Early recurrence and extensive retroperitoneal metastasis after surgery for high-grade mucinous tubular and spindle cell carcinoma: A case report and literature review

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Abstract. Mucinous tubular and spindle cell carcinoma (MTSCC) is a rare subtype of renal cancer. The present report details the treatment experience of a case of MTSCC, where the patient underwent a right-side laparoscopic nephrectomy in October 2020 at Zhuji People's Hospital (Zhuji, China). A total of 3 months post-operation, multiple metastases were discovered in the right renal area and retroperitoneum, with rapid disease progression observed in the subsequent 2 months. Treatment with tislelizumab combined with pazopanib was ineffective, and the patient subsequently died. Although MTSCC is generally considered a low-grade 'indolent' tumor, with most patients achieving long-term survival post-surgery, a minority of cases, especially those of a higher grade, may experience postoperative recurrence and metastasis. Due to the rarity of metastatic MTSCC, most studies are based on small sample sizes or case reports, and there is a lack of standardized systemic treatment and follow-up strategies for metastatic MTSCC. The present paper summarizes and analyzes the clinical features, treatment methods and prognosis of metastatic MTSCC cases reported in the literature, aiming to provide assistance for the treatment and follow-up management of metastatic MTSCC. Even in cases of distant metastasis, aggressive surgical treatment, metastasectomy combined with molecular targeted or immunotherapy, may still be recommended.

Introduction

Mucinous tubular and spindle cell carcinoma (MTSCC) represents a rare subtype of renal cell carcinoma characterized by unique biological features. In the 2004 WHO classification of renal tumors, it was first recognized as a distinct entity (1). However, in the 2016 edition of the classification standards, the description of it as malignant and low-grade tumor was removed (2). It has a wide age distribution (13-82 years), with a mean age of onset of 53 years, and is more common in women (3). Due to the lack of significant clinical manifestations and imaging characteristics, the diagnosis of MTSCC primarily relies on pathological histology and immunohistochemical examination (4). Pathologically, MTSCC is characterized by tightly packed, elongated tubules transitioning to spindle cell areas and mucinous stroma (5). Although surgery is the primary treatment modality and most patients have a favorable prognosis, the risk of recurrence and distant metastasis should not be overlooked (6). Ged *et al* (7) conducted a study of 25 cases at their institution, reporting a 3-year survival rate of 84.0%, with a median follow-up time of 3.9 years (range, 1 month to 10.3 years). The present article reports the treatment of a patient with MTSCC at Zhuji People's Hospital (Zhuji, China) in October 2020, who experienced renal recurrence and retroperitoneal metastasis shortly after surgery, with rapid deterioration of the condition. Additionally, it summarizes literature-reported metastatic cases, aiming to provide clinical insights by reviewing their clinical manifestations, treatment strategies and prognoses.

Case report

A 31-year-old male patient was admitted at Zhuji Fourth People's Hospital (Zhuji, China) in October 2020, with a half-month history of painless gross hematuria, which was continuous, light red without clots, and worsened after consuming spicy food. An initial urinary system ultrasound performed externally suggested the presence of a mass in the right kidney. The patient then sought treatment at Zhuji People's Hospital (Zhuji, China) in October 2020. A physical examination demonstrated no significant positive findings, including negative rebound tenderness in the abdomen, no tenderness upon percussion in the renal area and no palpable abdominal mass. Laboratory tests revealed the following: Urine white blood cell count, 233 U/μl (reference values, <25.0 U/μl); urine red blood cell count, 10,204/μl (reference values: 0.0-20.0 U/μl); uric acid level, 571 μmol/l (reference values: Male 202-416 μmol/l); lactate dehydrogenase, 296 U/l (reference values: 120-250 U/l); and BCA, creatinine, urea nitrogen and tumor markers (CEA, AFP, CA 19-9, CA 72-4

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and CA 125) were all negative. Further upper abdominal CT scans with and without contrast revealed a roughly circular mass at the lower pole of the right kidney with clear boundaries, smooth edges and uneven internal density, including patchy hemorrhage, necrosis and fine calcifications, measuring ~7.6x6.7 cm (Fig. 1A). Contrast-enhanced CT showed mild, uneven enhancement in the lesion area, no significant lymphadenopathy and thrombosis. Renal artery CT angiography indicated that the tumor was primarily supplied by the renal artery with sparse internal vasculature (Fig. 1B). A chest CT showed no metastatic lesions. Based on these findings, a preoperative diagnosis of a malignant tumor with insufficient right kidney blood supply was made.

