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Journal of the Chinese Medical Association 79 (2016) 554–558

www.jcma-online.com

Original Article

Clinical-radiologic correlation of mixed epithelial and stromal tumor of the kidneys: Cases analysis

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Received August 20, 2015; accepted February 26, 2016

Abstract

Background: Mixed epithelial and stromal tumor of the kidney (MESTK) is a rare tumor, with few malignant cases reported. Occurring mostly in middle-aged women, it is characterized by a biphasic pathological structure.
Methods: This study retrospectively reviewed the imaging findings and medical records of six MESTK cases of a single institution in a 10-year period.
Results: All of the patients were middle-aged women without hormone therapy history. The typical image was a renal tumor with varied cystic components. Half of the cases had sinus invagination, but only one had intratumor calcification. On imaging studies, four were Bosniak Category IV, one was Category III, and one presented as a solid tumor. The mean RENAL nephrometry score was 9.3. Five patients underwent partial nephrectomy, with no statistical renal functional deterioration after nephron-sparing surgery. There were no peri-operative complications.
Conclusion: Surgery remains the treatment of choice for MESTK, and nephron-sparing surgery should be considered in feasible cases.

Keywords: Bosniak category; computed tomography; mixed epithelial and stromal tumor of the kidney; nephron-sparing surgery

1. Introduction

Mixed epithelial and stromal tumor of the kidney (MESTK) is a rare neoplasm. The first case was described in 1998 by Michal and Syrucek.[1] Histopathologically, it is composed of epithelial and stromal components, thereby appearing as a cystic renal mass with varying proportions of solid components on imaging. Until 2010, approximately 150 cases had been reported,[2] although most reports focused on the pathologic and radiographic features.[3–5] However, preoperative diagnosis of MESTK is problematic, since most of these tumors are Bosniak Category IV or solid lesions. Therefore most cases are treated surgically.[4] This is a retrospective analysis of six cases of MESTK with detailed imaging profiles, treatment decision-making, and clinical outcomes.

2. Methods

Between March 2004 and November 2013, there were six cases of MESTK diagnosed histopathologically in a single institution. We followed the provisions of the Declaration of

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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http://dx.doi.org/10.1016/j.jcma.2016.02.012

Helsinki and obtained informed consent from all six patients. Patients' demographic data (i.e., age, sex, and menopausal status), laterality of the mass, hormone replacement, clinical symptoms, imaging findings, and peri-operative outcomes were reviewed.

Noncontrast and contrast-enhanced computed tomography (CT) before surgery were performed. The CT imaging included the largest diameter of the renal tumor, proportion of cystic component, calcification status, contrast enhancement, sinus invagination, septum, Bosniak category,[6] and RENAL nephrometry score.[7]

The peri-operative outcome variables assessed were surgical technique, estimated blood loss, operative time, ischemia time for partial nephrectomy, complications, and recurrence. Serum creatinine was checked preoperatively and at 3-months postoperatively. Measurement of effective renal plasma flow (ERPF) using scintigraphy with I-131-orthoiodohippurate was also done preoperatively and at 3–6-months postoperatively. The estimated glomerular filtration rate (eGFR) was calculated with the Modification of Diet in Renal Disease equation. The split renal function for the five patients who underwent partial nephrectomy was calculated as the percentage of ERPF of the diseased kidney divided by the total ERPF. Differences in renal function preoperatively and postoperatively were evaluated using Student *t* test for continuous variables.

3. Results

Based on the demographic parameters, all of the patients were female, with a mean age of 50.5 years (range, 44–68 years). Half of them were menopausal, but no patient received hormone replacement therapy. Two patients presented with ipsilateral flank pain, while the rest were incidental findings.

The CT imaging findings revealed that all of the patients had a contrast-enhanced renal tumor without satellite lesions (Fig. 1). The mean tumor diameter was 4.4 cm (range, 2.2–9.0 cm). Five tumors contained cystic components, but the proportion varied (10–80%); the other one presented as a solid renal tumor. Only one tumor had calcification (Fig. 2). Half of the tumors showed sinus invagination (Fig. 3). Based on the Bosniak classification, four tumors were Bosniak Category IV and one was Bosniak Category III (Table 1). The mean RENAL nephrometry score was 9.3 (range, 8–11). The clinico-radiological features of our series and other studies are summarized in Table 1.[4,12,14]

The peri-operative and functional outcomes are reported in Table 2. One patient with a tumor diameter of 9 cm underwent open radical nephrectomy. Another underwent laparoscopic partial nephrectomy, while four received open partial nephrectomy. The mean operative time was 262.5 minutes (range, 190–300 minutes). The mean estimated blood loss was 118.3 mL (range, 50–200 mL), and no patient required a blood transfusion. The mean ischemia time for the five patients who underwent partial nephrectomy was 43 minutes (range, 23–80 min). There were neither peri-operative nor postoperative complications. The average postoperative follow-up without tumor recurrence was 18 months (range, 4–55 months).

