Case Report

Case of renal mucinous tubular and spindle cell carcinoma with high nuclear grade

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Abbreviations & Acronyms
AMACR = α-methyl acyl CoA racemase
CD = cluster of differentiation
CK = cytokeratin
CT = computed tomography
NA = not available
OS = overall survival
PET = positron emission tomography
RCC = renal cell carcinoma
RFS = recurrence-free survival
RMTSCC = renal mucinous tubular and spindle cell carcinoma
RT = radiation therapy
WHO = World Health Organization

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Introduction: Renal mucinous tubular and spindle cell carcinoma is a rare subtype of renal cell carcinoma newly added to the World Health Organization classification in 2004. Although it has been considered as a tumor with good prognosis, aggressive cases have recently been reported.

Case presentation: A 52-year-old man was diagnosed as having left renal cell carcinoma. Open radical left nephrectomy and left-sided pelvic lymph nodes dissection were performed. Pathological diagnosis revealed a renal mucinous tubular and spindle cell carcinoma with high nuclear grade and extra-regional lymph nodes metastasis classified as pT3aN0M1. After nephrectomy, metastasis at second lumbar vertebra and lymph nodes recurrence were occurred.

Conclusion: This tumor with high nuclear grade may be potentially aggressive and carries a poor prognosis.

Key words: high nuclear grade, renal cell carcinoma, renal mucinous tubular and spindle cell carcinoma.

Keynote message

Some tumors of RMTSCC with high nuclear grade may have an aggressive course with poor prognosis. When diagnosing RMTSCC, clinicians should carefully observe the nuclear grade of the neoplastic cells and the area occupied by these cells with high nuclear grade.

Introduction

RMTSCC is a rare RCC that was newly classified in the WHO classification system in 2004.[1] RMTSCC predominantly occurs in middle-aged women (1:4 male-to-female ratio) and has been considered a tumor with good prognosis.[2,3] Histologically, this tumor is characterized by cuboidal cells with a tubular structure and spindle cells with cord-like architecture and mucinous stroma.[4,5] However, some aggressive cases with a poor prognosis have been recently reported,[6,7] and in the 2016 WHO classification, the description of RMTSCC as a carcinoma with a good prognosis was eliminated.[5] In this case report, we describe a case of RMTSCC with high nuclear grade that had metastasis at second lumbar vertebra and lymph nodes recurrence after nephrectomy.

Case presentation

A 52-year-old man was referred to our hospital because of a growing left renal tumor. A contrast-enhanced CT scan revealed the presence of a 93-mm tumor in the upper pole of the left

kidney (Fig. 1a,b) with tumor thrombus observed in the left renal vein (Fig. 1c). The tumor was gradually enhanced from the corticomedullary phase to the excretory phase. Enlarged lymph nodes were present at the left external iliac lesion; they were extra-regional lymph nodes and no other distant metastasis was observed (Fig. 1d). We diagnosed him as having left RCC classified as cT3aN0M1.

Open radical nephrectomy and dissection of left-sided pelvic lymph nodes were performed. The tumor and lymph nodes were examined macroscopically and microscopically. Macroscopically, a 80 × 80-mm, gray–whitish and solid tumor with necrotic tissue was located in the upper pole of the resected left kidney. Microscopically, the tumor consisted of a tubular and partly papillary structure (Fig. 2a). The neoplastic cells were cuboidal with eosinophilic cytoplasm. The Fuhrman nuclear grading system is used to describe the RMTSCC.[2,7] This case was classified as Fuhrman nuclear grade 3 (Fig. 2b). The tumor was invaded into left renal vein, and metastatic lymph nodes were found at the left external iliac area (Fig. 2c). Fascicular growth with spindle cells and mucin stained by Alcian blue stain were found (Fig. 3a). Immunohistochemical findings showed the neoplastic cells to be diffusely positive for AMACR (Fig. 3b) and CK 7 (Fig. 3c). CD 10 was negative in the neoplastic cells (Fig. 3d). Although Ki-67 and p53 were negative in the neoplastic cells with low nuclear grade, they were positive in the neoplastic cells with high nuclear grade (Fig. 3e,f). We subsequently diagnosed him as having left RMTSCC classified as pT3aN0M1.

