Ipsilateral Synchronous Papillary and Clear Cell Renal Cell Carcinoma: a Case Report and Literature Review

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Case Report

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Abstract

Background: The rare disease of ipsilateral synchronous papillary and clear cell renal cell carcinoma was often misdiagnosed as a single tumor with intra-renal metastasis or some other diseases preoperatively. Both of the effective management and long overall survival might be affected as the different prognosis of the two kinds of tumors. Here, we report a case of ipsilateral synchronous papillary and clear cell renal cell carcinoma, and present the clinicopathological features as well as review the literature in China.

Case presentation: A 70-year-old man presented with a single mass in the left renal revealed either by ultrasound or CT during a routine physical examination. The tumor was occurred as two isolated masses in the gross finding. Hematoxylin and eosin staining and immunohistochemistry were performed. Papillary cell carcinoma and clear cell renal cell carcinoma were the compositions of the tumors. Immunostainings were as follows: The papillary renal cell carcinoma showed positive for CK7, P504s, Pax8,Vimentin, and scatterly for CD10, the proliferation rates of Ki67 was just 3%; While the clear cell renal cell carcinoma was positive for Pax8,CAIX,Vimentin, and diffusely for CD10, but negative for CK7 and P504s, the Ki67 proliferation rates was 5%. The patient was diagnosed with ipsilateral synchronous papillary and clear cell renal cell carcinoma, and free from the disease 9 months after surgery.

Conclusions: Ipsilateral synchronous papillary and clear cell renal cell carcinoma is a rare condition without specific clinical manifestations. The understanding of the computed tomography features and increasing the awareness or experience of the disease may be helpful to improve the preoperative diagnosis accuracy. Precise diagnosis should be based on histopathological morphology and immunostaining. As the different prognosis of the two tumors, optimal surgical treatment should be performed to prolong the survival time.

Background

The renal cell carcinoma (RCC) is the third most frequent malignancy of the urology system, which commonly originated from epithelial cells of the tubules [1]. The most common subtype of RCC is clear cell (80%), beside papillary(10%) and chromophobe type RCC(5%) [2]. As the two most common subtypes, papillary renal cell carcinoma (PRCC) and clear cell renal cell carcinoma (CCRCC) within the same renal was very rare at one time in the literature reviewed. Accurately diagnosis of RCC is necessary not only for prognosis but also for evaluation of therapeutic response. In the clinical practice, ipsilateral synchronous PRCC and CCRCC are often misdiagnosed as an isolated mass or a multiple lesion due to the intra-renal metastasis preoperatively. As a result, the patients may have a limited survival after the disease is finally confirmed postoperatively. Herein we reported a 72 years old male with a complex renal mass in our institution, and reviewed the clinicopathological features and therapeutic strategies of the literature, with a purpose to improve the accuracy of the pre-operative diagnosis.

Case Presentation

A 72 years old male was admitted to the inpatient because of left renal mass found by physical examination with no other complain. The patient had a long history of hypertension for 20 years. No family history associated was discovered. The initial impression on the ultrasound revealed a hypoechoic lobular mass with a volume of 7.8cm × 4.8cm × 2.8 cm in the middle to lower pole of the left renal. The subsequent computed tomography(CT) scan had shown a single endophytic mass of 7.5 cm in diameter, contrast enhancing(Fig. 1a). The physical examination found no vital signs. A diagnosis of angiomyolipoma (AML) was considered preoperative. The patient underwent laparoscopic left radical nephrectomy month later. Grossly, it revealed a two ipsilateral synchronous kidney mass (Fig. 1b). The first lesion(Tumor I) was in the middle pole of the left renal with a fibrous pseudocapsule surrounded,

