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Renal mixed epithelial and stromal tumor: case report

Tumor epitelial-estromal misto do rim: relato de caso

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ABSTRACT

Mixed epithelial and stromal tumor (MEST) represents a recently described biphasic kidney neoplasm, which predominantly affects perimenopausal females. The authors report the case of a young male patient with a MEST exhibiting positivity for estrogen and progesterone receptors. Computed tomography/magnetic resonance imaging (CT/MRI) showed an expansive lesion affecting the right kidney. Grossly, a solid-cystic tumor was identified, which measured 5.7 × 3.5 × 2.4 cm. On microscopic examination, a biphasic tumor constituted by stromal and epithelial elements, without significant atypias, was identified. The stromal element was composed of spindle cells revealing positive immunoexpression for actin, desmin, vimentin, and estrogen receptors. The epithelial component exhibited a predominantly tubular pattern showing positive immunoreaction for cytokeratins. The diagnosis of MEST was then established.

Key words: kidney; neoplasias; mixed epithelial and stromal tumor; pathology; immunohistochemistry.

INTRODUCTION

Tumors of the kidney amount to 2% of the total human cancer burden, and renal cell carcinoma represents, on average, over 90% of all malignances of the kidney. Mixed epithelial and stromal tumor (MEST) is a complex renal neoplasm composed of a mixture of stromal and epithelial elements[1-3]. These rare lesions have been termed cystic hamartoma of renal pelvis, adult mesoblastic nephroma, leiomyomatous renal hamartoma, and mesoblastic nephroma[1, 4-6]. MEST is four to six times more common in women than in men. All patients have been adults, with a mean age of 46 years. Owing to the disparity between incidence rates in women and men, a hormonal influence on the development of MEST has been suggested[1-3, 6]. Herein the authors report the case of a male patient with a MEST exhibiting positive immunoexpression of estrogen and progesterone receptors, and discuss clinical and morphologic findings of this uncommon tumor.

CASE REPORT

A 26-year-old male patient was admitted to the nephrology service due to a 30-day history of macroscopic hematuria episodes. On physical examination, there were no clinical changes. There was no previous history of relevant disease. On laboratory investigation, glucose, hemoglobin, erythrocytes, creatinine, urea, liver enzymes, and cholesterol were within normal plasma levels. Serologic tests for hepatitis B virus, hepatitis C, and HIV were negative. Qualitative urinalysis revealed the presence of several red blood cells per field. Abdominal computed tomography/magnetic resonance imaging (CT/MRI) showed an expansive round lesion affecting the inferior pole of the right kidney. CT/MRI of the chest has not identified significant alterations. The patient underwent radical nephrectomy. On gross examination, an ovoid well-circumscribed solid-cystic pale tumor was identified, which measured 5.7 × 3.5 × 2.4 cm (**Figure 1**). The process did not compromise the renal capsule or the perinephric tissues.

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On microscopic examination, a biphasic tumor was found. The stromal element was composed of spindle cells arranged in short fascicles (**Figure 2**), and varying from hypocellular to fibrotic areas. The epithelial element was constituted by cuboidal to columnar cells showing clear or acidophilic cytoplasm and ovoid central nuclei. Epithelial cells were distributed in immature tubules exhibiting various degrees of luminal dilation, and/or forming micro- and macrocysts. Neither significant atypia nor necrosis was identified. The stromal element exhibited positive immunoexpression for actin, desmin, vimentin, and estrogen (**Figure 3**) and progesterone receptors. The epithelial component showed positive immunoreactions for cytokeratins (AE1/AE3) and vimentin. The tumor exhibited negative immunoexpression for melanocyte antigen (melan-A), and human melanoma black 45 (HMB-45). The diagnosis of kidney MEST was then established.

