Diagnostic Pathology

CASE REPORT

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Keratin 20 positive SDH-deficient renal cell carcinoma: a case report and literature review

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Abstract

This study aims to broaden the morphological scope of *SDH*-deficient renal cell carcinoma and to assist clinicians and pathologists in better understanding this entity to prevent misdiagnosis. This study used immunohistochemistry staining and the first-generation sequencing Sanger method for gene detection. It retrospectively analysed the clinical pathology, molecular characteristics, biological behaviour, and treatment information of one case of *SDH*-deficient renal cell carcinoma. The patient was a 57-year-old female with right back pain for more than 20 days and had no personal or family history of kidney tumours. In addition, the tumour cells had clear boundaries in morphology, and residual normal renal tubules could be seen around them. There were also ossification and adipose tissue around the tumour centre. The tumour cells were arranged in a glandular tubular and cord-like manner. Vacuolar and eosinophilic inclusion bodies could be observed in the cytoplasm. The nucleus was regular, the chromatin distribution was fine, and there were no obvious nucleoli. They were low-grade nuclei. In addition, no atypical mitosis or necrosis could been found. Furthermore, immunohistochemistry staining showed *SDHB*-negative and keratin 20 -positive tumour. Meanwhile, the first-generation sequencing also pointed out the presence of *SDHB* gene mutations in the tumour. After 12 months of follow-up, there was no evidence of disease recurrence in the patient. *SDH*-deficient renal cell carcinoma is a rare tumour associated with *SDH* gene germline mutations, and suspected cases should undergo *SDHB* immunohistochemistry staining. Most *SDH*-deficient renal cell carcinomas have a good prognosis, but undifferentiated cases require long-term follow-up.

Keywords *SDH*-deficient renal cell carcinoma, Keratin 20 positive, Differential diagnosis

Introduction

Succinate dehydrogenase (*SDH*) is an enzyme complex composed of four subunits (*SDHA*, *SDHB*, *SDHC*, and *SDHD*). In addition, *SDH* plays an important role in converting of succinate to succinate and in the mitochondrial electron transport chain. *SDH* is also essential for cellular energy metabolism. Whereas *SDH*-deficient renal cell carcinoma (*SDH*-deficient RCC) was first discovered in 2004 [1]. Then, it was included in the Vancouver classification of the International Society of Urological Pathology (ISUP) in 2013 [2] and was accepted by the World Health Organization as a morphologically unique subtype of RCC in 2016 [3, 4]. This type of renal cell carcinoma is rare, accounting for approximately 0.05% to 0.20% of all renal cell cancers [5]. At present, there are few reports on its clinical pathology and molecular characteristics. To improve our understanding of this type of

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renal cell carcinoma, we introduced a keratin 20-positive *SDH*-deficient RCC case and reviewed relevant literature.

Case presentation

Clinical information

A 57-year-old woman presented the right back pain 20 days ago without obvious cause, which aggravated after activity. For further treatment, she went to the outpatient department of our hospital few days later. The specialist examination revealed percussion pain in the right renal area. The patient was recently diagnosed with hypertension for 3 months. She denied other chronic medical histories and infectious diseases, underwent laparoscopic cholecystectomy was performed 15 years prior to presentation due to gallstones. She also denied other major trauma and surgery histories as well as any family history of hereditary diseases.

Imaging features

Enhanced computed tomography (CT) examination of the upper abdomen showed that a round-like abnormal enhancement was seen in the right kidney with a clear boundary, of about 3.5 cm. The uneven enhancement was also presented in the arterial phase, with patchy hypo-dense shadows and small flake fat density shadows (Fig. 1A). While the enhancement degree decreased in the venous phase and delayed phase (Fig. 1B-C). No enlarged lymph nodes were found in the periphery. To further confirm the diagnosis, the upper abdominal magnetic resonance imaging (MRI) plain scan was also performed and found a circular long T1 and T2 signal in the right kidney. The DWI signal was high, with a diameter of about 3.5 cm. The internal signal was uneven, with a slight fat signal (Fig. 1D-E). According to the preoperative imaging examination results, the patient was considered to have a tumour in the right kidney. Then, a right laparoscopic partial nephrectomy was operated. The postoperative CT plain scan of the upper abdominal showed the postoperative changes in the right kidney after mass resection, with a local absence of the right kidney. A dense strip-like shadow was visible in the surgical area, with mild exudation around the right kidney (Fig. 1F). There was no tumour recurrence after 12 months of tumour resection.

Diagnostic histological features

Resected tumour specimen was fixed in 10% neutral buffer formalin and immunohistochemistry staining was performed according to standard protocols. Paraffin-Embedded blocks were cut into 5 μm thick sections, and stained with hematoxylin and eosin, as well as various antibodies. The clones, working dilutions and commercial sources of those antibodies were listed in Table 1.

In gross examination, a piece of tissue was incised with a size of 4.5×3.0×2.8 cm. A mass of 4.5×3.0×2.3 cm was seen at 0.4 cm from the cut margin. The cut surface was greyish yellow, and the lesion area was dark red with an external capsule. A grey-white area could be seen in the centre of the mass, with calcification in the lesion area, ranging from approximately 0.5×0.4 cm.