All of the six tumors were benign MESTK that presented with a variable mixture of spindle and epithelial cell components. The spindle component varied from ovarian stroma to scar-like fibrous tissue (Fig. 4A). The epithelial component showed tubular, cystic, and glandular structures (Fig. 4B).

Based on the functional outcomes (Table 3), there was no difference in the preoperative and postoperative eGFR. Similarly, there was no difference in the preoperative and postoperative split renal function in the five patients who underwent partial nephrectomy.

4. Discussion

The main feature of MESTK is it's pathologically biphasic structure: the epithelial and matrix components. The epithelial component exhibits a cystic structure lined with flat, hobnail, and cuboidal epithelium. The matrix part surrounding the cyst is composed of spindle cells.

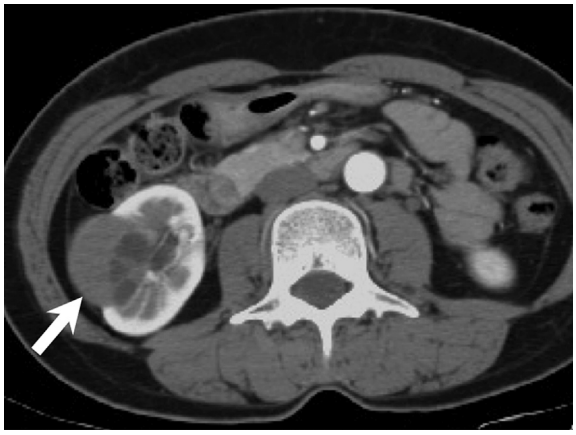

Fig. 1. Case 1: A 58-year-old woman with an epithelial and stromal tumor of the right kidney. Enhanced computed tomography scan in the corticomedullary phase showed a well-demarcated, moderately-enhanced, solid, and cystic renal mass (arrow).

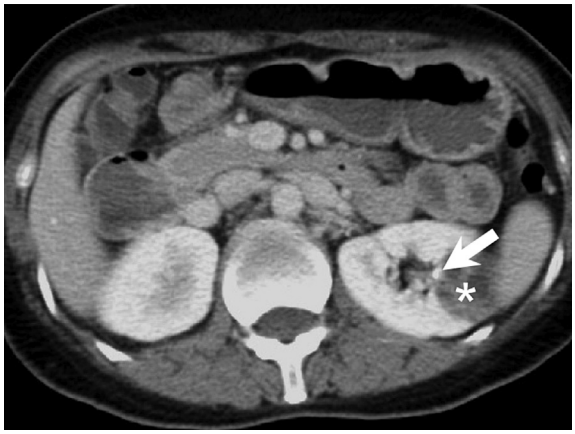

Fig. 2. Case 2: A 46-year-old woman with an epithelial and stromal tumor of the left kidney. Enhanced computed tomography imaging showed a solid and cystic mass (star), with calcification near the collecting system (arrow).

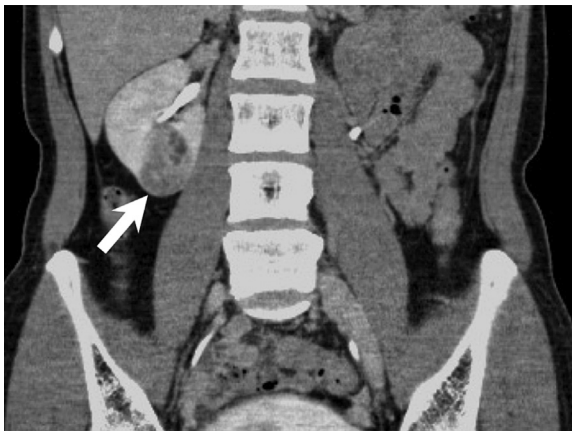

Fig. 3. Case 6: A 43-year-old woman with an epithelial and stromal tumor of the right kidney. Coronal reconstruction imaging during the postrenal phase demonstrated a tumor with renal sinus invagination (arrow).

