Case Report

Clinicopathological characteristics of kidney mucinous tubular and spindle cell carcinoma

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Abstract: Kidney mucinous tubular and spindle cell carcinoma (MTSpCC) is a rare renal low-grade pleomorphic epithelial neoplasm featured by tubular and spindle cells with a relatively indolent behavior. This study was designed to clinicopathologically characterize two cases of kidney MTSpCC. Similar to other tumors, the data showed the diagnosis of MTSpCC relies on histological examination. Tumor cells stained strongly for CK19, CK20, and CK7 within the epithelioid component. Whereas evaluating MTSpCC clinically showed no specific symptoms, analyzing MTSpCC microscopically showed multiple elongated tubular branches of tumor cells that are closely arranged in cord-like manner under lightly stained myxoid stroma. MTSpCC also has the spindle cell area; the single tumor cell is small and nucleus round or oval. Immunohistochemical analysis of cytokeratins, electron microscopy, or genetic tests all improves the diagnosis.

Keywords: Kidney, mucinous tubular, spindle cell carcinoma, pathology, immunohistochemistry

Introduction

Most common kidney cancers are renal cell carcinoma (RCC) and urothelial cell carcinoma (UCC), histologically. Clinically, kidney cancer symptoms are hematuria without pain or an abdomen mass, and additional symptoms include tiredness, loss of appetite, weight loss, or persistent abdomen pain. Distinct types of kidney cancers have different risk factors and treatment options [1], and survival of kidney cancer also depends on the type and stage of the disease. Thus, it is crucial for the differential diagnosis of kidney cancer and detection of them early in early stages. In this study, we characterized kidney mucinous tubular and spindle cell carcinoma (MTSpCC) that is rare in the kidney. MTSpcc is a low-grade pleomorphic renal epithelial neoplasm that is featured by tubular and spindle cells with a relatively indolent clinical behavior [2]. At the present, there have not been many studies on this type of kidney cancer since it is very rare. Herein, we report and discuss the clinicopathological and electron microscopic features in the characterization of MTSpCC.

Materials and methods

Case report

Case 1: A 26-year-old female patient was admitted to our hospital (Third Xiangya Hospital of The Central South University, Changsha, Hunan, China) because of vaginal bleeding and a cervical mass determined by colposcopy (Figure 1A). A pre-surgery CT scan revealed a huge solid mass within the parenchyma of the lower pole of the left kidney, suggesting kidney cancer. Platinum-based chemotherapy was given to the patient for the 16 days prior to surgery and during surgery. A solid mass with a size of 15 × 10 cm was found, which pushed the left kidney forward, and thus, a radical resection of the left kidney was performed. Grossly, the uterus size was 9 × 6 × 4 cm, the diameter of the cervix was 5 cm and the posterior lip of the cervix was hard and cauliflower-like, and the left kidney was 11 × 9 × 8 cm in size with a tumor mass of 8.5 × 6 × 5 cm localized at the lower pole. The tumor lesion was round, relatively homogenous texture with a clear border. The cut surface showed light brown color. After surgery, the patient further received two cycles of
Kidney mucinous tubular and spindle cell carcinoma

Platinum-based chemotherapy. During the seven-month-follow-up, there was no tumor recurrence or metastasis observed.

Case 2: A 52 year-old female patient had complained of gross hematuria and back pain. A CT scan revealed a huge solid mass within the parenchyma of the lower pole of the left kidney (Figure 2A). Surgery was performed on the patient and the tumor was resected and the lesion size on the left kidney was 7 × 6 × 6 cm. The tumor mass was round and had a clear border with a light brown cutting surface. After the seven-month post-surgery follow-up, there was no tumor recurrence or metastasis.

Histochemistry and Immunohistochemistry

The renal tumor tissue obtained from nephrectomy was fixed in 10% formalin and embedded in paraffin. Three-micrometer-thick sections were prepared and stained with hematoxylin-eosin stain and Alcian blue stain. Moreover, to assess gene expression, we performed immunohistochemistry according to a previous study [2]. Four-micrometer-thick tissue sections were immunostained in an automated immunostainer using antibodies against cytokeratin 7 (OV-TL12/30), cytokeratin 19 (A53-B/A2.26), CD56 (56C04), CD10 (MX002), Rcc (PN-15), Vimt (SP20), ALK (5A4), and Ki67 (SP6). All antibodies were obtained from THERMO (Waltham, MA, USA).

