Mixed epithelial and stromal tumor of the kidney: A case report

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Abstract. Mixed epithelial and stromal tumor (MEST) is a rare neoplasm of the kidney, affecting mostly women at menopausal age. While few cases of malignant transformation have been described in the literature, MEST is usually considered a benign tumor with minimal risk of local recurrence or distance metastases. The current study presents a case of a 18-year old male patient with a cystic tumor of the left kidney incidentally diagnosed on magnetic resonance imaging of the heart performed for other reasons. The patient underwent a partial nephrectomy, with perioperative course being uneventful. The pathology report revealed MEST of the kidney. No local recurrence nor disease progression have been observed in the patient during the one-year follow-up period. The present case report is evidence that may help in developing guidelines on the management of patients with benign renal masses.

Introduction

Mixed epithelial and stromal tumor (MEST) is a rare neoplasm of the kidney (1-9), with ~100 cases having been described in the up-to-date literature (1,2,4-5,9,10).

It has been recognized as a renal tumor since its introduction to the classification by World Health Organization in 2004 (4). MEST is most commonly diagnosed in women of menopausal age (1-11). Most of neoplasms were related to women with history of long estrogen therapy. Due to this information it can be considered that hormones are a risk factor for this tumor. The clinical presentation of MEST is similar to typical renal tumor (1,2,4-5,6,8,10-12). However approximately ¼ of known diagnosed MESTs were asymptomatic. Current treatment strategy is based on surgical operation. Imaging studies usually reveal a cystic lesion with soft tissue components (1-12). Microscopic findings consist of epithelium with mesenchymal tissue (1-12). The risk of malignant transformation in a patient with MEST is highly dependent on the individual characteristics of a tumor, but in vast majority of patients, the neoplasm was of benign character and the prognosis is good (1-12).

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Case report

An 18-year-old male patient was incidentally diagnosed with a lesion of the left kidney on magnetic resonance (MR) imaging of the heart, performed as part of diagnostic evaluation for a history of exercise-induced syncope episodes. Apart from familiar hypertension, treated with lisinopril, the past medical history of the patient was insignificant. The MR imaging revealed a 3-cm, well-demarcated, non-protruding, complex cystic lesion with a soft tissue component adjacent to its wall, located in the upper pole of the left kidney. The lesion was showing high signal intensity on T2-weighted imaging but no contrast enhancement (Fig. 1). The presence of the lesion was then confirmed on multiphase abdominal computed tomography (CT) scan (Fig. 2). The attenuation of the lesion on native-phase images was 30 Hounsfield units (HU), with minimal and non-significant contrast enhancement on subsequent phases, which was interpreted as indicative of cystic nature of the lesion. However, medially within the cyst a 7-mm soft-tissue tumor was revealed adjacent to the cystic wall, showing a moderate contrast-enhancement, which raised suspicions for malignant character of the lesion. The patient did not report hematuria, flank pain nor any other symptoms that could have indicated a renal tumor.

The patient was scheduled for surgery and a partial nephrectomy was performed, leading to a complete excision of the lesion. The perioperative course was uneventful. Gross examination of the nephrectomy specimen demonstrated 3 cm multicystic tumor of the renal medulla with 7 mm greyish solid component within the cyst. The tumor was non-encapsulated. No necrosis was found. Microscopically, appearance of the cystic component of the tumor resembled an adult cystic nephroma (Fig. 3). The cystic septa were covered with monolayer of benign flat and cuboidal epithelial cells. The histology of the solid component was typical for MEST with epithelial component consisted of branched glandular structures. The

