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Sporadic hemangioblastoma of the kidney; a rare entity and a potential diagnostic challenge

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ABSTRACT

Hemangioblastoma is a benign tumor of central nervous system (CNS) which may rarely occur in extraneural tissues. Renal hemangioblastoma (RH) occurs sporadic or in the setting of Von-hipple-lindau syndrome. It is usually misdiagnosed as other renal masses including renal cell carcinoma (RCC) due to their similar clinical and histologic features. In this paper, we present two cases of RH which resembled RCC, however immunohistochemical studies confirmed diagnosis of RH.

Keywords: Renal hemangioblastoma, Renal mass, Renal cell carcinoma, Immunohistochemistry

Case Report

Implication for health policy/practice/research/medical education:
Renal hemangioblastoma (RH) is a mimicker of real cell carcinoma, clinically and histologically. Attention to immunohistochemical profile of this tumor leads to the correct diagnosis and prevents unnecessary nephrectomy.

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Introduction

Hemangioblastoma is a tumor of mesenchymal cells that most often involves the central nervous system (CNS). It can be found as a sporadic finding, or it can be related to Von Hippel-Lindau (VHL) syndrome (1) . Extraneuraxial hemangioblastoma can be found in some other organs such as bone, liver, pancreas, lungs, urinary bladder, peripheral nervous system, and kidneys. Renal hemangioblastoma (RH) is a rare presentation of this tumor. It is usually linked to VHL syndrome, and the sporadic type of RH is even rarer (2,3). RH exhibits a morphologic pattern, similar to that observed in CNS hemangioblatoma. Both lesions display oval to polygonal cells with eosinophilic cytoplasm under the optic microscope. The presence of widespread vascularity characterized by thin to thick-walled blood vessels is also notable in both of them (4). On the other hand, there are histologic and clinical similarities recognized between RH and renal cell carcinoma (RCC) which is an invasive malignant tumor of the kidney (5). Accordingly, early diagnosis of benign RH leads to a more appropriate approach to the patients, thereby avoiding unnecessary diagnostic and therapeutic strategies (6).

Herein, we describe two cases of renal masses with no history and clinical features of VHL syndrome, initially presented with hematuria and flank pain. Both patients underwent nephrectomy. Subsequent pathologic and immunohistochemistry evaluation of these tumors confirmed the diagnosis of RH.

Case Presentation

Case 1

A 41-year-old female patient with no remarkable past medical history was referred to our hospital with gross hematuria and a constant pain localized in her right flank.

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She denied any history of trauma or vigrous exercise. Physical examination was negative for neurologic or muscular origin for this pain. Furthermore, she had no costovertebral angle tenderness. The laboratory data revealed no abnormalities but hematuria. On ultrasonography, a mass was detected in her right kidney, later confirmed by an abdominal computerized tomography (CT) scan (Figure 1).

The mass was highly suspicious for RCC. She underwent right sided partial nephrectomy. Then, the resected mass was sent to the pathology department for further evaluations (Figure 2).

Histologic features

On gross examination the tumor was well circumscribed with gray-white. Microscopically, hematoxylin and eosin (H&E) sections revealed epithelioid polygonal cells with bland-looking nuclei and eosinophilic to pale cytoplasm arranged in a vague lobular pattern intersected by fine fibrous stroma and a rich capillary network. Moreover, mitosis was absent (Figure 3).

Immunohistochemistry (IHC) showed diffuse and intense staining for neuron specific enolase (NSE) (Figure 4a) and less intensity for S100 (Figure 4b). CD34 and CD31 (Figure 4c), highlighted the capillary vessels but they were negative in clear cells. Moreover, HMB45 was negative.

According to the IHC evaluation, the diagnosis of RH was confirmed.

Case 2

A 40-year-old male patient was presented to the urology clinic complaining of gross hematuria and constant pain, localized in the right flank since few months ago. Evaluation for urolithiasis and urinary tract infections was performed for him previously and the results were negative. He denied any history of trauma. Hematuria was confirmed by the laboratory studies. A mass was detected in his abdominopelvic CT scan images (Figure 5), suspicious for RCC.

The patient underwent right sided nephrectomy. The tumoral kidney was sent to pathology department.