Under general anesthesia, the patient underwent laparoscopic right radical nephrectomy, which lasted 3.5 h with an estimated blood loss of ~200 ml. The resected kidney specimen (measuring ~8x7x7 cm) partially protruded from the kidney surface, with an intact capsule, and the cut surface revealed a soft tumor containing necrotic tissue without noticeable mass in the renal pelvis. A biopsy specimen was first fixed using Zhejiang Jinhua Tonghe Biotechnology Co., Ltd. Biological Tissue Fixative (10% neutral buffered formalin fixative; ready-to-use) at 25˚C for 12 h, after which samples were cut to 3 μm-thick. The sections were stained with HE stain at 25˚C for 45 min and imaged using a Zeiss Axio-Lab-A1 microscope. Microscopically, the tumor tissue showed infiltrative growth, invading the renal parenchyma but not the perirenal fat tissue (Fig. 2A). Tumor cells were partly plump and spindle-shaped, with eosinophilic cytoplasm, arranged in bundles. Certain cells had unclear boundaries and transparent cytoplasm, with oval nuclei and atypical mitoses (Fig. 2B). The stroma showed focal mucinous changes, vascular proliferation and extensive necrosis (Fig. 2C). No nerve, vascular invasion or intravascular tumor thrombus was seen. For immunohistochemistry, tissue sections (3-μm thick) were fixed in Zhejiang Jinhua Tonghe Biotechnology Co., Ltd., Biological Tissue Fixative (10% neutral buffered formalin) at 25˚C for 12 h, and embedded in paraffin. Staining was performed using the DAKO Autostainer Link 48 system (Agilent Technologies, Inc.). The following primary antibodies (prediluted by the manufacturer) from Guangzhou Anbiping Medical Laboratory Co., Ltd., were used: Ki67 (cat. no. IM098), CD10 (cat. no. IM025), EMA (cat. no. IR074), PAX-8 (cat. no. IR191), Vimentin (cat. no. IM142), CK7 (cat. no. IM061), CK (cat. no. IM067), CD34 (cat. no. IM034), P504s (cat. no. IR127), CK20 (cat. no. IR385), SMA (cat. no. IHC-M005), P53 (cat. no. IM123) and CD30 (cat. no. IM032). All primary antibodies were incubated with the samples at 25˚C for 30 min. The secondary antibodies EnVision FLEX+, Mouse, High pH (Link; prediluted by the manufacturer; cat. no. K8002; Agilent Technologies, Inc.; EnVision FLEX+) were used at 25˚C for 20 min. Blocking was performed with 3% peroxidase blocking reagent (cat. no. DAKO SM801; Agilent Technologies, Inc.) at 25˚C for 5 min, followed by incubation with EnVision FLEX/HRP (cat. no. DAKO SM802; Agilent Technologies, Inc.) at 25˚C for 20 min. DAB incubation was carried out at 25˚C for 5 min (cat. no. DAKO DM827). The microscope used for examination was an Olympus BX-51 microscope with a camera adaptor (Olympus U-TV0.5XC-3; Olympus Corporation) for obtaining images. Immunohistochemistry results revealed Ki-67 labeling index (~40%; Fig. 2D), CD10 (-; Fig. 2E), epithelial membrane antigen [EMA (++); Fig. 2F], paired box gene 8 [PAX8 (-); Fig. 2G],Vimentin (+++; Fig. 2H), CK7 (-; Fig. 2I), CK (++; Fig. 2J), α-methylacyl-CoA racemase [P504S (-) Fig. 2K], CD34 vessels (+; Fig. 2L),CK20 (-; data not shown), SMA (-; data not shown), P53 (-; data not shown), CD30 (-; data not shown), placental alkaline phosphatase (++; data not shown) and Desmin (-; data not shown). Based on morphology and immunohistochemistry, a final diagnosis of high-grade MTSCC (tumor size ~8x4x3.5 cm) was made. No tumor invasion was seen in the ipsilateral ureter or vascular margins. The tumor was classified as T2N0M0 (8), with extensive necrosis and atypical mitoses, World Health Organization (WHO)/International Society of Urological Pathology grade 3 (2), but without sarcomatoid transformation.

A total of 3 months post-operation, abdominal enhanced CT with contrast revealed scattered soft tissue nodules with clear boundaries next to the right renal area, one of which was associated with hemorrhage (Fig. 3A and B). CT values ranged from 23-56 Hu and the largest nodule measured ~1.9x1.3 cm, showing mild uneven enhancement. The patient sought further treatment at Zhejiang Cancer Hospital (Hangzhou, China) in March 2021, where a PET-CT scan indicated multiple recurrences or metastases around the right kidney surgical area (Fig. 3C-E), inferior vena cava, right psoas muscle (Fig. 3F), right mesentery, peritoneum and serosal surface of the right hemicolon, with possible hemorrhage within the masses. The right liver, diaphragm, right psoas muscle, right iliopsoas muscle and right abdominal wall muscles were involved, with potential emboli formation in the inferior vena cava and left common iliac artery. The treatment with 200 mg tislelizumab (intravenously once every 3 weeks) and 800 mg pazopanib (orally once a day) was initiated for one cycle, but the response was poor.