measuring 5.0cm × 4.5 cm × 4.5 cm and protruding the kidney capsule with no invasion; the second lesion (Tumor II) was in the lower pole closed to the first lesion, measuring 3.0cm × 3.0cm × 2.5 cm with an isolated capsule grossly(Fig. 2a). Both cutting surfaces of the tumors occurred solid and yellow-brown color, focal hemorrhage and no necrosis were shown. Histopathological examination of tumor I revealed tubular and papillary architectures containing a central fibrovascular core (Fig. 2b). The two growth patterns were both lined by cuboidal and columnar cells. The cells lining the papillary structures contained abundant eosinophlic and amphophilic cytoplasm. The nuclear features were moderate to large irregular nuclei containing coarse chromatin and prominent nucleoli. And neither geographic necrosis nor psammoma bodies were showed. Tumor II revealed a typical CCRCC features, tubular and nest patterns floating in a plexiform vascular pattem(Fig. 2c). The tumor cells were polygonal in shape with clear or eosinophilic cytoplasm. A pseudopapillary growth pattern without a true fibrovascular core was happened in some areas of the tumor II. Focal fibrosis and inflammatory infiltration was seen, but no necrosis was occurred. None of vessel invasion or peripheral fat infiltration was exhibited in both tumors. The PRCC showed positive for CK7,P504s,Pax8,Vimentin, and scatterly for CD10, the proliferation rates of Ki67 was just 3%(Fig. 2d,f,h); While the CCRCC was positive for Pax8,CAIX, Vimentin, and diffusely for CD10, but negative for CK7 and P504s, the Ki67 proliferation rates was 5%(Fig. 2e,g,i).The final diagnosis was ipsilateral synchronous papillary cell carcinoma (WHO grade II-III) and clear cell renal cell carcinoma(WHO grade II-III) in the left kidney. The patient was discharged at the sixth day with no complication postoperatively. At the first nine month follow-up, the patient was free from the disease with no recurrence or metastasis.

Discussion And Conclusion

The RCC is the most common solid mass of the kidney and comprises 2 to 3% of all cancers in adults [1]. Over the past years, RCC had been divided into clear cell and non-clear cell subtypes, while the most common subtype of non-clear cell RCC was the PRCC. Even rare, combination of different subtypes had been reported [3]. The histology mainly focused on the PRCC and CCRCC, which might present a challenge for the accurate diagnosis. The incidence of the ipsilateral synchronous PRCC and CCRCC was about 4.8% by Richstone et al [4]. The rare conditions were only about 12 cases that had been reported in the literature ranged from 1990 to 2020 in China. Therefore the rarity of the disease may contribute to the misdiagnosis in clinical practice. As in our case, an initial diagnosis of AML was impressed.

The underlying etiology and histogenesis of ipsilateral synchronous PRCC and CCRCC are still unclear, which partly affect the cognition of the clinician. The best known possible etiological factors for RCC are smoking, obesity, and hypertension [5]. Smoking is implicated to be the key for the etiology of RCC, with an increasing risk of dose-dependent. Nonetheless, the relationship between obesity or hypertension and the disease are not yet firmly established. For our case, a history of hypertension for almost 20 years was mentioned. Interestingly, 7 cases of ipsilateral synchronous PRCC and CCRCC came from the same area were discovered by reviewing the literature in China. Further studies may be essential to consider whether the exposure to such a geogenic factor is a risk for the issue development.

Underwent ultrasound or abdominal CT could reveal the lesion preoperatively. Most CCRCC are hypervascular, the degree of enhancement performs a quickly decreasing in the phase of parenchyma, medullary and delayed, showing as “fast in and fast out”. In contrast, there is no predominent difference of the enhancement shown in the three phases of the PRCC by the CT scan, as the vessels of the fibrovascular core are thin and sparse in the papilla [6]. Unfortunately, there is still a risk of 3.5% missing the coexisting tumors [4]. High to 70% of multifocal lesions were missed on preoperative imaging due to the small size or the adjacent location in Chinese cases reviewed. There were

3 cases diagnosed as an isolated mass both by ultrasound and CT; 4 cases were diagnosed as a single mass by the ultrasound and a multiple lesions was found by the CT scan latterly; only 3 cases were diagnosed as a multiple-lesion mass by both imaging techniques initially (Table 1). Our case was also diagnosed as a single mass by the ultrasound and CT scan preoperatively. Missing the second mass was not only a radiological misdiagnosis, but also reflect lacking awareness of the imaging features of ipsilateral synchronous PRCC and CCRCC, and these may lead to a heavy effect on the treatment strategies latterly. As a result, Excessive dependence on radiological findings to obtain an accurate preoperative diagnosis of ipsilateral synchronous PRCC and CCRCC is undesirable.

