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°C, 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

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**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.

References

1. Chang H, Li J, Wang P, Lu X, Li B. Microsurgical treatment of cervical spinal hemangioblastoma. Neurochirurgie. 2020;66(1):56-60.
2. Byun J, Yoo HJ, Kim JH, Kim YH, Cho YH, Hong SH et al. Growth rate and fate of untreated hemangioblastomas: Clinical assessment of the experience of a single institution. J Neurooncol. 2019;144(1):147-54.
3. Salama Y, Albanyan S, Szybowska M, Bullivant G, Gallinger B, Giles RH et al. Comprehensive characterization of a canadian cohort of von hippel-lindau disease patients. Clin Genet. 2019;96(5):461-7.
4. Wang J, Cao W, Wang Z, Zhu H. Novel gene mutation in von hippel-lindau disease - a report of two cases. BMC Med Genet. 2019;20(1):194.
5. Launbjerg K, Bache I, Galanakis M, Bisgaard ML, Binderup MLM. Von hippel-lindau development in children and adolescents. Am J Med Genet A. 2017;173(9):2381-94.
6. Chen X, Xu G, Bi Q, Huang Y, Shao H, Jin M et al. Cauda equina syndrome as first manifestation of von hippel-lindau disease. World Neurosurg. 2019;125:316-9.
7. McGrath LA, Mudhar HS, Salvi SM. Optic nerve haemangioblastoma: Signs of chronicity. Ocul Oncol Pathol. 2018;4(6):370-4.
8. Darbari S, Meena RK, Sawarkar D, Doddamani RS. Optic nerve hemangioblastoma: Review. World Neurosurg. 2019;128:211-5.
9. Jalikis FG, Hoch BL, Bakthavatsalam R, Montenovo MI. Sporadic retroperitoneal hemangioblastoma: Report of a case and review of the literature. Case Rep Pathol. 2017;2017:4206489.
10. Huang Y, Han XC, Lv GS. Sporadic hemangioblastoma of the retroperitoneum. Int J Clin Exp Pathol. 2014;7(4):1777-81.
11. Shi H, Li H, Zhen T, Zhang F, Han A. Hemangioblastoma of pelvic cavity: Report of a case and review of literature. Int J Clin Exp Pathol. 2014;7(10):7054-8.
12. Patton KT, Satcher RL, Jr., Laskin WB. Capillary hemangioblastoma of soft tissue: Report of a case and review of the literature. Hum Pathol. 2005;36(10):1135-9.
13. Panelos J, Beltrami G, Capanna R, Franchi A. Primary capillary hemangioblastoma of bone: Report of a case arising in the sacrum. Int J Surg Pathol. 2010;18(6):580-3.
14. Deb P, Pal S, Dutta V, Srivastava A, Bhargava A, Yadav KK. Adrenal haemangioblastoma presenting as phaeochromocytoma: A rare manifestation of extraneural hemangioblastoma. Endocr Pathol. 2012;23(3):187-90.
15. McGrath FP, Gibney RG, Morris DC, Owen DA, Erb SR. Case report: Multiple hepatic and pulmonary haemangioblastomas—a new manifestation of von hippel-lindau disease. Clin Radiol. 1992;45(1):37-9.
16. Nonaka D, Rodriguez J, Rosai J. Extraneural hemangioblastoma: A report of 5 cases. Am J Surg Pathol. 2007;31(10):1545-51.
17. Zhao M, Williamson SR, Yu J, Xia W, Li C, Zheng J et al. Pax8 expression in sporadic hemangioblastoma of the kidney supports a primary renal cell lineage: Implications for differential diagnosis. Hum Pathol. 2013;44(10):2247-55.
18. Wang CC, Wang SM, Liau JY. Sporadic hemangioblastoma of the kidney in a 29-year-old man. Int J Surg Pathol. 2012;20(5):519-22.
19. Jiang JG, Rao Q, Xia QY, Tu P, Lu ZF, Shen Q et al. Sporadic hemangioblastoma of the kidney with pax2 and focal cd10 expression: Report of a case. Int J Clin Exp Pathol. 2013;6(9):1953-6.
20. Liu Y, Qiu XS, Wang EH. Sporadic hemangioblastoma of the kidney: A rare renal tumor. Diagn Pathol. 2012;7:49.
21. Ip YT, Yuan JQ, Cheung H, Chan JK. Sporadic hemangioblastoma of the kidney: An underrecognized pseudomalignant tumor? Am J Surg Pathol. 2010;34(11):1695-700.
22. Wang Y, Wei C, Mou L, Zhang Q, Cui Z, Li X et al. Sporadic renal haemangioblastoma: Case report and review of the literature. Oncol Lett. 2013;5(1):360-2.
23. Oberhammer L, Mitterberger MJ, Lusuardi L, Kunit T, Drerup M, Colleselli D et al. Sporadic renal hemangioblastoma: A case report of a rare benign renal tumor. Clin Case Rep. 2019;7(12):2321-6.
24. Wu Y, Wang T, Zhang PP, Yang X, Wang J, Wang CF. Extraneural hemangioblastoma of the kidney: The challenge for clinicopathological diagnosis. J Clin Pathol. 2015;68(12):1020-5.