Three months after nephrectomy, a PET-CT scan showed metastasis at the second lumbar vertebra with a maximum standard uptake value of 5.7 (data not shown). Six months after nephrectomy, vertebrectomy was performed for metastasis at the second lumbar vertebra. The pathological findings showed metastasis of the RMTSCC to the second lumbar vertebra. Nine months after nephrectomy, another PET-CT scan showed two 10-mm lymph nodes at the left internal iliac lesion with a maximum standard uptake value of 5.1 (data not shown). These were not regional lymph nodes of RCC, but he was not suffering from other causative diseases such as prostate or rectal cancer. Therefore, we diagnosed these lymph nodes as metastasis of RMTSCC. We are planning on administration of tyrosine kinase inhibitor.

Discussion

To date, around 100 cases of RMTSCC have been reported. Most of them have described RMTSCC with low nuclear grade and a favorable prognosis.[2] However, several recent reports have shown recurrence or metastasis in RMTSCC with high nuclear grade.[7,8] To our knowledge, around 20 cases of recurrence after nephrectomy in RMTSCC have been reported. Among them, the detailed clinical course and prognosis after nephrectomy have been reported in 10 cases,[6,7,9–15] which are summarized in Table 1. The median patient age was 67.5 (range 32–82) years. The 10 cases comprised eight male and two female patients. Of note, histological findings revealed that seven patients had neoplastic cells with high nuclear grade. After recurrence, three patients were treated with sunitinib, one with pazopanib and RT, one underwent resection of the recurrent metastatic tumor, two underwent chemotherapy, and details of treatment were not described in three patients. We performed Kaplan–Meier survival analysis in the seven cases of RMTSCC with high nuclear grade. The median RFS was 5.5 months (95% CI 1.0–28 months), and the median OS was 9.0 months (95% CI 1.0–48 months). One patient with good progress after resection of her recurrent metastatic tumor was reported who had been alive for 23 years after the initial surgery.[15] However, it should be noted that this patient had RMTSCC with low nuclear grade. Collectively, these findings indicate that the prognosis of RMTSCC with high nuclear grade is unfavorable.

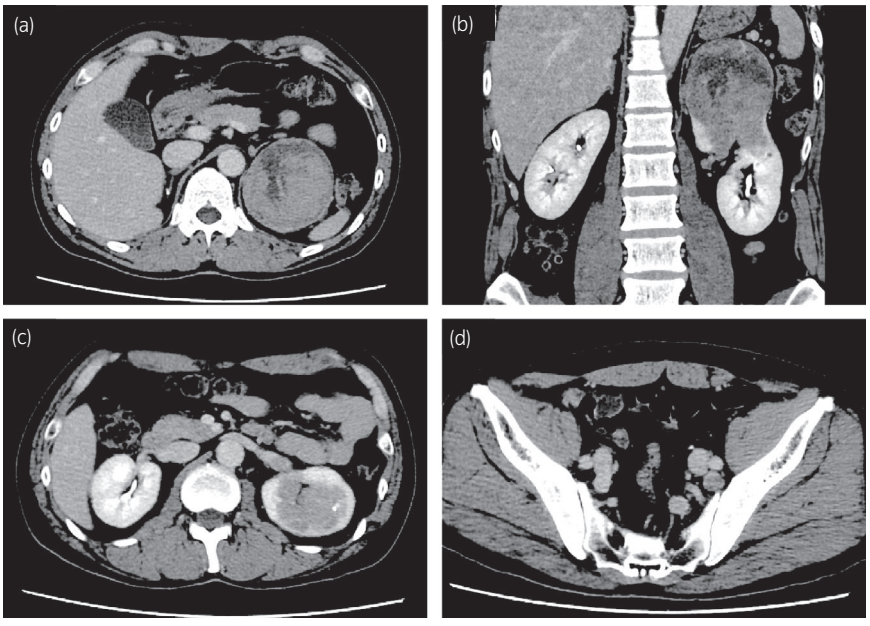

Fig. 1 CT imaging findings before nephrectomy. (a) Abdominal enhanced CT showed the size of the left renal tumor as 74 mm on axial imaging and (b) as 93 mm on coronal imaging. (c) Abdominal enhanced CT axial image of the left renal tumor and tumor thrombus in the left renal vein. (d) Abdominal enhanced CT of the 16-mm lymph node at the left external iliac area.