Pathologic features

The tumor was surrounded by a thick fibrotic capsule, made of polygonal mesenchymal cells with round nuclei and acidophilic cytoplasm. A vascular stroma in addition to some interstitial edema and hemorrhage and scattered hemosiderophages were observed which can be characteristic for hemangioblastoma. No necrosis or mitosis was observed. In addition, renal main vessels, ureter margin, and vessel margins were free of tumor. Lymphovascular invasion was not seen and renal hilum lymph nodes were intact. Immunohistochemistry showed that CD10, HMB45, CD117, desmin, myogenin, and melan-A were negative in tumor cells (Figure 6a); however,

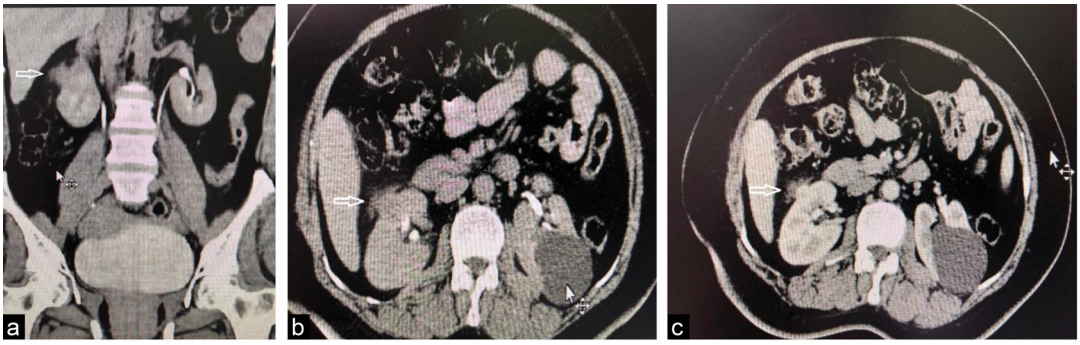

Figure 1. CT scan of the kidney. a: the hypodense mass in the upper pole of right kidney is marked in the coronal view in latent phase. b and c: the mass is marked in the axial view.

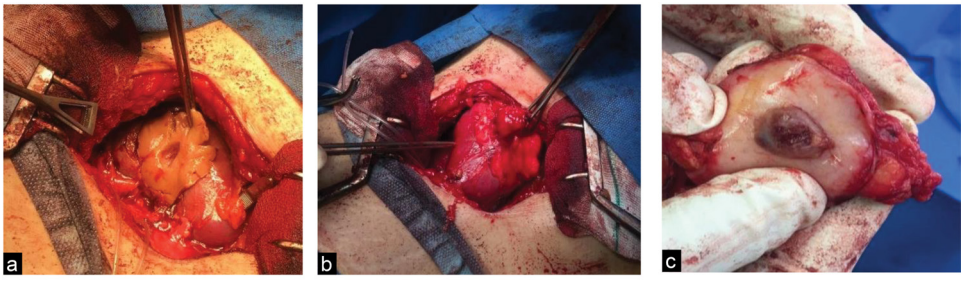

Figure 2. a and b: Renal mass surrounded by perinephric fat. c: The cut surface shows a brownish round nodule embedded in renal parenchyma.

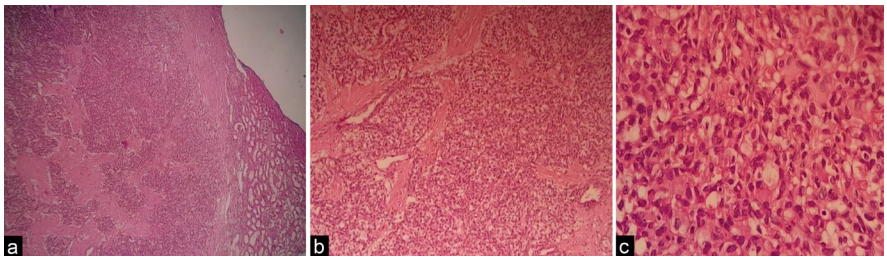

Figure 3. Microscopic examination shows a well circumscribed tumor with vague lobular pattern (3a; H&E, ×40). Lobules of epithelioid polygonal cells are noted with bland-looking nuclei and eosinophilic to pale cytoplasm intersected by fine fibrous stroma (3b; H&E, ×100) and a rich capillary network (3c; H&E, ×400).

inhibin, CD34, vimentin, and NSE were positive in the tumor cells (Figure 6b, 6c). Negative cytokeratin and nonspecific staining for S100 were also reported. These findings suggested RH as the final diagnosis.