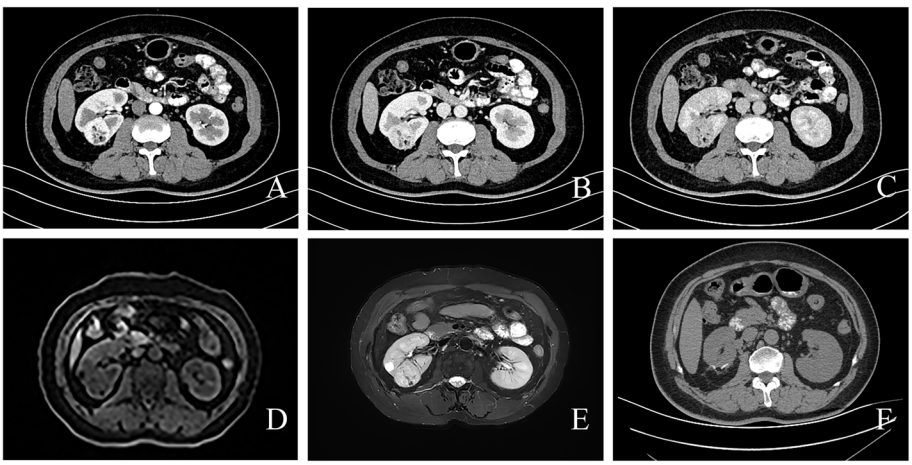

Fig. 1 CT and MRI scans showed a tumour in the right kidney. **A** Enhanced CT examination of the upper abdomen showed that a round-like anomaly enhancement may be seen in the right kidney, the boundaries were still clear, about 3.5 cm, and the arterial phase of the enhanced scanning was unevenly enhanced, with patchy hypo dense shadows and small flake fat density shadows in it. **B-C** The degree of enhancement in the venous phase and delayed phase was reduced. **D-E** Upper abdominal MRI plain scan found a circular long T1 and T2 signal on the right kidney, and a diameter of about 3.5 cm. The internal signal was uneven and there was a slight fat signal. **F** Postoperative upper abdominal CT plain scan showed postoperative changes in the right kidney after mass resection, with a local absence of the right kidney. A dense strip-like shadow was observed in the surgical area, with slight exudation around the right kidney

Table 1 Antibodies used in this case

Antibodies	Clone	Dilution	Source	Location	Result
SDHB	Mouse mAb	-	Maixin Bio	C	Negative
SDHA	Mouse mAb	1:200	Abcam	C	Positive
keratin 7	Mouse mAb	-	ZSGB-BIO	C	Negative
keratin 20	Mouse mAb	-	ZSGB-BIO	C	Positive
CD10	Mouse mAb	-	Maixin Bio	C/M	Negative
CD117	Rabbit mAb	-	Maixin Bio	M/C	Mast Cell Positive
CA9	Rabbit pAb	-	Maixin Bio	M	Negative
Ki-67	Mouse mAb	1:150	ZSGB-BIO	Cell	3%

Abbreviations: *C* Cytoplasm, *M* Membrane

Histologically, low magnification showed that the tumour cells had clear boundaries, with fibrous capsule-like tissue on the outside and residual normal renal tubules around (Fig. 2A). Ossification and adipose tissue were presented in the centre of the tumour, with haemorrhage in some areas (Fig. 2B). The tumour cells were arranged in a glandular tubular and cord-like pattern, with vitreous stroma, benign tubules invasion, and scattered mast cells (Fig. 2C-D). Under the high-power microscope, tumour cells were cubic or elliptical, flocculent cytoplasm, vacuolar or eosinophilic cytoplasm, eosinophilic inclusion bodies, regular nuclei, fine chromatin, and indistinct nucleoli (Fig. 2E-F).

Immunohistochemistry results

IHC showed diffuse cytoplasmic positivity of SDHA (Fig. 3A). Tumour cells showed negative expression of SDHB (Fig. 3B), keratin 7 (Fig. 3C), CD10 (Fig. 3D), and carbonic anhydrase 9 (CA9). Mast cells scattered throughout the tumour expressed CD117 (Fig. 3E), while tumour cells diffusely expressed keratin 20 (Fig. 3F). The Ki-67 positive marker index for tumour cell proliferation was 3% (Table 1).

Molecular detection results

The first-generation sequencing Sanger method was used for gene testing, and the results showed two mutations. Heterozygous mutation in exon 3 of *SDHB*: C.201-36G > T. Heterozygous mutation occurred in exon 8 of *SDHB*: C.725G > A (Fig. 4). Based on these morphological features, as well as immunohistochemistry and genetic testing results, *SDHB*-deficient renal cell carcinoma was diagnosed pathologically.

