some echo of blood flow inside. CT and MRI findings are shown in Figure 1B-D and Figure 2 A-G, respectively. A round, soft tissue density or signal mass was seen inside the lower pole of the left kidney. In the periphery of the mass, some small high-density areas in CT images of the precontrast phase and hypointensities in fat-suppressed T2-weighted images and diffusion-weighted images suggested hemorrhage. After contrast agent injection, the mass showed peripheral nodular enhancement in both CT and MR images of the corticomedullary phase, and progressive centripetal enhancement in CT and MR images of the posterior enhanced phase. In the center of the mass, a hyperintensity in fat-suppressed T2-weighted images and diffusion-weighted images that was not enhanced suggested necrosis. We made a radiologic diagnosis of renal clear cell carcinoma because the mass showed a rich blood supply with hemorrhage and necrosis.

Given the suspicion for renal cell carcinoma (RCC), the patient underwent laparoscopic right partial nephrectomy. The pathological results showed RH (Fig. 2H). Immunohistochemical results were cytokeratin (CK)-pan (partially +), CD31 (-), CD34 (-), inhibin alpha (+), neuron-specific enolase (NSE)

(partially +), vimentin (+), and Ki-67 (1%+). The patient's recovery was uneventful, and there was no evidence of local recurrence or metastasis 4 months after surgery.

Case 2

In December 2017, a 42-year-old female patient presented to our institution due to a mass in the left kidney found during ultrasound examination in the local hospital. The patient had a history of cesarean section 16 years earlier and no special family history. Her respiratory frequency was 21 times per minute, with body temperature 36.5°, pulse rate 78 times per minute, and blood pressure 100/58 mmHg. Physical examination revealed no obvious tenderness or percussion pain in the renal region or ureteral walking area, and there was no obvious mass. Routine blood and urine tests were normal, and serum carbohydrate antigen 199, carbohydrate antigen 125, alpha-fetoprotein, carcinoembryonic antigen, and prostate-specific antigen were negative. No obvious lesions were found on chest X-ray or ultrasonography of the liver, gallbladder, pancreas, and spleen.

MRI findings are shown in Figure 3 A–G. A 29×26×28 mm round, soft tissue signal mass was seen inside the left kidney. The mass showed significant hyperintensity in fat-suppressed T2-weighted images and diffusion-weighted images, which could be described as the "light bulb sign." After contrast agent injection, the mass exhibited peripheral nodular enhancement in MR images of the corticomedullary phase, and progressive centripetal enhancement in MR images of the nephrographic and delayed phases, with almost complete "filling in" in the delayed phase. The radiologic diagnosis was uncertain because the renal mass showed unique findings that we had not previously seen in renal masses.

Given the suspicion for RCC, the patient underwent da Vinci robotic-assisted left partial nephrectomy. The pathological results showed RH, and the tumor was surrounded by a fibrous capsule (Fig. 3H). Immunohistochemical results were CK-pan (-), CD31 (-), CD34 (-), inhibin alpha (+), NSE (+), PAX-8 (+), RCC (-), and S-100 (+).

Discussion

The latest 2016 World Health Organization classification of tumors of the urinary system and male genital organs now includes RH as a mesenchymal tumor, which is similar to the CNS hemangioblastoma[28]. However, a correlation between VHL syndrome and VHL gene mutation has not been reported, and the biological behavior of the tumor is benign. RH is a rare, slow-growing, and benign renal tumor. It usually affects the middle-aged and elderly but can also occur in younger patients[18, 20]. Compared with women, men are 1.5 to 2 times more likely to develop RH[29]. In sporadic cases like the two described here, there is no VHL-related disease and no associated family history of VHL disease in the patient (so-called "isolated" RH)[26].

