

Case Report

High-Grade Renal Mucinous Tubular and Spindle Cell Carcinoma

Kyotaro Fukuta^a Ryoichi Nakanishi^b Takahiro Moriyama^a
Hirofumi Izaki^c Takumi Kakimoto^d Takeshi Oya^e Tomoya Fukawa^f
Kunihisa Yamaguchi^f Yasuyo Yamamoto^f Masayuki Takahashi^f
Yasushi Sutou^a Hiro-omi Kanayama^f

^aDepartment of Urology, Tsurugi Municipal Handa Hospital, Tsurugi, Japan; ^bDepartment of Urology, Tokushima Prefectural Miyoshi Hospital, Miyoshi, Japan; ^cDepartment of Urology, Tokushima Prefectural Central Hospital, Tokushima, Japan; ^dDepartment of Pathology and Laboratory Medicine, Tokushima University Graduate School of Biomedical Sciences, Tokushima, Japan; ^eDepartment of Molecular Pathology, Tokushima University Graduate School of Biomedical Sciences, Tokushima, Japan; ^fDepartment of Urology, Tokushima University Graduate School of Biomedical Sciences, Tokushima, Japan

Keywords

Renal mucinous tubular and spindle cell carcinoma · Renal cell carcinoma · Radical nephrectomy

Abstract

Mucinous tubular and spindle cell carcinoma (MTSCC) is a rare subtype of renal cell carcinoma. Although usually indolent, high-grade MTSCC has been reported to exhibit an aggressive clinical course. Herein, we report a case of high-grade renal MTSCC. An 86-year-old man visited our hospital with fever and fatigue. Based on contrast-enhanced computed tomography findings, the patient was diagnosed with clinical stage T2aN0M0 right renal cell carcinoma and underwent laparoscopic radical nephrectomy. Histological examination showed tubular to tubulopapillary structures accompanied by mucinous stroma, suggesting high-grade renal MTSCC. He remained recurrence- and metastasis-free 6 months after nephrectomy. Since high-grade renal MTSCC may have an aggressive clinical course, such patients should be observed carefully after radical nephrectomy.

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Introduction

Mucinous tubular and spindle cell carcinoma (MTSCC) is a rare subtype of renal cell carcinoma (RCC) with specific histological features [1]. Although usually following an indolent clinical course, MTSCC may exhibit high-grade features with an aggressive clinical course and a poor prognosis [1]. The optimal treatment in patients with metastatic MTSCC remains unclear irrespective of advances in immunotherapy for metastatic RCC [2, 3]. Few cases of high-grade MTSCC have been reported due to its rarity. Here we present a case of high-grade MTSCC successfully managed by radical nephrectomy.

Case Presentation

An 86-year-old man visited our hospital for fever and fatigue. Abdominal contrast-enhanced computed tomography (CT) revealed a 72 × 71 mm avascular mass in the lower pole of the right kidney (Fig. 1a, b). We diagnosed right RCC (clinical stage T2aN0M0) and performed a laparoscopic transperitoneal radical nephrectomy. No perioperative complications were observed, and his fatigue gradually improved after the nephrectomy. Macroscopically, a 75 × 70 mm, pale yellowish, solid tumor with necrosis was observed in the lower pole of the right kidney (Fig. 2a, b). Histologically, the tumor was predominantly composed of low-grade cuboidal cells, showing tubular to tubulopapillary structures, sometimes forming tubules merging with bland spindle cells, and accompanied by mucinous stroma with Alcian blue-positive extracellular mucin (Fig. 2c, d). Some of the tumor cells had clear or oncocytic cytoplasm, and foci of foamy macrophages were also observed in the stroma. In the low-grade components, mitoses were rare, and necrosis was absent. Although high-grade components were observed in less than half of the tumor, these components comprised pleomorphic to spindle/sarcomatoid cells with marked nuclear atypia, increased mitoses, and extensive necrosis, and showed infiltrative growth in the kidney without extrarenal extension or vascular invasion (Fig. 2e). Immunohistochemical analysis was diffusely positive for cytokeratin 7 (Fig. 2f) and α -methylacyl coenzyme A racemase (AMACR) (Fig. 2g), and negative for cluster of differentiation 10 (CD-10) (Fig. 2h). Based on these findings, the patient was diagnosed with high-grade MTSCC. He has been followed up carefully for 6 months after nephrectomy without recurrence or metastasis.