25. Bisceglia M, Muscarella LA, Galliani CA, Zidar N, Ben-Dor D, Pasquinelli G et al. Extraneuraxial hemangioblastoma: Clinicopathologic features and review of the literature. Adv Anat Pathol. 2018;25(3):197-215.
26. Muscarella LA, Bisceglia M, Galliani CA, Zidar N, Ben-Dor DJ, Pasquinelli G et al. Extraneuraxial hemangioblastoma: A clinicopathologic study of 10 cases with molecular analysis of the vhl gene. Pathol Res Pract. 2018;214(8):1156-65.
27. Kuroda N, Agatsuma Y, Tamura M, Martinek P, Hes O, Michal M. Sporadic renal hemangioblastoma with ca9, pax2 and pax8 expression: Diagnostic pitfall in the differential diagnosis from clear cell renal cell carcinoma. Int J Clin Exp Pathol. 2015;8(2):2131-8.
28. Moch H, Humphrey PA, Ulbright TM, Reuter VE. The WHO classification of tumours of the urinary system and male genital organs. Lyon. France: International agency for research on cancer press: 2016.
29. Ahadi M, Zham H, Rakhshan A, Rafizadeh M, Talebi Bayazi D, Baikpour M et al. Hemangioblastoma of the central nervous system: A case series of patients surgically treated at shohada-e-tajrish hospital, tehran, iran during 2004-2014. Iran J Child Neurol. 2019;13(2):163-9.
30. Jung SM, Kuo TT. Immunoreactivity of cd10 and inhibin alpha in differentiating hemangioblastoma of central nervous system from metastatic clear cell renal cell carcinoma. Mod Pathol. 2005;18(6):788-94.
31. Hoang MP, Amirkhan RH. Inhibin alpha distinguishes hemangioblastoma from clear cell renal cell carcinoma. Am J Surg Pathol. 2003;27(8):1152-6.
32. Eichberg DG, Buttrick S, White K, Gultekin SH, Komotar RJ. Pax8 expression variability in cerebellar hemangioblastoma: Case series and review of the literature. Appl Immunohistochem Mol Morphol. 2019;27(6):477-81.
33. Carney EM, Banerjee P, Ellis CL, Albadine R, Sharma R, Chaux AM et al. Pax2(-)/pax8(-)/inhibin a(+) immunoprofile in hemangioblastoma: A helpful combination in the differential diagnosis with metastatic clear cell renal cell carcinoma to the central nervous system. Am J Surg Pathol. 2011;35(2):262-7.
34. Dilauro M, Quon M, McInnes MD, Vakili M, Chung A, Flood TA et al. Comparison of contrast-enhanced multiphase renal protocol ct versus mri for diagnosis of papillary renal cell carcinoma. AJR Am J Roentgenol. 2016;206(2):319-25.
35. Woo S, Suh CH, Cho JY, Kim SY, Kim SH. Diagnostic performance of ct for diagnosis of fat-poor angiomylipoma in patients with renal masses: A systematic review and meta-analysis. AJR Am J Roentgenol. 2017;209(5):W297-w307.
36. Lim RS, Flood TA, McInnes MDF, Lavallee LT, Schieda N. Renal angiomylipoma without visible fat: Can we make the diagnosis using ct and mri? Eur Radiol. 2018;28(2):542-53.
37. Schieda N, Thornhill RE, Al-Subhi M, McInnes MD, Shabana WM, van der Pol CB et al. Diagnosis of sarcomatoid renal cell carcinoma with ct: Evaluation by qualitative imaging features and texture analysis. AJR Am J Roentgenol. 2015;204(5):1013-23.
38. Rachinger J, Buslei R, Prell J, Strauss C. Solid haemangioblastomas of the cns: A review of 17 consecutive cases. Neurosurg Rev. 2009;32(1):37-47; discussion -8.
39. Lan Z, Richard SA, Zhang Y. Cystic-solid hemangioblastoma at the cerebellopontine angle: A case report. Medicine (Baltimore). 2020;99(3):e18871.
40. Lee SR, Sanches J, Mark AS, Dillon WP, Norman D, Newton TH. Posterior fossa hemangioblastomas: Mr imaging. Radiology. 1989;171(2):463-8.
41. Wang Q, Zhang S, Cheng J, Liu W, Hui X. Radiologic features and surgical strategy of hemangioblastomas with enhanced cyst wall. World Neurosurg. 2017;108:143-50.
42. Jinhu Y, Jianping D, Xin L, Yuanli Z. Dynamic enhancement features of cavernous sinus cavernous hemangiomas on conventional contrast-enhanced mr imaging. AJNR Am J Neuroradiol. 2008;29(3):577-81.

43. Gaa J, Saini S, Ferrucci JT. Perfusion characteristics of hepatic cavernous hemangioma using intravenous ct angiography (ivcta). Eur J Radiol. 1991;12(3):228-33.

44. Soyer P, Dufresne AC, Somveille E, Lenormand S, Scherrer A, Rymer R. Differentiation between hepatic cavernous hemangioma and malignant tumor with t2-weighted mri: Comparison of fast spin-echo and breathhold fast spin-echo pulse sequences. Clin Imaging. 1998;22(3):200-10.

45. Huang Y, Chan L, Bai HX, Li X, Zhang Z, Wang Y et al. Assessment of care pattern and outcome in hemangioblastoma. Sci Rep. 2018;8(1):11144.