The gross features of RH include a predominantly solid tumor rich in capillaries with a well-demarcated border from the surrounding renal parenchyma, which is consistent with what we saw in the surgical specimens. Microscopically, RH is a morphologically distinctive vascular neoplasm with rich capillary

networks and lipid-rich stromal cells[18, 20, 29]. Based on the stromal cell components, they could be divided into three types: capillary-dominated, interstitial cell-dominated, and classic type (intermediate between the other two types). Unfortunately, although the stromal cells of RH appear normal, they may show obvious nuclear pleomorphism, similar to malignant tumors. Therefore, RH can be easily misdiagnosed as RCC and other malignant tumors[29].

Because it is difficult to distinguish RH from renal clear cell carcinoma by routine hematoxylin and eosin (HE) staining alone, immunohistochemical examination is helpful for differential diagnosis. Studies have shown that labeling with inhibin alpha, S-100, and CD10 help to distinguish RH from renal clear cell carcinoma. Inhibin alpha and S-100 are usually positive in RH and negative in renal clear cell carcinoma and contrast; CD10 is usually positive in renal clear cell carcinoma and negative in RH[30-33]. Our cases are also consistent with the results of the above studies.

CT and MRI are very useful examination methods that have been widely used in the diagnosis and differential diagnosis of diseases in various systems. Both have gained increased acceptance for accurate diagnosis and differential diagnosis of renal tumors[34-37].

Most hemangioblastomas are in the cerebellum and can be divided into three types: solid, solid-cystic, or predominantly cystic with small mural nodules[38, 39]. The most common and typical radiologic findings correspond to the last type and show a markedly enhanced small mural nodule attached to a large unenhanced cyst wall[40, 41]. There is limited literature describing the imaging findings of RH, but they report RH as a solid, heterogeneously enhanced mass, which is consistent with our cases[17, 22, 23]. However, they do not correspond with the most common and typical radiologic findings of hemangioblastoma in the cerebellum. This discrepancy may be related to the different tumor growth environments.

In addition to being solid tumors, the CT and MRI findings of our two patients were similar to that of cavernous hemangiomas of the liver, including peripheral nodular enhancement in the corticomedullary phase, progressive centripetal enhancement in the nephrographic and delayed phases, and sometimes complete “filling in” in the delayed phase[42, 43]. Other renal tumors do not exhibit these enhancement patterns, which could be unique to RH. At present, these findings have not been mentioned in the literature. It may be that others have not noticed this feature, or they may not have performed contrast enhancement multiphase scanning with CT and MRI. T2WI also helps during differential diagnosis. The high signal intensity on T2WI indicated slow blood flow in the neoplastic vascular channel, which is of great significance to angiogenic tumors. The first case was less typical due to bleeding, but the second case was similar to cavernous hemangioma of the liver, showing a significantly high signal intensity known as the “light bulb sign”[44].

Because RHs are indolent neoplasms, asymptomatic tumors may be managed with observation. Gross total resection is the most suitable treatment if intervention is required[45]. If the correct preoperative diagnosis was made, these two patients may have received different treatments. Unfortunately, RH can easily be misdiagnosed as renal clear cell carcinoma, the most common malignant tumor of the kidney,

which can lead to overtreatment. Characteristic CT and MRI manifestations may help guide preoperative diagnosis. At the same time, once RH is surgically confirmed, a comprehensive examination should be performed to determine if the tumor is associated with VHL disease.

Conclusions

In conclusion, RH is a rare benign tumor that is easily misdiagnosed as clear cell carcinoma. Characteristic manifestations on CT and MRI may help us make a preoperative diagnosis to avoid surgery or indicate nephron-sparing surgery. This highlights the importance of accurate preoperative radiologic diagnosis.

Abbreviations

CNS:Central nervous system; VHL:Von-Hippel-Lindau; PVHL:VHL protein; RH:Renal hemangioblastoma; MRI: Magnetic resonance imaging; CT:Computed tomography; RCC: Renal cell carcinoma; CK:Cytokeratin; NSE:Neuron-specific enolase; HE:Hematoxylin and eosin

Declarations

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Not applicable

Authors' contributions

JH and NL carried out the studies, participated in collecting data, and drafted the manuscript. QFW and WLZ participated in its design. WWL prepared histology figures and provided pathological analysis. HH participated in the acquisition and analysis or interpretation of data. All authors read and approved the final manuscript.

