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Mucinous Tubular and Spindle Cell Carcinoma of the Kidney: A Case Report

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Key Words

Mucinous tubular and spindle cell carcinoma · Renal carcinoma · Kidney

Abstract

Background: Mucinous tubular and spindle cell carcinoma (MTSC) is a rare and newly described type of renal cell carcinoma (RCC) with relatively indolent behavior. Although there are small series of this clinical entity in the literature, its histogenetic origin or line of differentiation remains unclear.

Patients and Methods: A 67-year-old woman was hospitalized for flank pain; imaging studies revealed a 6.5-cm mass in the right kidney. She was referred for fine needle aspiration of the lesion, which showed an epithelial tumor with round to oval nuclei associated with strands of metachromatic stromal tissue. Cytopathologic diagnosis was consistent with RCC.

Results: Subsequent right heminephrectomy was performed and the surgical pathology specimen showed an MTSC of the kidney. The patient has done well postoperatively, with 24 months of benign follow-up.

Conclusion: A precise differential diagnosis between MTSC and other renal carcinomas (e.g. papillary RCC with sarcomatoid transformation) is important for predicting patient prognosis. Even though MTSC is a rare cause of renal masses, it should be included in the differential diagnosis, especially because its imaging might be misleading, mimicking other benign renal diseases. Heminephrectomy is the preferred treatment in these subjects.

Introduction

Beginning in the late 1990s, several groups described a unique group of renal neoplasms composed of cytologically low-grade cells organized in tubules and spindled cords and set in an abundant extracellular mucinous matrix [1–4]. With the codification of these lesions as mucinous tubular and spindle cell carcinoma (MTSC) in the 2004 World Health Organization (WHO) Classification of Tumors of the Urinary System and Male Genital Organs [5], this entity has been accepted as a distinct subgroup of renal cell carcinoma (RCC) [6]. In fact, this classification summarized the achievements and contributions of previous classifications, in particular the University of Mainz (1986) [7] and Heidelberg (1997) [8] classifications. It described categories and entities based on pathologic and genetic analyses [9, 10].

Since the initial recognition of MTSC, several additional cases and small series have been reported. The histopathologic findings have been well characterized and include interconnecting tubular and spindled cells with low-grade nuclei within myxoid/mucinous stroma. According to Parwani et al. [11] and Srigley [5], morphologic, immunohistochemical, and ultrastructural features of these tumors indicate differentiation toward distal nephron segments, possibly the collecting duct or the loop of Henle. Markers of the proximal nephron such as CD10 and villin are generally absent. On the other hand, molecular studies indicate that MTSC lacks alterations associated with more common renal epithelial tumors [11, 12].

Case Report

A 67-year-old woman was hospitalized due to flank pain associated with a right renal tumor that was found during a medical examination. The patient had no medical or family history of any malignancy. Her medical history revealed stress disorders, hypercholesterolemia, diabetes mellitus, hypertension and obesity. Physical and laboratory examinations showed no remarkable findings, except for glucose and cholesterol which were remarkably high.

First, an ultrasound was performed that revealed a mass lesion involving the medial aspect of the right kidney. Subsequently, abdominal computed tomography (CT) revealed an enhanced tumor (6.2 cm) at the lower pole of the right kidney, adjacent to and possibly involving the renal pelvis. No lymphadenopathy was seen.

The primary differential diagnosis based on the radiographic studies was RCC and urothelial carcinoma of the renal pelvis. The patient was referred for fine needle aspiration of the lesion, which was performed with CT guidance. Only 1 aspiration, with 1 pass of the tumor, was performed and the yield was sufficient to make 4 smears; 2 were alcohol-fixed for Papanicolaou staining and 2 were air-dried for Diff-Quik staining. The case displayed atypical-appearing epithelial proliferation thought to be consistent with an RCC and the tumor was diagnosed as a right RCC, cT1aN0M0 according to the tumor-node-metastasis (TNM) system.

Subsequently, the patient underwent right heminephrectomy guided by intraoperative ultrasound (fig. 1). Macroscopically, the tumor was present in the lower pole of the right kidney and exhibited a well-circumscribed, regular, grayish-white cut surface. It was 7.0 × 6.0 × 5.0 cm in size (its maximum diameter was 4 cm), without hemorrhage or necrosis, and did not extend beyond the renal pelvis. Moreover, no invasion of the renal vein or perinephric fat was observed.

Tissue samples were fixed in 10% neutral buffered formalin, embedded in paraffin, and stained with H&E, periodic acid-Schiff and Alcian blue. Pathologic evaluation of the tumor showed that it consisted of cuboidal and oval or spindle cells arranged in tubular and trabecular patterns embedded in a myxoid stroma (fig. 2, fig. 3). Detailed morphologic features as well as their

immunohistochemical profile established with markers of proximal renal tubules (RCC marker antigen, CD15, and α -methylacyl-CoA racemase) and of distal renal tubules [kidney-specific cadherin and cytokeratin (CK) 7], were studied. Immunohistochemical analysis showed positive staining for epithelial membrane antigen (EMA) and CK7. The tumor was also immunoreactive for a CK cocktail including CK7, CK20, CK19, CK8/18. The markers CD10 and vimentin were negative. Alcian blue staining revealed abundant mucin in the intervening fibrous stroma. The final pathologic diagnosis was a renal MTSCC-K, pT1a, INF-a, v(-). After the operation, the patient's convalescence was uneventful and there was no evidence of recurrence after 24 months of benign follow-up. The patient was not subjected to adjuvant therapy (chemo-radiotherapy or immunotherapy).