Discussion

Hemangioblastoma is a primary CNS tumor, but it can present as extraneuraxial neoplasm in other organs of the body. This tumor rarely develops in the kidney (2,7,8). RH is a rare neoplasm which can present as sporadic form or as part of VHL (2,3,8). To the best of our knowledge, less than 30 cases of sporadic RH were reported to date (5,8-11). Because of its rare occurrence, its natural course has not been thoroughly studied. In the kidney, RH may mimic other primary benign and malignant lesions of this organ. Not only it is difficult to diagnose RH based only on clinicoradiologic pattern, but also is it challenging with relying only on routine microscopic studies such as H&E staining. By optic microscopic studies, the histological presentation of RH may overlap with other neoplastic lesions of the kidney, especially RCC, and epithelioid variants of angiomyolipoma, specially on a core needle biopsy (12); however, it is so important to differentiate these lesions from one another because of different management plans and different prognoses.

Both RH and RCC, can present with eosinophilic cells with focal rhabdoid and spindle cells and haphazardly arranged delicate and arborizing capillary networks, and distinguishing between these two entities morphologically can be extremely challenging on a small needle biopsy. Moreover, both lesions can show solid sheets or a nested pattern. However, these two lesions may be differentiated based on their distinctive IHC markers. Almost all cases of RH show strong positivity for α-inhibin, S100, and NSE, unlike RCC. Furthermore, RCC shows positivity for AE1/AE3, EMA, PAX8, PAX2, CD10, and RCC (13). Like our cases, RH may be associated with flank pain and hematuria, as well as RCC.

In our both patients the first possible diagnosis was RCC due to their clinical manifestation and imaging findings, while pheochromocytoma was less suspected according to the absence of its typical symptoms. Our patients did not

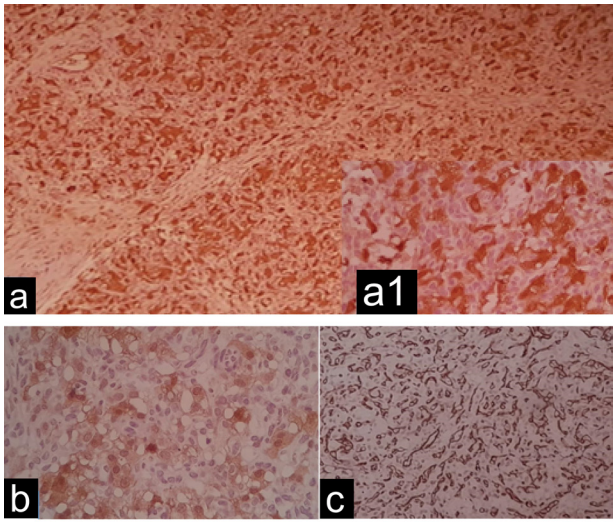

Figure 4. Immunohistochemistry examination shows positive immunoreactivity for NSE in tumoral cells (4a, ×100) and its zooming (4a.1, ×400), positive immunoreactivity for S100 (4b, ×100) and negative immunoreactivity for CD31 in epithelioid clear cells (4c, ×100).

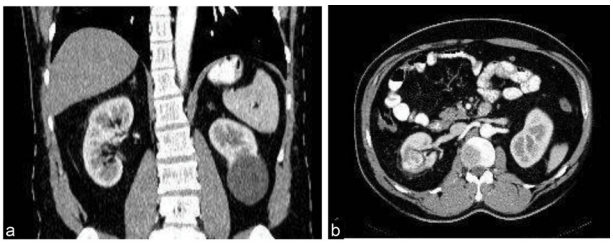

Figure 5. Computed tomography (CT scan) image of hypodense mass of the right kidney in coronal (5a) and axial (5b) view.

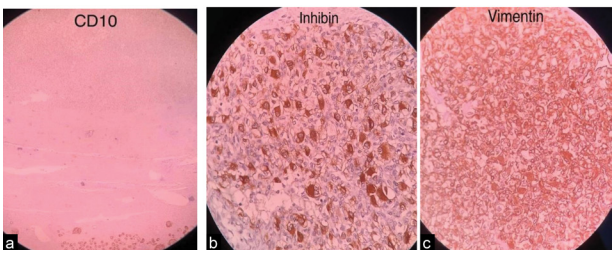

Figure 6. Immunohistochemistry staining showed negative immunoreactivity for CD10 (6a, ×100), but positive immunoreactivity for Vimentin and Inhibin (6b, c; ×400).

develop hematomas and massive hematuria, even though angiosarcoma must be considered as a life-threatening condition in any patient with a renal mass presented with hematuria.