A total of 5 months post-operation, the patient was readmitted at Zhuji People's Hospital (Zhuji, China) in March 2021 due to a fever, and a full abdominal enhanced CT identified multiple soft tissue nodules and mass shadows in the right renal area, retroperitoneum, paraspinal muscles and surrounding the ascending colon and inguinal area (Fig. 4A). Certain nodules fused into masses with internal bleeding and necrosis, the largest mass measured ~12.3x7.2 cm, with areas showing mild uneven enhancement. Moreover, chest CT revealed inflammation in the lower lobe of the right lung, without obvious metastatic lesions (Fig. 4B). The patient was treated with intravenous linezolid glucose injection (every 12 h), combined with 0.3 g biapenem (every 8 h) and 10 ml oral ibuprofen suspension for fever reduction. Despite these interventions, the high fever persisted, leading to progressive severe anemia and oliguria. The patient was administered transfusions of packed red blood cells (1.5 U) to improve oxygen-carrying capacity, antipyretics (ibuprofen suspension 10 ml/6 h) and linezolid glucose injection (0.6 g IV infusion once every 12 h) combined with biapenem (0.3 g IV infusion once every 8 h) for anti-infection treatment. However, no significant improvement was recorded. Subsequently, the patient developed Gram-positive bacterial sepsis and acute renal failure, and was discharged in April 2021, at the request of the patient. Follow-up via phone later that month confirmed the patient had died.

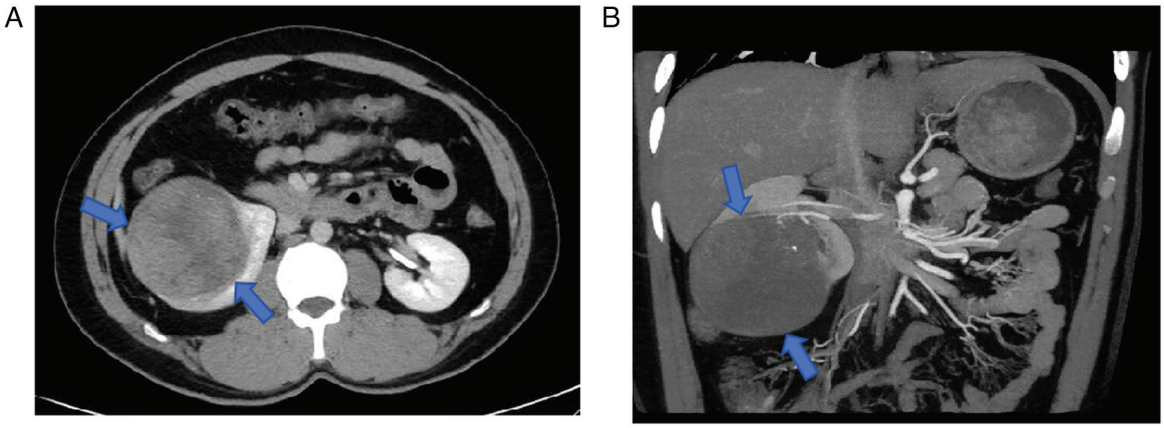

Figure 1. Preoperative CT findings. (A) Abdominal enhanced CT reveals that a lesion (blue arrows) is visible in the mid-lower pole of the right kidney showing progressively mild and uneven enhancement. (B) The right renal CT angiography reveals arterial supply from the right renal artery, with relatively sparse internal vascularity within the tumor (blue arrows).