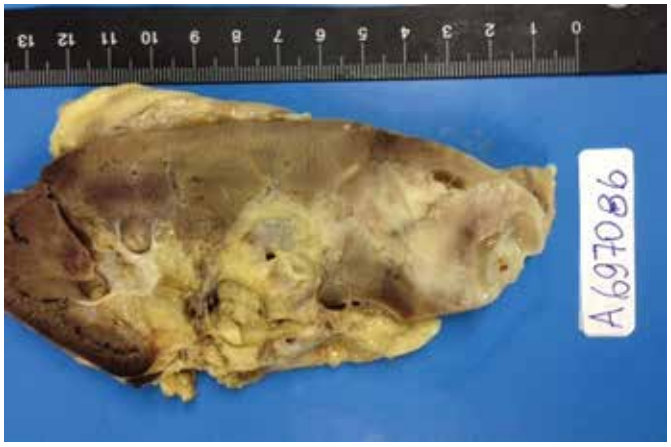

FIGURE 1 – *Mixed epithelial and stromal tumor of the kidney: a circumscribed, light brown, solid tumor, with cystic areas*

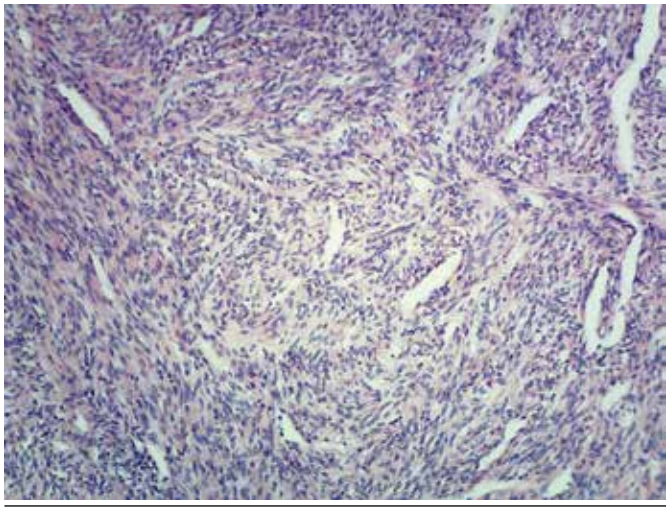

FIGURE 2 – *Mixed epithelial and stromal tumor: spindle cells arranged in short fascicles, hematoxylin-eosin, 200×.*

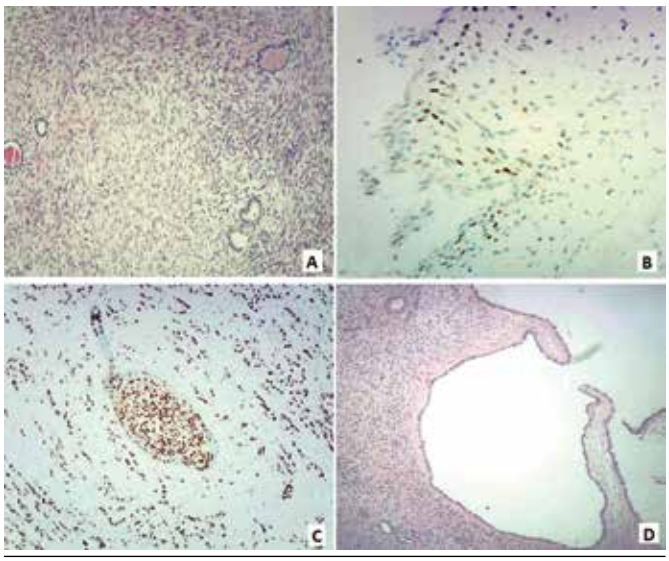

FIGURE 3 – *Mixed epithelial and stromal tumor*
A) a biphasic tumor composed by spindle cells and epithelial elements; B) positive immunoexpression for estrogen receptor in the stromal component, streptavidin-biotin, 400×; C) positive control for estrogen receptors in breast invasive ductal carcinoma, streptavidin-biotin, 200×; D) epithelial covering cystic formations, hematoxylin-eosin, 40×.

DISCUSSION

MEST comprises a rare tumor of the kidney that is more common in women than in men (6:1, respectively). In general, patients are adults, with a mean age of 45 years. MEST lacks the translocation characteristic of cellular congenital mesoblastic nephroma, and most reported cases are benign tumors[1, 2, 7, 8]. The presenting symptoms are flank pain, hematuria, or symptoms of the urinary tract. The lesion corresponds to an incidental finding in 25% of the patients[1, 2, 7-9]. On gross examination, MEST is a centrally located, circumscribed, solid-cystic kidney lesion that frequently extends into the renal pelvis. A partial or complete capsule is often present. The tumor infrequently shows an infiltrative border. Mean tumor size reported in the literature was 6 cm[1, 2, 8-14].

