

Case – Mixed epithelial and stromal tumours: A rare pediatric renal tumour

Elena G. Gibson¹; Neha Batra¹; Jennifer B Gordetsky¹; David Kelly²; Pankaj P. Dangle²

¹University of Alabama at Birmingham School of Medicine; ²Children's Hospital of Alabama, University of Alabama at Birmingham; Birmingham, AL, United States

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Introduction

Mixed epithelial and stromal tumour (MEST) is a renal neoplasm with a mixture of solid and cystic components and microscopic findings of epithelial and stromal cells within the tumour.¹ MESTs are most often seen in adult females, commonly during peri-menopausal ages (40-50 years).¹

Some believe MEST and cystic nephroma (CN) represent a spectrum of the same tumour process, and the term “renal and epithelial stromal tumour” was first proposed by Turbiner, et al. in 2007 to better encapsulate both MEST and CN.^{1,2} More recently, the 2016 World Health Organization classification of tumours combined adult CN and MEST under the term “mixed epithelial and stromal tumour family”.³ Although CN/MEST is recognized as one diagnosis in adults, recent studies describe pathologic and genetic differences between adult CN/MEST and pediatric CN.^{3,4} Since similar relationships between pediatric MEST and CN have not been defined, it is important to recognize MEST as a distinct potential diagnosis in a pediatric patient with a renal neoplasm.

Case report

A previously healthy 14-year-old male presented to the emergency department with blunt trauma to his right flank resulting from a football injury. With signs of gross hematuria present, a computerized tomography (CT) scan was performed. The CT scan revealed a cystic, heterogeneous (Bosniak IIF/III) mass in the anteromedial aspect of the right kidney, measuring about 6 x 8 cm in size with evidence of hemorrhage and enhancement (**Figure 1 A-D**). The mass was well circumscribed, and there was no evidence of metastases, other masses, perinephric hematoma, or regional adenopathy. A urinalysis was consistent with hematuria.

Options to perform a robotic, laparoscopic or open nephrectomy were discussed with the family, and the decision was made to proceed with a robotic procedure. Due to concerns regarding malignancy, a right robotic radical nephrectomy and regional lymphadenectomy were performed. Although a partial nephrectomy would be ideal in a patient this age, the case was discussed with multiple adult and pediatric urologists, and a complete nephrectomy was recommended due to the centralized location of the tumour and suspicions for malignancy.

Histopathologic evaluation of the renal tumour revealed a well-circumscribed lesion with mixed stromal and cystic elements. The epithelium consisted of tubules with microcystic and macrocystic dilatation, and epithelial cells ranged from low cuboidal to columnar. The cyst septa contained excess smooth muscle and a small number of mononuclear inflammatory cells, but no sheets of embryonal blastemal cells. The absence of blastemal cells ruled out cystic nephroblastoma and cystic partially differentiated nephroblastoma, and the excess smooth muscle in the septa was suggestive of MEST rather than cystic nephroma, in which cystic components with thin fibrous septa would be expected.^{3, 5, 6} Special positive immunoperoxidase stains in the septal stromal cells for estrogen and progesterone receptors confirmed the presence of MEST and ruled out pediatric cystic nephroma (Fig. 2 A- D). Evaluation of the right hilar lymph nodes revealed mild sinus histiocytosis, and mild patchy hemorrhage, with no evidence of metastasis.

The patient recovered well from the surgery and a decision to follow-up with abdominal ultrasound and chest radiograph every 6 months for two years was made. At his 18-month follow-up visit, the patient was symptom free and imaging showed a normal left kidney and no evidence of recurrence or metastasis. The patient and his family decided against genetic testing for DICER1 mutations.