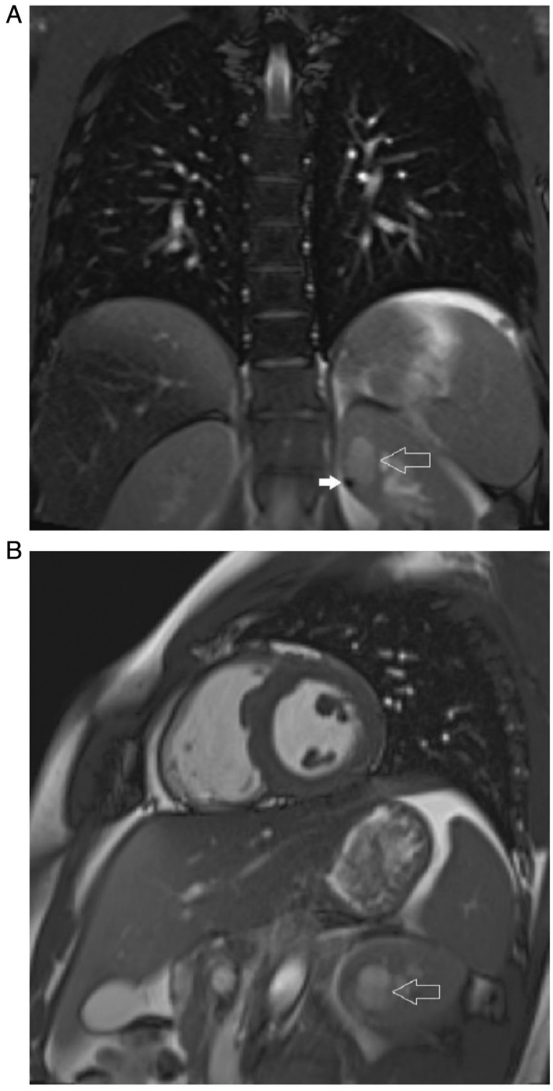

Figure 1. Lesion as observed using magnetic resonance imaging. (A) Frontal plane and (B) sagittal plane. The images indicate an incidentally revealed pathologic lesion of the left kidney (hollow arrow) containing a small solid component adjacent to its wall (filled arrow). The lesion is well-demarcated and shows high signal intensity on T2-weighted imaging.