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Availability of data and materials

All the data in this report have been presented in the manuscript.

Ethics approval and consent to participate

Written informed consent was obtained from the two patients for publication of this case report and any accompanying images. This case report has been approved by the ethics committee at Sir Run Run Shaw Hospital, Zhejiang University School of Medicine（No. 20201014-41）.

Consent for publication

The patients gave their written informed consent for the publication of their data.

Competing interests

The authors declare that they have no competing interests.

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Figures

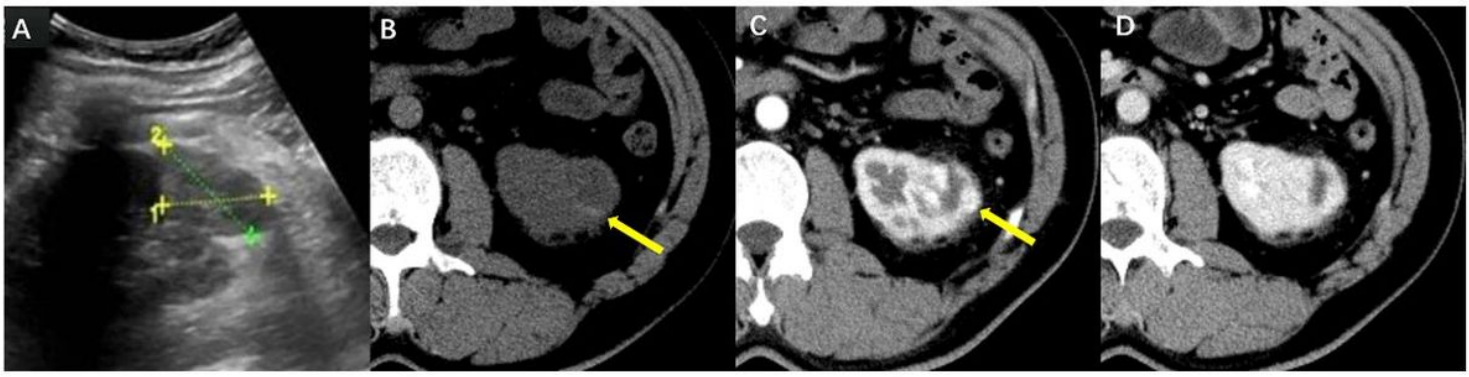

Figure 1

A 45-year-old man with a round mass in the left kidney diagnosed as hemangioblastoma. (A) Ultrasonography revealed a 37×42 mm heterogeneous echo mass inside the lower pole of the left kidney that had an irregular shape and a distinct margin. (B) Axial CT images of the precontrast phase of the abdomen showed a round soft tissue mass in the lower pole of the left kidney, and a small high-density shadow could be seen in the periphery of the mass (yellow arrow), which suggested a hemorrhage. (C) In axial CT images of the corticomedullary phase, the mass showed peripheral nodular enhancement (yellow arrow), similar to that of the abdominal aorta at the same level. (D) Axial CT images of the nephrographic phase showed slight progressive centripetal enhancement.