Electron microscopy

Fresh tissues were sliced into fragments of less than 1 mm³ and fixed in 3% glutaraldehyde in 0.1 M cacodylate buffer, pH 7.3, followed by fixed in 1% osmium tetroxide in the same buffer and 0.5% uranyl acetate in 0.1 M acetate acetic acid buffer, pH 5. After being dehydrated in ethanol and passaged epoxypropane, the tissue samples were embedded in epoxy resin. Ultrathin sections were prepared and stained with uranyl acetate and lead citrate and then examined under a transmission electron microscope and photographed.

Results

Clinical characteristics (include CT or other exam)

Clinically, MTSpCC showed no specific symptoms. A huge solid mass was protruding out of the kidney border, with a large cross section. The value of the plain CT scan for the mass was about 36-40 HU. No obvious enhancement was observed during an enhancing scan and the value was about 50-82 HU, which was lower than the normal renal parenchyma. The border between the mass and renal parenchyma was clear. No enlarged lymph nodes were observed within the region of renal hilum and retroperitoneal area.
Kidney mucinous tubular and spindle cell carcinoma

Histology

The border between the renal tumor and surrounding tissue was clear and the mass was observed to grow expansively (Figure 2B). The tumor was composed of small and elongated tubular cells that were closely arranged, and myxoid stroma cells were located between the tubular cells. The cells within the tumor were arranged cord-like. Some lumens were not clear and no obvious tubular structure was observed because the lumens were small, elongated, and in collapsed manner. The tubular cells described resembled spindle cells (Figure 2C, 2D). At higher magnification, the tumor cells were observed to be cubic or columnar, arranged in tubular manner, with less cytoplasm, relatively homogenous size, obvious nucleolus, insignificant nuclear atypia, and rare mitotic figures. In contrast, tumor cells of the cervix in Case 1 displayed obvious cellular atypia (Figure 1B). Foam cells and mild lymphocytic infiltration were observed within focal lesions. The tumor cells stained strongly for CK19, CD56, and CK7 within the epithelioid component, but were negative for Vimentin, CD10, ALK, and RCC. Ki67 scores (cell proliferation index) were approximately 3-5%. Under a transmission electron microscope, spindle cells showed characteristics of epithelial differentiation. Large amount of mitochondria and endoplasmic reticulum were observed in the cytoplasm. Lipid droplets were seldom observed. The nucleus was small and round, with nucleus easily observed. Microvilli were observed on the cavity surface and the cells were closely arranged (Figure 3).

Discussion

Adenosquamous cervical cancer is not clinically rare, but MTSpCC recently was a novel renal...
Kidney mucinous tubular and spindle cell carcinoma

epithelial tumor defined in WHO Classification of Tumors of the Urinary System and Male Genital (2004 edition) [2]. Parwani et al. [3] referred MTSpCC as a low-grade malignant renal epithelial mucinous tumor that differentiated towards distal renal units. Razoky et al. [4] described the histopathological and genetic characteristics of this tumor and speculated that it originated from the distal renal units for the ultrastructure of MTSpCC and resembles the Henle’s loop of distal renal units. However, other studies indicated that expression of proximal tubule-related marker AMACR in MTSpCC almost reached 100% in this kind of tumor [5]. Therefore, the true origin of MTSpCC still requires further exploration. However, Hes et al. [5] suggested that development of MTSpCC could be related to a kidney stone, because of the total 11 cases they reported, three patients had kidney stone history and regional lymph node metastasis occurred in one patient [6].

After reviewing the literature, we can summarize the clinical and pathological characteristics of MTSpCC as the following: i) Clinical characteristics: MTSpCC is often occurring in female patients [3, 4, 6, 7]. Among all 44 cases reviewed, 27 were for female patients and 17 were for male patients (a ratio of 1.58), but there is no age preference (age ranged from 22 to 84). Most patients have no specific complaints about symptoms, but certain patients complained of back pain, recurring urinary tract infection, and hematuria. Ultrasound examination showed an abdominal mass and most was single. ii) Pathological characteristics: Tumor mass is usually localized in the renal parenchyma with most tumor lesions being away from the medulla, and thus in within non-central region. The cutting surface of the tumor lesion is gray or light brown. The tumor lesion is usually homogeneous with micro focal hemorrhage, but necrosis is rare and the border between the mass and surrounding tissue is clear, without an intact capsule. Microscopically: Multiple small and elongated branches arranged cord-like tumor cells could be observed in lightly stained myxoid stroma and area of spindle cells could also be observed. PAS staining shows that the tubular was surrounded by the basilar membrane. The tumor cell is small with cubic or oval shape, less cytoplasm that is transparent, pale and acidophilus. The nuclear grade of the tumor is usually low and size of nucleolus was low to medium. Necrosis is occasionally observed and foam cell infiltration and chronic inflammatory cell infiltration are common. Myxoid stroma staining revealed acidic mucus with positive Alcian blue. Previous studies did report high nuclear grade MTSpCC [8, 9]. The main pathological characteristics were defined as enlarged nucleus of tumor cells and obvious cell atypia. In addition, special MTSpCCs were also reported [10, 11]. However, the sarcomatoid area, such as fibrosarcoma-like, was observed besides the typical appearance of the tumor as described above. A large area of necrosis within the tumor lesion is common and tumor cell proliferation index is high. Cytokeratin CK7 and CK19, and Rcc could be expressed in both MTSpCC and renal cell carcinoma. However CD10 is lowly expressed in MTSpCC, indicating that CD10 may be a useful marker to differentially diagnose these tumors [12, 13].