Discussion

Renal MTSCC is a rare epithelial neoplasm accounting for less than 1% of all renal tumors with characteristic histological features [4]. It was first reported in 2001 [5] and classified in the World Health Organization (WHO) classification system in 2004 [6], and fewer than 100 cases have been reported so far.

Most MTSCC cases are incidentally detected on abdominal imaging [4]. On imaging, MTSCCs show a hypovascular pattern and require differentiation from other hypovascular tumors such as papillary and chromophobe RCC. This case was an example of a RCC with hypovascularity that was detected by chance on contrast-enhanced CT for the investigation of fever and general fatigue. Distinguishing MTSCC from papillary and chromophobe RCC is challenging, as indicated by our initial suspicion of papillary and chromophobe RCC based on the CT findings and their proportion.

Histopathological diagnosis of MTSCC is also challenging, and immunohistochemical evaluation may be required to differentiate it from papillary RCC. Srigley et al. [7] reported

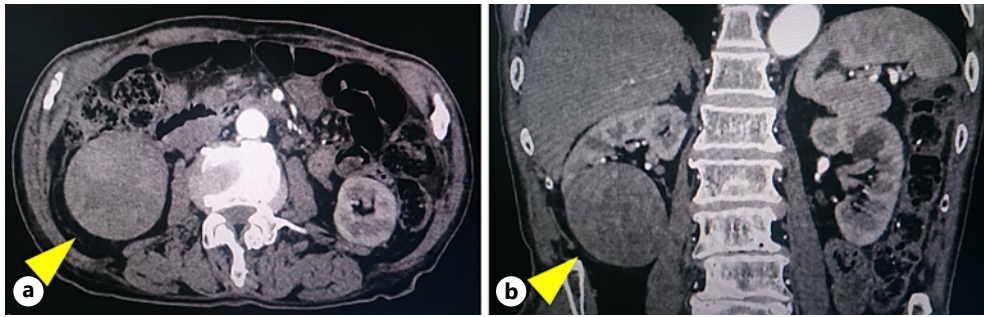


Fig. 1. Results of preoperative abdominal contrast-enhanced CT (**a**, **b**). Abdominal contrast-enhanced CT shows a 72 × 71 mm avascular tumor in the lower pole of the right kidney.

that mucinous change and negative staining for CD-10 helped to distinguish MTSCC from papillary RCC. Sarsik et al. [8] also reported that the immunoreactivity for AMACR and CK7 are similar in MTSCC and papillary RCC (AMACR 100%, CK7 100% and AMACR 100%, CK7 90%, respectively), while that for CD-10 differs (11% and 80%, respectively), corresponding to our case that showed diffuse positivity for AMACR and CK7, and negativity for CD-10.

Although MTSCC is typically indolent, some cases have been reported that exhibit an aggressive clinical course. Yang et al. [1] reported 10 locally advanced/metastatic cases in 33 MTSCC patients. Other series also identified metastasis in 9.5–24% of patients [9, 10]. Moreover, these aggressive MTSCCs have been reported to be accompanied by sarcomatoid changes and high-grade transformation [1, 10, 11]. Yang et al. [1] also reported that 8 of 12 patients (67%) with sarcomatoid transformation and/or epithelial high nuclear grade died of MTSCC. Consequently, this subtype is no longer defined as a low-grade RCC in the 2016 WHO classification of tumors [12].