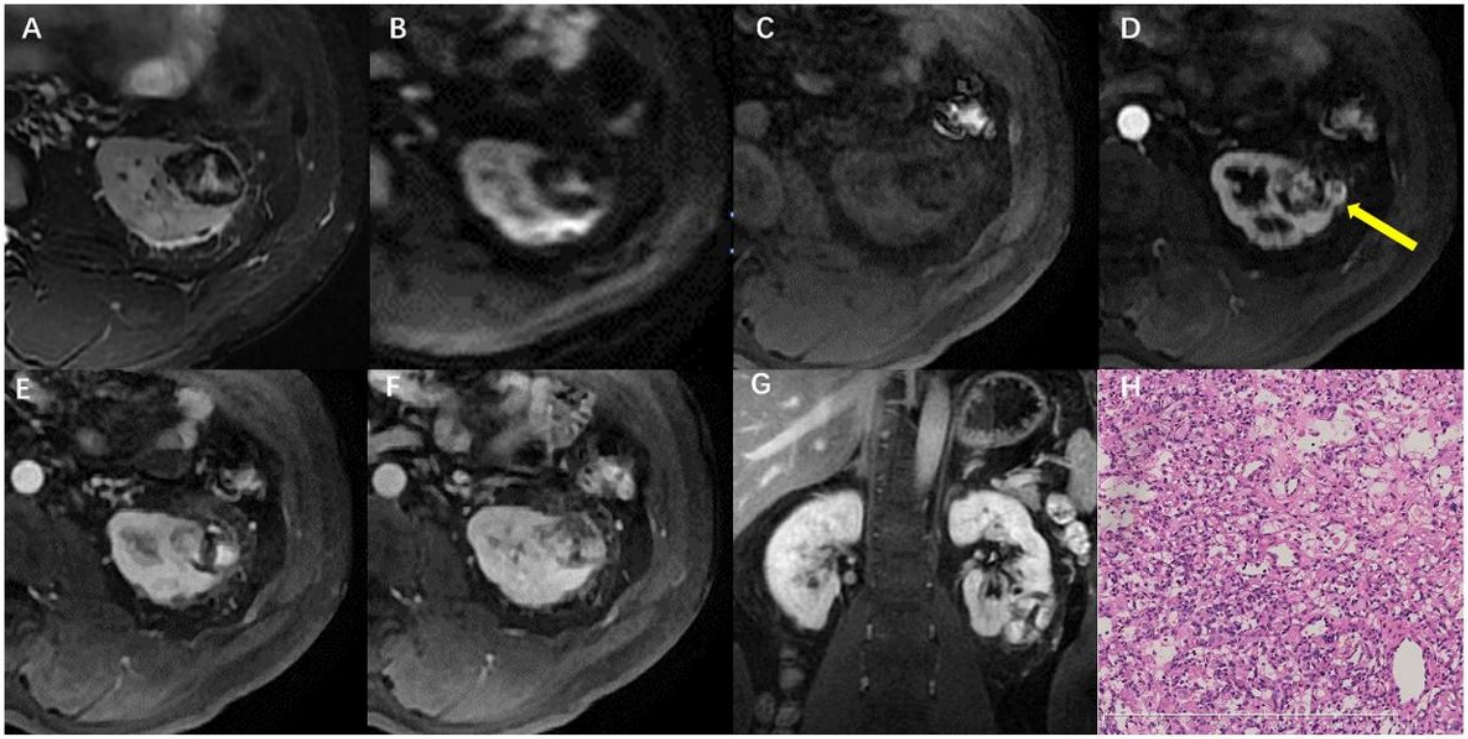

Figure 2

(A) Axial fat-suppressed, T2-weighted image and (B) diffusion-weighted image showing hypointensity in the periphery of the mass suggesting hemorrhage, and hyperintensity in the center of the mass indicative of necrosis. (C) In axial, precontrast, fat-suppressed, T1-weighted images, the mass appeared heterogeneously hypointense compared with the renal parenchyma. (D) Axial, corticomedullary phase, fat-suppressed, gadolinium-enhanced, T1-weighted images showed peripheral nodular enhancement (yellow arrow). (E) Axial nephrographic phase, (F) axial delayed phase and (G) coronal delayed phase fat-suppressed, gadolinium-enhanced, T1-weighted images showed progressive centripetal enhancement. An area in the center of the mass was not enhanced. (H) Histological examination demonstrated an RH. The tumor was mainly composed of a rich vascular network interspersed with polygonal cells, HE×100.

