

Mixed Epithelial and Stromal Tumor of the Kidney – A Case Report

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A 45-year-old woman had gross hematuria without flank pain for two weeks. She visited our hospital and a renal echo showed a heterogenous mass on the left kidney. Abdominal computed tomography showed a multicystic tumor, about 7 cm, on the left renal pelvis and the proximal ureter. The tumor was enhanced after contrast injection. Ureteroscopy showed an intraluminal polypoid tumor. Cystic renal cell carcinoma or urothelial carcinoma was suspected preoperatively. We performed a hand-assisted laparoscopic nephroureterectomy, and the post-operative course was uneventful. The pathology report demonstrated that the tumor was composed of an admixture of stroma and flattened to cuboidal urothelium. The tumor stromal cells expressed both estrogen and progesterone receptors, and no malignant cells were found. There has been no recurrence or deterioration of the patient's renal function since surgery. We suggest keeping in mind the diagnosis of mixed epithelial and stromal tumor of the kidney when encountering perimenopausal women with renal cystic tumors. (*Chang Gung Med J* 2010;33:693-8)

Key words: mixed epithelial and stromal tumor of the kidney, kidney neoplasm, hematuria, laparoscopic nephroureterectomy

Mixed epithelial stromal tumor of the kidney (MESTK) is a rare genitourinary tract tumor. It was first described by Michal and Syrucek in 1998.⁽¹⁾ This benign tumor demonstrates a marked female predominance, and has a connection to female sex hormones.⁽²⁾ We report a 45-year old Taiwanese woman who presented with painless hematuria. A malignant renal tumor was suspected according to the pre-operative image study. However, the pathology report after the operation revealed MESTK.

CASE REPORT

This 45-year-old woman presented with gross hematuria for two weeks. There was no fever,

dysuria, or flank pain. In addition, the results of her physical examination showed no remarkable abnormality, and her laboratory examination was generally normal except for hematuria in the urinalysis. She had worked in a barbershop about 15 years ago, and had frequent contact with hair dye. She denied hormone therapy but her left ovary had been removed via laparoscopy because of a ruptured chocolate cyst in 1997. Her older brother had a history of buccal cancer.

Renal ultrasonography revealed a heterogenous mass on her left renal pelvis and the lower calyx, which caused hydronephrosis. Further abdominal computed tomography showed a multi-cystic lesion, about 7.8 x 5.5 x 6.4 cm, arising from the lower pole

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of the left kidney and extending to the renal pelvis and proximal ureter. It resulted in remarkable hydronephrosis and decreased cortex thickness (Fig. 1). There was no enlarged lymph node in the paraaortic or pelvic region. The favored diagnosis included advanced renal cell carcinoma or urothelial carcinoma because of enhancement of the heterogeneous mass after contrast injection.

After a detailed discussion with the patient and her family, she decided to have the possible malignant tumor surgically removed. The ureteroscopy showed an intraluminal polypoid tumor, and a hand-assisted left nephroureterectomy was performed smoothly. There was a well circumscribed cystic tumor, about 7.0 x 5.5 x 3.4 cm, protruding into the renal pelvic cavity (Fig. 2). Pathology reports demonstrated that the tumor was composed of cystic lesions of various sizes and shapes (Fig. 3A). The cysts were lined by flattened to cuboidal urothelium (Fig. 3B), and there was no atypia no mitotic activity. The stroma was composed of spindle fibers and smooth muscle (Fig. 3C). Immunohistochemically, the tumor stromal cells displayed expression of

estrogen, progesterone, and desmin receptors. (Fig. 3D, E and F). According to the pathologic features, a diagnosis of mixed epithelial and stromal tumor of the kidney was made.

The patient was discharged from the hospital four days after the operation. There was no recur-

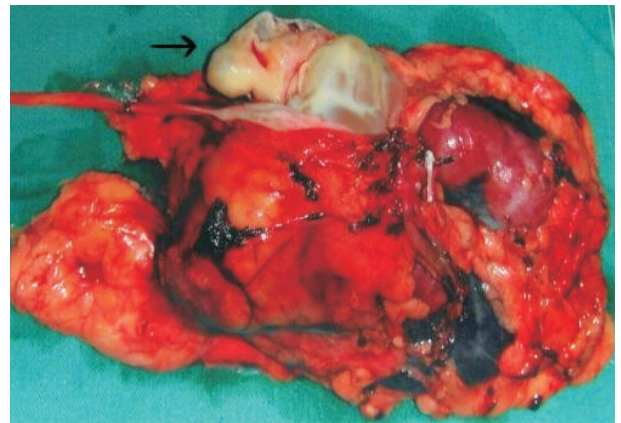


Fig. 2 The extracted kidney is about 11.0 x 5.5 x 5.0 cm and weighs 113 grams. The tumor, shown by the arrow, is composed of solid parts and multiple cysts of variable sizes.

