**CLINICAL CASE**

**Mixed epithelial and stromal tumor of the kidney: a case report and literature review**

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**Abstract**  Mixed epithelial and stromal tumor of the kidney is a rare benign kidney neoplasia that predominantly occurs in middle-aged women. It presents as a well-defined biphasic lesion with solid and cystic components in both tomography and magnetic resonance imaging, reflecting the proliferation of the stromal element and the presence of multiple cysts that are the manifestation of the epithelial element. Malignant transformation, recurrence, and metastasis are rare, but isolated cases and small series have been reported in the literature.

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**PALABRAS CLAVES**  
Tumores mixtos epiteliales y estromales del riñón; Neoplasia; Benigna; Bifásica; Quistes

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**Tumor mixto epitelial y estromal del riñón. Presentación de un caso y revisión de la literatura**

**Resumen**  Los tumores mixtos epiteliales y estromales del riñón comprenden un grupo de neoplasias benignas del riñón, poco frecuente, que principalmente aparece en mujeres de mediana edad. Se presenta como una lesión bien delimitada bifásica, con un componente sólido y quístico tanto en la tomografía como en la resonancia magnética, que refleja la proliferación de componente estromal así como la presencia de múltiples quistes como principal manifestación del componente epitelial. La transformación maligna, recurrencia y metástasis son raras, sin embargo recientemente se han descrito casos en la literatura.

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Introduction

Mixed epithelial and stromal tumors (MEST) of the kidney are biphasic tumors with complex stromal and epithelial elements that were first described by Michal and Syrucek in 1998. They are considered a relatively new pathology and recent reports have described their pathologic clinical characteristics. These tumors, together with cystic nephroma, were grouped into the mixed epithelial and mesenchymatous tumors in 2004, according to the World Health Organization classification of renal tumors. Following several studies, the unifying term renal epithelial and stromal tumors was proposed that would include the 2 pathologies. They are uncommon entities representing 0.20-0.28% of all renal neoplasias and have been reported as isolated cases or in small case series, totaling 100 reports in the international medical literature. The mean age at the time of diagnosis is 46 years and the woman:man ratio is 6:1. These lesions are incidental findings in 25% of the cases and they tend to be asymptomatic. Macroscopically, they are solid tumors with cystic components. The cysts vary in size from millimeters to various centimeters at their largest diameter. Their microscopic characteristics show stromal and epithelial components. The appearance of MEST in imaging studies is nonspecific and they can be confused with complex cystic lesions. Surgical resection of the lesion is curative in the majority of cases. The behavior of these tumors is usually benign, although there are reports of malignant sarcomatoid or carcinomatous transformation that generally progress with a high mortality rate.

Clinical case

An asymptomatic 40-year-old woman had an unremarkable family history. She was a tobacco smoker for 20 years with a smoking index of 20. Physical examination revealed no relevant data and laboratory tests were within normal parameters. During the routine medical evaluation, a right complex renal cyst was identified through ultrasound (fig. 1). The study was complemented with a contrast-enhanced abdominopelvic tomography scan that identified a right renal cystic lesion with 7 HU in the non-contrast phase, measuring 1.7 cm at its largest diameter and heterogeneous heterogeneous enhancement up to 35 HU in the contrast-enhanced phase. The cysts were covered with cells that went from cubical to flattened, some of which were tuck-shaped. The epithelial component expressed vimentin, smooth-muscle actin, and desmin, as well as estrogen and progesterone receptors. (figs. 5-7).

At the third month of follow-up, the patient is asymptomatic and awaiting control studies.

Discussion

MEST is a recently described neoplasia that, despite its low incidence, should be considered in the differential diagnosis of renal tumors. It shows predilection for the female sex, peri-menopausal women, or patients with a history of hormone therapy. There are 8 cases reported in men, and the relevant history in the majority of cases is hormone deprivation therapy for prostate cancer. These tumors are generally asymptomatic, but the most frequent clinical manifestations are palpable mass (31.8%), gross hematuria (27.3%), and flank pain (22.7%). They present as a central lesion of the kidney with expansive growth and frequent compression of the renal pelvis. However, no destructive invasion into the pelvic wall or adjacent parenchyma has been demonstrated, but there is occasional invasion of the renal sinus fat.