Microscopically, MEST can be composed of cysts, microcysts, tubules, and complex branching glandular formations. In some, there are leaflike arrangements resembling those seen in phyllodes tumor. Epithelial component ranges from low cuboidal to columnar or hobnail, with clear to pale, eosinophilic, or vacuolated cytoplasm[2-4, 8, 15, 16]. Ciliated cells, urothelium, presence of mucin, or epithelial cells exhibiting müllerian findings have been described. The architecture of the microcysts varies from simple microcysts with abundant stroma to densely packed clusters of microcysts, or even to complex branching channels which may be dilated[3, 4, 8, 10, 11, 15, 17-19]. The stromal component exhibits spindle cells with plump nuclei and abundant cytoplasm. Stromal areas can vary from hypocellular, collagenous and fibrotic to densely cellular, with a

woven pattern resembling ovarian stroma[2, 8, 11, 16-18, 20]. Fascicles of smooth muscle cells or areas exhibiting a myxoid stroma can be found. Adipose tissue is occasionally present[2, 3, 4, 15, 16, 20, 21]. Neither the stromal nor the epithelial component shows mitotic figures or cytological atypia. Mitotic figures, hemorrhage, and necrosis have not been found in most cases of indolent MEST[2, 8, 11, 16-18, 20]. The **Table** shows cases of MEST found in the international literature and comparable to the present report.

TABLE – Summary of published cases of MEST of the kidney

Authors	Age/gender	Clinical findings	Topography	Treatment modality	Positive immunoexpression	Negative immunoexpression	Outcome
Demiralay *et al.*[22]	60/F	Incidental	Right kidney	Total nephrectomy	SC: SMA, desmin, ER and PR EE: EMA, and E1/AE3	SC: HMB-45	Unavailable
Ekici *et al.*[23]	51/F	Abdominal pain	Right kidney	Partial nephrectomy	SC: desmin, SMA, ER, and PR EE: AE1/AE3 and EMA	SC and EE: HMB-45, and CD34	No recurrence or metastases after 24-month follow-up
Horikawa *et al.*[8]	61/F	Hematuria	Left kidney	Total nephrectomy	SC: Vimentin, SMA, PR, bcl-2, CD99, and desmin EE: AE1/AE3, and EMA	SC: ER	No recurrence or metastases after 10-month follow-up
Hou *et al.*[24]	45/F	Hematuria	Left kidney	Total nephrectomy	SC: ER, PR, and desmin	Not described	No recurrence or metastases after 12-month follow-up
Menéndez *et al.*[9]	62/F	Abdominal pain	Left kidney	Total nephrectomy	SC: vimentin, CD10, SMA, desmin, CD56, bcl-2, and ER EE: AE1/AE3, CK7, EMA, and CK5/6	Not described	No recurrence or metastases after 36-month follow-up
Nakagawa *et al.*[6]	43/F	Incidental	Right kidney	Total nephrectomy	SC: vimentin, and SMA EE: CKM, EMA	Not described	Developed recurrence/ died after 43 months
Rao *et al.*[25]	35/F	Flank pain	Right kidney	Total nephrectomy	SC: vimentin, ER, and PR EE: CKM	Not described	No recurrence or metastases after 12-month follow-up
Richter *et al.*[26]	47/F	Flank pain	Left kidney	Partial nephrectomy	ST: vimentin, desmin, SMA, CD10, alpha-inhibin, ER, and PR EE: CKM, CK7	Not described	Unavailable
Sukov *et al.*[20]	84/F	Incidental	Left kidney	Total nephrectomy	SC: WT-1, CD99, CD56, ER, and actin EE: CK7, CAM 5.2, AE1/AE3, EMA	SC: desmin, myogenin, progesterone receptor	Unavailable
Suzuki *et al.*[27]	67/M	Incidental	Right kidney	Total nephrectomy	SC: vimentin, ER, PR, WT-1, CD99, bcl-2 EE: AE1/AE3 and EMA	SC: CD99, SMA, desmin	Unavailable
Teklali *et al.*[21]	12/M	Hematuria	Right kidney	Partial nephrectomy	SC: vimentin, SMA, desmin, ER, PR EE: AE1/AE3, and EM	Not described	No recurrence or metastases after 24-month follow-up
Wang *et al.*[14]	60/M	Incidental	Not described	Total nephrectomy	SC: PR, SMA, desmin, and vimentin EE: AE1/AE3	Not described	No recurrence or metastases after 06-month follow-up
Wang *et al.*[14]	58/M	Incidental	Not described	Total nephrectomy	SC: CD10, ER, PR, vimentin, and desmin EE: AE1/AE3	SC: melan-A, and HMB-45	No recurrence or metastases after 23-month follow-up
Zou *et al.*[28]	19/M	Abdominal discomfort and right flank pain	Right kidney	Total nephrectomy	SC: vimentin, CD99, bcl-2, WT-1, and EMA EE: AE1/AE3, and EMA	SC and EE: CD10, CD34, CD117, S-100, desmin, SMA, HMB-45, Melan-A, ER, EP	Unavailable
Present case	26/M	Hematuria	Right kidney	Total nephrectomy	SC: actin, desmin, vimentin, and estrogen and progesterone receptors EE: AE1/AE3, and vimentin	SC/EE: melan-A, and HMB-45	No recurrence or metastases after 03-month follow-up