According to the differential diagnosis described above, IHC plays an important role in confirming the final diagnosis. In 2019 Oberhammer et al (6) reported a case of hemangioblastoma accidentally found in an abdominal CT scan, with no urinary symptoms. The results of IHC evaluation showed immunoreactivity to vimentin, inhibin, NSE, CD-10, S-100, and WTI. Additionally, necrotic cells were observed. They designed a table comparing the results of IHC studies of his patient to 11 other patients diagnosed with RH in the literature. S-100, inhibin, and NSE were frequently positive in the previous cases. The evaluation of cytokeratin was positive in approximately 50% of cases. Most of the patients were middle-aged complaining of flank pain and hematuria.

Previousely, Luo et al reported a case of RH presented with unilateral flank pain in a 43-year-old woman (14). The patient underwent laparoscopic heminephrectomy and the resected tumor was evaluated pathologically. Tumoral cells with eosinophilic cytoplasm were observed along with hemorrhagic and necrotic lesions. The immunostaining was positive for inhibin, NSE, S-100, vimentin, and CD-10. Similarly, He J et al reported a case of renal hemangioblastoma with no urinary symptoms. A 43-year-old female asymptomatic patient with a renal mass as an incidental finding of abdominal ultrasonography, later diagnosed as hemangioblastoma. Similarly, He J et al presented a 45-year-old male patient complaining of dull abdominal pain for only 2 weeks with no urinary symptoms, diagnosed as RH (11). They suggested some diagnostic clues regarding to the findings of contrast-enhanced multiphase scanning with MRI and CT. Some unique enhancement patterns for renal hemangoblastoma were described in the study.

Recently, Raja et al preseneted a male case of sporadic RH with complaint of nonspecific unilateral flank pain for three days. The imaging findings confirmed a 2.4 cm mixed solid-cystic mass lesion located on the superior pole of the left kidney . The morphologic features in addition to the unique immunophenotype, were suggestive of RH (2).

Additionally, Malagic Polutak et al in 2023 reported a case of sporadic retroperitoneal hemangioblastoma. The patient was an 87-year-old male patient, whose abdominal CT scan performed due to kidney stones had incidentally revealed a mass in the retroperitoneum posterior to the inferior vena cava. Histopathological and immunohistochemical studies confirmed the diagnosis of hemangioblastoma (15).

Conclusion

RH is a benign neoplasm which can be mistaken with more prevalent tumors of the kidney, such as RCC. Clinical features and radiographic presentations, along with routine histologic analyses are not sufficient for diagnosis, so almost always it is diagnosed by IHC studies. All clinicians must be aware of this mimicker of RCC which has a very different natural course and treatment. The evidence suggests that RH usually occurs in middle-aged patients, sporadically or in the setting of VHL. The clinical presentation may vary from being asymptomatic to hematuria and flank pain. It is usually mistaken for other renal masses including RCC which is clinically and histologically similar to it. The imaging modalities such as MRI and CT scan are usually not capable of distinguishing between RH and other renal masses. An immunohistochemistry examination is required to confirm the diagnosis. In addition to the diagnostic workup, evaluation for VHL is strongly recommended.

Authors' contribution

Conceptualization: Shirin Taraz Jamshidi.
Data curation: Tina Zeraati.
Formal analysis: Ali Emadzadeh, Tina Zeraati.
Investigation: Salman Soltani, Hamidreza Ghorbani.
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Resources: Shirin Taraz Jamshidi, Ali Emadzadeh.
Software: Tina Zeraati.
Supervision: Shirin Taraz Jamshidi.
Validation: Tina Zeraati.
Visualization: Salman Soltani, Hamidreza Ghorbani.
Writing–original draft: Tina Zeraati.
Writing–review & editing: Shirin Taraz Jamshidi, Ali Emadzadeh.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

This case report was conducted in accordance with the World Medical Association Declaration of Helsinki. Written informed consent was obtained from patients for publication as a case report. Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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