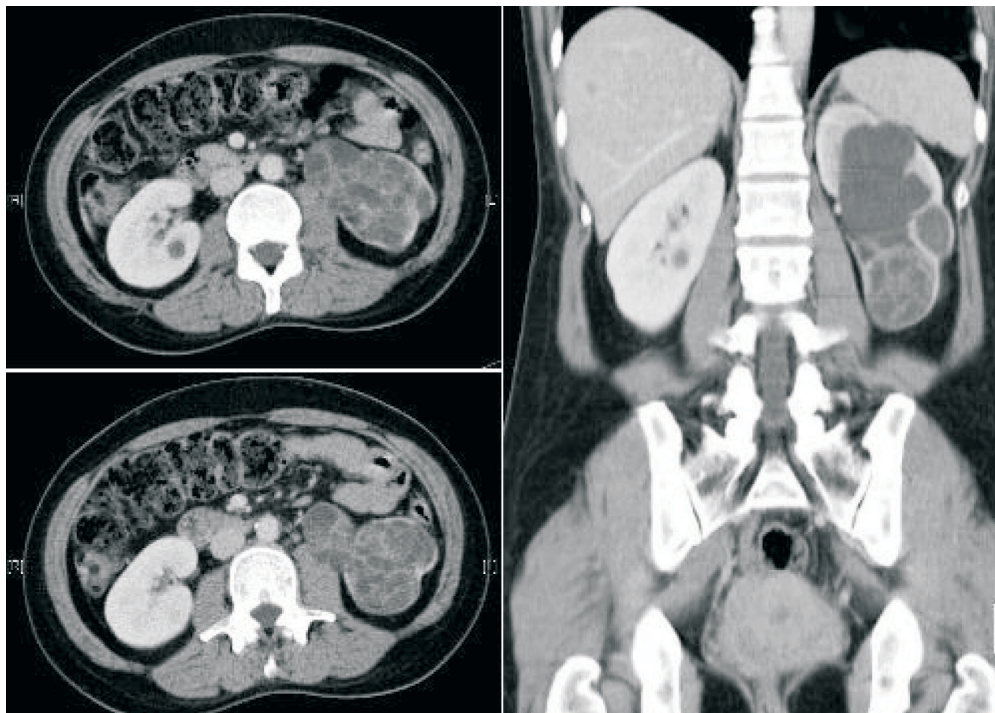


Fig. 1 Abdominal computed tomography with contrast showing a cystic lesion, about 7.8 x 5.5 x 6.4 cm, on the left kidney, resulting in remarkable hydronephrosis and mass effect on the left psoas muscle. There is no enlarged lymph node in the paraaortic or pelvic region.