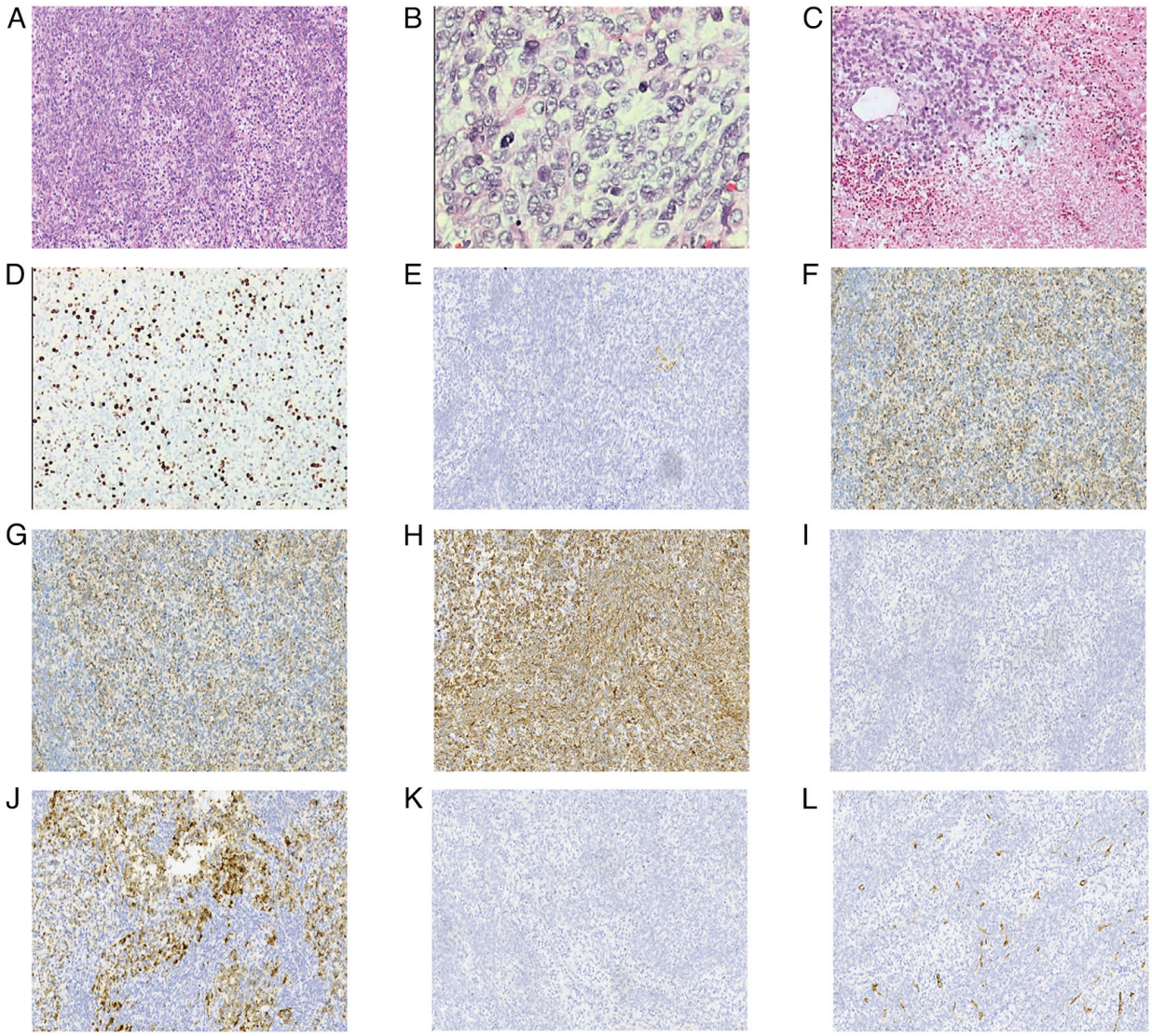

Figure 2. Histological and immunohistochemical findings. (A) Tumor cells are partly plump and spindle-shaped, with eosinophilic cytoplasm, arranged in bundles (magnification, x200). (B) Certain cells had unclear boundaries and transparent cytoplasm, with oval nuclei and atypical mitoses (magnification, x400). (C) The stroma revealed focal mucinous changes, vascular proliferation and extensive necrosis (magnification, x200). (D) Positive cytoplasmic staining of Ki-67 (magnification, x200). (E) Negative cytoplasmic staining of CD10 (magnification, x200). (F) Positive cytoplasmic staining of epithelial membrane antigen (magnification, x200). (G) Negative cytoplasmic staining of paired box gene 8 (magnification, x200). (H) Positive cytoplasmic staining of Vimentin (magnification, x200). (I) Negative cytoplasmic staining of CK7 (magnification, x200). (J) Positive cytoplasmic staining of CK (magnification, x200). (K) Negative cytoplasmic staining of P504S (magnification, x200). (L) Positive cytoplasmic staining of CD34 vessels (magnification, x200).