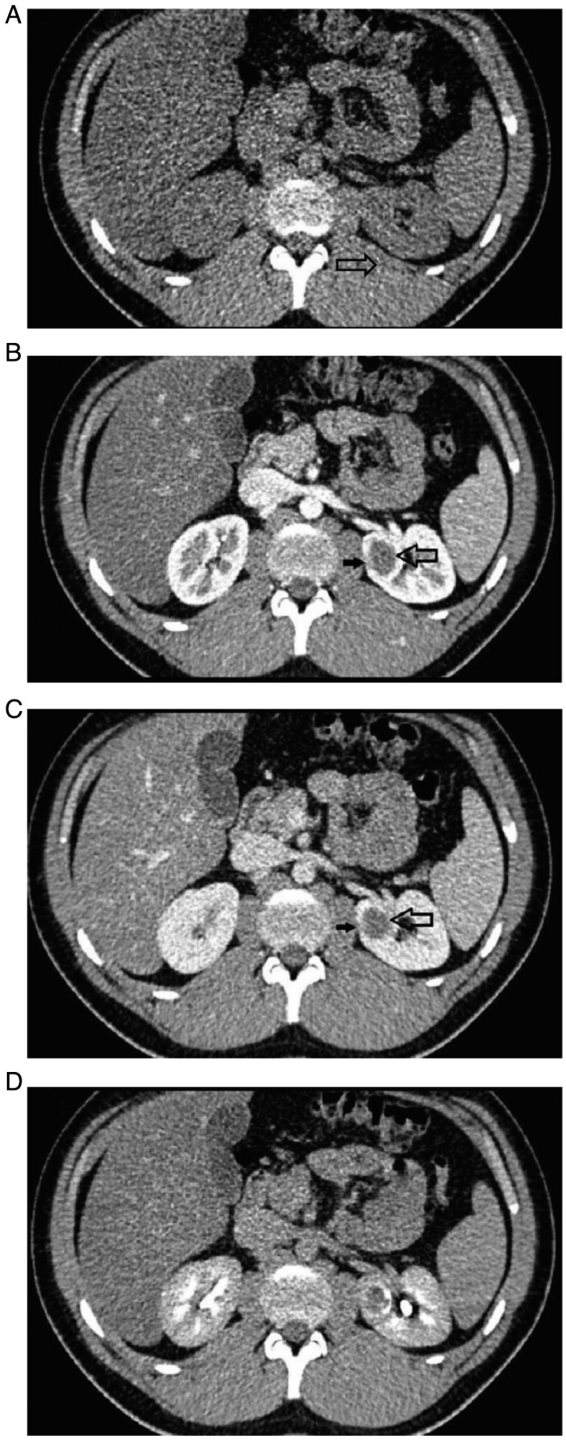

Figure 2. Lesion as observed using multiphase computer tomography scans. The present study confirmed the presence of the lesion in the upper pole of the left kidney (empty arrow). (A) Native phase. The cystic lesion shows low intensity and nonsignificant contrast enhancement in both (B) early and (C) late arterial phases, as well as in (D) delayed phase. There is a small contrast-enhancing tumor visible adjacent to the cystic wall (filled arrow).

stromal component contained elongated spindle-shaped smooth muscle-like cells with vesicular nuclei surrounded by hypocellular highly collagenized matrix with flattened vessels (Fig. 4). Apart from these findings, the solid tumor contained scattered small tubular structures lined with transitional cells with amphiphilic or clear cytoplasm. Eosinophilic secretions were seen inside the tubules (Fig. 5). Some of the tubules were protruding among the papillary ducts (Fig. 6). The cells of both epithelial and stromal components did not show atypia or mitoses. The stromal cells were, immunohistochemically, positive for ER [Dako, catalog number IR084 RTU, 30'Ab, room temperature] (Fig. 7), PgR [Dako IR068 RTU, 30'Ab, room temperature], SMA [Dako IR611 RTU, 30'Ab, room temperature] (Fig. 8) and caldesmon. The epithelial component was positive for GATA-3 [Ventana L50-823, 30'Ab, room temperature] and PAX-8 [Cell Marque MRQ-50, 30'Ab, room temperature] (Fig. 9). Immunostains for inhibin [Dako IR058 RTU, 30'Ab, room temperature], calretinin [Dako IR627 RTU, 30'Ab, room temperature] and CD-10 [Dako IR648 RTU, 30'Ab, room temperature] were negative. Until now, no disease recurrence nor progression has been observed in the patient during the one-year follow-up.

Discussion

MEST is a rare neoplasm of the kidney (1-9). Up to date, ~100 of cases have been described in the literature (1,2,4-5,8,10).

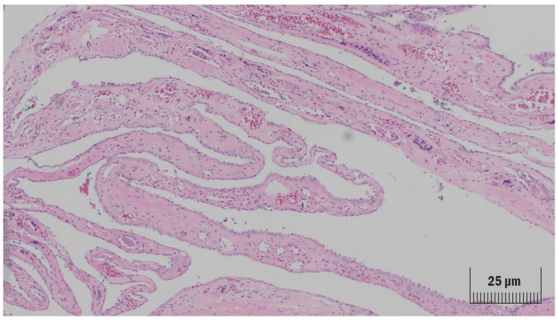

Figure 3. Cystic component of the mixed epithelial and stromal tumor. Hematoxylin-eosin staining (magnification, x40).

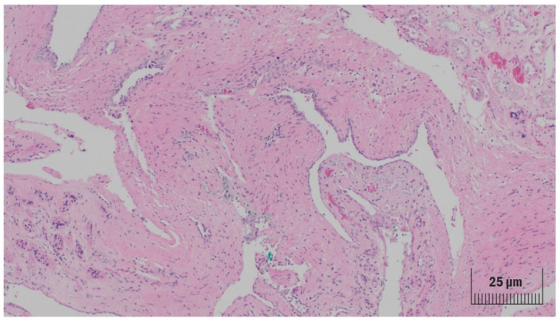

Figure 4. Solid component of the mixed epithelial and stromal tumor. Branched glandular structures of smooth-muscle-like bundles covered with cuboidal epithelium. Hematoxylin-eosin staining (magnification, x40).