Discussion

Succinate dehydrogenase (*SDH*), also known as mitochondrial complex 2, is a key enzyme that oxidizes succinate to fumaric acid in the tricarboxylic acid cycle. It consists of *SDHA*, *SDHB*, *SDHC*, and *SDHD* protein subunits. It also participates in the tricarboxylic acid cycle, mitochondrial electron transfer chain, as well as electron transfer in the respiratory chain [6]. The absence of any subunit of *SDH* may lead to the instability of these complexes, resulting in complete loss of enzyme function, accumulation of succinic acid in cells and induction of tumour development. In addition, mutations or abnormal expression of *SDH*-related genes are associated with

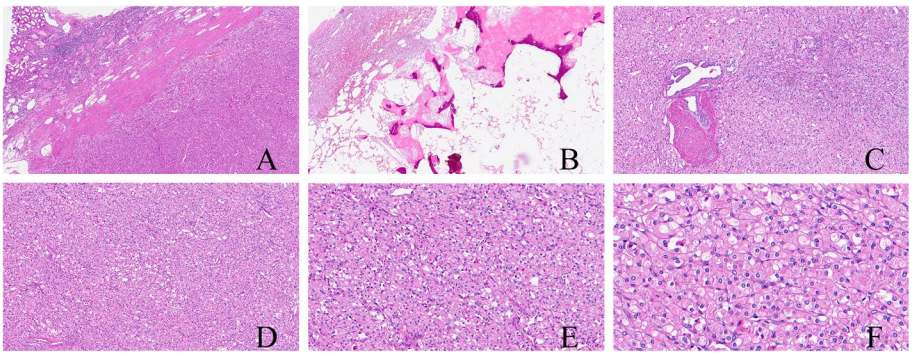

Fig. 2 Microphotographs showing the histopathological features of the tumour. **A** The tumour cells had clear boundaries, with fibrous capsule-like tissue on the outside, and residual normal renal tubules could be seen around them (H&E; × 40). **B** There was ossification and adipose tissue in the centre of the tumour, and some areas were bleeding (H&E; × 40). **C** The tumour cells were arranged in a glandular tubular and cord-like pattern, with glassy stroma and benign tubule invading (H&E; × 100). **D** The tumour cells were arranged in a glandular tubular and cord-like pattern, with many scattered mast cells visible within the tumour (H&E; × 100). **E** Tumour cells appeared cubic or oval in shape, with flocculent cytoplasm and vacuolar or eosinophilic cytoplasm (H&E; × 200). **F** Eosinophilic inclusion bodies could be seen, with regular nuclei, delicate chromatin, and indistinct nucleoli (H&E; × 400)

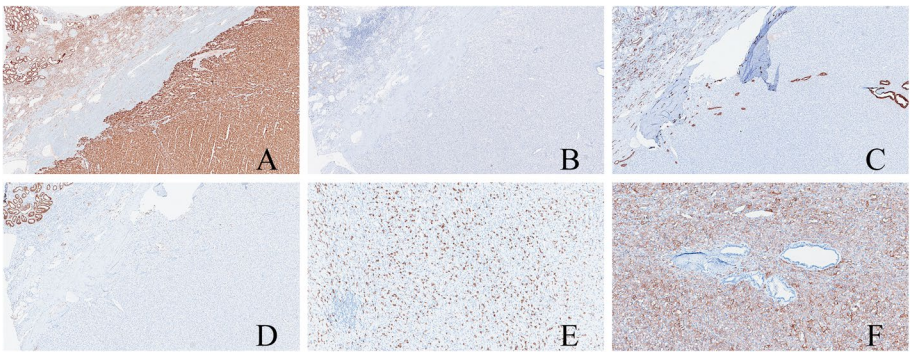

Fig. 3 Immunohistochemically analysis of the tumour. **A** IHC showed diffuse cytoplasmic positivity of tumour cells towards SDHA (original magnification × 40). **B** Tumour cells showed negative expression for SDHB in the IHC image (original magnification × 40). **C** IHC image showing cells were negative for keratin 7 (original magnification × 40). **D** IHC image showing cells were negative for CD10 (original magnification × 40). **E** Mast cells scattered throughout the tumour expressed CD117 in the IHC image (original magnification × 100). **F** IHC of keratin 20 showing diffuse cytoplasm positivity (original magnification × 100)

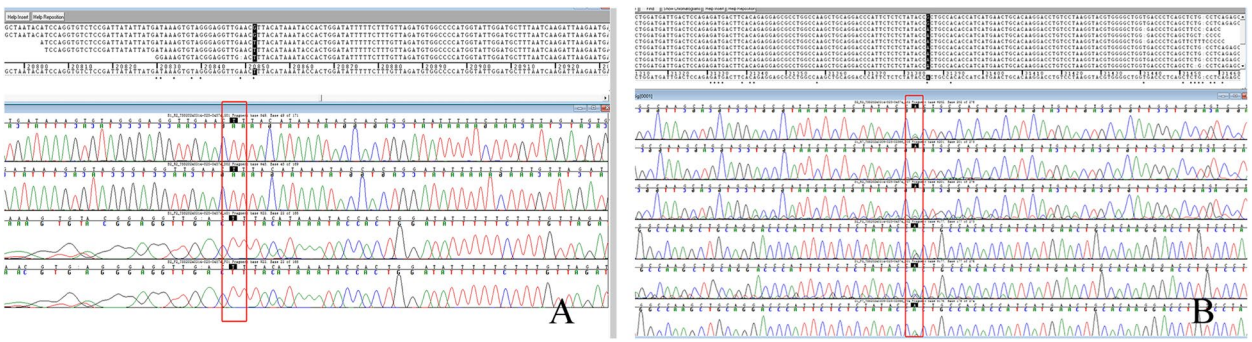

Fig. 4 Sanger sequencing test results. **A** Heterozygous mutation in exon 3 of *SDHB*: C.201-36G > T. **B** Heterozygous mutation in exon 8 of *SDHB*: C.725G > A

a variety of diseases, including pheochromocytoma/ paraganglioma, gastrointestinal stromal tumours, renal cell carcinoma, and pituitary adenoma.

