Mucinous Tubular and Spindle Cell Carcinoma of the Kidney: Touch Imprint Cytologic and Histologic Findings — A Case Report —

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The recent WHO classification has recognized mucinous tubular and spindle cell carcinoma (MTSCC) as a distinct entity of renal cell carcinoma, exhibiting a mixed pattern of tubules and a surrounding spindle cell proliferation within a myxoid stroma, with low-grade nuclear features. A 51-year-old woman had an incidentally discovered renal mass. Radiologic examination revealed a large, well defined mass in the lower pole of the right kidney; a right radical nephrectomy was performed. Imprint cytologic smears from fresh surgical specimens showed cellular, cohesive clusters with thick, broad trabecular arrangements and branching structures. On high power fields, the tumor was composed of round-to-oval low-grade nuclei with vesicular chromatin and small nucleoli. The tumor cells had indistinct borders and pale, eosinophilic cytoplasm, In some areas, round-to-elongated tubular structures and spindle cell patterns were noted. Chronic inflammatory cell infiltration was noted, along with a mucinous background and occasional psammoma bodies. Neither significant cytologic atypia nor mitosis was seen.

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Key Words: Kidney neoplasms, Carcinoma, Cytology, Kidney tubules

INTRODUCTION

Mucinous tubular and spindle cell carcinoma (MTSCC) of the kidney is a recently described, low-grade renal cell tumor that has been recognized as a distinct entity by the World Health Organization 2004 classification.¹ Since its initial recognition, several additional cases and small case series¹ have been reported. The histopathologic findings are well characterized and include interconnecting tubular and spindled cells with low grade nuclei within a myxoid and mucinous stroma. Ultrastructural studies suggest the presence of distal nephron differentiation, and molecular studies indicate that MTSCC lacks alterations associated with more common renal epithelial tumors.² The tumor has a good prognosis; thus, a correct diagnosis is very important. There is little information in the literature regarding the cytopathologic findings in MTSCC.³-⁶ We...
describe the imprint cytologic characteristics and histologic findings associated with this rare tumor.

**CASE**

**Clinical Presentation**

A 51-year-old woman visited the urology department with an incidentally discovered renal mass. She denied urinary and constitutional symptoms, and her past medical history was unremarkable. CT scan showed a well defined, exophytic, heterogeneous, high attenuation mass (Fig. 1). Laparoscopic radical nephrectomy was performed. The patient received no adjuvant treatment and was well 2 months after nephrectomy. The specimen exhibited a huge lobulating contour. The cut surface showed a well-circumscribed, round, gray-white to yellow mass measuring $7.4 \times 6 \times 5.5$ cm in size. Foci of hemorrhage were found, but no necrotic areas were noted (Fig. 2). A number of touch imprint smears were performed on the surgical specimen, and these were stained with hematoxylin and eosin. The surgical specimen was fixed in 10% neutral buffered formalin and embedded in paraffin.

**Cytologic Findings**

On the basis of the histologic diagnosis, we reviewed the smears to investigate the morphologic correlation between cytologic and histologic features. The touch imprint smear showed moderately cellularity. On low power fields, branching pseudo-papillary structures were observed. Closer inspection revealed that most tumor cells were bland-appearing with fragile cytoplasm and uniform round-to-oval nuclei. Some tumor cells had characteristic long process-like cytoplasm. Others formed a pseudo-papillary pattern lacking a fibrovascular core. A transition from a monolayered epithelial sheet to a spindle cell pattern was noted (Fig. 3A). A small portion of the tumor cells formed characteristic tubule-like structure (Fig. 3C). Spindled whirling pattern areas were also noted (Fig. 3E), as were occasional psammoma bodies (Fig. 3G). Tumor cells were admixed with chronic inflammatory cells, including plasma cells, eosinophils, and lymphocytes, all against a mucinous background (Fig. 3I). Scattered foamy histiocytes and mast cells were also observed. Neither mitosis nor atypia was noted. In focal areas, tumor cells displayed prominent nucleoli corresponding to Fuhrman grade 2. In general, these tumor cells had bland-looking low-grade features.
Fig. 3. Comparison of cytology (A, C, E, G, I) and Histology (B, D, F, H, J). (A) Cytologic smear shows transition from monolayered epithelial sheet to spindle cell pattern. (B) Histologic section shows abrupt transitions between the tubular (left half) and spindled (right half) areas. (C) Cytologic smear shows round to elongated tubule-like structure (arrow). (D) Histologic section shows elongated tubules separated by pale mucinous stroma, the tubules are composed of small bland-looking cuboidal cells with pale eosinophilic cytoplasm. (E) Cytologic smear shows spindle cell pattern with round to oval low nuclear grade. (F) Histologic section shows spindle cell areas with chronic inflammatory cell infiltration. (G) Cytologic smear shows psammoma bodies, (H) Histologic section shows a psammoma body. (I) Cytologic smear shows chronic inflammatory cells including plasma cells, eosinophils, lymphocytes in mucinous background. (A-I : H&E). (J) Alcian blue staining of histologic section reveals extracellular mucinous materials (Alcian blue).
Histologic Findings

On microscopic examination of the kidney tumor, distinctive histologic features were found. The tumor was well demarcated with a non-infiltrative border. Two different patterns were present: tubule structures and vaguely swirling spindle cell areas. There was an abrupt transition between the tubular and spindled areas composed of similar cells (Fig. 3B). Tubular structures made up the predominant pattern. In tubular areas, elongated tubules were separated by pale mucinous stroma, and the tubules were composed of small, bland-looking cuboidal cells with pale eosinophilic cytoplasm (Fig. 3D). The nuclei were usually spherical or oval and had a few small chromatin clumps and small nucleoli. Mitotic figures were not identified. Whirling spindle cell areas were also found in small portions (Fig. 3F). In spindle cell areas, there were short interlacing fascicles and vague storiform areas. The tumor cells were also bland-looking, with no mitosis or pleomorphism noted. No papillary structures or desmoplastic stroma were noted, either. Interestingly, tumor tissues were infiltrated by lymphocytes, plasma cells, and eosinophils (Fig. 3F). Occasional foamy histiocytes were present within the tumor, particularly in the mucinous areas. A few mast cell aggregates were observed. Scattered psammoma bodies were noted (Fig. 3H). No necrosis was noted, nor was vascular or lymphatic invasion observed. The tumor was limited to the kidney (pT2).

