

available at www.sciencedirect.com
journal homepage: www.eu-openscience.europeanurology.com



European Association of Urology

Case Report

Mucinous Tubular and Spindle Cell Carcinoma of the Kidney with Nodal Metastasis Managed with Surgical Resection

Article info

Article history:

Accepted April 20, 2021

Associate Editor:

Silvia Proietti

Keywords:

Kidney neoplasms
Radical nephrectomy
Retroperitoneal
lymphadenectomy

Abstract

Mucinous tubular and spindle cell carcinoma (MTSCC) is a rare renal malignancy that usually follows an indolent course. The few existing reports of metastatic MTSCC show poor response to systemic therapy. Here we describe the unusual case of a 39-yr-old male with MTSCC presenting as a large renal mass with bulky retroperitoneal lymphadenopathy managed with complete resection of disease. He has remained free of recurrence for 1 yr postoperatively. On the basis of the experience reported here, aggressive surgical resection of MTSCC with isolated nodal metastases may be considered for similar patients in the future given the historically poor response rates to systemic therapy.

© 2021 The Authors. Published by Elsevier B.V. on behalf of European Association of Urology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

1. Case report

Mucinous tubular and spindle cell carcinoma (MTSCC) of the kidney is a very rare renal epithelial malignant lesion with fewer than 100 cases reported in the literature to date [1–3]. MTSCC generally follows an indolent course and most cases are managed successfully with partial or radical nephrectomy [4]. However, a small subset of patients present with metastatic disease; given the rarity of this clinical phenomenon, there is no consensus regarding the optimal therapeutic approach for these cases. The literature suggests that MTSCC responds poorly to systemic therapy, and therefore current treatment paradigms which prioritize systemic therapy prior to surgery for advanced renal cell carcinoma (RCC) may not apply to this rare subtype [4–6]. Here we report a case of MTSCC with bulky nodal metastases managed with radical nephrectomy and retroperitoneal lymphadenectomy.

A 39-yr-old otherwise healthy African American male presented to an external institution with gross hematuria. He underwent an abdominal and pelvic computed tomography (CT) scan with intravenous contrast, which revealed a 14-cm left renal mass with bulky preaortic and

para-aortic adenopathy measuring up to 8 cm. A renal mass core biopsy was performed at the external institution. On referral to our center, pathologic reinterpretation revealed MTSCC. Chest CT was negative for metastases and abdominal magnetic resonance imaging did not reveal tumor thrombus (Fig. 1). All laboratory values were within normal limits, placing the patient in the International Metastatic RCC Database Consortium favorable risk category [7].

The patient's care was discussed at our multidisciplinary genitourinary tumor board. Given the large nature of the mass with bulky lymphadenopathy, the absence of distant metastases, the patient's young age with excellent performance status, and prior reports that MTSCC responds poorly to systemic therapy, the consensus decision was to pursue surgical resection. Input from our colleagues in medical oncology and pathology was invaluable and highlights the importance of referral of such complex cases to high-volume centers.

The patient underwent open left radical nephrectomy and bilateral template retroperitoneal lymphadenectomy via a midline incision in October 2019. Tissue anterior to the left common iliac artery was split and rolled, and the

<http://dx.doi.org/10.1016/j.euros.2021.04.006>

2666-1683/© 2021 The Authors. Published by Elsevier B.V. on behalf of European Association of Urology. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).



dissection proceeded cranially on the anterior surface of the aorta until the left renal vein was encountered. The origin of the left renal artery was identified, ligated, and divided. Once the kidney was removed, a full bilateral template retroperitoneal lymph node dissection was performed, with the borders of the renal vessels superiorly, the ureters

laterally, the ureteral crossing of the iliac arteries inferiorly, and the anterior spinous ligament posteriorly. Two inter-aortocaval postganglionic sympathetic nerve fibers were prospectively identified and preserved. All lumbar vessels were divided to ensure complete removal of all retrocaval and retroaortic tissue.