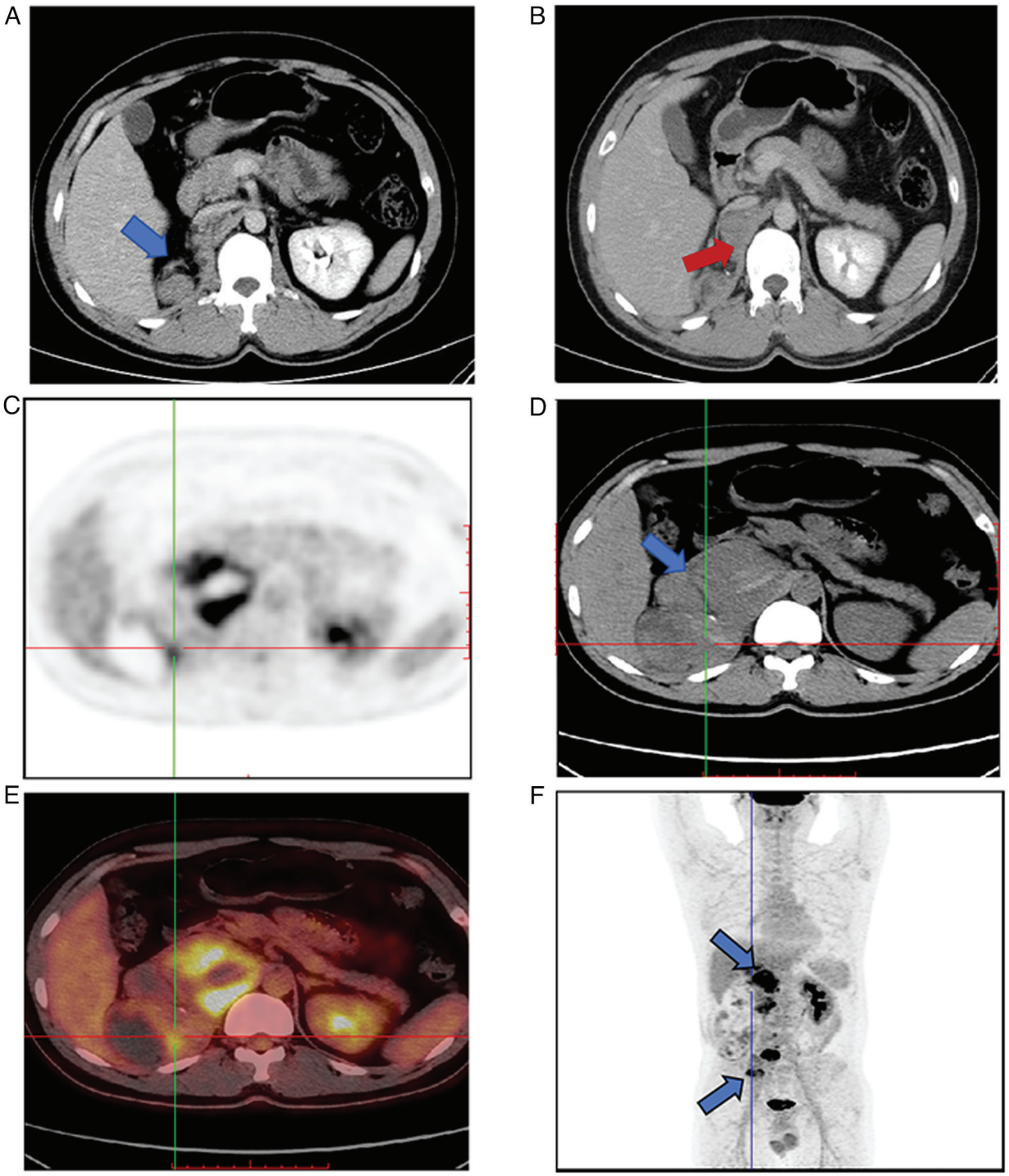

Figure 3. Post-operation abdominal enhanced CT and PET-CT findings. A total of three months post-operation, an abdominal enhanced CT reveals: (A) a nodule (blue arrow) in the right renal region, and (B) a nodule (red arrows) in the surgical area. PET-CT indicates post-radical nephrectomy for right kidney cancer with (C) abnormal radiotracer uptake. Additionally, (D) multiple cystic-solid irregular soft tissue density nodules and masses (blue arrow) are observed in the surgical area, with clear borders encasing the inferior vena cava. (E) The anteromedial aspect of the mass shows hypermetabolism. (F) The solid portions of both the renal region mass and the psoas major muscle mass also demonstrate abnormal radiotracer uptake (blue arrow).

Discussion

MTSCC is a rare subtype of renal cancer that typically manifests as a low-grade and indolent tumor, and accounts for <1% of all renal cancer incidences (9). However, the exact incidence of MTSCC is unclear. In the study by Xu *et al* (10), it is reported that the incidence of MTSCC at their institution was 0.52% of all cases of renal cell cancer (22/4,197 cases). MTSCC is distinguished by its unique morphology of renal tubules and spindle cells, along with a mucinous extracellular matrix, classified by the WHO in 2004 as a low-grade polymorphic renal epithelial tumor (11). Although MTSCC affects a wide age range, with a male-to-female ratio of ~1:4, most cases are incidentally discovered during physical examinations, with a minority presenting with flank pain or painless hematuria (12). The patient in the present case was male and

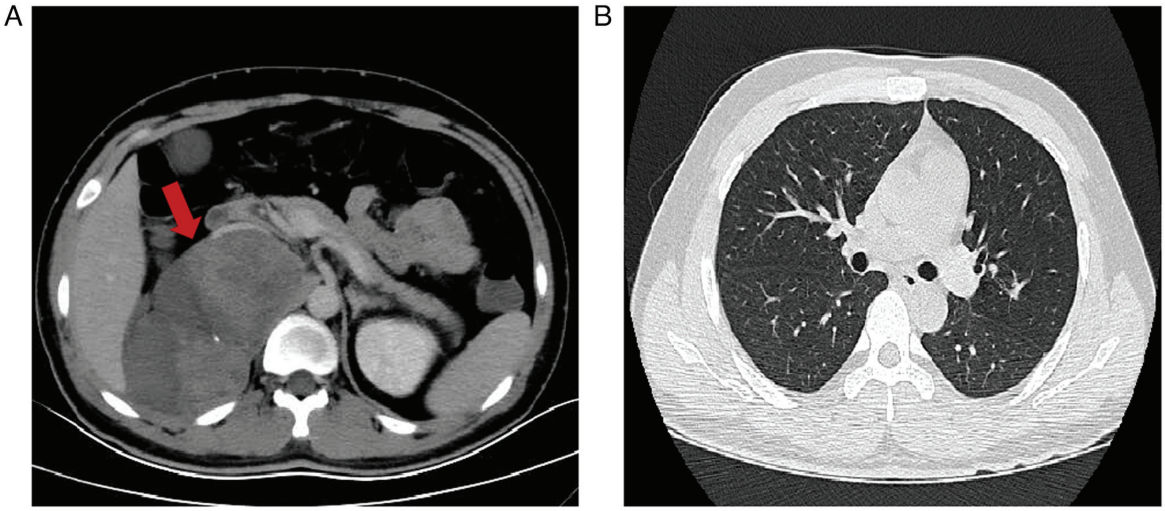

Figure 4. CT findings 5 months post-operation. (A) A significant increase in the size of nodules in the surgical area is observed, with certain nodules in retroperitoneum merging into masses (red arrow). (B) No metastatic lesions were observed on the chest CT.

presented with painless hematuria, which is consistent with reported cases (6,7,12). Imaging findings for MTSCC tumors typically reveal a solitary solid lesion located within the kidney, sometimes protruding from the renal parenchyma (13). These lesions have relatively uniform density, with occasional punctate or patchy calcifications, small areas of hemorrhage or cystic necrosis (14). Enhanced CT shows that tumor enhancement during the cortical phase is usually lower than that of the renal parenchyma, whilst in the renal parenchymal and excretory phases, it exhibits gradual and persistent mild enhancement (15). The tumor characteristics of the patient described in the present report study are consistent with those reported in the literature, presenting as a solitary roundish mass within the renal parenchyma, accompanied by scattered patchy hemorrhage, necrosis and fine punctate calcifications, with persistent mild enhancement.