Table 1
Ipsilateral synchronous PRCC and CCRCC reported in the Chinese literature

Case	Authors	Years	Age/Sex	Discovery path	Symptoms /signs	Location	Num.of mass (Ultrasound/ CT)	Treatment
1	Sheng HL et al.	2011	78/M	Lumbago	No	L	1/2	LRN
2	Zhang D et al.	2014	70/M	PE	No	L	-/-	NSS
3	Zhang D et al.	2014	63/M	PE	No	L	1/1	NSS
4	Zhu DF et al.	2016	47/M	PE	No	R	2/2	NNS
5	Wang JJ et al.	2018	52/M	abdominal discomfort	No	L	-/2	LRN
6	Chen JS et al.	2018	45/M	ESWL	No	L	-/-	LRN
7	Chen JS et al.	2018	64/F	PE	No	L	1/2	LRN
8	Chen JS et al.	2018	74/M	hematuria	Hematuria	L	1/2	LRN
9	Chen JS et al.	2018	70/M	PE	Microhematuria	L	2/2	NSS
10	Chen JS et al.	2018	63/M	PE	Microhematuria	L	1/1	NSS
11	Chen JS et al.	2018	47/M	PE	No	R	2/2	NSS
12	Chen JS et al.	2018	78/M	Lumbago	Microhematuria	L	1/2	LRN
13	Present case	2020	72/M	PE	No	L	1/1	LRN

M, male; F, female; PE, physical examination; ESWL, Extracorporeal shock wave lithotripsy; L, left; R, right; CT, computed tomography; PRCC, papillary renal cell carcinoma; CCRCC, clear renal cell carcinoma; LRN, Laparoscopic radical nephrectomy; NSS, nephron sparing surgery;"-", no data available.

Diagnosis and subclassification of RCC must be based primarily on pathology. The most two common subtypes PRCC and CCRCC generally show the typical architectural and cytological characters prominently. But our case was diagnosed as the AML initially, because of the similar gross features. A cutting surface of yellow-brown color could make a confusion with the AML, as the latter is well circumscribed and has pushing the borders, also contains soft yellow regions admixed with firm tan regions. Elsewhere, the majority of PRCC is bilateral and multifocal, as well as areas of hemorrhage and necrosis are commonly seen in PRCC, a confusion with others is not hard to comprehend.

While, on microscopic, PRCC may be confused with CCRCC when a solid growth with clear cytoplasm exhibited, and CCRCC with papillary pattern or esophilia cytoplasm occurs as a confusion with PRCC. In this condition, the classic morphology features of the two tumors provide a great help to distinguish them, such as whether a pseudopapillary pattern was exhibited or not. And because of the different immunoprofiles shown in PRCC and CCRCC, immunohistochemical staining may also offer an important clue to the diagnosis. PRCC is strongly positive for CK8/18, CK7and P504s, while CCRCC is positive for CD10, CAIX and Vim strongly.CK7 may be expressed in both tumors, but PRCC often shows diffuse cytoplasm positive with CK7, while no positivity is observed in CCRCC. The result of our own case was the same as the literature, a strong positive of CK7 in PRCC and negative for CCRCC (Fig. 2D, E).

Besides that, a differentiation might be necessary between PRCC and collecting duct carcinoma, when the latter had a papillary pattern. Nevertheless, the collecting duct carcinoma often exhibits as a high grade tumor with predominent desmoplastic stroma, and occur in the medulla. CK7 may be expressed in both tumors, but negativity for CEA, 34βE12 and some other biomarkers can help to exclude the PRCC. When thinking back to our initial gross diagnosis, if the epithelioid subtype of AML was exhibited, CCRCC might be misclassified as AML firstly. CCRCC is always positive for Vim, CD10 and CAIX, but negative for the biomarkers of AML, such as HMB45 and SMA. A careful attention to the morphology and immunohistochemistry may help to establish the correct diagnosis.