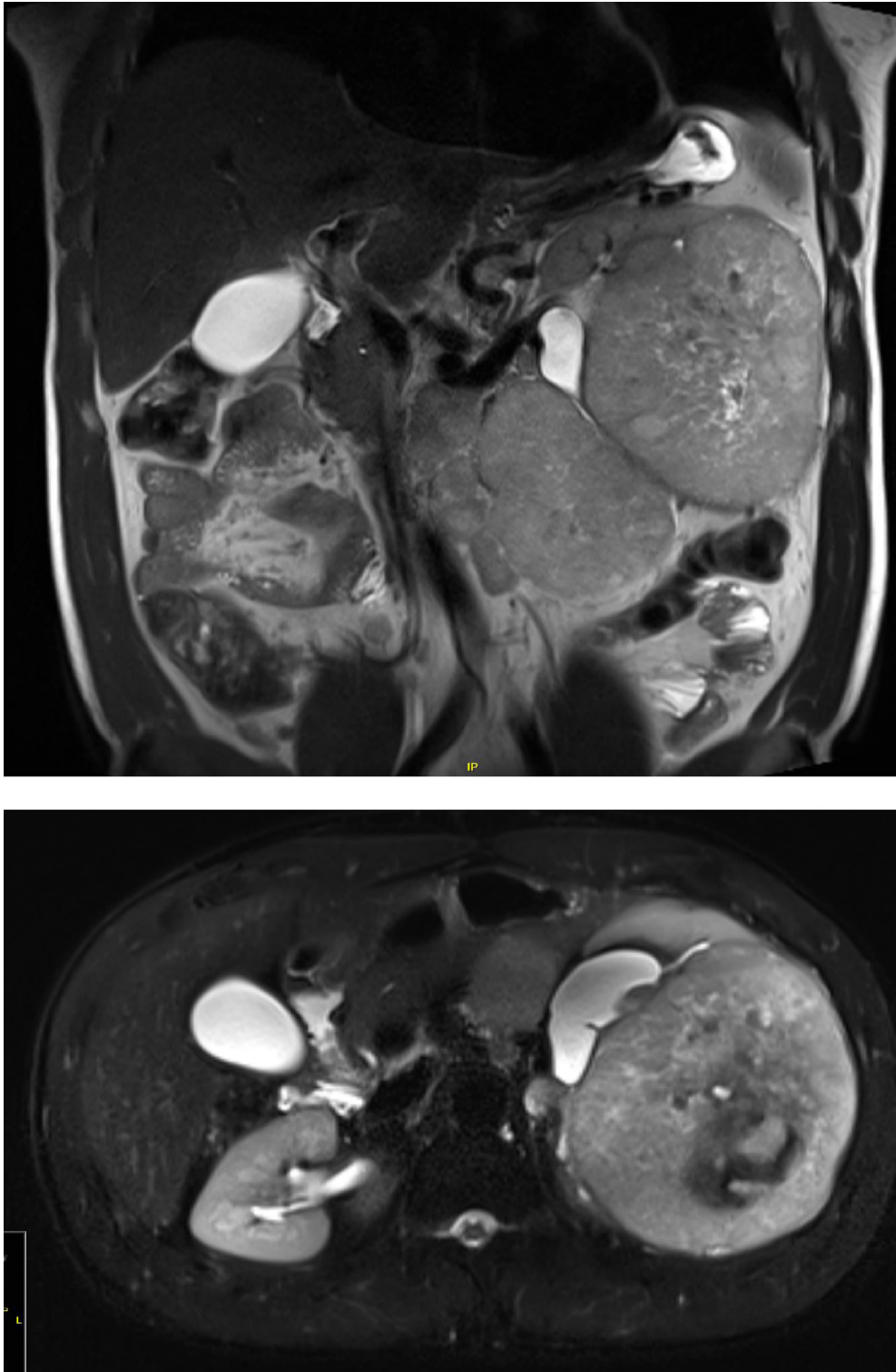


Fig. 1 – (A) Axial and (B) coronal T2-weighted magnetic resonance images showing a large left renal mass and associated retroperitoneal lymphadenopathy.

The patient did well postoperatively and was discharged home on postoperative day 5. He experienced no intraoperative complications (grade 0 on the European Association of Urology guideline classification scheme) and no deviations from the normal postoperative course. Final pathology confirmed a 14-cm MTSCC of the left kidney. Histologically, the tumor exhibited a tubulocystic growth pattern with extracellular mucin, giving a “bubbly” appearance in areas (Fig. 2). Clusters of cells had a spindle cell appearance. The nuclei had low-grade features with prominent nucleoli, without cytologic atypia. The tumor cells were positive for CK7, AMACR, and PAX-8, and negative for CD10, confirming the diagnosis of MTSCC. There was focal necrosis in the tumor (10%) without sarcomatoid elements. Eleven of 31 lymph nodes were positive for metastatic tumor. Final pathology staging was pT2bN1 with negative surgical margins. Adjuvant therapy was not recommended.

Repeat imaging at 1 yr postoperatively revealed no evidence of recurrent disease (Fig. 3). The patient experienced no late postoperative complications, and antegrade ejaculation was preserved.