From a pathological perspective, typical MTSCC features include spindle cells and tubular structures interspersed with mucinous stroma, with varying proportions of different components within the tumor (16). Although the vast majority of MTSCCs are low-grade, with inconspicuous nucleoli and minimal atypia, literature reports have also described high-grade MTSCCs, characterized by larger nuclei, prominent nucleoli, coagulative necrosis and areas of sarcomatoid transformation, indicating the malignant potential of MTSCC (17). This present case showed prominent nucleoli, atypical mitoses and extensive necrosis, with no invasion into perirenal fat, vessels or nerves, diagnosed as pT2a stage. Although no sarcomatoid transformation was observed, it indicates the malignant potential of MTSCC.

Immunohistochemically, MTSCC typically expresses distal renal tubular markers such as cytokeratin, vimentin and EMA, whilst proximal tubular markers such as CD10 and villin are often negative (18). The literature reports that vimentin, PAX8, EMA, P504S and low molecular weight cytokeratins (such as, CK7, CK8/18 and 34βE12) are usually positively expressed, whilst CD10 is partially positive. Markers such as carbonic anhydrase IX, CK20 and GATA binding protein 3 are typically negative, and the Ki-67 index may be elevated in high-grade tumors (19). The present case demonstrated a positive expression of EMA and vimentin, and a negative expression of PAX8, CK7 and CD10. Combined with its morphological appearance and immunohistochemistry, the diagnosis was MTSCC. Furthermore, the Ki-67 index of ~40% suggested a high-grade tumor.

Despite being generally regarded as low-grade and indolent tumors, reports of lymph node and distant metastases of MTSCC have gradually increased in recent years, highlighting its potential malignancy (6,12,15-19). A review of the literature and a summary of metastatic cases, including this case, totaled 22 cases (6,12,15-29), in which there were 16 male and 6 female patients, with a male-to-female ratio of 2.6:1, and the median age was 64 years (range, 31-82 years). Although MTSCC can occur at any age and is more common in females, the summarized cases demonstrated that middle-aged and older males may be more at risk of metastasis in MTSCC, consistent with the report by Huang *et al* (24). However, a larger number of cases is needed to verify this. Furthermore, the average size of the tumor was ~7.1 cm (range, 1-18 cm). A total of two cases were located within the renal pelvis and 14 cases were in the renal parenchyma near the medullary region, with larger lesions protruding beyond the renal outline externally and inward toward the renal sinus. Imaging of 12 cases (54%) showed heterogeneous density with necrosis, hemorrhage or cystic changes. Preoperative imaging and postoperative pathology indicated that 12 cases (60%) had invasion into the perirenal fat, lymphatic vessels or veins, with one case developing an inferior vena cava thrombus. This indicates that when tumors are large, located deep within the kidney (near the medullary sinus area) and accompanied by infiltration of surrounding tissues, lymphatic vessels or veins, as well as the presence of necrosis or hemorrhage, the aggressiveness of the tumor increases, consistent with reports by Ursani *et al* (6) and Uchida *et al* (12) (Table I). Furthermore, of the summarized cases, 6 showed sarcomatoid transformation, 10 had necrosis, and 8 exhibited atypical mitoses of grade ≥3. A total of 5 cases (22%) suggested low-grade tumors, and among these, 3 had metastasis preoperatively, 1 showed inferior vena cava thrombus

Table I. Summary of the characteristics of cases of mucinous tubular and spindle cell carcinoma in the literature.