Discussion

To the best of our knowledge, only 5 cases of MEST in a pediatric patient have been reported in the current literature, and only two occurred in young males.^{2, 7-9} Similar to our patient, most reports of pediatric MEST occurred during adolescence.^{2, 7-9} Details of MEST cases in pediatric males are outlined in **Table 1**. The two previously reported cases in adolescent males were diagnosed during evaluations of hematuria (microscopic and gross), and both patients underwent a partial nephrectomy.^{2, 7} Similar microscopic findings of epithelial and stromal components diagnosed the tumours as MEST in all three cases. On immunohistochemical evaluation, stains revealed estrogen receptor and desmin or actin expression within the stromal cells of all three tumours, and progesterone receptor expression was reported in two of the cases, including ours.^{2, 7, 8}

In addition to MEST, the differential diagnosis for this type of renal lesion in an adolescent includes a cystic partially differentiated nephroblastoma, a cystic nephroblastoma, and a cystic nephroma.^{5, 6, 10} All of these may present with or without a palpable mass and symptoms such as flank pain, hematuria and abdominal pain.⁶ However, partially differentiated nephroblastomas (peak before 2 years old) cystic nephroblastomas (peak 3-4 years old), and

cystic nephromas (peak before 2 years old) typically occur at younger ages compared to pediatric cases of MEST (12-14 years old).⁵

Radiologic features among pediatric cystic renal lesions can be similar; therefore, histologic evaluation is necessary to establish a final diagnosis.⁶ In our case, the absence of blastic components, atypical cells and mitoses helped us rule out cystic nephroblastoma and congenital mesoblastic nephroma.^{5,6} Differentiating a MEST from a CN is often more difficult because of shared clinical and morphological characteristics.^{2,3,7}

Although CN/MEST is recognized as one diagnosis in adults, pediatric CN remains distinct from both adult CN/MEST and pediatric MEST. Adult CNs often demonstrate a wavy,ropy collagen with a cellular stroma uncommon in pediatric CNs.³ While both adult and pediatric CNs exhibit estrogen receptor activity, pediatric CNs more often express DICER1 mutations and lack inhibin reactivity.^{3,11} In addition to differences from adult CN, typical histologic characteristics of pediatric CN^{3,5} differ from findings in pediatric MEST.^{2,7,8} In children, CNs are primarily cystic structures with fibrous septa, but reports of MEST in children describe tumours with solid and stromal components as well as spindle cells on pathologic examination.^{2,3,7,8} The presence of DICER1 mutations in pediatric CN, but not adult CN/MEST, may warrant future evaluations of DICER1 mutations in pediatric MESTs.³ In addition to PCN, DICER1 mutations are associated with other neoplasms including familial pleuropulmonary blastomas, ovarian sex cord-stromal tumours and embryonal rhabdomyosarcomas.¹¹ Determining the status of DICER1 mutations in pediatric MEST patients could not only help describe the relationship between pediatric CN and MEST, but findings could influence patient care and future surveillance activity.

MESTs are typically benign lesions, although a few cases of malignant transformation have been reported in adult patients; thus, surveillance for recurrence or metastasis is required.¹² In all reported cases of pediatric MEST, surgical treatment was successful, and there were no signs of recurrence or metastases on follow-up.^{2,7-9}

In conclusion, similarities in presentation and differences in management exist among pediatric patients presenting with cystic renal tumours.^{5,6} Increasing the awareness and understanding of pediatric MEST could help provide the most appropriate and effective care for these patients.

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Figures and Tables

Fig. 1. Computed tomography (CT) images of abdomen showing renal mass.