SDH-deficient renal cell carcinoma (RCC) is a rare subtype of RCC, accounting for approximately 0.05%-0.20% of all RCCs [5], and was recently recognized as a unique subtype in the 2016 World Health Organization classification [3, 4]. The RCC with *SDH* deficiency is mainly seen in young people, with an average age of 37 (patients 14 to 76 years old), with males predominating, with a male-to-female ratio of 1.7:1 [6, 7]. Tumours are highly correlated with genetics. Patients often have germline mutations in *SDH*-related genes, mainly *SDHB* mutations, followed by *SDHC*, *SDHA*, and *SDHD*, which are rare and cause mitochondrial complex 2 dysfunctions, leading to tumour development. It is estimated that the lifetime risk of developing kidney tumours in patients with *SDHB* gene mutations is 14% [7]. Clinically, most *SDH*-deficient renal cell carcinoma presents as small organ-localized tumours occasionally found on imaging, or as lower back pain or accidental findings. In rare cases, tumours may manifest as metastatic diseases. At long-term follow-up, approximately 30% of patients presented with multifocal or bilateral renal tumours, 15% had a personal history of gastrointestinal stromal tumours (GIST), 15% had a personal history of paragangliomas (PGL), 22% had a family history of RCC, 26% had a family history of PGL positivity, and 4% had a family history of GIST positivity [6, 7]. Our patient was a 57-year-old woman with a right renal mass due to back pain. No personal or family history of renal cell carcinoma, GIST, pheochromocytoma, or PGL exists. The clinical presentation of this patient differs from previous reports, which may expand the clinical spectrum of the disease.

Pathologically, the tumour is 0.7 to 20.0 cm in size, with an average of 5.1 cm [8]. The tumour is well-defined and can be surrounded by a pseudo capsule. Its cross-section is brownish or reddish brown. Haemorrhage or partial cystic changes can also be seen, usually without necrosis. Microscopically, *SDH*-deficient RCC has clear boundaries, but it is often seen that glomeruli and renal tubules are located at the "edge" (i.e. outside) of the tumour, but interestingly, they are sometimes located within the tumour. Tumours are

arranged in solid patchy or glandular tubular shapes, with tumour cells appearing round or oval in shape, round nuclei, evenly distributed chromatin, and blurry nucleoli. The most typical features are eosinophilic, vacuolar, or flocculent inclusion bodies in the cytoplasm of tumours. In most cases, *SDH*-deficient RCC is a low-grade tumour, but high-grade nucleoli, sarcomatous changes, or coagulation necrosis may also be present. In addition, mast cell infiltration might be seen in the tumour stroma. The morphologic appearance of our patients essentially maintained the described typical appearance caused by *SDH*-deficient RCC.

When any component of mitochondrial complex 2 undergoes genetic inactivation, the entire complex becomes unstable, leading to the degradation of *SDHB* subunits. Therefore, the absence of *SDHB* immunohistochemistry staining is necessary for diagnosing *SDH*-deficient RCC. In RCC with *SDHB*, *SDHC*, and *SDHD* deficiency, tumour cells show *SDHB*-negative while *SDHA*-positive. In contrast, tumour cells in *SDHA*-deficient RCC are negative for both *SDHA* and *SDHB* [9], and the immunohistochemical interpretation of *SDHB* expression requires comparison with surrounding normal renal tissue. *SDH*-deficient RCC typically exhibits immune reactivity to PAX-8, EMA, and Ksp-cadherin, but is negative for keratin 7, keratin 20, AE1/AE3, CD117, RCC antigens, P63, CA9 and vimentin. Neuroendocrine and epithelial markers are also generally negative, but CD117 may highlight mast cells in tumours. Under electron microscopy, in *SDH*-deficient RCC, the cytoplasm of tumour cells contains abundant mitochondria, and the cytoplasmic inclusion bodies correspond to mitochondria with degenerated or compressed cristae and matrix abnormalities [10] Molecular genetics indicates that *SDH*-deficient RCC has strong heritability and a germline mutation in one of the *SDH*-related genes. Among them, *SDHB* mutations are the most common, followed by *SDHC* and *SDHD*. Ricketts et al. [11] studied 14 cases of *SDHB*-deficient renal cell carcinoma and found that 8 exons of the *SDHB* gene could be mutated. Our patient had heterozygous mutations in exons 3 and 8 of *SDHB*, C.201–36 G > T; C.725 G > A. All of the above mutations can affect the expression of proteins, which is consistent with the *SDHB*-negative result detected by immunohistochemistry. There had been many reports of mutations in the third exon of *SDHB*, while in the cases reported by Zhu Q et al. [6], there were gene mutations at the same site as our cases: C.725 G > A (guanine > adenine), resulting in changes in amino acids R242H (arginine > histidine), which had been reported as a pathogenic mutation [12]. In addition, our patient showed a positive expression for keratin 20. We reviewed previous cases (Table 2) [6, 13–25] and literature [7] and found that 5 patients underwent keratin 20 staining [7, 14, 15, 23], and we were the first reported case of *SDHB*-deficient RCC expressing keratin 20.