2. Discussion

To the best of our knowledge, our experience reported here is the first published case of a durable clinical response following surgical resection for MTSCC of the kidney with nodal metastasis. MTSCC of the kidney is an extremely rare disease, with fewer than 100 cases reported since it was recognized as a discrete pathologic entity in 2004 [2]. The majority of cases reported have been in females, with a 2:1 female predominance, and an average age presentation in the sixth decade [1]. Most cases appear to follow an indolent clinical course after resection, with 3-yr overall survival of 85% reported [5].

The differential diagnosis of MTSCC includes papillary RCC, sarcomatoid RCC, smooth muscle tumor, and inflammatory myofibroblastic tumor. The mucinous change seen in MTSCC helps to differentiate it from papillary RCC. CD10 is frequently positive in papillary RCC, but was negative in this case; furthermore, the chromosome 7 and 17 gains and Y chromosome loss that are characteristic of papillary RCC are not found in MTSCC. Sarcomatoid RCC is characterized by large pleomorphic nuclei with significant mitotic activity, which were not observed here. Smooth muscle tumors have a more distinct fascicular pattern and are negative for cytokeratin; this tumor was positive for CK7. Our patient's tumor also lacked the inflammatory background typically seen in myofibroblastic tumors.

A small subset of MTSCC patients may develop metastatic disease, and given the rarity of this clinical scenario, optimal treatment protocols are not well defined. Of the largest reported series of 25 cases, six (24%) involved metastatic disease, with three of these presenting with de novo metastases and two with nodal metastases [5]. High-grade histologic features or sarcomatoid dedifferentiation were found in five of six metastatic cases, compared with

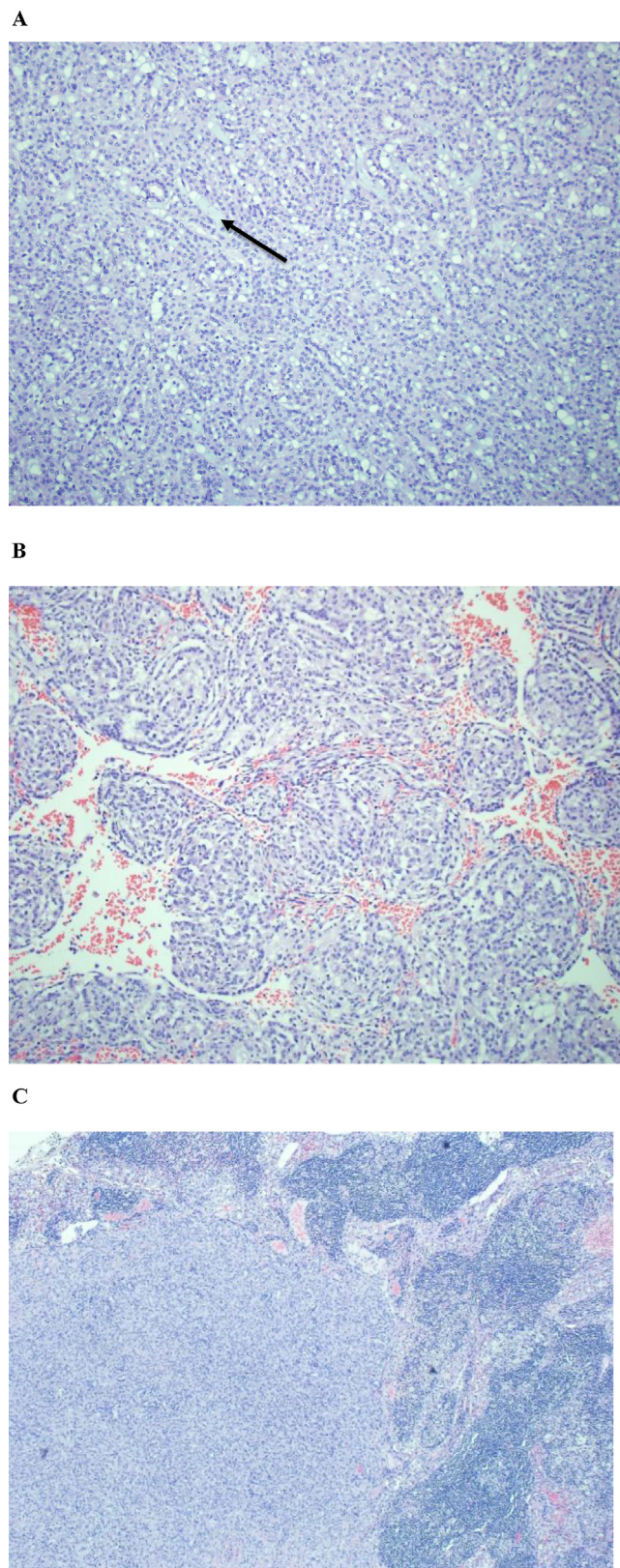


Fig. 2 – Tumor exhibiting (A) a tubulocystic pattern with mucin (arrow), causing a “bubbly” appearance in the tissue (4×), while (B) other areas contained spindle cell pattern (4×). (C) Metastatic tumor within one of the lymph nodes exhibited a similar histologic appearance, consisting of a tubulocystic pattern with mucin interspersed with a spindle cell pattern (2×).