The aim of surgical management for patient with multifocal renal tumors is not only to prevent recurrence and metastasis, but also to minimize the number of surgical procedures and to prolong kidney function as long as possible. Both laparoscopic, robotic and partial nephrectomy for multiple lesions of the ipislateral renal tumors have been reported [7–9].Although laparoscopic radical nephrectomy has been the standard therapy for sporadic multifocal renal tumors, nephron sparing surgery (NSS) is now a good option for the mass with a diameter less than 3 cm. No matter which operation mode is selected, a right balance between oncologic control and renal functional preservation need to be considered. Even there had been a diagnosis of a single mass preoperatively, our patient still underwent the laparoscopic radical nephrectomy with a purpose to achieve a long survival time. And in the Chinese cases reviewed, 2 of the 3 cases diagnosed as a single mass underwent the NSS, and 3 cases diagnosed as a multiple-lesions mass with the considering of an intra-renal metastasis preoperatively, also underwent the NSS (Table 1). If a single mass or a multiple intra-renal metastasis lesion was confirmed, to preserve more renal function and improve the life quality of the patient, a NSS may performed. So in such condition, whether an adequate surgical range obtained, or whether a long life-time survival achieved, should be considered renew. Obviously, a precisely preoperative diagnosis is also the key to access a long survival time.

The prognosis of PRCC is more favorable than CCRCC, as the former behaves less aggressively than CCRCC. By now there was still not sufficient data concerning survival to compare the subtypes of RCC with multifocality in the same kidney. Capaccio et al. reported three cases with ipsilateral synchronous PRCC and CCRCC [10]. All of the patients underwent laparoscopic radical nephrectomy, and one died from the cancer after a 5 years long survival. In the present case, the patient was free from the disease with no recurrence or metastasis for nine month.

As the incidence of ipsilateral synchronous PRCC and CCRCC was quite low. A lack of awareness or experience may exist among most clinicians. If there is a multifocality mass in a single kidney, intra-renal metastasis will be considered initially, the possibility of the existing of ipsilateral synchronous PRCC and CCRCC may be ignored. But as the prognosis of PRCC and CCRCC are quite different, the therapy strategies may be performed differently, such as operation mode or adjuvant chemotherapy. So even they represent a low incidence rate, different histological subtypes of multiple ipsilateral synchronous RCC need to be classified as a special entity postoperatively, because of the different therapy strategies performed latterly.

In conclusion, we presented a case of ipsilateral synchronous PRCC and CCRCC. The diagnosis of ipsilateral synchronous PRCC and CCRCC can be achieved through the detail clinical history, imaging findings, pathological examination and immunohistochemical staining. As the different prognosis of the two tumors, careful clinical decision and appropriate surgical management are required to manage the disease. The above descriptions are expected to understand the disease, to help clinicians, and to improve the diagnostic work in future. If optimally applied, these tactics can be related with a long life expectation and a long term preservation of renal function for most patients with ipsilateral synchronous PRCC and CCRCC.

Abbreviations

CCRCC: clear cell renal cell carcinoma; CT: computed tomography; EWL: Extracorporeal Shock Wave Lithotripsy; AML: angiomyolipoma; LRN: laparoscopic radical nephrectomy; NSS: nephron sparing surgery; PRCC: papillary renal cell carcinoma; RCC: renal cell carcinoma; RRN: robotic radical nephrectomy; WHO: World Health Organization; CK7: cytokeratin 7; CAIX: carbonic antydrase IX; CK8/18: cytokeratin8/18; CEA: carcinoma embryo antigen; 34βE12: cytokeratin Multi; SMA: smooth muscle actin.

Declarations

Informed consent statement

Informed consent was obtained from the patient.

Written informed consent

Patient has provided informed consent for publication of the case.