The differential diagnosis of *SDH*-deficient RCC is mainly other renal tumours with eosinophilic morphology, such as oncocytoma, chromophobe renal cell carcinoma, clear cell renal cell carcinoma, eosinophilic solid cystic renal cell carcinoma, etc. Oncocytoma exhibits characteristic island-like structures, central scar, round or oval nucleus, and relatively mild nuclear atypia. Immunohistochemistry mostly expresses CD117, while keratin 7 is scattered or focal stained. Most *SDH*-deficient RCCs usually show negative results for CD117 and keratin 7. In addition, one of the diagnostic features of *SDH*-deficient RCC is the presence of eosinophilic, vacuolar, or flocculent inclusion bodies in the cytoplasm. Whereas, eosinophilic cells are usually absent in oncocytoma. Chromophobe cells of the eosinophilic subtype RCC are also a factor to consider in differential diagnosis. The tumour cell membrane is clear, the nucleus is wrinkled like a raisin, and paranuclear halos are often visible. Immunohistochemistry expressions of keratin 7, CD117, and *SDHB* are associated with the absence of intracytoplasmic inclusion bodies, which helps to distinguish this entity from *SDH*-deficient RCC. When eosinophilic cytoplasm appears in clear cell RCC, it is mostly a high-grade nucleus, and the classic clear cell region may exist elsewhere. Immunohistochemistry shows positive results for *SDHB*, CA9, vimentin, and CD10, all of which are different from *SDH*-deficient RCC. Eosinophilic solid cystic renal cell carcinoma (ESC RCC) is a tumour with or without nodular sclerosis. The tumour is mainly composed of eosinophils, forming solid and cystic structures. Tumours also have abundant eosinophilic cytoplasm, and in some cases, eosinophilic glomeruli and vacuoles can be seen in the cytoplasm. The characteristic immunohistochemistry in ESC RCC is keratin 20 positivity (patchy or diffuse), keratin 7 deficiency or weak positivity, and CD117 is usually negative [26]. And the RCC with TFEB amplification can also be positive for keratin 20 [27]. However, in this case, *SDHB*-deficient RCC also expressed keratin 20. Therefore, keratin 20 positivity cannot distinguish these three types of tumours, and gene abnormalities need to be detected through immunohistochemically expression and sequencing of *SDHB* and *SDHA*. Attention should also be paid to distinguishing *SDH*-deficient RCC from RCC/*FH*-deficient RCC associated with hereditary leiomyomatosis and RCC syndrome. A few *FH*-deficient RCCs have also been reported to exhibit low-grade eosinophilic morphology [28]. Tumours have flocculent and vacuolated eosinophilic cytoplasm, which is very similar to *SDH*-deficient RCC. However, immunohistochemistry shows *FH* deficiency, of 2-succinylcysteine (2-SC) overexpression and *SDHB* retention, all different from *SDH*-deficient RCC.

There are no evidence-based medical guidelines for the treatment of *SDH*-deficient renal cell carcinoma.

Table 2 The clinical and pathological characteristics of SDH-deficient RCC were reported in the past five years

Author/Year	Number of cases	Age(years) /Sex	Size (cm)	IHC	Gene detection for SDH	Treatment/recurrence/metastasis	FU(months)
Gupta S（2019）[13]	3	28/M	Bilateral; Right: 9, Left: 2.5	SDHA (+), SDHB (-)	NA	Partial/radical nephrectomy	NED（37）
		34/M	10.7	SDHA (+), SDHB (-)	NA		NED（20）
		65/F	3	SDHA (+), SDHB (-)	NA		DOOD（1）
Ugarte-Camara M (2019) [14]	1	29/M	8.5 × 7.5 × 5.5	EMA (+), keratin 7 (-), keratin 20 (-), Vimentin (-), CD10 (-), SDHB (-)	SDHB (C.166_170del p.Pro56Tyrfs*5) in exon 2	Radical right nephrectomy	NED (84)
Xiao Q (2019) [15]	2	32/M	7 × 6 × 6	SDHA (+), SDHB (-), PAX-8 (+), CA9 (-), CD10 (-), keratin 7 (-), keratin 20 (-), CD10 (-), TFE-3 (-), CD56 (-), CgA (-), Syn (-).	SDHB NM_OO30002：C.268C>T R[CGA]>*[TGA];NP_002991.2：P.Arg90Ter R (Arg) >* (Ter) in exon 3	Radical resection of renal cell carcinoma	NED (15)
		60/M	4 × 3.5 × 3.5		SDHB NM_OO30002：C.785_786insG;NP_002991.2：p.I1e263fs in exon 8	Radical resection of renal cell carcinoma	NED (10)
Zhu Q (2020)[6]	2	58/F	2.5 × 2.0 × 2.0	PAX-8 (+), EMA (+), P504S (+), Vimentin (-), keratin 7 (-), CA9 (-), SDHB (-), HMB45 (-), TFE-3 (-).	SDHB（C.725G > Ap.R242H）	Left nephrectomy	NA
		47/M	5.8×4.3×3.2	PAX-8 (+), P504S (+), keratin 7 (-), SDHB (-), HMB4 5(-), TFE-3 (-).	NA	Left nephrectomy	NA
Kumar RA（2021）[16]	1	37/F	4.0×3.5×2.0	PAX-8 (+), SDHB (-).	NA	Robot assisted partial nephrectomy	NED(6)
Milionis V (2021) [17]	1	40/F	5.0	PAX-8 (+), EMA (+), SDHB (-), CD10 (-), keratin 7 (-), CgA (-), SDHA (+), CD117 (mast cells +).	Heterozygous variation NM_003000.3：C.412G>T，p.（Asp138Tyr） in SDHB	Laparoscopic partial nephrectomy	NED (12)
Fuchs TL（2022）[18]	59	19-80，M：F = 1.6：1	NA	SDHB (-), SDHA (+).	(18/59) Germline mutations in the SDH gene	(9/59) Metastatic disease occurred	(3/59)DOD
Yamaguchi Y（2022）[19]	1	50/M	1.5	SDHB (-), CgA (-), Syn (-).	Germline mutations in the SDHB gene	Right nephrectomy, 17 months later, lymph node metastasis of paraganglioma occurred. Afterwards, sunitinib started anti-angiogenic treatment	NA
Higashi S（2022）[20]	1	75/F	3.8×2.8 and 1.2×1.1	SDHB (-), SDHA (+)	SDHB NM_003000.3：C.642 G > C） in exon 6	Robot assisted partial nephrectomy	NED（15）
Wang XT（2022）[21]	11	24-62，7M and 4F	NA	SDHA (+), (8/11) SDHB (-), (3/11) SDHB (focal or patchy weak +), PAX-8 (+), FH (+), keratin 7 (-), CA9 (-).	(7/11) Mutations in the SDHB gene (4 cases of missense mutations, 1 case of frameshift mutation, 1 case of splicing mutation, and 1 case of termination codon mutation); (4/11) NA	(8/11) Radical nephrectomy, (3/11) Simple nephrectomy	5 patients NED（28-116）；5 patients NA