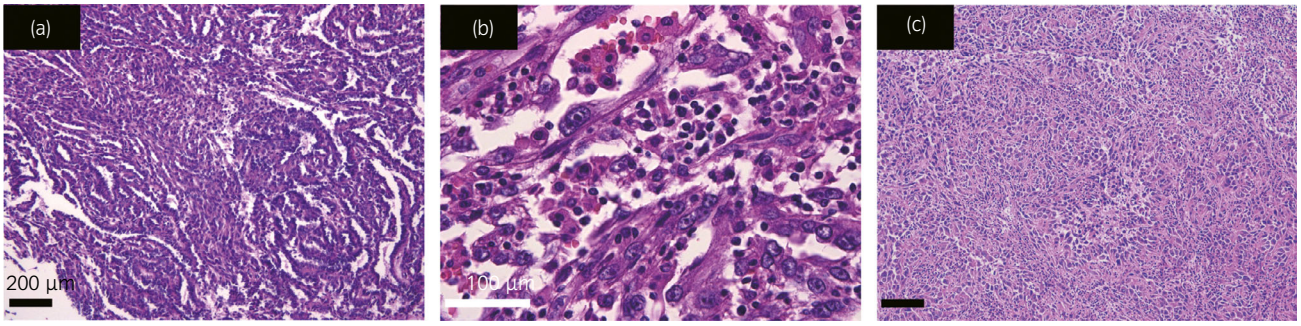

Fig. 2 Pathological findings of hematoxylin and eosin staining. (a) H&E staining of the renal tumor show the tubular and papillary structure and spindle component. (b) H&E staining of the renal tumor showed the high nuclear grade (Furman grade 3) and (c) the left external iliac lymph node showing mainly the spindle component.