Conflict-of-interest statement

The authors declare that there is no conflict of interest related to this report

Ethics approval and consent to participate

Written informed consent was obtained from all participants. Ethical approval was obtained from the Ethics Committee of Tianjin Fifth Central Hospital, China, in accordance with the ethical guidelines of the 1975 Declaration of Helsinki. Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor in-Chief of this journal.

Consent for publication

Written informed consent for publication was obtained from all participants.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Jing Yin was involved in acquisition of data and drafting and completing the manuscript. Mo Zheng was involved in the review of literature. Baojiang Li participated in the critical review of the paper. All authors gave final approval for publication. All authors jointly take full responsibility for the work as a whole, including the study design, access to data, and the decision to submit and publish the manuscript.

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Figures

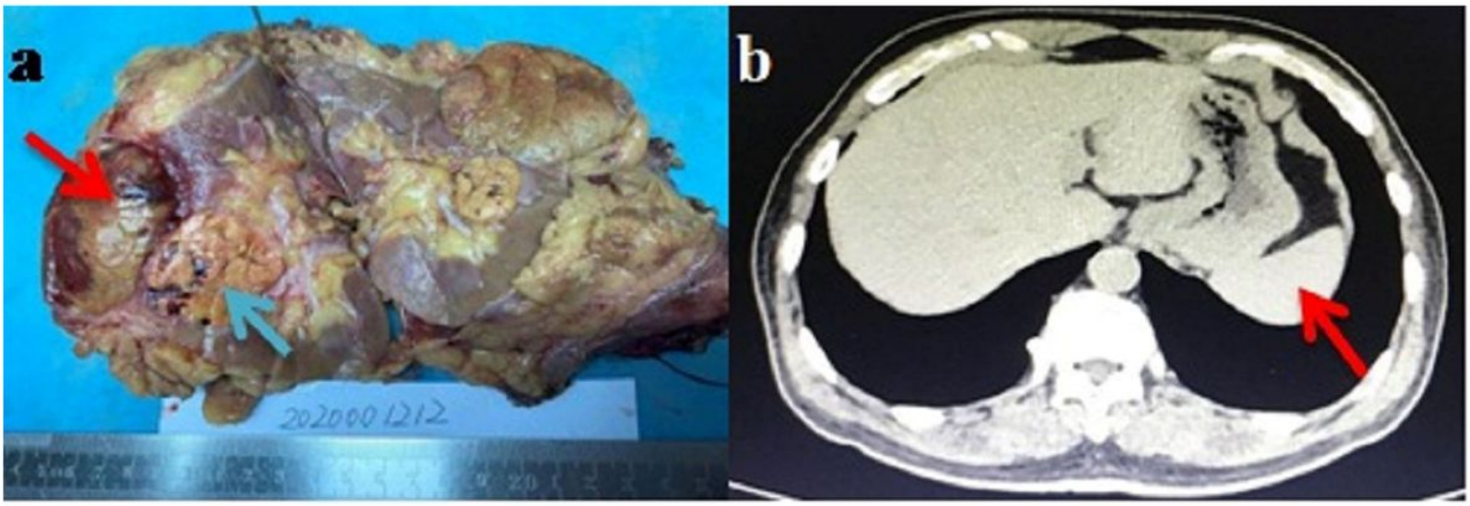

Figure 1

Macroscopic features and Conventional CT findings. a) the gross surface showed two lesions in the middle-lower pole of the kidney, PRCC(blue arrow) and CCRCC(red arrow). b) Conventional CT demonstrated a single endophytic mass in the lower pole of the kidney, contrast enhancing (red arrow).