Table 2 (continued)

Author/Year	Number of cases	Age(years) /Sex	Size (cm)	IHC	Gene detection for SDH	Treatment/recurrence/ metastasis	FU(months)
Kodare D（2023） [22]	1	37/F	15.0×13.6×13.0	PAX-8 (+), keratin 7 (-), SDHB (-), CD117 (mast cells +).	NA	Right radical nephrectomy	NA
Liu W(2023) [23]	1	50/M	4.1	PAX-8 (+), TFE-3 (+), SDHB (-), keratin 7 (-), keratin 20 (-), RCC (-), CA9 (-), CD10 (-).	NA	Surgical resection	NED（7）
Sun X（2023 [24]	1	28/M	20.5×19.5×9.5	SDHB (-)	NA	Preoperative renal artery embolization followed by open radical nephrectomy	NED（10）
Pulford C (2023) [25]	1	19/M	3.5 and 3.4	SDHB (-), CA9 (-), keratin 7 (-), FH (+).	SDHB germline mutation positive	Robot assisted partial nephrectomy	NA
Dong SS*	1	57/F	4.5×3.0×2.3	SDHA (+), keratin 20 (+), SDHB (-), keratin 7 (-), CD10 (-), CA9 (-), CD117 (mast cells +).	SDHB(C.201-36G>T; C.725G>A)	Right laparoscopic partial nephrectomy	NED (12)

Abbreviations: FU follow-up, *F* female, *M* male, *NA* not available, *DOD* dead of disease, *DOOD* dead of other disease, *NED* no evidence of disease

* Present case

Surgical resection is still the preferred treatment method. If the tumour is early or small, partial nephrectomy or tumour ablation is usually chosen to preserve the kidney. For advanced renal cell carcinoma, FDG-PET examination is recommended to determine the current growth status of the tumour. For metastatic diseases, molecular targeted therapy with vascular endothelial growth factor (VEGF), mammalian target of rapamycin (mTOR), and tyrosine kinase (TK) has been previously administered [8, 29]. It is suggested that molecular analysis of *SDHB* may not be necessary if the patient is over 40–45 years old and has no family history of renal tumours. However, for patients under the age of 45, even if there is no family history, the possible diagnosis of *SDH*-deficient RCC should be considered [30]. Through this case, we find that for patients with kidney tumours, it is necessary to inquire about the disease condition and family history of the tumour in detail. Regardless of the patient's age, *SDHB* immunohistochemically staining and genetic testing are necessary for diagnosis and can guide clinical treatment decisions.

Most *SDH*-deficient RCCs are low-grade tumours with good prognosis. Long-term follow-up shows that the metastasis rate is about 11% [31], which can be cured by complete resection alone. However, coagulation necrosis, high-grade nuclei, and sarcomatous changes have been reported in some tumours, and they have more positive progression and higher metastasis rates (possibly up to 70%) [5], requiring curative treatment. Metastasis in the lungs, liver, bones, brain, and lymph nodes has been reported [30]. Therefore, it is necessary to conduct long-term follow-up and monitoring of *SDH*-deficient tumours.