Special staining and immunohistochemical findings

Alcian blue (pH 2.5) and PAS staining of the MTSCC revealed the presence of extracellular mucinous material in the tubular areas (Fig. 3J). However, the extracellular mucinous material of the tumor was negative for mucicarmine staining. The MTSCC tumor cells showed positive staining for vimentin. Epithelial membrane antigen and cytokeratin 7 (CK7) were strongly expressed in tubular cells compared to the spindle cell area, CD10 was not expressed in tumor cells. The Ki-67 index showed less than 1% positive expression.

DISCUSSION

The recent WHO classification system has recognized MTSCC as a distinct entity under the heading of renal cell carcinoma (RCC) that exhibits a mixed pattern of tubules within a myxoid stroma along with spindle cell proliferation and low-grade nuclear features. The reported cases have shown a female predominance and benign clinical outcomes.7 MTSCC can be easily diagnosed based on histology alone, because of its characteristic histologic appearance. However, MTSCC is morphologically diverse, and diagnostic difficulty may arise when the histologic features are not typical. To date, fewer than 100 cases of MTSCC have been reported.1 Moreover, the cytologic findings of MTSCC have been addressed in only a few cases.3-6

The cell lineage and origin of MTSCC still remain undetermined. Initially, Parwani et al. suggested that the morphologic and ultrastructural configurations of MTSCC are similar to the normal loop of Henle; they therefore believed that the tumor originated from the distal nephron.2 However, more recently, there have been reports showing immunohistochemical overlap with papillary RCC, suggesting proximal tubular differentiation. Thus, some reports have suggested that MTSCC actually represents a variant of papillary RCC with spindle cell features.7-8 Our study showed that CD10, which is more specific to the proximal tubules, was not expressed in tumor cells. A previous study showed that the majority of MTSCCs exhibited no immunoreactivity with CD10.7 We found that CK7 was positive in tubular and spindle cells. In the non-neoplastic kidney, strong cytoplasmic reactivity with CK7 is present in the distal convoluted tubules.1 However, the prior observation of high CK7 expression in both papillary RCC and MTSCC was confirmed. Therefore, CK7 is of no value in differentiating MTSCC and papillary
RCC.\(^7\) Expression of p53 and overexpression of Ki-67 may correlate with aggressive behavior and may be related to lymph node metastasis.\(^1,10,11\) In the present case, the Ki-67 index showed less than 1% positive expression, as the majority of MTSCCs have a benign presentation.\(^2,7\) Diagnosis is clinically important to avoid overtreatment. The differential diagnosis includes clear cell RCC, sarcomatoid RCC, papillary RCC, and collecting duct carcinoma. Additionally, non-epithelial tumors such as angiomylipoma should also be considered. Immunohistochemical, cytologic, and histologic findings are very helpful in formulating a differential diagnosis for these tumors.

With regard to cytologic investigation, the branching pseudo-papillary arrangements seen in MTSCC can also be seen in conventional RCC. However, clear cell RCC would be expected to have more cells with vacuolated cytoplasm and perivascular nesting of tumor cells. The branching pseudo-papillary structures of MTSCC also resemble papillary RCC, but MTSCC shows a relative lack of foamy cells and true vascular cores.\(^6\) In clear cell RCC and papillary RCC, the myxomatous stroma is absent.\(^12\) Sarcomatoid RCC is also a consideration because of the spindled morphology of many of the tumor cells. However, MTSCC lacks significant anisokaryosis and atypia, with prominent nucleoli in spindled areas.\(^11\) In the present case, focal nuclear pleomorphism and prominent nucleoli were seen. However, neither significant anisokaryosis nor atypia was noted. Thus, these findings should not be used as exclusion criteria.\(^4\) Collecting duct carcinomas exhibit tubular, sheet-like structures, and the population of papillary structures is more scant. The tumor cells have granular cytoplasm. The nuclei are large and highly atypical and contain increased coarse granular or vesicular chromatin with prominent nucleoli.\(^13,14\)

On the basis of the cytologic findings in our case, we noted that MTSCC has distinctive features. The tumor cells generally had bland cytologic features with oval to spindled nuclei with long process-like cytoplasm. Most tumor cells lacked prominent nucleoli. However, in focal areas, nuclear grooving and prominent nucleoli were observed. The most important findings were distinct tubular structures and whirling spindle cell patterns. An admixture of tumor cells and chronic inflammatory cells such as plasma cells, lymphocytes, eosinophils, and mast cells was also characteristic. A few foamy histiocytes and occasional psammoma bodies were also present.

MTSCC appears to exhibit distinctive cytomorphologic features, including a uniform population of epithelial cells with round nuclei against a background of abundant mucinous material. According to these cytologic findings, aspiration cytology should be applicable for the diagnosis of kidney tumors. Imprint cytology, obtained from fresh surgical specimens at the time of frozen section diagnosis, is helpful in classifying this rare renal tumor that has an indolent clinical course.

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