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Cytological and Ultrastructural Findings of Mucinous Tubular and Spindle Cell Carcinoma: A Case Report

Takahashi M*, Fukuda M, Yamada M, Yuzawa K, Yoshino M, Yamamoto M, Aso T, Unno K, Takahashi K, Mizguchi K, Nagashima Y and Kawamoto M

Department of Diagnostic Pathology, University Hospital, Mizonokuchi, Teikyo University School of Medicine, Kawasaki-Shi, Kanagawa-ken, Japan

Abstract

The 2016 World Health Organization Classification of Tumors recognized mucinous tubular and spindle cell carcinoma (MTSCC) as a rare histological variant of renal cell carcinoma (RCC). To date, a limited number of studies have reported this tumor concerning histology, and only a handful of those have reported cytological and ultrastructural features. This study aims to report a case of MTSCC in a female patient in her early 50s who presented with a chief complaint of gross hematuria, and to discuss relevant cytological and ultrastructural findings. Imaging revealed a 30 mm tumor in the left kidney, suggesting the presence of RCC, and left nephrectomy was performed. In addition, scratched cytology of tumor surface revealed clusters of tumor cells with clear cell boundaries extending two-dimensionally in papillary or dendritic arrangements with interspersed blood vessels and stromal components that were stained light green. Histologically, the tumor was composed of small and uniform cells arranged in elongated tubular architectures and spindle fascicles with occasional papillary structures; the stroma was acidophilic and contained colloidal substances that tested positive for Alcian blue and periodic acid-Schiff stain. Concordant with immunohistochemical results, the tumor was diagnosed with MTSCC. Furthermore, transmission electron microscopy revealed tubular structures with microvilli, abundance of mitochondria in the cytoplasm, cellular interdigitations and widened interstitium.

Keywords: Renal tumor; Mucinous tubular; Spindle cell carcinoma; Cytology; Transmission electron microscopy

Introduction

Incorporated as a rare histological variant of renal cell carcinoma (RCC) in the 2004 World Health Organization Classification of Tumors, mucinous tubular and spindle cell carcinoma (MTSCC) reportedly occurs in less than 1% of all renal neoplasms [1,2]. While a majority of PubMed results feature clinical or histopathological images of MTSCC including immunohistochemical findings, only 2 literatures discuss cytology [3,4] and 4 reports describe electron microscopic finding [5-8]. This study aims to report our experience with a patient with MTSCC and discuss our tumor cell findings, including microstructures, observed by transmission electron microscopy.

Case Report

The patient is a female in her early 50s who presented with gross hematuria. Clinical work-up included computed tomography scan and magnetic resonance image which revealed 3 cm mass in the left kidney (Figure 1). The mass was diagnosed with renal cell carcinoma clinically, and a left radical nephrectomy was performed. After 17 months follow-up without any adjuvant therapy, the patient has not had recurrence.

Cytological findings

Prior to fixation, cut surface of the tumor was scratched, then Papanicolaou and Giemsa stains were performed. Smears showed abundant clusters of tumor cells with inflammatory cell background composed mainly of plasma cells with a few foamy macrophages. The clusters were composed of monotonous tumor cells and matrix, some of those had fibrovascular core. The tumor cells showed vague cell boundary, round to ovoid nuclei with small nucleoli (Figures 2A and 2B). Tumor cell clusters were admixed with long dendritic matrix stained light green with Papanicolaou stain and Giemsa stain revealed that most tumor-cell clusters had metachromatic mucoid material (Figures 3A and 3B). Urine cytology obtained prior to the operation showed one small clusters of small atypical cells of obscure origin containing densely stained nuclei against a bloody/inflammatory background, which were classified as “indeterminate significance” (Figure 4).

Gross findings

Macroscopic examination revealed a 3.5 × 3.0 cm well circumscribed yellowish-white solid tumor (Figure 5).

Histological findings

Histologically, the tumor was surrounded by a fibrous pseudo capsule. The tumor cells nearly the uniform size of renal tubular epithelium (Fuhrman grade 2) form tubular or slit-like structures (Figures 6A and 6B). The stromal mucinous and colloidal substances were positive for Alcian blue and Periodic acid-Schiff stains (Figure 7).

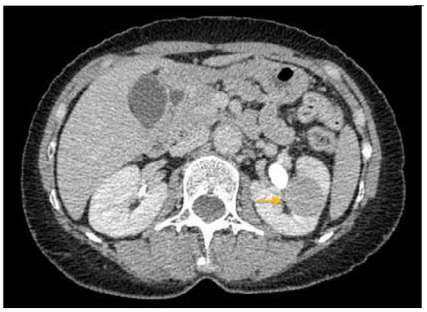

Figure 1: Contrast-enhanced abdominal CT scan; Uniform formation of the internal structure of the renal mass is observed (arrow).