In conclusion, *SDH*-deficient RCC is a rare tumour associated with *SDH* gene germline mutations, with unique clinical and pathological features. For renal eosinophilic tumours with inclusion bodies in the cytoplasm, pathologists should consider the possibility of *SDH*-deficient RCC. Even if there is no inclusion body or inclusion body is not obvious, *SDHB* immunohistochemistry staining should be performed on suspected cases. After diagnosis, patients and immediate family members should monitor other *SDH*-deficient tumours, including pheochromocytoma, paraganglioma, and GIST. Most *SDH*-deficient RCCs have a good prognosis, but for undifferentiated cases, the prognosis is poor and requires long-term follow-up. For tumours without adverse pathological features, separate resection may be a reasonable choice. With the improvement of physician awareness, patients can receive correct diagnosis and timely treatment. Therefore, pathologists and clinicians should hold a highly sceptical attitude towards this eosinophilic renal tumour.

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This article constitutes first presentation to this case report.

Informed consent
Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Registry and the registration no. of the study/trial
N/A.

Animal studies
N/A.

Author's contributions
D.S.S, W.Z.Y and X.Q wrote the main manuscript text and T.X.C, W.C.M, X.Q, X.C, Y.W and G.X.W prepared Figs. 1, 2, 3, and 4. All authors reviewed the manuscript.

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Availability of data and materials
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The images did not contain the patient records and information. This study obtained ethical approval and participation consent by the Clinical Research Ethics board of the Northern Jiangsu People's Hospital Affiliated to Yangzhou University.

Competing interests
The authors declare no competing interests.

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References

1. Vanharanta S, Buchta M, McWhinney SR, et al. Early-onset renal cell carcinoma as a novel extraparaganglial component of SDHB-associated heritable paraganglioma. Am J Hum Genet. 2004;74:153–9. https://doi.org/10.1086/381054.
2. Srigley JR, Delahunt B, Eble JN, et al. The International Society of Urological Pathology (ISUP) Vancouver classification of renal neoplasia. Am J Surg Pathol. 2013;37(10):1469–89. https://doi.org/10.1097/PAS.0b013e318299f2d1.
3. Gill AJ, Amin MB, Smith SC, Trpkov K. Succinate dehydrogenase-deficient renal cell carcinoma. In: Holger M, Humphrey PA, Ulbright TM, Reuter VE, editors. WHO Classification of Tumors of the Urinary System and Male Genital Organs. 4th ed. Lyon, France: International Agency for Research on Cancer; 2016. p. 35–6.
4. Williamson SR, Eble JN, Amin MB, et al. Succinate dehydrogenase-deficient renal cell carcinoma: detailed characterization of 11 tumors defining a unique subtype of renal cell carcinoma. Mod Pathol. 2015;28(1):80–94. https://doi.org/10.1038/modpathol.2014.86.
5. Gill AJ, Hes O, Papathomas T, et al. Succinate dehydrogenase (SDH)-deficient renal carcinoma: a morphologically distinct entity: a clinicopathologic series of 36 tumors from 27 patients. Am J Surg Pathol. 2014;38(12):1588–602. https://doi.org/10.1097/PAS.0000000000000292.
6. Zhu Q, Wu X, Huang Y, Tang M, Wu L. Clinicopathologic features of succinate dehydrogenase deficiencient renal cell carcinoma. Int J Clin Exp Pathol. 2020;13(6):1403–7.