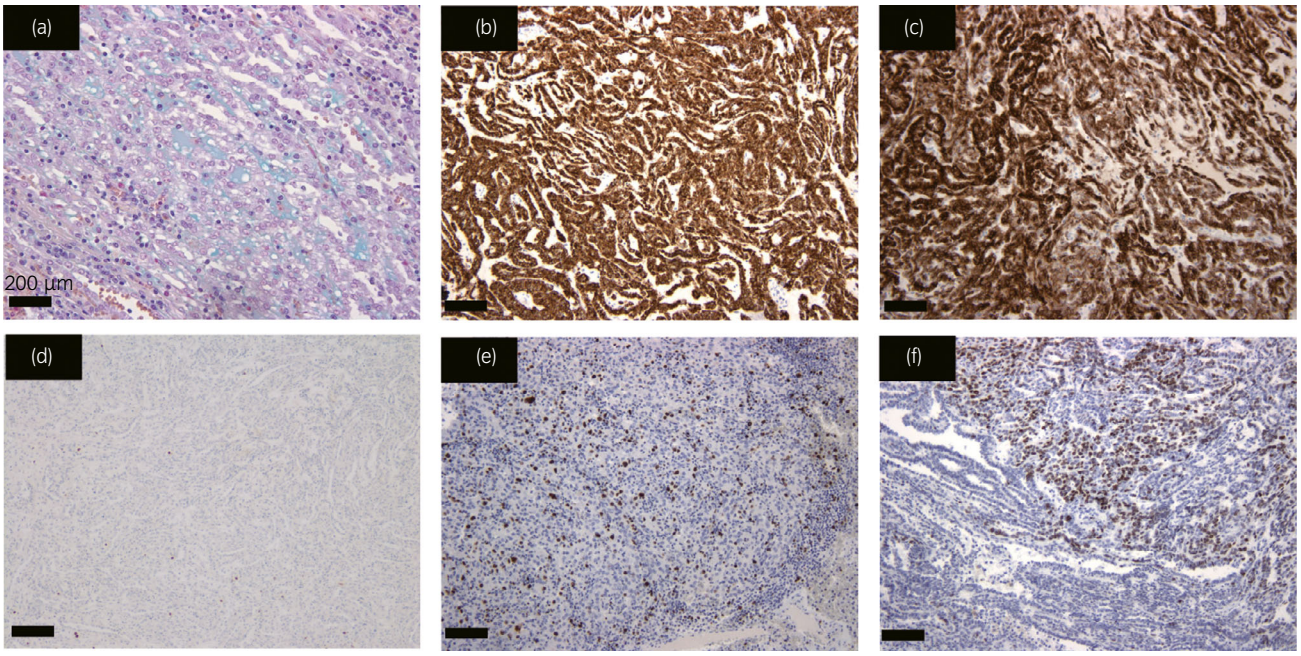

Fig. 3 Pathological findings of immunohistochemical and special staining. (a) Alcian blue staining of the renal tumor showed stained mucinous stroma. (b) Immunohistochemical staining of the renal tumor showed that AMACR and (c) CK7 are diffusely positive, (d) CD10 is negative, (e) Ki-67 was positive in the neoplastic cells with high nuclear grade and negative in the neoplastic cells with low nuclear grade, and (f) p-53 was positive in the neoplastic cells with high nuclear grade and negative in the neoplastic cells with low nuclear grade.

Table 1 Clinical and pathological details of renal mucinous tubular and spindle cell carcinoma cases with recurrence after nephrectomy

	Age	Sex	R/L	cT	*N*	M	pT	Nuclear grade	RFS (months)	OS (months)	Additional treatment	Reference
1	49	M	RL	1a	0	0	1a	Low	24	29	Pazopanib + RT	9
2	82	M	R	1a	1	0	1a	High	5	6	Sunitinib	10
3	71	M	R	1a	0	0	1a	High	1	24	Sunitinib, temsirolimus, axitinib	7
4	64	M	R	2a	NA	NA	1b	High	6	9	Chemotherapy	7
5	76	M	R	1a	NA	NA	1a	High	NA	48	Sunitinib	11
6	71	M	L	1a	0	0	1a	Low	9	NA	NA	12
7	64	M	L	2b	0	0	2b	High	NA	8	NA	13
8	75	M	NA	NA	NA	NA	NA	High	NA	1	Chemotherapy	6
9	57	F	R	1b	0	0	1b	High	28	48	NA	14
10	32	F	R	1b	0	0	1b	Low	96	NA	Operation	15

There is no currently recommended systemic therapy for recurrence or metastasis of RMTSCC. In our investigation, one case was reported with a good response to sunitinib in RMTSCC with low nuclear grade.[16] In contrast, other RMTSCCs with high nuclear grade did not respond to chemotherapy that included sunitinib, axitinib, and temsirolimus. As the second-line therapy, one paper has reported about efficacy of nivolumab in non-clear cell RCC patients including one case of RMTSCC.[17] CT showed a stable tumor at 6 months after nivolumab treatment, but the nivolumab was stopped at 8 months because of tumor progression. In the future, we will report the detail of clinical course after recurrence.

Conclusion

We presented a case of RMTSCC with high nuclear grade. After nephrectomy, metastasis at second lumbar vertebra and lymph nodes recurrence occurred. The prognosis of RMTSCC with high nuclear grade is considered to be unfavorable. Further studies with a large number of cases are required to compile evidence on the follow-up course and therapeutic algorithm in RMTSCC. Additionally, biomarkers to predict the prognosis of RMTSCC are required because recurrence and metastasis occurred even in RMTSCC with low nuclear grade. When diagnosing RMTSCC, clinicians should carefully observe the nuclear grade of the neoplastic cells and the area occupied by these cells with high nuclear grade.

Ethics

We obtained written informed consent from the subject.

Acknowledgement

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Conflict of interest

The authors declare no conflict of interest.

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Editorial Comment

Editorial Comment to Case of renal mucinous tubular and spindle cell carcinoma with high nuclear grade

Renal mucinous tubular and spindle cell carcinoma (RMTSCC) is a relatively rare type of malignancy arising from renal parenchyma, which can be characterized by tiny, long tubules lined by cuboidal cells with or without spindled cells separated by pale mucinous stroma.[1] Although