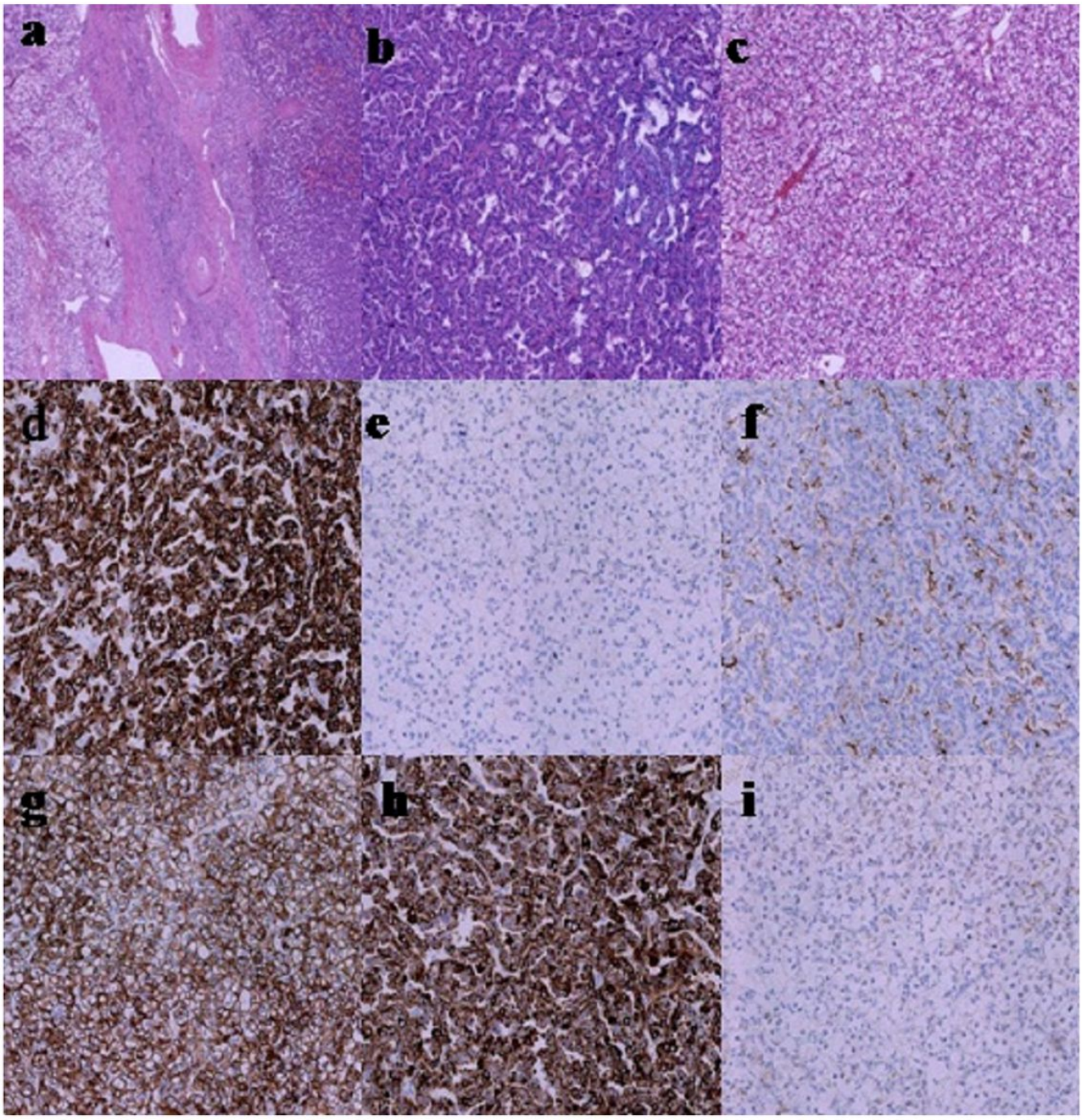

Figure 2

Histopathology findings. a) Hematoxylin-eosin staining showed the clear bordance between CCRCC(left) and PRCC(right)(200X). b) hematoxylin and eosin (H&E) staining of PRCC (200X). c) hematoxylin and eosin (H&E) staining of CCRCC (200X). d)-f) Immunohistochemistry staining showed the CK7 was positive for PRCC(200X) and negative for CCRCC(200X). f)-g) Immunohistochemistry staining showed the CD10 was positive for PRCC(200X) scattered and positive for CCRCC diffuse y(200X). h)-i) Immunohistochemistry staining showed the P504s was positive for PRCC(200X) and negative for CCRCC(200X).

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