MEST is a biphasic tumor composed of a mixture of solid areas formed by stromal components with spindle cells and epithelial components that can vary from small tubules to complex glandular structures and the formation of cysts. It presents with thick septa and a greater percentage of the stromal component (54.6%). The lesions have a mean size of 4.5 cm (1.7-18 cm). The stroma is frequently formed by elements that are similar to those of the ovary and can even present data of hyalinization and luteinization. It presents with thick septa and a greater percentage of the stromal component (54.6%). The lesions have a mean size of 4.5 cm (1.7-18 cm).

Immunohistochemical study usually shows expression of the stromal component with desmin, smooth-muscle actin, caldesmon, and estrogen and progesterone receptors, such as CD10, whereas the epithelial component generally is expressed through CK7. The connection between sex hormones and the expression of estrogen and progesterone receptors in the stromal cells of these tumors suggests that the hormonal influence is a significant factor in the development of MEST.

Given the similarity between the stroma of MEST and the stroma of the Müllerian tubules in the majority of cases, the presence of ectopic Müllerian stroma in the kidney has also been proposed as the possible origin of these lesions. This suggests that these tumors develop from the neoplastic transformation of the kidney stromal cells that have Müllerian stromal characteristics, with or
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without melanocytic differentiation. These stromal cells that are similar to Müllerian stroma have the potential to stimulate growth of the epithelium through contact, inducing Müllerian differentiation in the renal tubules involved. Several theories could explain the extragonadal presence of Müllerian stroma; one posits the presence of primitive fetal mesenchyme in the kidney, pancreas, liver, and other sites that can respond and proliferate when there is a hormonal imbalance, and another suggests the abnormal migration of ovarian stromal cells during embryogenesis.

The behavior of these tumors is benign, but some cases of malignization have been reported, including carcinomatous or sarcomatous transformation. Malignant transformation can be observed in both the epithelial and stromal components, characterized by increased cellularity, cytologic atypia, ovoid and vacuolated nuclei with a prominent nucleolus, and high mitotic index (15-25 mitoses per 10 high power fields). Macroscopic observation usually includes hemorrhage and necrosis.

According to authors of small MEST case series, diagnosis should be considered in: a) middle-aged female patients, b) women with a history of hormone replacement with estrogen, c) cystic renal tumors with delayed enhancement after contrast medium administration, and d) lesions originating in the renal pelvis with negative urinary cytology.

MEST is considered in the differential diagnosis of complex cystic lesions such as cystic nephron in the adult, multilocular cystic renal cell carcinoma, and angiomyolipoma with epithelial cysts, among others. Appearance in imaging studies is nonspecific and a Bosniak III or IV cyst is usually reported, described as a single solid lesion or cystic tumor with a solid component that has intermediate or late contrast enhancement.

Treatment has been surgical due to the difficulty in differentiating these lesions from possible malignant tumors, for which these patients have undergone partial nephrectomy, radical nephrectomy, and there have even been some cases of radical nephroureterectomy due to suspicion of urothelial tumor. There are no predictive prognoses for these tumors and their histogenesis and clinical behavior require future studies.

Conclusions

MEST is a clinically uncommon entity that is considered a benign neoplastic group with good outcome, but its malignant transformation is possible. These tumors must be differentiated from other renal neoplasms given that they share certain clinical and radiologic characteristics. Their diagnosis should be contemplated in the presence of a cystic renal mass, especially in peri-menopausal women or patients with a history of hormone therapy. Further studies are required to determine the etiology, pathogenesis, and natural history of these lesions.

Ethical responsibilities

Protection of persons and animals. The authors declare that no experiments were performed on humans or animals for this study.

Data confidentiality. The authors declare that they have followed the protocols of their work center in relation to the publication of patient data.

Right to privacy and informed consent. The authors have obtained the informed consent of the patients and/or subjects referred to in the article. This document is in the possession of the corresponding author.
Figure 2  Tomographic scan of the abdomen and pelvis with intravenous contrast medium. Anterolateral cortical lesion with a solid component in its interior that takes up the contrast medium (Bosniak IV complex cyst).

Figure 3  At low magnification, a neoplastic lesion made up of a solid, cystic component can be observed.

Figure 4  The mesenchymal component is similar to ovarian stroma and is densely cellular with fusiform cells.

Figure 5  Immunostaining with smooth muscle actin that is expressed in cells with a stromal component.

Figure 6  Immunostaining for progesterone receptors that shows nuclear positivity.

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Conflict of interest
The authors declare that there is no conflict of interest.

References


Figure 7  Estrogen receptors with nuclear positivity in fusiform cells.