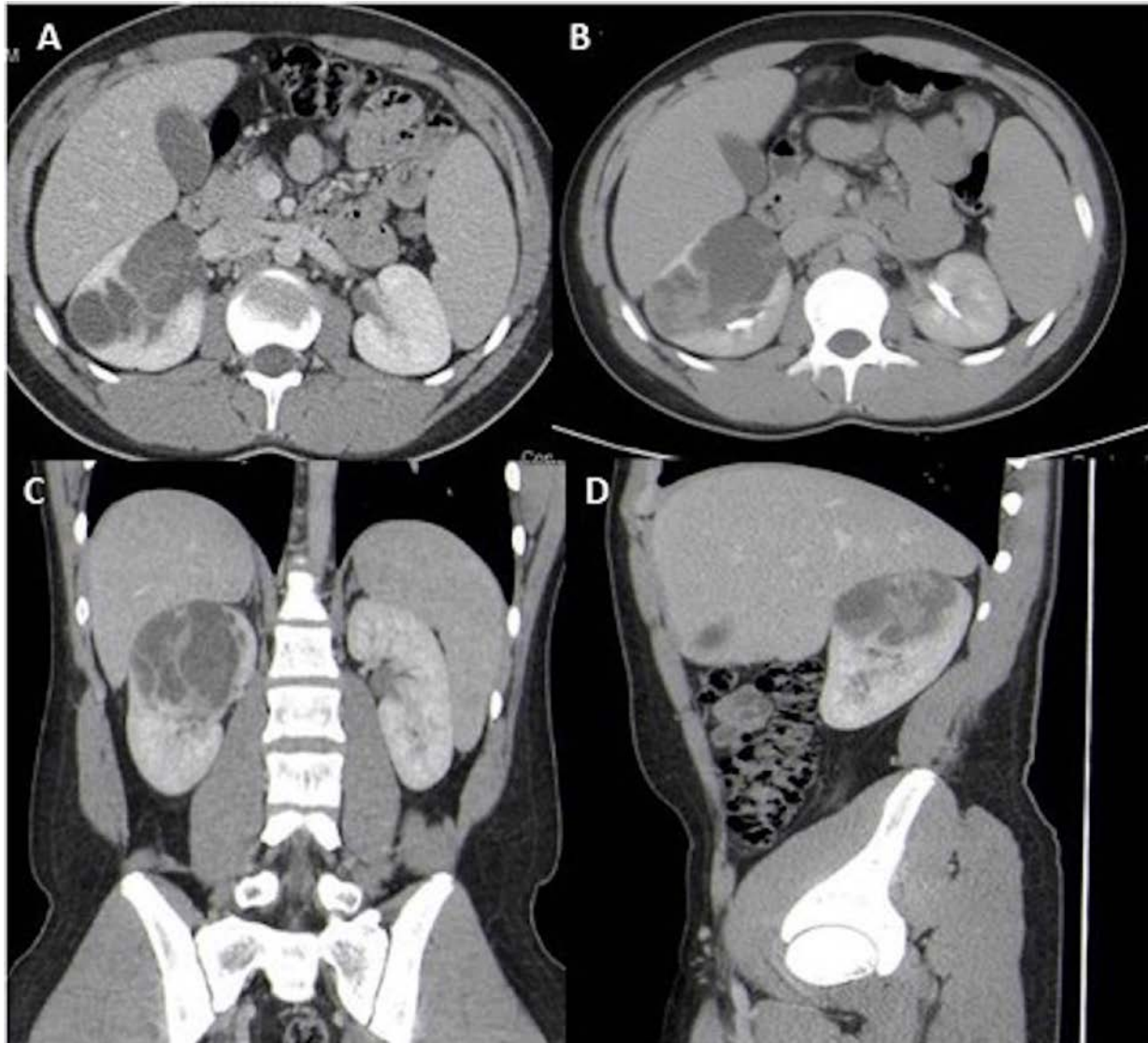


Fig. 2. (A) Low magnification of cystic renal tumour. (B) Thin septae with cuboidal epithelial lining. The cells lack cytologic atypia or mitoses, but stroma contains spindled cells and some simple tubules. (C) Estrogen receptor positivity in spindled stromal cells. (D) Progesterone receptor positivity in spindled stromal cells.