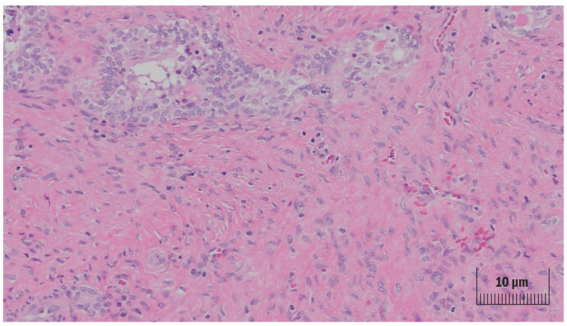

Figure 5. Sample of tumor. Small, scattered tubular structures, lined with transitional cells with amphiphilic or clear cytoplasm, with eosinophilic secretions inside the tubules. Hematoxylin-eosin staining (magnification, x100).

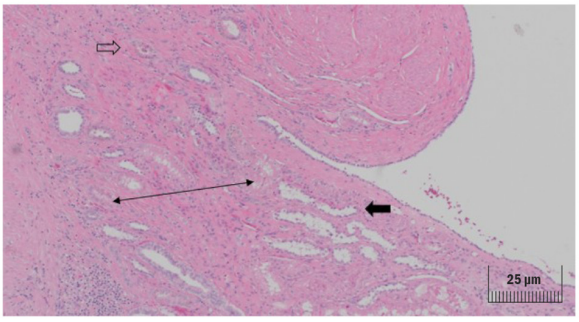

Figure 6. Segment of neoplasm. Tumor pattern (black hollow arrow) and the borders of the tumor (double arrow). Collecting ducts are marked with a black filled arrow. Hematoxylin-eosin staining (magnification, x40; scale bar, 10 μm).

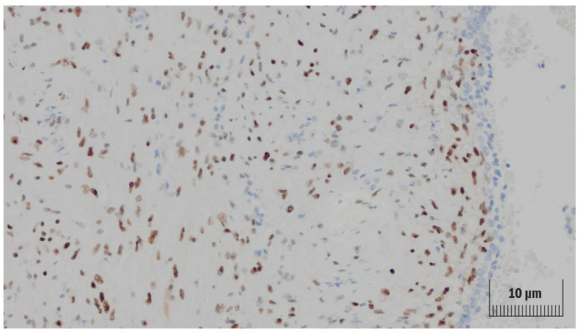

Figure 7. Positive staining for estrogen receptors within the mixed epithelial and stromal tumor stroma (magnification, x100).

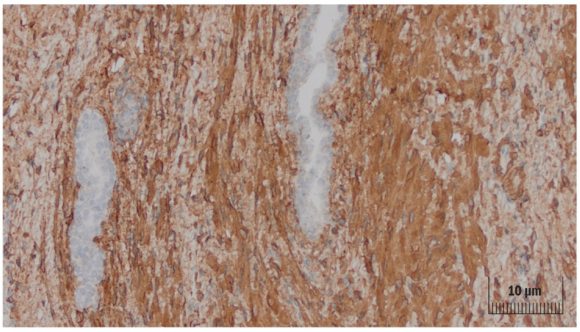

Figure 8. Positive staining for actine fiber within the mixed epithelial and stromal tumor stroma (magnification, x100).

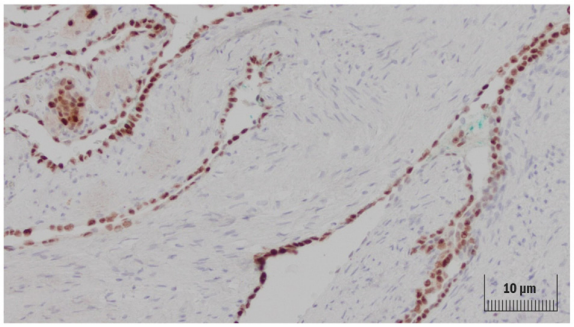

Figure 9. Positive staining of the mixed epithelial and stromal tumor epithelium with paired box gene 8 antibody (magnification, x100).

The majority of diagnosed tumors occurred in women at menopausal age (1-11) and only a few cases have been described in men (1,2,4-5,7-8), with a female-to-male ratio of 10 to 1 (1,2,4,8,11,12). The age of diagnosis varied from 17 to 78 in cases described in the literature, most commonly being ~50 (1,2,4,6,7,12), with a single pediatric case having been reported (7). MEST appears to be more common in women with a history of prolonged estrogen replacement therapy, as well as in men treated with some forms of hormonal therapy, reflecting a possible role of sex hormones in the etiology and development of these tumors.