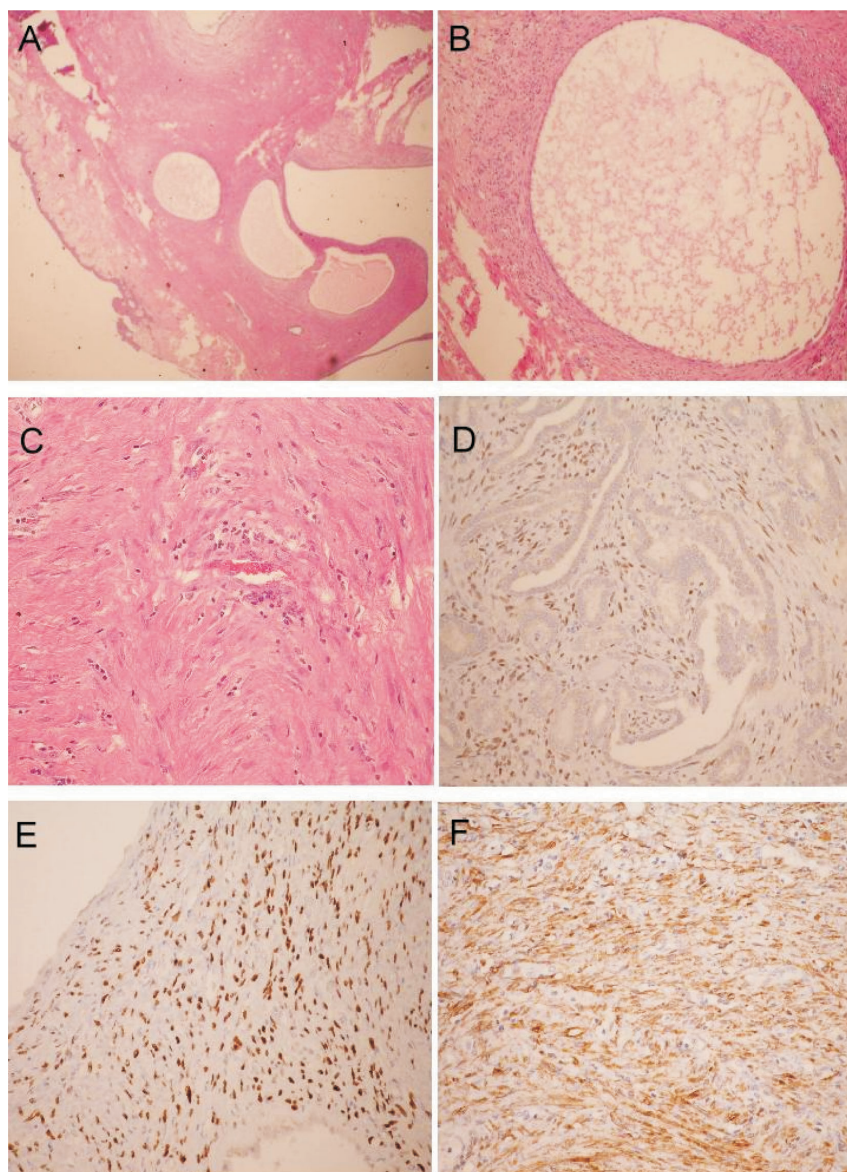


Fig. 3 (A) A hematoxylin and eosin stain shows that the tumor is composed of cystic lesions of different sizes and shapes. (B) The cyst is lined by flattened to cuboidal urothelium. (C) The stroma is composed of spindle cell fibers and smooth muscle. (D) Stains for estrogen receptors, and (E) progesterone receptors are positive. (F) The stroma shows a positive reaction against desmin.

rence during the one year follow-up. Her renal function remains normal as of this report.

DISCUSSION

MESTK is a rare and recently defined entity. It was first proposed by Michal and Syrucek in 1998.⁽¹⁾

This biphasic benign tumor is composed of spindle cell stroma and epithelial components ranging from small tubules and gland-like structures, to cystic-like cavities. Most of the reported patients with MESTK have been middle-aged women, patients with long term oral contraceptive use, and those with hyper-estrogenic conditions.⁽²⁾ Also, this tumor usually

occurs in perimenopausal women, and the mean age for occurrence is about 46 years.^(2,3) In the past, it was usually misinterpreted as a cystic nephroma, cystic hamartoma or mesoblastic nephroma. However, recent studies have shown that MESTK is a unique renal neoplasm.⁽⁴⁾ MESTK is different from cystic nephroma because the former contains grossly apparent solid tissue, whereas the latter has no obvious solid area.⁽⁵⁾ Also, MESTK differs from a renal pelvis cystic in that MESTK is not a developmental disorder and the spindle cells are mostly muscular rather than fibrous.⁽⁵⁾ Furthermore, MESTK has stromal and epithelial components, which differentiates it from a mesoblastic nephroma, which is a pure mesenchymal tumor. Besides, MESTK occurs mostly in female adults while mesoblastic nephroma affects both genders equally.⁽⁵⁾