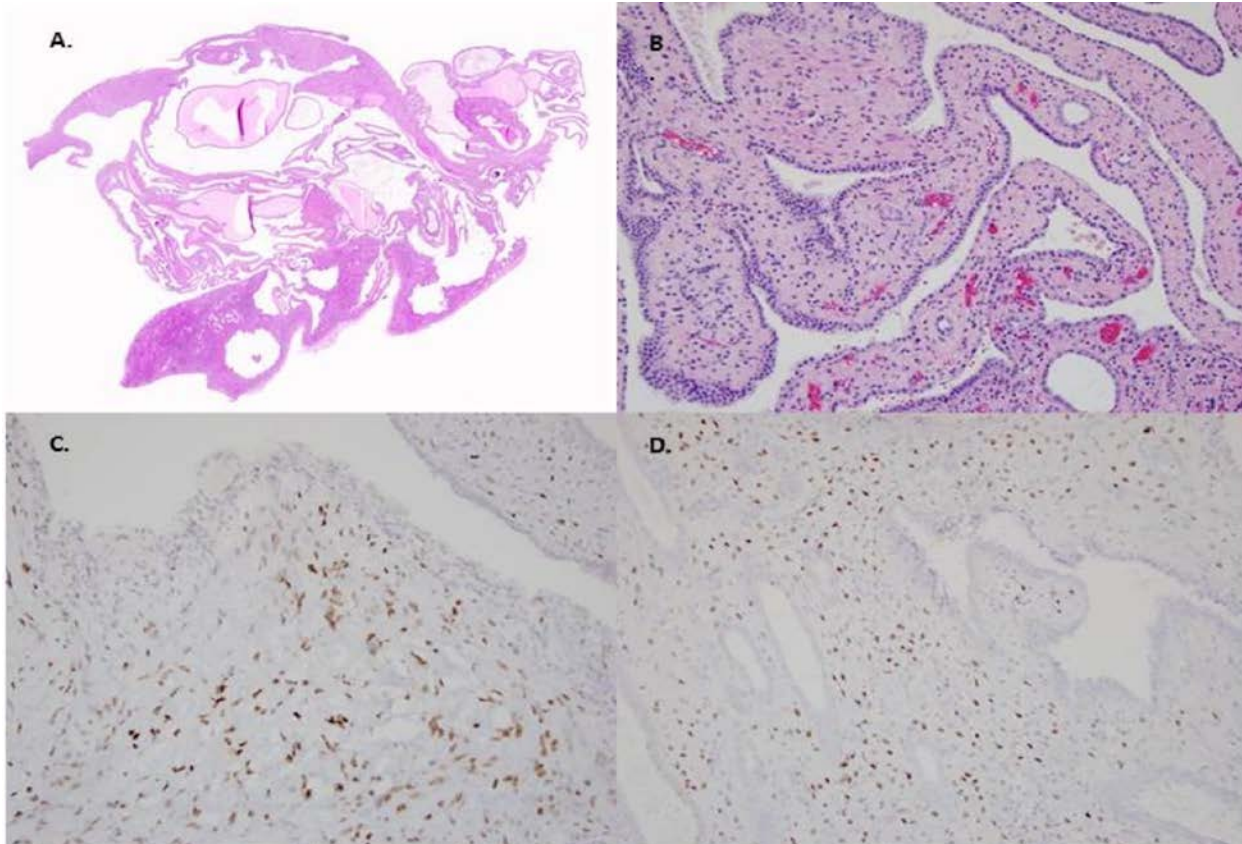


Table 1. Mixed epithelial and stromal tumour cases in pediatric males							
Case	Age	Presentation	Size (cm)	Location	Surgery	Pathology	No recurrence
Choy et al ²	14	Microscopic hematuria	2.0 x 1.5 x 0.8	R lower pole	Robotic partial nephrectomy	Epithelial & stromal Stromal ER +, PR +, actin +	9 months
Teklali et al ⁷	12	Gross hematuria	5.0	L upper pole	Partial nephrectomy	Epithelial & stromal Stromal ER +, actin +, desmin +, PR: NA	48 months
Present	14	Blunt trauma hematuria	7.0 x 4.0 x 3.0	R anteromedial	Robotic radical nephrectomy	Epithelial and stromal elements Stromal cells ER+, PR+, desmin+	18 months

ER: estrogen receptor; L: left; NA: not available; PR: progesterone receptor; R: right.