iii) Electron microscopic examination shows epithelial differentiation of MTSpCC, but this technique has less application value compared to regular pathological examination. iv) Genetic test: FISH show losses on chromosomes 1 and 8, and gains of chromosomes 7 and 17 [14]. A previous study [15] showed that high-grade mucinous tubular and spindle cell carcinoma had a gain of chromosomes 1q, 7, 16, 19q, and Y, but loss of chromosomes 1p, 6p, 8p, 11q [del (11) (q23)], and 13. G-band karyotype showed gain of chromosomes 2, 3, 5, 7, 12, 16, and 20, but loss of chromosome 15. MTSpCC was defined by WHO Classification as a novel renal epithelial tumor;
Kidney mucinous tubular and spindle cell carcinoma

thus, awareness and differential diagnosis are the keys to make MTSpCC diagnosis. For differential diagnosis, we have to distinguish it from: A) Papillary renal cell carcinoma, showing invasive tumor growth. Histologically, papillary tumor cells are arranged in papillary/trabecular configuration or papillary/entity configuration. The typical papillary configuration has clear branch with neoplastic epithelial cells coated. The fibrous axis composed of small blood vessels located in the center and foam cells could easily be observed within the axis. Both small and round nucleus that was not clear and large and irregular nucleus with coarse chromatin could be observed. In contrast, the border of MTSpCC has clear border between the tumor lesion and the surrounding tissue. Single tumor cells are small, cube-shaped or oval with less cytoplasm. B) Collecting duct carcinoma, typically occurs in the central area of the kidney with small masses located in renal pyramids. Collecting duct carcinoma often has irregular tube or structure of papillary configuration and fibrous stroma. Usually, the border is not clear and the tumor grows invasively within the renal parenchyma [16]. In contrast, MTSpCC is localized in renal parenchyma and away from the medulla and in a non-central region. The border between the mass and surrounding tissue was clear, although there is no an intact capsule. C) Metanephric adenoma of the kidney: Branched and staghorn-like tubules were often observed in metanephric adenoma. Abundant tumor cells within metanephric adenoma were closely arranged, with unclear stroma that was loose and edematous. Papillary structures were observed in 50% of the metanephric adenoma cases. The large and blunt papillary structure observed within the capsule resembles immature glomeruli. Psammoma bodies could always be observed. Diffused positive of CK and EMA could not be observed. However, MTSpCC cells often have cubic shape, less cytoplasm unobvious nuclear atypia, and long tubular structure with loose stroma, which resembles metanephric adenoma but myxoid background could not be observed in metanephric adenoma. D) Metastatic cancer: Tumor cells displayed obvious cellular atypia with invasive and multi-nodular growth patterns.

Renal carcinoma is notorious for its low sensitivity to chemotherapy and radiotherapy. However, in the last years, several new treatment modalities have been introduced. With this progress, exact histological diagnosis have become of prime practical importance [17]. MTSpCC usually has a good prognosis. During the seven and 23-month-follow-up of these two cases, tumor recurrence or metastasis was not observed. However, previous studies [8, 18] did report distant metastasis that caused death in a case with high grade MTSpCC. If there is a metastasis, MTSpCC with sarcoma differentiation often causes pulmonary or renal hilar lymph nodes metastasis. Pathological examination revealed similar metastases as in sarcoma [18]. However, another recent study showed distant metastasis of classic MTSpCC [9]. Thus, it is speculated that MTSpCC without necrosis, karyokinesis and cellular atypia may also be invasive and cause metastasis.

In summary, MTSpCC is a rare kidney tumor, and pathology and additional biomarkers could make the diagnosis. MTSpCC usually has a good prognosis, but it does metastasize distantly and treatment options include surgery and chemotherapy.

Disclosure of conflict of interest

None.

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Kidney mucinous tubular and spindle cell carcinoma