***Corresponding author:** Takahashi M, Department of Diagnostic Pathology, University Hospital, Mizonokuchi, Teikyo University School of Medicine, Kawasaki-Shi, Kanagawa-ken, Japan, Tel: +81-44-844-3333; E-mail: mitakahashi@med.teikyo-u.ac.jp

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Some areas displayed clear cytoplasm resembling clear cell RCC, and some other areas displayed spindle cells (Figure 8).

Immunohistochemical stains for cytokeratin 7 (CK7), high molecular weight CK (HMW-CK), PAX8, cytokeratin (clone CAM5.2), and α-methyl acyl CoA racemase (AMACR) were positive and that CD10 and vimentin were negative; therefore, the tumor was diagnosed with MTSCC (Figure 9).

Ultra structurally, abundant collagenous stroma laid along tumor cells. Other than those, tumor cells also formed tubular structures with microvilli. Interdigitation between the tumor cells were observed and numerous mitochondria were in the cytoplasm (Figures 10A-10D). Neurosecretory granules were not detected.

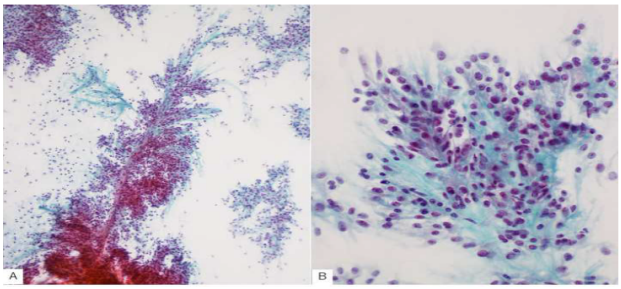

Figure 2: Scratched cytology of the tumor. A: Papillary or dendritic shaped tumor cell clusters accompanied by fibrovascular core (Papanicolaou stain, 20x); B: The nuclei of tumor cells were round, oval, or spindle-shaped, and the nucleoli is small, but clearly defined (Papanicolaou stain, 40x).

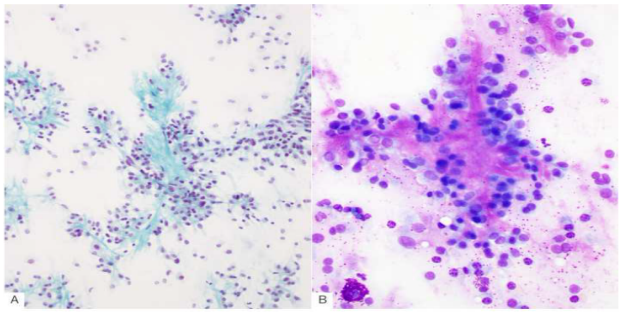

Figure 3: Scratched cytology of the tumor. A: Interspersed fibrillary material stained light green (Papanicolaou stain, 20x); B: Abundant metachromatic mucoid material in tumor cell cluster (Giemsa stain, 20x).

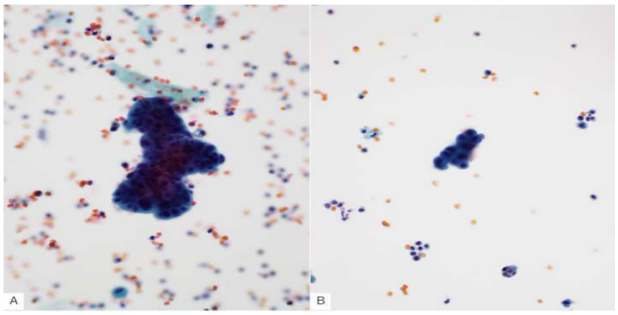

Figure 4: Urinary cytology. A: Few clusters of branching papillary structure composed of small urothelial-like cells are observed (Papanicolaou stain 60x); B: A cluster of small cells with obscure origin (Papanicolaou stain, 60x).

Figure 5: Macroscopic observations of the left renal tumor; Formalin-fixed cut surface of left kidney shows 3.5 cm yellowish-white solid tumor with a clear border.

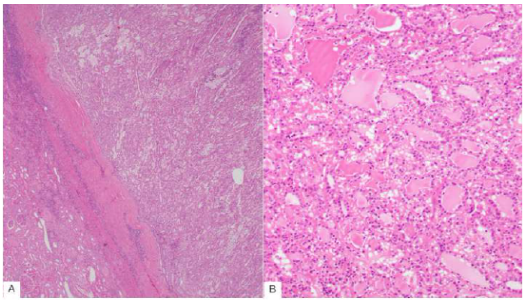

Figure 6: Histological findings. A: Pseudocapsular structure is observed on the surface of the tumor (H and E stain, 4x); B: Follicle like tubular structure and slit-like structure are observed (H and E stain, 4x).

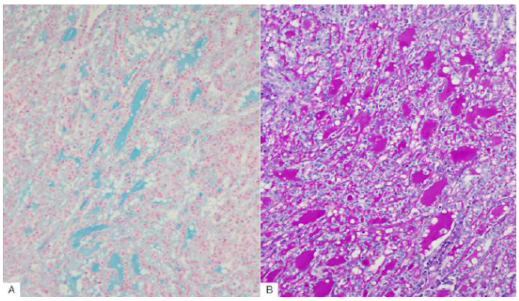

Figure 7: Mucinous substance observed both slit-like region and inside the tubular structure. A: Mucinous substance is stained blue with Alcian blue stain (20x). B: Mucinous substance is stained purple-magenta with Periodic acid–Schiff stain (20x).