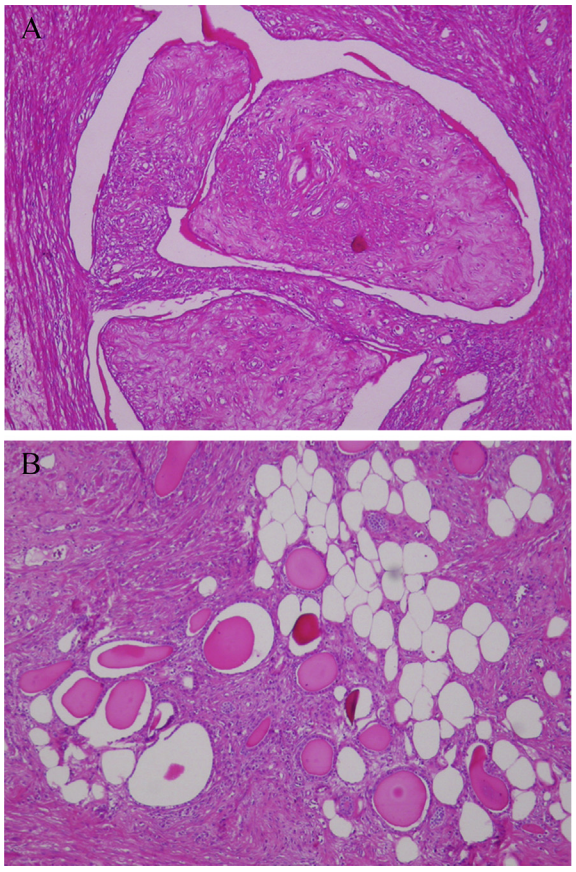

Fig. 4. Case 3: A 68-year-old woman with an epithelial and stromal tumor of the right kidney. (A) Microscopically, the stromal component revealed hyalinizing stroma and phyllodes-like structure; (B) the epithelial component showed numerous tubular and microcystic structures with variable linings, including clear, oncocytic, or hobnail cells.

According to different cell distributions ranging from loose to dense, the matrix part manifests as hyalinizing stroma to ovarian-like stroma.[3]

The pathogenesis of MESTK remains unknown. Most cases are benign, but malignant transformation has been reported.[8] Also, most cases occur in middle-aged, peri-menopausal or postmenopausal women.[3] Some patients receive estrogen as hormone replacement treatment,[9,10] suggesting that estrogen and the pathogenesis of MESTK may be related. Nonetheless, some male cases of MESTK have also been reported, including one who received estrogen therapy for underlying prostate cancer.[10] In this series, all six women were middle-aged, but none of them had undergone estrogen therapy. Thus, the hormone etiology hypothesis cannot explain all cases of MESTK.

The typical clinical symptomatology of MESTK includes hematuria, lower back pain, and a palpable mass.[11] However, recent literature and this study reveal an increasing number of asymptomatic cases.[12] The possible reason may be advances in imaging modalities and the prevalence of health examinations.

Table 1
Clinico-radiological comparison of mixed epithelial and stromal tumor of the kidney series.

	Lane BR et al[15,a]	Sahni VA et al[5,b]	Chu LC et al[4]	Wang C et al[12]	Present series
Clinical features	$n = 9$	$n = 5$	$n = 5$	$n = 8$	$n = 6$
Mean age	52	55.6	58.2	38	50.5
Female:male	9:0	5:0	5:0	6:2	6:0
Symptomatic	6 (67%)	1 (20%)	2 (40%)	1 (13%)	2 (33%)
Menopause	3 (33%)	NA	NA	NA	3 (50%)
Hormone replacement	2 (22%)	NA	NA	0	0
Image features					
Cystic					
Bosniak III	3 (30%)	3 (60%)	5 (100%)	NA	1 (17%)
Bosniak IV	3 (30%)	2 (50%)	0	NA	4 (66%)
Solid	4 (40%)	0	0	NA	1 (17%)
Mean size, cm (range)	4.5 (1.7–18)	6.4 (2.6–12.4)	13.3 (4–20)	4.9 (3.5–7)	4.4 (2.2–9)
Calcification	NA	4 (80%)	2 (40%)	NA	1 (17%)
Sinus invagination	10 (100%)	2 (40%)	5 (100%)	NA	3 (50%)
Nephron-sparing surgery	NA	3 (60%)	1(20%)	2 (25%)	5 (83%)
Malignant transformation	1 (10%)	0	0	0	0

NA = not applicable.
[a] There was one case of bilateral MEST.
[b] There was one case without a tumor size record.

