Mixed epithelial stromal renal tumor with dystrophic ossification: a case report and literature review

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A 25-year-old female presented with worsening right flank pain and a 9 year history of a slow growing 4 centimeter calcified renal mass. The lesion was resected by laparoscopic partial nephrectomy revealing a mixed epithelial and stromal tumor (MEST). This tumor has unusual features including the extensive amount of dystrophic calcification and the young age at presentation. Herein, we present a focused review of the literature regarding MESTs, as well as a discussion of calcified renal mass management. We conclude that laparoscopy may be utilized to safely perform nephron sparing surgery for select, calcified renal masses.

Key Words: mixed epithelial stromal tumor, calcification, dystrophic ossification, renal mass

Introduction

Mixed epithelial stromal tumor (MEST) is a recently described benign neoplasm of the kidney that shares some morphologic features with cystic nephroma.[1,2] These tumors are predominantly well circumscribed, and consist of variable proportions and sizes of epithelial tubular structures and a variably dense ovarian type stromal component. These lesions appear most commonly in middle aged women. The presence of estrogen and progesterone receptors in the spindle component of the masses suggests a hormonal role in the development of the mass. The only male in Adsay et al's series had a long history of sex steroid use.[1] Their review consisted of twelve patients, mean age of 56 years, of whom 50% presented with symptoms including pain and infection. These lesions are well circumscribed and benign in nature. Turbiner et al reported on 14 MEST tumors with a mean size of 9.7 cm in diameter, and these masses showed no evidence of recurrence after a mean follow up of 2.5 years.[2] Calcification was present in 4 of their 14 cases (29%), with focal dystrophic ossification in one of these tumors.

Herein, we report on the case of a 25-year-old female with a MEST who presented with an extensively calcified right renal mass. Surgical management included a technically challenging laparoscopic nephrectomy.

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Materials and methods

Case report

A 25-year-old woman presented to our institution with 6 months of worsening right flank pain. At age 16, the patient underwent obstetrical ultrasound that incidentally noted a 2.5 cm calcified upper pole renal mass thought to represent a hemorrhagic cyst. This mass was 3 cm in diameter on CT imaging at age 20 during workup for a ruptured ovarian cyst. Six months prior to presentation, CT scan measured the mass at 4.3 cm x 4.1 cm; at the time of surgery, contrast enhanced CT demonstrated a 4.8 cm x 4.1 cm calcified right upper pole mass with no regional adenopathy, Figure 1. There was no radiographic evidence of hydronephrosis, nephrolithiasis, or cholelithiasis. The patient was gravida 5, para 1 with a history of asthma and no previous surgical history. Other than mild right flank tenderness to deep palpation, her physical exam was unremarkable.

Thereafter, the patient underwent elective laparoscopic right partial nephrectomy. Technical difficulties with the lesion included the abutment of the mass to the collecting system. After defatting the kidney, the margins of the mass were visually apparent. Endoscopic ultrasound was employed while a monopolar hook was used to further demarcate the necessary resection margins. Following renal hilar clamping, the kidney was irrigated with 4 degree Celsius saline irrigation. During tumor resection, the collecting system was entered and subsequently repaired with a running Lapra-Ty 2-0 Vicryl suture. Five 0-Vicryl Lapra-Ty figure-of-eight stitches were utilized to close the parencymal defect after application of Floseal.[3] Warm ischemia time was 34 minutes. The mass was placed in an Endocatch bag and removed periumbilically. The extraction site was 5 cm; the hardness of the mass required us to fashion this larger extraction site as to prevent fatigue of the bag and potential spillage of tumor. Estimated blood loss was 50 cc. Postoperatively, the patient ambulated, tolerated a regular diet, received non narcotic analgesia and was discharged on postoperative day one. Imaging at 6 months demonstrated no evidence of disease recurrence.

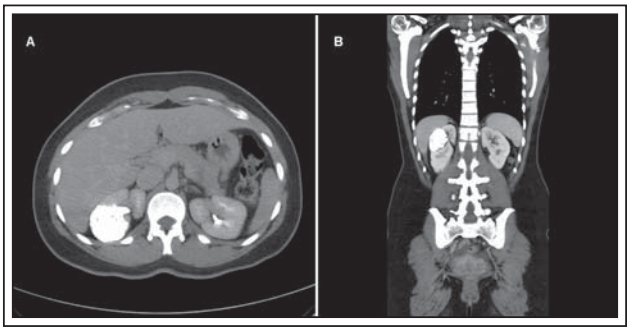

Figure 1. Axial (A) and coronal (B) reconstruction of abdominal CT scan revealing 4.8 cm calcified right renal mass.