First author/s, year	Case	Sex	Age, years	Location	Size, cm	pTNM stage	Invasion of surrounding tissues	Pre-operative metastasis	Neph-rectomy	Necrosis	Nuclear grade[a]	Sarcomat-oid trans-formation	Adjuvant therapy	Postoperative metastasis sites	Prognosis	(Refs.)
Present case	1	Male	31	Right	8	T2aN0M0	No	No	RN	Yes	High (grade 3)	No	Tislelizumab and pazopanib	Retroperito-neum, muscle and mesentery (3 months)	DOD (5 weeks)	-
Ursani *et al*, 2010	2	Female	64	Left	18	T3aN1M1	Perirenal fat	Liver and LN	RN	No	Low	No	No	Liver and LN	AWD (16 months)	(6)
Uchida *et al*, 2017	3	Male	71	Right	3	T3aN0M0	Blood vessel	No	PN	No	High (grade 3)	No	Sunitinib, temsirolimus and axitinib	Lung, bone, liver and pleura) (1 months	DOD (24 months)	(12)
	4	Male	64	Right	8	T3aN0M0	Blood vessel	No	RN	No	High (grade 3)	No	No	Lung (6 months)	DOD (9 months)	
Gong *et al*, 2020	5	Male	70	Left	4.4	T3aN0M1	No	Bladder	RN	Yes	Low	No	Sunitinib, gemcitabine and cisplatin	None	NED (36 months)	(15)
	6	Male	61	Left	10.7	T3aN1M0	Blood vessel	No	RN	Yes	Low	No	No	None	NED (80 months)	
Sakatani *et al*, 2017	7	Male	82	Right	2.1	T3aN1M0	Lymphatic vessel	LN	RN	No	High (grade 3)	No	No	LN, liver and brain (5 months)	DOD (5 months)	(16)
Ivey *et al*, 2021	8	Male	39	Left	14	T2bN1M0	No	LN	RN	Yes	Low	No	No	None	NED (12 months)	(17)
Kubota *et al*, 2018	9	Male	72	Right	4.6	T3aN2M1	Perirenal fat	LN	RN	Yes	High (grade 3)	Yes	No	Lung, Bone and pleura (12 months)	DOD (66 months)	(18)
	10	Male	64	Right	11	T3bN0M0	Perirenal fat	No	RN	Yes	High (grade 4)	Yes	No	Mesentery (24 months)	AWD (130 months)	
Shen et al, 2023	11	Female	77	Left	2	T1aN0M0	No	No	RN	Yes	Low	No	Unknown	Lung (6 months)	DOD (15 months)	(19)
	12	Male	69	Left	5.5	T3aN0M0	Perirenal fat	No	RN	No	High (grade 3)	No	No	Lung (6 months)	DOD (6 months)	
Isono *et al*, 2020	13	Male	43	Left	5	T3aN1M0	Lymphatic vessel	LN	RN	No	Low	No	Sunitinib, axitinib and nivolumab	Peritoneum (4 months)	DOD (12 months)	(20)
Miura *et al*, 2020	14	Female	77	Left	1	T3aN1M0	Vein	LN	RN	No	High (grade 4)	Yes	Pazopanib and axitinib	Lung, LN and bone (15 months)	AWD (25 months)	(21)
Takahashi *et al*, 2019	15	Male	68	Right	6.4	T3aN1M0	Perirenal fat	LN	RN	No	Low	No	Axitinib and nivolumab	Lung and bone (7 months)	AWD (12 months)	(22)
Kobayashi *et al*, 2019	16	Female	75	Left	3.5	T3aN0M0	Renal sinus fat	No	RN	No	Low	No	No	Lung, LN and bone (1 months)	DOD (4 months)	(23)

Table I. Continued.

First author/s, year	Case	Sex	Age, years	Location	Size, cm	pTNM stage	Invasion of surrounding tissues	Pre-operative metastasis	Neph-rectomy	Necrosis	Nuclear grade[a]	Sarcomat-oid trans-formation	Adjuvant therapy	Postoperative metastasis sites	Prognosis	(Refs.)
Huang *et al*, 2018	17	Male	60	Left	3.7	T1aN0M1	Renal capsule	Bone	RN	No	Low	No	No	Bone	AWD	(24)
Mikami *et al*, 2017	18	Male	87	Right	6.5	T1bN0M0	No	No	RN	No	Low	No	No	LN (91 months)	AWD (115 months)	(25)
Larkin *et al*, 2010	19	Female	61	Right	3.5	T1aN1M1	No	LN, bone and AdG	No	No	Low	No	Sunitinib	LN, bone and AdG	AWD (7 months)	(26)
Simon *et al*, 2008	20	Female	64	Left	15	T3aN0M1	Perirenal fat	Bone and AdG	RN	Yes	Low	Yes	Radiotherapy	Liver and bone (3W)	DOD (3 weeks)	(27)
Kobari *et al*, 2023	21	Male	53	Left	11.5	T3aN0M0	Perirenal fat	AdG, LN and liver	RN	Yes	Low	Yes	Radiotherapy, pazopanib and axitinib	AdG, LN and liver (2 months)	DOD (24 months)	(28)
Fuchizawa *et al*, 2021	22	Male	69	Left	9	T2aN0M1	No	Bone	CN	Yes	High (grade 3)	Yes	Ipilimumab and nivolumab	None	NED (21 months)	(29)

pTNM, pathological tumor-node-metastasis. [a]Low (grade 1-2) and high (grade 3-4). LN, lymph node; AdG, adrenal gland; RN, radical nephrectomy; PN, partial nephrectomy; CN, cytoreductive nephrectomy; NED, no evidence of disease; AWD, alive with disease; DOD, dead of disease.