Table 2
Peri-operative profile.

Case	Surgery	RENAL score	Estimated blood loss (mL)	Ischemia time (min)[a]	Operative time (min)	Complications
1	OPN	10	180	80	295	None
2	LPN	9	180	45	280	None
3	ORN	11	200	0	300	None
4	OPN	9	50	23	270	None
5	OPN	9	50	49	190	None
6	OPN	8	50	63	240	None

LPN = laparoscopic partial nephrectomy; OPN = open partial nephrectomy; ORN = open radical nephrectomy.
[a] Only one patient who received laparoscopic partial nephrectomy experienced warm ischemia for hilum control. In the remaining four open partial nephrectomy cases cold ischemia technique was applied.

Table 3
Evaluation of renal function in five patients who received nephron-sparing surgery.

	Preoperatively	3-mo postoperatively	p[a]
eGFR (SD)[b]	89.17 (23.01)	82.83 (27.79)	0.6764
SRF% (diseased kidney)[c]	50.35 (5.71)	43.44 (6.93)	0.1236

eGFR = estimated glomerular filtration rate; SD = standard deviation; SRF = split renal function.
[a] Student t test.
[b] eGFR (mL/min/1.73 m^2) = 186 × $(S_{cr})^{-1.154}$ × $(age)^{-0.203}$ × (0.742 if female) × (1.212 if African-American).
[c] SRF (%) = effective renal plasma flow of diseased kidney/total effective renal plasma flow.

Radiographically, diagnosis of MESTK reported in literature often relies on CT as a diagnostic imaging tool.[12,13] All patients in Table 1 had received CT preoperatively. On CT, MESTK appears as a multilocular cystic mass with variable cystic components. In this series, the range of difference was 0−80%, and calcification was noted occasionally. The cases belong to Bosniak Categories III to IV or pure solid on imaging. Common differential diagnoses of MESTK on CT include cystic renal cell carcinoma and cystic nephroma. Preoperative radiologic diagnosis of MESTK is problematic. According to literature on the management of cystic renal mass, Bosniak Category III lesions have 30−100% chance of malignancy and surgery is recommended, whereas Bosniak Category IV is deemed malignant until proven otherwise, and surgery is strongly indicated.[13,14] Also, the role of needle core biopsy is not recommended for cystic renal masses, unless areas with a solid pattern are present.[14] Therefore, surgery is strongly indicated in most MESTK cases.

Common differential diagnoses of MESTK on CT include cystic renal cell carcinoma and cystic nephroma. Half of the MESTK cases in this series revealed renal sinus invagination, which made nephron-sparing surgery more difficult. The anatomic features of renal tumors are evaluated using RENAL nephrometry. The mean RENAL score in the six patients was 9.3 (range, 8−11), which means moderate-to-high complexity of the lesions.[7]

Although the vast majority of MESTK cases are benign and prognosis is good, management should follow the renal cell carcinoma protocol.[10,15] More than half of patients with MESTK undergo radical nephrectomy.[2,8,10,12] Nephron-sparing surgery cannot be done in cases with a very large tumor size, sinus invagination, or endophytic growth. In this series, five of the six MESTK cases had moderate-to-high complexity and underwent partial nephrectomy. Multi-planar reformation of the CT image improved the identification of tumor margins and clarified the interface between the tumor and the collecting system (Fig. 3), and was performed on four patients to facilitate the nephron-sparing surgery. Five patients had no peri-operative complications and no statistical difference in preoperative and postoperative split renal function (SRF) and eGFR. There was also no tumor recurrence noted.

MESTK should be considered in middle-aged women who may have hormone replacement history with contrast-enhanced cystic renal tumors. Twenty percent to 60% of our MESTK cases were managed with nephon-sparing surgery (Table 1). In our series, only one underwent radical nephrectomy for a large tumor and high RENAL score (11 points). However, the remaining five who received partial nephrectomy still had tumors with moderate-to-high complexity (RENAL score 8−10 points).[7] Based on the current findings, partial nephrectomy is suitable as a treatment for MESTK, even for difficult cases. Kamel et al[16] report partial nephrectomy for very large MESTK.

Limitations of this study are the small case number, retrospective design, and scarcity of MESTK cases. With advances in imaging modalities and the rising popularity of health examination, diagnosis of asymptomatic and small MESTK will increase. With the benign nature of MESTK and the development of minimally invasive techniques, nephron-sparing surgery may be the treatment of choice in the future.

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