Pathologic findings

The tumor consisted of a 5.8 cm x 4.4 cm x 4.0 cm, well circumscribed, hard mass with a heterogeneous yellow to white cut surface with extensive calcification. There were no grossly cystic areas. Microscopic examination after decalcification revealed a tumor consisting of a mixture of tubular and microcystic (epithelial) structures in a paucicellular stromal component, Figure 2. The tubular component was present circumferentially at the periphery of the tumor, both adjacent to normal parenchyma as well as on the contralateral aspect of the lesion. Tubules were also present in the middle of the tumor as small tubular clusters surrounded by calcific and hyalinized stroma. The predominant lining of the tubolocystic component was cuboidal to flat with occasional hobnailing. By immunohistochemistry, the epithelial component was reactive with CK7, CAM 5.2, A1/A3, focal AMACR and CD57.

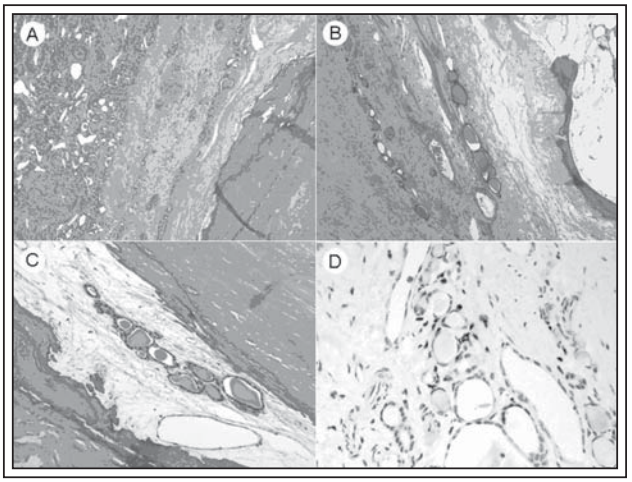

Figure 2. MEST consisting clusters of small tubules in a paucicellular stroma and adjacent areas of calcification (A), hematoxylin and eosin, original magnification X40. Focal areas of ossification and adipose tissue adjacent to tubular structures (B), hematoxylin and eosin, original magnification X100. Tubular structure in the center of the calcific mass surrounded by dense calcifications (C), hematoxylin and eosin, original magnification X100. Stromal elements immunoreactive with progesterone receptor (D), progesterone receptor, original magnification X100.

TABLE 1. **Reported cases of MEST in patients less than 25 years of age**

Author	Age (yrs)	Sex	Tumor size (mm)	Symptoms	Follow up	Original report	Reclassification*
Smida, 1989[4]	18	F	60	Asymptomatic	NA	MN	MEST*
Mahalati, 1994[5]	18	M	46	Asymptomatic	NED 6 mos	MN	MEST*
Levin, 1982[6]	19	F	130	Unknown	Recurrence	MN	MEST*
Van Velden, 1990[7]	20	F	80	Asymptomatic	NED 12 mos	MN	MEST*
Ishibashi, 1994[8]	22	F	NA	Abdominal pain	NED 36 mos	AMN	MEST*
Iraqi, 1984[9]	22	F	NA	Abdominal fullness	NED 30 mos	MN	MEST*
Ogawa, 1989[10]	24	F	NA	Flank pain	NED 18 mos	GH, AMN	MEST*
Hara, 2005[11]	12	F	14	NA	NED 40mos	MEST	

NA = not available; NED = no evidence of disease; mos = months; MN = mesoblastic nephroma; AMN = adult mature nephroblastoma; GH = giant hamartoma
*In coining "MEST," Adsay et al reclassified 38 cases in the literature as probable cases of MEST. This reclassification was based upon morphologic characteristics of the tumors.

The stromal component had undergone extensive calcification with focal osseous, adipocytic and smooth muscle metaplasia. These are unusual findings in such tumors but have been previously reported.[2,3] The stroma had areas of focal cellular condensation as well as hypocellular collagenized foci. The stromal component was immunoreactive with vimentin, progesterone receptor, desmin and SMA and negative for estrogen receptor, inhibin and calretinin, Figure 2.