Despite the limited incidence of cases with high-grade features or aggressive behavior, several previous studies have identified chromosomal alterations and/or cytogenetic features [1, 8, 13]. While most of MTSCCs share common chromosomal alterations including the loss of heterozygosity of chromosomes 1p, 4, 6, 8, 9, 13, 14, 15, and 22 [1, 8, 13], Yang et al. [1] showed that the gain of 1q at the location of some oncogenes was the most common chromosomal alteration distinguishing locally advanced/metastatic MTSCC from indolent MTSCC. This study also provided new evidence that CDKN2A/B deletion and additional complex genomic abnormalities were frequently identified in aggressive MTSCCs [1]. Moreover, the new WHO classification of tumors indicated that CDKN2A/B deletion and additional complex genomic abnormalities may be present in high-grade MTSCCs [14]. Thus, these cytogenetic and/or molecular features may help identify aggressive MTSCCs in the near future.

Although no recurrence or metastasis has occurred, this patient should be followed up carefully, as the tumor showed unfavorable histologic features such as necrosis, solid growth, sarcomatoid transformation, and increased mitoses. The optimal treatment for MTSCC remains unclear due to its rarity. Although most MTSCCs are successfully treated with radical nephrectomy, the efficacy of systemic therapy for metastatic MTSCC is controversial. Larkin et al. [15] presented a case of metastatic MTSCC that responded to sunitinib (tyrosine kinase inhibitor). In addition, Fuchizawa et al. [16] presented a case of metastatic MTSCC that achieved lasting complete remission of bone metastases after cytoreductive nephrectomy followed by the combination of immune-oncology (IO) drugs nivolumab and ipilimumab. They also reported that immunohistochemical analyses of the tumor-infiltrating immune