and 2 died during follow-up. Although most metastatic behaviors are observed in high-grade MTSCC, the possibility of high malignancy and metastasis in low-grade tumors cannot be entirely excluded (6,20,23,25,26), emphasizing the importance of regular postoperative follow-ups. Moreover, of the 22 summarized cases, 7 had distant metastasis preoperatively and 9 had lymph node metastasis. Except for one patient who received sunitinib treatment without surgery, the remaining 19 patients underwent partial or radical nephrectomy, with 8 receiving adjuvant therapy (such as tyrosine kinase inhibitors, monoclonal antibodies and radiotherapy). Following aggressive treatment, 11 patients were still alive during follow-up, with survival times ranging from 3 weeks to 130 months. A total of four cases achieved tumor-free status, whilst 7 cases exhibited coexistence with the disease. Prior to surgery, seven patients were diagnosed with a clinical stage of IV; however, following active treatment, five patients remained alive. Even if MTSCC has metastasized distantly, aggressive surgical treatment, metastasectomy and molecular targeted or immunosuppressive therapy remain recommended treatment methods, helping to control disease progression (17,24,25). Furthermore, out of the summarized cases, during the follow-up period, the shortest time to first detection of metastasis after surgery was 3 weeks in one case (27), and the longest was 91 months (25), indicating a wide time span. This highlights the importance of developing personalized follow-up strategies for early detection of disease recurrence or metastasis.

Due to the rarity of metastatic MTSCC, there is currently no recommended systemic treatment. In case 3 (12), partial nephrectomy was followed by treatment with sunitinib, temsirolimus and axitinib, along with palliative radiation to the left ribs to control pain. However, the patient showed no significant response and died of respiratory failure 2 years later. In case 5 (15), preoperative bladder metastasis was treated with radical nephroureterectomy and bladder resection, followed by 1.2 g gemcitabine and 60 mg cisplatin chemotherapy, with no metastasis observed during a 36-month follow-up. This suggests that a combination of sunitinib and gemcitabine + cisplatin chemotherapy may be effective. In case 13 (20), peritoneal metastasis was treated with sunitinib, resulting in a reduction of disseminated tumors and stable disease for 3 months. However, 9 months post-operation, the patient developed ascites and was treated with axitinib and nivolumab, but with poor outcomes, dying 12 months post-operation. In case 14 (21), preoperative chemotherapy (gemcitabine + cisplatin for 1 month, and methotrexate, vinblastine, doxorubicin and cisplatin for 4 cycles) failed to control the tumor, leading to a left nephrectomy and regional lymphadenectomy. Postoperatively, the patient received 600 mg/day pazopanib and later switched to 10 mg/day axitinib. However, 15 months later, CT revealed lung and supraclavicular lymph node metastases. Despite continued treatment, the patient remained alive but continued to experience tumor metastasis and recurrence. In case 15 (22), postoperative lung, vertebral and iliac metastases were treated with axitinib and later nivolumab as second-line therapy, resulting in complete remission of metastatic sites. In case 19 (26), preoperative multiple metastases were treated with sunitinib for 7 months with a positive response. In case 20 (27), preoperative vertebral and ipsilateral adrenal metastases were treated with radiation, tumor embolization and radical nephrectomy, but the patient died 3 weeks post-operation due to further metastases. In case 21 (28), preoperative multiple distant and lymph node metastases were treated with a radical nephrectomy and metastasectomy, followed by continuous systemic treatment with tyrosine kinase inhibitors, pazopanib and axitinib, with radiotherapy to all metastatic sites. However, the outcomes were poor and the patient died 2 years later. In case 22 (29), multiple preoperative bone metastases were treated with cytoreductive nephrectomy, followed by ipilimumab and nivolumab combined therapy, resulting in controlled disease, with the patient remaining disease-free. Therefore, immune checkpoint inhibitors appear effective against metastatic MTSCC. In summary, the primary treatment strategy for MTSCC involves radical or partial nephrectomy and for metastatic cases, aggressive surgical treatment, metastasectomy and molecular targeted or immunosuppressive therapy may be effective treatment methods.

In conclusion, based on the literature that is currently available, treatment strategies for MTSCC need to follow a detailed protocol. Before surgical treatment, a thorough imaging assessment is essential to determine the size and location of the tumor, and its invasion of adjacent tissues, and to evaluate the presence of lymph node spread or distant metastasis. After surgery, comprehensive pathological and immunohistochemical analysis of the resected tumor is crucial to identify the tumor grade, especially the presence of high-grade features such as sarcomatoid changes, mitotic activity and areas of necrosis. To develop and optimize comprehensive treatment plans for MTSCC, including selecting the appropriate surgical technique, determining adjuvant treatment options and formulating follow-up strategies, there is an urgent need to expand the scope of research and increase the sample size of cases. Additionally, more genetic and molecular biology studies are necessary to fully understand the pathogenesis and therapeutic targets of MTSCC. Such expanded research will provide deeper insights, making the management of MTSCC more precise and effective.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

XM, JX and JF designed the study and participated in the literature search. XM obtained medical images, contributed to the literature review, and prepared the draft manuscript. XM and JF critically revised the manuscript for important intellectual content and provided general supervision. XM, XY, FY, and ZW were instrumental in revising the manuscript, participating in data analysis and providing treatment

recommendations for the patient. XM and JF confirm the authenticity of all the raw data. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was approved by the Ethics Committee of Zhuji People's Hospital [Zhuji, China; approval no. (2024) MedEthics no. (0115)].

Patient consent for publication

Written consent for publication was obtained from the family of the patient.

Competing interests

The authors declare that they have no competing interests.

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