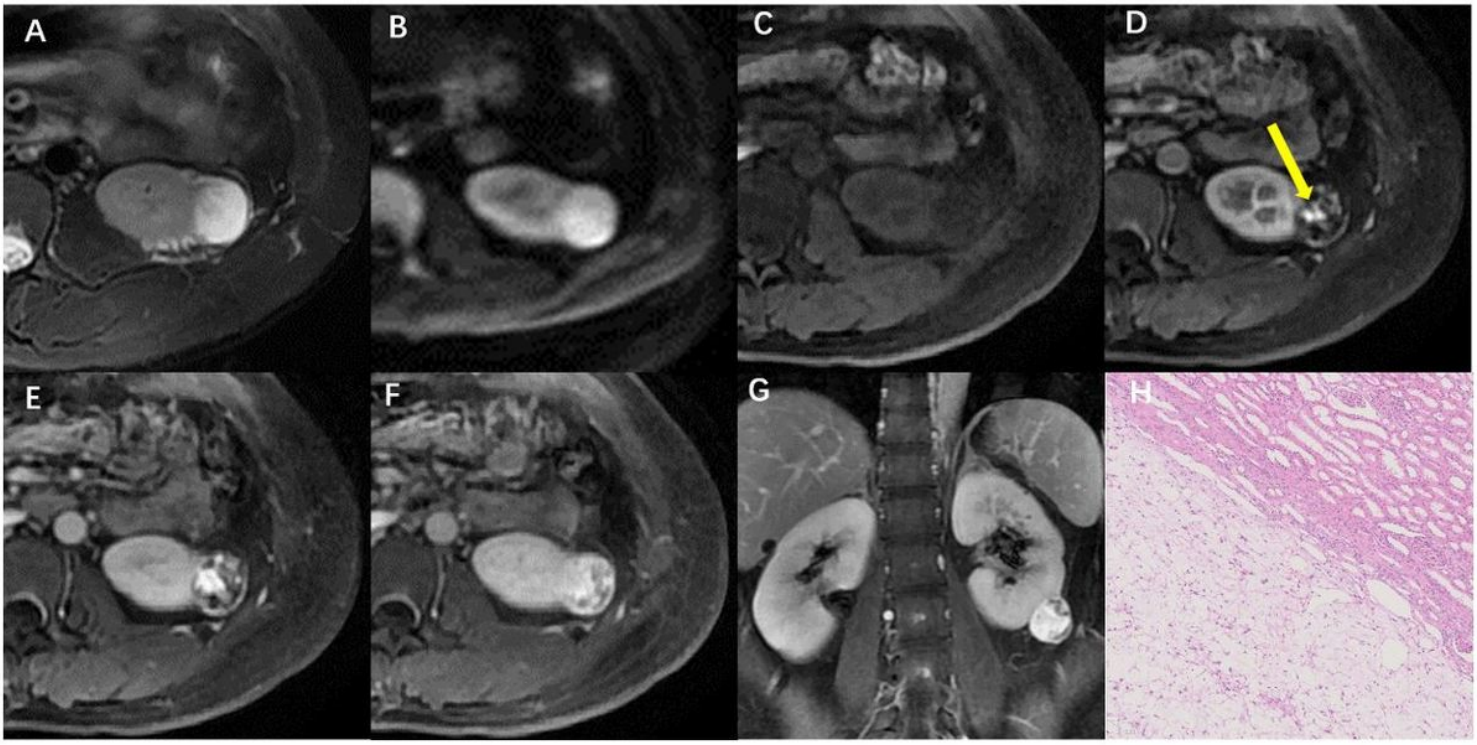

Figure 3

A 42-year-old woman with a 29×26×28 mm round mass in the left kidney diagnosed as hemangioblastoma. (A) Axial, fat-suppressed, T2-weighted images and (B) diffusion-weighted images showed significant hyperintensity of the mass. (C) In axial precontrast, fat-suppressed, T1-weighted images, the mass appeared hypointense compared with the renal parenchyma. (D) Axial corticomedullary phase fat-suppressed, gadolinium-enhanced, T1-weighted images showed peripheral nodular enhancement (yellow arrow). (E) Axial nephrographic phase, (F) axial delayed phase, and (G) coronal delayed phase fat-suppressed, gadolinium-enhanced, T1-weighted images showed progressive centripetal enhancement and almost complete “filling in” in the delayed phase. (H) The tumor was surrounded by a fibrous capsule and had a well-demarcated border against the surrounding renal parenchyma, HE×100.