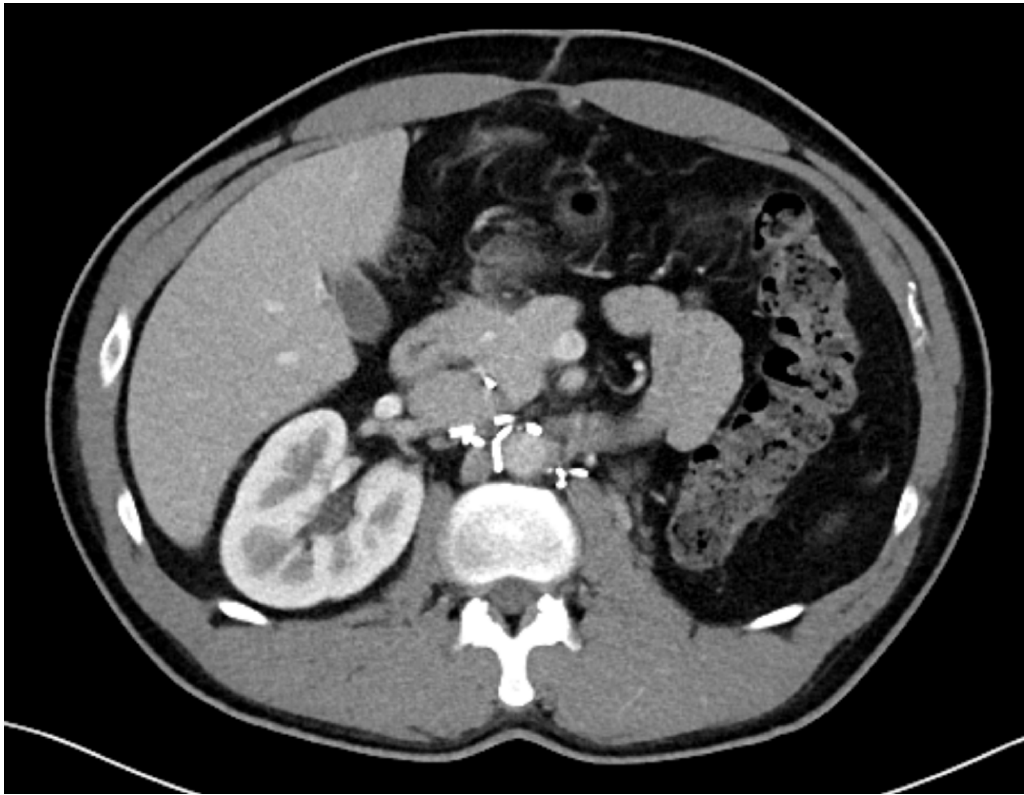


Fig. 3 – Axial 1-yr postoperative computed tomography scan demonstrating no evidence of recurrent disease.

zero of 19 nonmetastatic cases. Responses to systemic therapy were generally poor; of the four patients treated, one showed a meaningful response to sunitinib with a time to treatment failure of 30.6 mo, while the remaining patients treated with tyrosine kinase inhibitors and/or checkpoint inhibitors experienced rapid disease progression with treatment failure within 1–4 mo. Notably, none of the agents used are considered standard of care for metastatic RCC today, and there remains an unmet need to investigate the activity of newer systemic agents for this rare pathologic entity.

The favorable postoperative outcome reported here appears particularly relevant in the context of previous data suggesting the absence of an oncologic benefit from lymphadenectomy among patients with clinically node-positive RCC [8]. Differences in tumor biology may underlie this difference observed, although we acknowledge that follow-up beyond 1 yr is needed to establish the definitive outcome for our patient. Our experience stands in notable contrast to a case of a 43-yr-old male with a 5-cm MTSCC and retroperitoneal adenopathy reported by Isono et al [9]. Despite undergoing radical nephrectomy and retroperitoneal lymphadenectomy, this patient developed peritoneal carcinomatosis within 4 months of surgery and died within 12 months of diagnosis. Of note, this patient's tumor had high grade features, and the marked difference in outcome compared to our patient raises the question of whether adjuvant systemic therapy should be considered

after resection of poorly differentiated MTSCC, even though adjuvant targeted therapy has largely proven to be ineffective. Surgical factors also influence outcome, and although limited details were presented in this paper, we strongly advocate for referral of these cases to high-volume centers as complete removal of all retroperitoneal tissue without violation likely provides the best chance for a favorable outcome.