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Discussion

MTSC is a recently recognized subtype of low-grade RCC that has characteristic histologic morphology and appears to be distinct from the more common RCC on molecular grounds as well [13, 14]. Proper classification is important, because this tumor behaves in a benign fashion in the overwhelming majority of cases. As a result, it may be confused with metanephric adenoma and fluorescence in situ hybridization (FISH) is useful in distinguishing benign from malignant renal neoplasms. Although generally considered uncommon, the proportion of renal tumors that are MTSC may be higher because of prior misclassification as compact/solid variants of papillary RCC or unclassified RCC [15].

MTSC was first recognized as a specific entity in the WHO 2004 Classification [10, 15]. It is a rare type of RCC composed of low-grade polymorphic renal epithelial neoplasms with mucinous tubular and spindle cell features. It has been suggested that MTSCs are reminiscent of and derived from the loop of Henle or collecting duct. Patients exhibit a wide age range of 17 to 82 (mean 53) years and a female predominance with a male to female ratio of 1:4. MTSC is sometimes associated with nephrolithiasis. On the basis of cytomorphologic features, the differential diagnosis in this case would include conventional (clear cell) RCC, sarcomatoid (spindled) RCC, and papillary RCC. Additionally, nonepithelial tumors such as angiomyolipoma should also be considered. They usually present as asymptomatic masses often found on ultrasound. Occasionally, patients may present with flank pain or hematuria.

Macroscopically, MTSCs are well circumscribed and have grey or light tan cut surfaces. Histologically, they are composed of tightly packed small elongated tubules separated by pale mucinous stroma. These tumors simulate leiomyoma or sarcoma. Many of them had been previously diagnosed and classified by pathologists as variants of solid papillary carcinomas with compressed and elongated papillae, metanephric adenomas and sarcomatoid carcinomas. Individual cells are small with cuboidal or oval shapes and low-grade nuclear features. Occasionally, areas of necrosis form cell deposits and chronic inflammation may be present. The mucinous stroma is highlighted with stains for acid mucins. These tumors also have a complex immunophenotype and stain for a wide variety of CKs including low-molecular-weight keratins (CAM 5.2, MAK 6), CK7, CK18 and CK19. EMA is commonly present and vimentin and CD15 staining may be seen. Markers of the proximal nephron such as CD10 and villin are generally absent. The spindle cells show epithelial features like tight junctions, desmosomes,

microvillus borders and occasional tonofilaments. In the literature, cytogenetic data indicate various chromosomal losses and gains but no loss of 3p or trisomy 7 and/or trisomy 17. Using comparative genomic hybridization and FISH, there is a characteristic combination of chromosome losses generally involving chromosomes 1, 4, 6, 8, 13 and 14, and gains of chromosome 7, 11, 16 and 17. The prognosis seems to be favorable; only 1 example has been reported with metastasis and this tumor is best considered as a low-grade carcinoma.

Prognosis was favorable in our case; during 24 months of follow-up, the renal function of the reminiscent right and left kidney was sufficient. The radiologic investigation showed no local or systematic recurrence. Further investigation is required to determine the frequency and true prognosis of these tumors which are easily identifiable morphologically.

Finally, it is very important for diagnostic pathologists to recognize MTSC on differential diagnosis because papillary RCC with low-grade spindle cell foci or clear cell papillary RCC have been recently reported. In conclusion, it could be said that any suspicious mass that might be revealed in an asymptomatic patient should be thoroughly examined in order to exclude and cure early malignant tumors.

Disclosure Statement

The authors declare that they have no competing interests.



Fig. 1. Intraoperative ultrasonography.

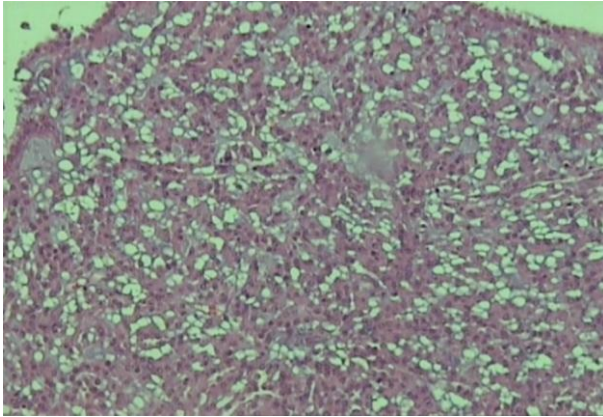


Fig. 2. MTSC with a highly packed appearance and extracellular mucinous material.

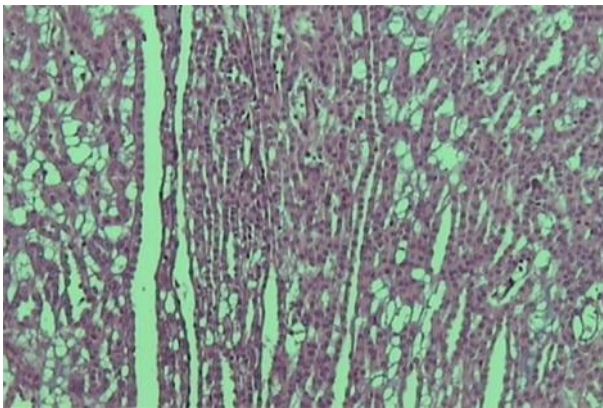


Fig. 3. Cord-like morphology of the neoplasm.

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