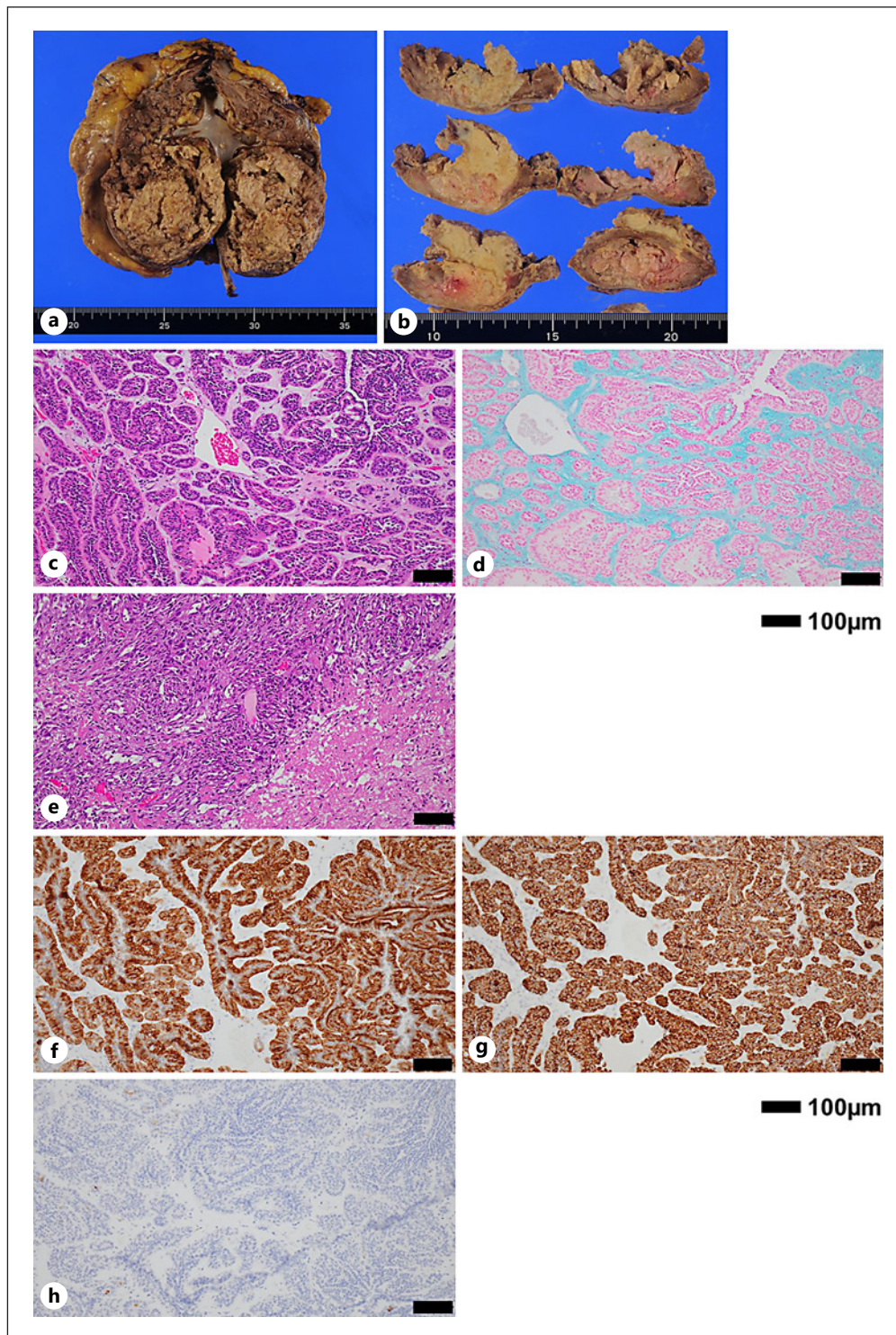


Fig. 2. Macro- and microscopic findings of the renal tumor. **a** A 75 × 70 mm, pale yellow, solid tumor with necrosis is located in the lower pole of the right kidney. **b** The cross-sectional surface of the tumor. **c, d** Hematoxylin and eosin-stained renal tumor, containing tubulopapillary lesions (**c**) and mucinous stroma positive for Alcian blue staining (**d**). **e** High-grade features with diffuse necrosis. **f–h** Immunohistological evaluation of CK7 (**f**), AMACR (**g**), CD-10 (**h**).

cells predicted the efficacy of immune checkpoint inhibitors for nonclear RCCs including MTSCC [16]. We will consider the IO combination or IO-tyrosine kinase inhibitor combination according to the International Metastatic RCC Database Consortium (IMDC) risk classification if recurrence is observed. The limitation of this case report includes the findings of aggressive behavior in high-grade MTSCC have been accumulated by several case reports due to the rareness of MTSCC. Further studies are required to establish the optimal systemic therapy for metastatic MTSCC.

Conclusion

In conclusion, we encountered a case of high-grade MTSCC. Since high-grade MTSCC may have an aggressive clinical course, such patients should be followed up carefully after radical nephrectomy.

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Statement of Ethics

Ethical approval was not required for this study in accordance with local or national guidelines. Written informed consent for publication of this case report and any accompanying images was obtained from the patient.

Conflict of Interest Statement

The authors declare no conflict of interest.

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Author Contributions

Kyotaro Fukuta reviewed the literature and drafted the manuscript. Kyotaro Fukuta, Ryoichi Nakanishi, and Hirofumi Izaki performed the surgery. Tomoya Fukawa, Kuniyoshi Yamaguchi, Yasuyo Yamamoto, Masayuki Takahashi, and Hiro-omi Kanayama critically revised the manuscript. Kyotaro Fukuta, Ryoichi Nakanishi, Takahiro Moriyama, Hirofumi Izaki, Takumi Kakimoto, Takeshi Oya, and Yasushi Sutou performed examinations before and after surgery, provided photographs, and drafted the first version of the manuscript. Kyotaro Fukuta, Ryoichi Nakanishi, Takahiro Moriyama, Hirofumi Izaki, Takumi Kakimoto, Takeshi Oya, Tomoya Fukawa, Kuniyoshi Yamaguchi, Yasuyo Yamamoto, Masayuki Takahashi, Yasushi Sutou, and Hiro-omi Kanayama approved the final manuscript.

Data Availability Statement

All data generated or analyzed in this study are included in this article. Further inquiries can be directed to the corresponding authors.

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