The presenting symptoms of MESTK may include flank pain, hematuria, or urinary tract infection-like symptoms, although up to a quarter of cases have been identified incidentally.⁽⁶⁾ The expression of estrogen and progesterone receptors in the stromal cells suggests that female sex hormones are an important factor for the development of MESTK. This is evident in a recent report which revealed 62% estrogen receptor and 85% progesterone receptor expression in the stromal component of MESTK.⁽⁷⁾ Although the pathogenesis of MESTK is not clear, it has been hypothesized that this tumor is related to the presence of fetal primitive mesenchyme in the kidney or the abnormal migration of ovarian stromal cells during embryogenesis. It is possible for ovarian stromal cells to become incorporated in metanephritic tissue, which could then be activated and transformed by hormone imbalance.⁽⁷⁾ This hypothesis helps explain why most patients with MESTK were either perimenopausal women or women who were under long-term female hormone therapy. The tumor epithelium reacts to cytokeratin AE1/3 and epithelial membrane antigen. The stromal cells are positive for mesenchymal markers such as vimentin, CD 34, and desmin, which are very important immunohistochemical clues under the microscope.⁽⁸⁾ The definite criteria of image diagnosis of MESTK have not been well established, and this benign tumor usually masquerades as advanced renal cell carcinoma or urothelial carcinoma pre-operatively, especially when the tumor is large. However, Hee et al. suggested that MESTK should be considered upon encountering a

single solid or solid and cystic renal mass with delayed contrast enhancement, especially in perimenopausal women or patients who have received female hormone therapy.⁽⁹⁾

Our patient was a 45-year-old perimenopausal woman, and her main symptom was painless gross hematuria. The tumor stromal cells displayed expression of estrogen, progesterone, and desmin receptors. These characteristics were compatible with previously reported features, although she had not taken oral contraceptives or received hormone therapy. She had a history of an ovarian chocolate cyst, which is a hallmark of endometriosis. Nevertheless, the relationship between the development of MESTK and endometriosis is unclear and we found no related reports.

Although this disease is predominant in women, four cases in men have been reported. Three of the reported patients had received long term estrogen therapy for prostate adenocarcinoma.^(2,5) Colombo et al., however, presented a case of non-hormone-induced mixed epithelia and stromal tumor of the kidney in a man, which is even rarer.⁽⁸⁾

Overall, about 70 cases of MESTK have been reported so far in the literature, and we could find no report of recurrence.⁽⁷⁾ According to these past studies, MESTK generally behaves in a benign fashion. However, a small number of cases have shown malignant transformation.⁽¹⁰⁻¹³⁾ All the patients reported in the malignant cases were female, with a mean age of 43 years (24-56 years). In addition, 5 of the 7 patients who experienced malignant transformation died within an average follow-up time of 20 months. The latest case reports by Jung et al. in 2008 documented two patients with follow-up periods of 8 and 36 months who both survived the disease without recurrence.⁽¹³⁾

Malignant MESTK cells have large nuclei with chromatin condensed around the nuclear membrane. The tissue has small cubic cells forming vascularized solid sheets with few signs of cohesion, producing a mosaic pattern. Fortunately, the patient in our case study had relatively uniform, round to oval nuclei without atypia or mitotic activity.

In conclusion, it is important to bear in mind the diagnosis of mixed epithelial and stromal tumor of the kidney in a perimenopausal woman with a renal cystic tumor. Those who have received female hormone replacement therapy are especially at high risk.

Despite the benign behavior of this neoplasm in the majority of cases, malignant transformation is still possible. In addition, most reported cases of MESTK occurred in Caucasians. Only one other case has been reported in a Taiwanese subject.⁽¹⁴⁾ Most Taiwanese urologists are not familiar with this new entity. In order to better determine the etiology, pathology, and optimal treatment of MESTK, more native serial studies are needed.

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腎臟混合上皮(及)基質腫瘤—病例報告

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腎臟混合上皮(及)基質腫瘤是很少見的泌尿系統腫瘤。我們報告一位45歲女性，主訴無痛血尿兩週。腹部電腦斷層顯示左腎及近端輸尿管有一個約七公分的多囊性腫瘤。輸尿管鏡檢查發現左側近端輸尿管內有瘰肉狀的病灶。術前鑑別診斷包括腎細胞癌或尿路上皮癌。我們實行腹腔鏡左側腎臟輸尿管切除術。術後病理檢查發現此腫瘤乃由上皮細胞與基質細胞共同組成，並無發現惡性細胞。此腫瘤對雌性素、黃體激素受體染色均呈陽性反應，故病理報告為腎臟混合上皮(及)基質腫瘤。術後病人情況穩定，門診追蹤並未發現復發或腎功能惡化。(長庚醫誌 2010;33:693-8)

關鍵詞：腎臟混合上皮(及)基質腫瘤，腎臟腫瘤，血尿，腹腔鏡腎臟輸尿管切除術

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