The clinical presentation of MEST may include flank pain, hematuria, urinary tract infections and a palpable abdominal mass, which comprise for typical symptoms of a renal tumor (1,2,4,5,6,8,10-12). However, approximately a

quarter of patient diagnosed with MEST were asymptomatic with the tumor being incidentally diagnosed on abdominal imaging (1,2,4,5,8,10-12).

The vast majority of MESTs are benign lesions, showing no local recurrence nor distant metastases. The risk of malignant transformation in a patient with MEST is highly dependent on the individual characteristics of a tumor. A few cases of malignant transformation have been described in the literature, affecting both epithelium or stromal tumor (1-8,10-12), including transformation into sarcoma, rhabdomyosarcoma, chondrosarcoma or papillary renal cell carcinoma. Thus, the differential diagnosis of MEST should include the above malignancies (1-7,11,12).

MESTs of the kidney present as unilateral and solitary lesions. Usually the tumor is well-demarcated, with the size of 3 to 24 cm having been reported in the literature (1-4,6-7,12). It can develop both in the renal cortex and in the medulla (1,2,4). CT scan commonly reveals cystic lesions, described as III or IV in the Bosniak classification, with solid components demonstrating contrast enhancement on the delayed phase (1,2,4,5,8,12). MR imaging usually shows complex cysts with cystic components of low and high signal intensity on T1 and T2-weighted imaging, respectively, and solid components of high and low signal intensity on T1 and T2-weighted imaging, respectively (9). Tissue sections show a tumor with cystic and solid components (1-12). While the cystic component is more prominent in adult nephroma, the composition of MEST is mainly stromal. The microscopic appearance of both epithelial and stromal compounds of MEST is highly variable. The spindle-shaped stromal cells may have hyperchromatic nuclei with scant cytoplasm, or vesicular nuclei with abundant cytoplasm, may present as cells with elongated nuclei or barrel-shaped cells with abundant cytoplasm. The stromal component may vary in terms of cellularity, which is higher if adjacent to cystic components, but may also be lower and accompanied by collagenized or myxoid patterns. The regions with high cellularity may be organized in bundles that appear similar to smooth-muscle fibers, occasionally resembling ovarian stroma (1-5,7,8,11-12). The epithelial component may comprise of small glands or branching tubular structures with flat, cuboid or hobnail cells lining (1-3,11).

Approximately 90% of spindle-shaped stromal cells demonstrate positive immunohistochemistry staining for smooth muscle actine, desmin, ER and PR. Positive staining for CD-10, CD-34 and WT1 occurs in ~50% of cases. The epithelial component stains positive for epithelial markers: PAX8 and GATA3. MEST tumor cells are immune-negative for inhibin, SF1, HMB45 and catepsine (1-3,7,8,10-12).

In conclusion, MEST of the kidney is a rare neoplasm. It is most commonly diagnosed in women at menopausal age. It is a neoplasm of benign character and good prognosis, although local recurrences and malignant transformations have been reported in the literature. As the up-to-date evidence in regard to the prognosis and survival of patients with MEST of the kidney is insufficient, reporting new cases could help in developing guidelines on the diagnosis and treatment of patients with this condition.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

PK wrote the manuscript, obtained data, and made substantial contributions to conception and design of the manuscript. TK, TD, HK, BA and JK performed the operation (TK was the first surgeon who performed the operation), receiving cancer tissues that could be used as material for study, performing acquisition of data. TK carried out microscopic examination of the tissue obtaining data and made substantial contributions to the interpretation of data. PK and KS confirm the authenticity of all the raw data. KS carried out the histopathology examination. JP carried out radiology studies, such as CT, and wrote a description for radiology images, interpreting the data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The patient provided written informed consent for participation in the study.

Patient consent for publication

The patient provided written informed consent for the publication of any data and/or accompanying images.

Competing interests

The authors declare that they have no competing interests.

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