Our patient presented from an outside institution having already undergone percutaneous biopsy. We do not routinely obtain biopsies for locally advanced renal tumors, but do so selectively if pathologic findings may lead us to offer preoperative systemic therapy. Given this patient's young age and African American race, both renal medullary carcinoma and a primitive neuroectodermal tumor were in the differential, and therefore preoperative biopsy appears prudent. We acknowledge that biopsy cannot reliably identify histologic grade or sarcomatoid features owing to intratumoral heterogeneity. [10] Such decisions highlight the advantages of caring for complex patients at high-volume centers, where multidisciplinary consultation is commonplace and the entire surgical team has expertise operating on large tumors near the great vessels.

On the basis of our experience, and in the context of poor response rates to systemic therapy reported for this extremely rare disease, aggressive surgical management of MTSCC with regional nodal metastases may be considered for similar patients in the future.

Conflicts of interest: The authors have nothing to disclose.

Ethical considerations: No identifiable patient information is included in this case report, so informed consent from the patient was not necessary.

References

- [1] Ferlicot S, Allory Y, Comp erat E, et al. Mucinous tubular and spindle cell carcinoma: a report of 15 cases and a review of the literature. *Virchows Arch* 2005;447:978–83.
- [2] Gaafar A, Valent  C, Echevarria C, Laforga JB, L pez JI. Renal mucinous and tubular spindle cell carcinoma: a clinicopathological study of 4 cases. *Ann Saudi Med* 2006;26:466–70.
- [3] Grigore A, Toma L, Stoicea M, Dinu M, Ardeleanu C. Rare renal tumor—mucinous tubular and spindle cell carcinoma. *Rom J Morphol Embryol* 2012;53:167–71.
- [4] Miura K, Adachi Y, Shirahase T, et al. A case of high-grade mucinous tubular and spindle cell carcinoma. *J Surg Case Rep* 2020;2020:rjaa014.
- [5] Ged Y, Chen YB, Knezevic A, et al. Mucinous tubular and spindle-cell carcinoma of the kidney: clinical features, genomic profiles, and treatment outcomes. *Clin Genitourin Cancer* 2019;17:268–274.e1.
- [6] Psutka SP, Chang SL, Cahn D, Uzzo RG, McGregor BA. Reassessing the role of cytoreductive nephrectomy for metastatic renal cell carcinoma in 2019. *Am Soc Clin Oncol Educ Book* 2019;39:276–83.
- [7] Heng DY, Xie W, Regan MM, et al. External validation and comparison with other models of the International Metastatic Renal-Cell Carcinoma Database Consortium prognostic model: a population-based study. *Lancet Oncol* 2013;14:141–8.
- [8] Gershman B, Thompson RH, Boorjian SA, et al. Radical nephrectomy with or without lymph node dissection for high risk nonmetastatic renal cell carcinoma: a multi-institutional analysis. *J Urol* 2018;199:1143–8.
- [9] Isono M, Seguchi K, Yamanaka M, Miyai K, Okubo K, Ito K. Rapid progression of mucinous tubular and spindle cell carcinoma of the kidney without sarcomatoid changes: a case report. *Urol Case Rep* 2020;31:101162.
- [10] Abel EJ, Carrasco A, Culp SH, et al. Limitations of preoperative biopsy in patients with metastatic renal cell carcinoma: comparison to surgical pathology in 405 cases. *BJU Int* 2012;110:1742–6.

J. Alexander IveyIII^a
Cherise Cortese^b
Bryce A. Baird^a
David D. Thiel^a
Timothy D. Lyon^{a,*}

^aDepartment of Urology, Mayo Clinic, Jacksonville, FL, USA

^bDepartment of Laboratory Medicine and Pathology, Mayo Clinic, Jacksonville, FL, USA

*Corresponding author. Department of Urology, Mayo Clinic, 4500 San Pablo Road, Jacksonville, FL 32224, USA. Tel.: +1 904 953 2000; Fax: +1 904 953 2218. E-mail address: lyon.timothy@mayo.edu (T.D. Lyon).