7. Kumar R, Bonert M, Naqvi A, Zbuk K, Kapoor A. SDH-deficient renal cell carcinoma - clinical, pathologic and genetic correlates: a case report. BMC Urol. 2018;18(1):109. https://doi.org/10.1186/s12894-018-0422-8.
8. Wang G, Rao P. Succinate Dehydrogenase-Deficient Renal Cell Carcinoma: A Short Review. Arch Pathol Lab Med. 2018;142(10):1284–8. https://doi.org/10.5858/arpa.2017-0199-RS.
9. Yakirevich E, Ali SM, Mega A, et al. A Novel SDHA-deficient Renal Cell Carcinoma Revealed by Comprehensive Genomic Profiling. Am J Surg Pathol. 2015;39(6):858–63. https://doi.org/10.1097/PAS.0000000000000403.
10. Housley SL, Lindsay RS, Young B, et al. Renal carcinoma with giant mitochondria associated with germ-line mutation and somatic loss of the succinate dehydrogenase B gene. Histopathology. 2010;56(3):405–8. https://doi.org/10.1111/j.1365-2559.2010.03482.x.
11. Ricketts CJ, Shuch B, Vocke CD, et al. Succinate dehydrogenase kidney cancer: an aggressive example of the Warburg effect in cancer. J Urol. 2012;188(6):2063–71. https://doi.org/10.1016/j.juro.2012.08.030.
12. Neumann HP, Bausch B, McWhinney SR, et al. Germ-line mutations in nonsyndromic pheochromocytoma. N Engl J Med. 2002;346(19):1459–66. https://doi.org/10.1056/NEJMoa020152.
13. Gupta S, Swanson AA, Chen YB, et al. Incidence of succinate dehydrogenase and fumarate hydratase-deficient renal cell carcinoma based on immunohistochemical screening with SDHA/SDHB and FH/2SC. Hum Pathol. 2019;91:114–22. https://doi.org/10.1016/j.humpath.2019.07.004.
14. Ugarte-Camara M, Fernandez-Prado R, Lorda I, et al. Positive/retained SDHB immunostaining in renal cell carcinomas associated to germline SDHB-deficiency: case report. Diagn Pathol. 2019;14(1):42. https://doi.org/10.1186/s13000-019-0812-6.
15. Xiao Q, Chen J, Liu D, Wang CM, Xu Q, Gu XW. [Clinicopathological features of succinate dehydrogenase-deficient renal cell carcinoma]. Zhonghua Bing Li Xue Za Zhi. 2019;48(10):796–798. Chinese. https://doi.org/10.3760/cma.j.issn.0529-5807.
16. Kumar RA, Miyagi H, Mittal V, Crispen P, Kumar U. Succinate dehydrogenase deficient renal cell carcinoma: A case report. Urol Case Rep. 2021;12(40):101885. https://doi.org/10.1016/j.eucr.2021.101885.
17. Milionis V, Goutas D, Vlachodimitropoulos D, et al. SDH-deficient renal cell carcinoma: A case report associated with a novel germline mutation. Clin Case Rep. 2021;9(10):e04605. https://doi.org/10.1002/ccr3.4605.
18. Fuchs TL, Maclean F, Turchini J, et al. Expanding the clinicopathological spectrum of succinate dehydrogenase-deficient renal cell carcinoma with a focus on variant morphologies: a study of 62 new tumors in 59 patients. Mod Pathol. 2022;35(6):836–49. https://doi.org/10.1038/s41379-021-00998-1.
19. Yamaguchi Y, Yokoyama M, Takemoto A, et al. Succinate dehydrogenase-deficient malignant paraganglioma complicated by succinate dehydrogenase-deficient renal cell carcinoma. IJU Case Rep. 2022;5(6):480–3. https://doi.org/10.1002/iju5.12520.
20. Higashi S, Sasaki T, Uchida K, et al. Succinate dehydrogenase B-deficient renal cell carcinoma with a germline variant in a Japanese patient: a case report. Hum Genome Var. 2022;9(1):25. https://doi.org/10.1038/s41439-022-00202-z.
21. Wang XT, Wang X, Zhang RS, Cheng K, Xia QY, Rao Q. [Succinate dehydrogenase-deficient renal cell carcinoma:a clinicopathological, ultrastructural and molecular analysis]. Zhonghua Bing Li Xue Za Zhi. 2022;51(1):12–16. Chinese. https://doi.org/10.3760/cma.j.cn112151-20210823-00590.
22. Kodare D, Menon S, Prakash G, Desai S. Succinate dehydrogenase deficient renal cell carcinoma: A case report of an uncommon renal cancer. Indian J Cancer. 2023;60(4):583–5. https://doi.org/10.4103/ijc.ijc_801_21.
23. Liu W, Chen G, Meng J, Liao X, Xie Y. Imaging findings of succinate dehydrogenase-deficient renal cell carcinoma. Clin Case Rep. 2023;11(8):e7799. https://doi.org/10.1002/ccr3.7799.
24. Sun X, Wang G, Huang Z, et al. Succinate Dehydrogenase Defects Giant Renal Cell Carcinoma. Urol Int. 2023;107(8):819–22. https://doi.org/10.1159/000531059.
25. Pulford C, Keating K, Eames R, Holdren C, Peifer D, Maatman T. Adolescent male with bilateral succinate dehydrogenase-deficient renal cell carcinoma in a horseshoe kidney managed successfully with staged bilateral robotic-assisted partial nephrectomies: A case report. Urol Case Rep. 2023;9(49):102412. https://doi.org/10.1016/j.eucr.2023.102412.
26. Sharma R, Thirunavukkarasu B, Elhence P, Rodha MS, Sureka B. Eosinophilic Solid and Cystic Renal Cell Carcinoma: From Unclassified to Classified, A Case Report. Turk Patoloji Derg. 2022;38(1):60–5. https://doi.org/10.5146/tjpath.2021.01531.
27. Lobo J, Rechsteiner M, Helmchen BM, Rupp NJ, Weber A, Moch H. Eosinophilic solid and cystic renal cell carcinoma and renal cell carcinomas with TFEB alterations: a comparative study. Histopathology. 2022;81(1):32–43. https://doi.org/10.1111/his.14663.
28. Smith SC, Sirohi D, Ohe C, et al. A distinctive, low-grade oncocytic fumarate hydratase-deficient renal cell carcinoma, morphologically reminiscent of succinate dehydrogenase-deficient renal cell carcinoma. Histopathology. 2017;71(1):42–52. https://doi.org/10.1111/his.13183.
29. Paik JY, Toon CW, Benn DE, et al. Renal carcinoma associated with succinate dehydrogenase B mutation: a new and unique subtype of renal carcinoma. J Clin Oncol. 2014;32(6):e10–3. https://doi.org/10.1200/JCO.2012.47.2647.
30. Kuroda N, Yorita K, Nagasaki M, et al. Review of succinate dehydrogenase-deficient renal cell carcinoma with focus on clinical and pathobiological aspects. Pol J Pathol. 2016;67(1):3–7. https://doi.org/10.5114/pjp.2016.59227.
31. Gill AJ, Pachter NS, Chou A, et al. Renal tumors associated with germline SDHB mutation show distinctive morphology. Am J Surg Pathol. 2011;35(10):1578–85. https://doi.org/10.1097/PAS.0b013e318227e7f4.

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