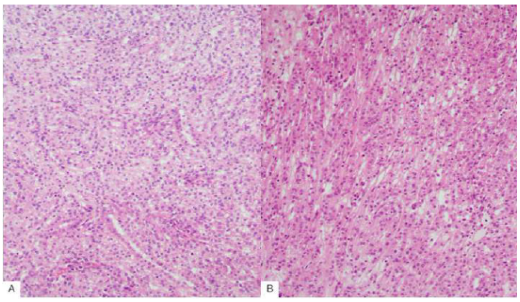

Figure 8: Partial findings of tumor cells. A: Translucent cytoplasm resembling clear cell RCC (H and E stain, 20x). B: Spindle shape in some parts of the tumor cell (H and E stain, 20x).

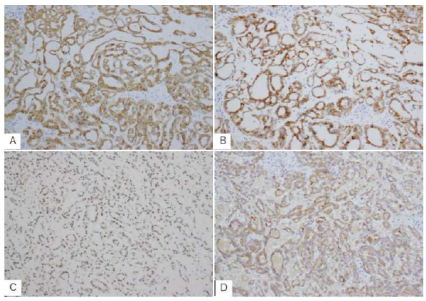

Figure 9: Immunohistochemical findings. A, CK7 (20x); B, HMW-CK (20x); C, PAX8 (20x); and D, AMACR (20x) are all shown positive reaction.

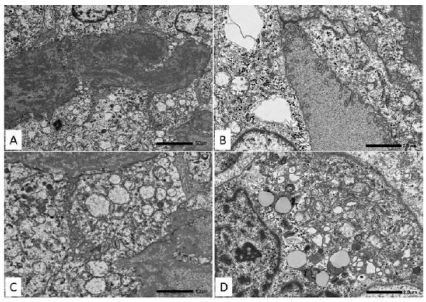

Figure 10: Ultrastructural findings. A: Widened interstitium with fibrous change (scale bar: 50 μm). B: Microvilli along glandular lumen (scale bar: 2 μm). C: Cellular interdigitation (scale bar: 13 μm), D: Abundant mitochondria within the cytoplasm of tumor cell (scale bar: 2 μm).

Discussion

Although exceptional poor prognosis is reported [7,9], MTSCC is generally classified as a tumor of low-grade atypia with a favorable prognosis compared to clear cell RCC [1-10]. In this context, understanding of histological feature of MTSCC from other type of tumors is important.

Regarding cytological feature of MTSCC, Huimiao et al. reported that in the background of mucinous stroma, there were small-to-large clusters and branching sheet formations of cells with uniformly shaped nuclei and small nucleoli or pseudopapillary clusters that had no visible fibrovascular core [3]. In our case, papillary clusters with fibrovascular core were observed in addition to the preceding cytological findings. Furthermore, we observed mucinous stroma with metachromasia by Giemsa staining, and this is characteristic and may be useful to differentiate MTSCC from other renal tumors. Ultrastructural findings observed in our case, such as tubular structures with microvilli along glandular lumens, abundant mitochondria within the cytoplasm and cellular interdigitations between the adjacent tumor cells, were partially described in previous reports [5-8]. Metachromatic mucinous material in cytological specimen may correspond to collagenous stroma observed by transmission electron microscope, and colloidal substance in tubular structure observed by Alcian blue and Periodic acid-Schiff stain is compatible with the amorphous material observed in tubular structure surrounded by microvilli, but the latter is not precisely identified as epithelial mucin produced by the tumor cells ultrastructurally due to the lack of apparent intracytoplasmic mucin pool. Although the suggestion of a normal counterpart of MTSCC cells have been described in some previous reports, it is still controversial [10]. Tubular structure observed in our case is reminiscent of renal tubules, but microvilli along glandular lumen have short length and low density compared to proximal tubule, and not quite similar to distal tubule and collecting duct. We cannot suggest an appropriate normal counterpart of MTSCC cell other than "may be renal tubular cell", and further elucidation including genetic features is needed to answer this question.

Conclusion

Since MTSCC was classified as a rare histological variant of RCC, the cytological findings about MTSCC were described in only 2 reports. In our case, scratched cytology of tumor surface revealed clusters composed of monotonous tumor cells, matrix with fibrovascular core and stroma had components stained light green by Papanicolaou stain and metachromatic material by Giemsa stain. These characteristics may be useful to differentiate MTSCC from other renal tumors. Furthermore, although ultrastructural findings such as tumor cells formed tubular structures with microvilli, interdigitation between the tumor cells and numerous mitochondria in the cytoplasm were observed, we cannot suggest an appropriate normal counterpart of MTSCC cell.

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