F: female; M: male; SC: stromal componente; SMA: smooth muscle actin; ER: estrogen receptor; PR: progesterone receptor; EE: epithelial element; EMA: epithelial membrane antigen; AE1/AE3: pan-cytokeratins; bcl-2: B-cell lymphoma; CD: cluster determinant; CK: cytokeratin.

Spindle cells show positive immunoexpression for actins, desmin, vimentin, smooth muscle actin, and estrogen and progesterone receptors. The epithelial component exhibits positive immunoexpression for cytokeratins and often vimentin. Positivity for estrogen receptor has been described in the epithelial element, and it has also been noted in male patients who have received anti-androgenic therapy for prostate cancer. MEST has been considered a cystic nephroma that has acquired cellular, ovarian-like stroma secondary to hormonal influences[1, 3, 14, 19, 23, 27, 28]. In the present report, authors described immunopositivity for estrogen receptor in the stromal component of a male patient who developed a MEST of the kidney. Some authors consider this unexpected finding associated with tumor loss differentiation and the activation of estrogen-related protein p29, which is a possible factor of influence on some gender-specific estrogen-associated tumors[4, 6, 8, 9, 14, 18, 23].

The histogenesis of MEST is unknown. Hormonal imbalance during the perimenopausal period can be related to the activation of a misplaced immature or fetal mesenchyme, which harbors the capacity for a dual, epithelial and mesenchymal differentiation. Some authors suggest the hypothesis of müllerian remnants developing neoplastic transformation due to excessive hormonal stimulation[1, 2, 6, 8, 11, 18, 23, 27].

The differential diagnosis includes adult nephroblastoma, cystic nephroma, and sarcomatoid renal cell carcinoma. The lack of cellular anaplasia rules out these tumors. The absence of blastema excludes nephroblastoma, and cystic nephroma typically shows a thin and fibrous stroma. MEST have been treated with surgical excision, and a few cases of recurrence, malignant transformation, and metastases development have been reported[6, 8, 9, 11, 13, 15, 16, 23, 24, 27].

RESUMO

O tumor epitelial e estromal misto (TESM) representa uma neoplasia renal bifásica descrita recentemente que afeta predominantemente mulheres na perimenopausa. Os autores relatam o caso de um paciente jovem, do sexo masculino, com TESM exibindo positividade para receptores de estrogênio e progesterona. A tomografia computadorizada/ressonância magnética (TC/RM) mostrou lesão expansiva no rim direito. Ao exame macroscópico, identificou-se tumor sólido-cístico medindo 5,7 × 3,5 × 2,4 cm. À microscopia, foi encontrado tumor bifásico constituído por elementos estromais e epiteliais, sem atipias significativas. O componente estromal era composto por células fusiformes, exibindo imunoexpressão positiva para actina, desmina, vimentina e receptores de estrogênio. Os elementos epiteliais mostraram padrão predominantemente tubular e exibiram imunorreação positiva para citoqueratinas. O diagnóstico de TESM foi então estabelecido.

Unitermos: *rim; neoplasias; tumor misto epitelial e estromal; patologia; imuno-histoquímica.*

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