Mixed epithelial and stromal tumors of the kidney discovered incidentally at autopsy

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Mixed epithelial and stromal tumors (MEST) of the kidney are uncommon neoplasms that were added to the World Health Organization's renal tumor classification in 2004. These entities are biphasic and contain both epithelial and mesenchymal components. MEST most commonly occur in women. Presented are two cases of MEST incidentally discovered at autopsy.

Mixed epithelial and stromal tumors (MEST) are rare, recently recognized benign renal neoplasms (1). Microscopically, they are biphasic and include both epithelial and mesenchymal components. These neoplasms are more prevalent in women than in men, and malignant transformation, metastasis, and recurrences are exceedingly uncommon. MEST often display immunoreactivity for estrogen and progesterone receptors, but this is not necessary for diagnosis, as morphology is sufficient. We present two cases of MEST discovered incidentally at autopsy.

CASE 1

A 42-year-old black woman with a complicated history including bipolar disorder, hypertension, type 2 diabetes mellitus, sarcoidosis, secondary hyperparathyroidism, IgA nephropathy, and dialysis-dependent end-stage renal disease complained of stomach upset and vomiting. En route to her dialysis unit, she became increasingly dyspneic and collapsed. She lost consciousness and became asystolic. Cardiopulmonary resuscitation established a pulse, and she was then transferred to the emergency department. Upon arrival, she experienced cardiac arrest again and resuscitative efforts reestablished a pulse of 30 beats a minute. She was intubated and transferred to the intensive care unit. However, global anoxic encephalopathy proved irreversible, and she died 2 days later. Her body mass index was 35.6 kg/m².

At autopsy, the right and left kidneys weighed 95 and 75 g, respectively. Bilateral renal cortices had finely granular surfaces. Cut sections of the kidneys showed marked cortical thinning. The right kidney had a gray-white, well-demarcated cortical nodule measuring 1.1 × 0.9 × 0.5 cm. Microscopically, the nodule was composed of spindle cells admixed with scattered tubular structures lined by flattened epithelium (*Figure 1a*).

Areas of fibrosis and cystic change were also present in the adjacent tissue. The stromal portion did not stain by estrogen and progesterone receptor immunohistochemistry. The epithelial component displayed strong immunohistochemical reactivity for low- and high-molecular-weight cytokeratins. No malignant changes were identified. Additional autopsy findings included cardiomegaly (545 g), hypertensive cardiovascular disease, global ischemic-anoxic encephalopathy, and widespread microocclusive intravascular sickling. Heart blood analysis disclosed a hemoglobin A1 of 61.4%, hemoglobin S of 32.4%, hemoglobin A2 of 3%, and hemoglobin F of 0%, all consistent with sickle cell trait.

CASE 2

A 58-year-old white woman with end-stage cryptogenic cirrhosis, Sjogren's syndrome, and hypothyroidism was discharged from the hospital on oral antibiotics for an atypical pulmonary infection. She presented 1 week later with increasing bilirubin levels and persistent lung infiltrates by computed tomography. Her white blood cell count was 7.1 K/uL; hemoglobin, 11.2 g/dL; hematocrit, 31.2%; platelets, 106 K/uL; albumin, 2.9 g/dL; alkaline phosphatase, 297 U/L; aspartate aminotransferase, 237 U/L; alanine aminotransferase, 107 U/L; and direct bilirubin, 30.9 mg/dL. She was icteric. Chest radiograph showed ground-glass opacities and scattered calcified granulomas in both lungs. Over the next few days, her direct bilirubin level remained elevated (29.8 mg/dL), and her total bilirubin measured 39.1 mg/dL. She developed septic shock, disseminated intravascular coagulopathy, and worsening encephalopathy, and she died.

At necropsy, 2000 mL of clear yellow-green fluid was found in the abdominal cavity. All internal organs were markedly icteric. The right and left kidney each weighed 250 g. A 0.8-cm yellow nodule was in the upper pole of the left kidney. Histologically, the nodule comprised a mixture of spindle cells that resembled ovarian stroma and tubular elements lined by flattened epithelium with eosinophilic cytoplasm (*Figure 1b*). The

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Figure 1. Microscopic images of mixed epithelial and stromal tumors. **(a)** Sections of the tumor showing admixed epithelial and mesenchymal components in Case 1 (hematoxylin and eosin, 100 $\times$). **(b)** Tubules surrounded by a mesenchymal component resembling ovarian stroma in Case 2 (hematoxylin and eosin, 100 $\times$).

stromal portion was highlighted by estrogen and progesterone receptor immunohistochemical stains. The epithelial portion showed similar immunohistochemical reactivity for low- and high-molecular-weight cytokeratins, as in the previous case, and this nodule was also consistent with a MEST. Other significant autopsy findings included end-stage cryptogenic cirrhosis, fibrotic pulmonary granulomas, moderate cardiomegaly (415 g), dural icterus, and chronic thyroiditis. A yellow-black stone obstructed the proximal lumen of the common bile duct near its junction with the hepatic hilum and adjacent to the clip from a previous cholecystectomy. Postmortem cultures were positive for *Candida albicans*.

DISCUSSION

MEST was first described by Michal and Syrucek in 1998 (1), and in 2004 it was included in the World Health Organization's renal tumor classification (2), accounting for 1.6% of all renal neoplasms (3). These tumors have been reported under various names such as leiomyomatous renal hamartoma, congenital mesoblastic nephroma, cystic hamartoma of the renal pelvis, solitary multilocular cysts of the kidney, multilocular renal cyst with müllerian-like stroma, and adult metanephric stromal tumor (4–12).

Microscopically, the neoplasm is biphasic with both epithelial and spindle cell elements. The epithelial component consists of clusters of tubules lined by flattened to cuboidal epithelium with eosinophilic cytoplasm and a hobnail appearance. The mesenchymal portion usually resembles ovarian stroma, but can range from scar-like fibrous tissue to interlacing fascicles (13). Most of these tumors behave in a benign fashion, but rare cases of metastasis, recurrence (6), and malignant transformation have been reported in the literature (14–16). Malignant features can occur in either component of the tumor and include increased cellularity, nuclear atypia, round to ovoid vacuolated nuclei with prominent nucleoli, and increased mitotic activity (15 to 25 mitotic figures per 10 high-power fields) (17).

These neoplasms are predominantly found in middle-aged, perimenopausal and older women (18), many with a history of long-term estrogen replacement (17). Clinical symptoms may include a palpable abdominal mass, flank pain, and hematuria (19) or can be discovered incidentally. On computed tomography and magnetic resonance imaging scans, MEST appears as a well-circumscribed multiseptate cystic mass with solid components and thick or thin septae (20, 21). Patients usually have an excellent prognosis postoperatively (17).

The mesenchymal element is immunohistochemically reactive for smooth muscle markers such as desmin and smooth muscle actin. The epithelial component is positive for low- and high-molecular-weight cytokeratins and *Ulex europaeus* (17). The mesenchymal portion also displays reactivity for estrogen and progesterone receptors in many cases (12). Expression of CD10, calretinin, and inhibin has also been described (18); however, morphology remains the most important factor for diagnosis.

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