Literature review

A MEDLINE review of the English literature was performed evaluating adolescent MEST tumor and calcification. As summarized in Table 1, this is the second reported case of MEST in a patient 25 years of age or younger. Of note, seven masses in females less than 25 years old that were previously reported as mesoblastic nephromas have been reviewed and categorized as "probable mixed epithelial and stromal tumor" by Adsay et al.[1] This case is the second reported MEST with extensive dystrophic ossification.[2]

Discussion

The current patient's initial radiographic documentation of a calcified renal mass occurred at age sixteen. Presently, the mechanism for development of mixed epithelial and stromal tumor remains unknown. Two features of this patient's tumor are of particular interest: the dystrophic calcification of the mass and her relatively young age of presentation.

Radiographically calcified renal masses in adolescents are of utmost concern for renal cell carcinoma.[12] Calcification is seen on CT in 33% of pediatric RCC cases versus 5%-10% in adults.[13,14] The prevalence of calcified MEST is currently unknown. Calcified masses have also been reported in vascular, infectious and cystic masses as well as Wilm's tumors, neuroblastomas, and sarcomas.[15] The distribution of calcium within a mass – central, circumferential, curvilinear, stippled - does not have predictive oncologic value.[16] Likewise, uniform, radiographic calcification in a mass does not necessarily imply ossification, as homogeneously calcified fluid filled cysts have also been reported.[17]

In addition to MEST, the differential diagnosis for this patient's calcified renal mass includes a metanephric adenoma and less likely a nephrogenic adenoma/metaplasia. However, the overall histopathologic features and additional immunostains including lack of expression of CA-125 and WT-1 support the exclusion of these less likely diagnoses. Due to the presence of adipocytic and muscular components, an angiomyolipoma was considered, noting that some angiomyolipomas have recently been reported to contain a cystic component.[21] However, myomelanocytic markers melan-A and HMB-45 were negative. Although unusual, fat containing MEST have been noted in series as well as case reports, with some tumors characterized by fat predominance.[2,22] Adipose tissue has been associated with osseous metaplasias in many organs that may or may not additionally include hematopoietic elements. Recent genomic and histopathologic testing indicates that cystic nephroma and MEST are closely related, perhaps at opposite ends of the same pathologic spectrum.[18-20]

Only one article contemporary to the coining of "MEST" notes tumor presence in an individual less than 25 years of age. Hara et al report the presence of MEST in a 12-year-old female with previous estrogen exposure.[11] In Adsay et al's review, they posited that seven historical cases of mesoblastic nephroma in individuals less than 25 years of age would be better characterized as MEST; of their twelve contemporary cases, eight had estrogen exposure.[1,4-9] Estrogen and progesterone receptors were present in 62% and 82% of Turbiner et al.'s 14 tumors.[2] The patient in this case report had received oral contraceptives for 2 years prior to the discovery of her mass, and continued to take them for an additional 9 years of follow up.

Conclusions

MEST should be added to differential diagnosis for a calcified renal mass that also includes renal cell carcinoma, cystic disease, xanthogranulomatous pyelonephritis, Wilm's tumor, neuroblastoma, transitional cell carcinoma, osteosarcoma, abscess, schistosomiasis, tuberculosis, hematoma, arteriovenous fistula and arteriovenous malformation.[15] In skilled hands, laparoscopic nephron sparing surgery can be safely performed to manage the calcified renal lesion. Although rare, MEST tumors should be considered in the differential diagnosis of renal masses, especially in young females. Surgery is still needed to exclude malignancy. □

References

1. Adsay NV, Eble JN, Srigley JR et al. Mixed epithelial and stromal tumor of the kidney. *Am J Surg Pathol* 2000;24(7):958-970.
2. Turbiner J, Amin MB, Humphrey PA et al. Cystic nephroma and mixed epithelial and stromal tumor of kidney: a detailed clinicopathologic analysis of 34 cases and proposal for renal epithelial and stromal tumor (REST) as a unifying term. *Am J Surg Pathol* 2007;31(4):489-500.
3. Shalhav AS, Orvieto MA, Chien GW et al. Minimizing knot tying during reconstructive laparoscopic urology. *J Urol* 2006;68(3):508-513.
4. Smida L, Taief YL, Rebai T. [Mesoblastic nephroma. Unusual renal tumor in adults. Apropos of a case] [Article in French]. *J Urol* 1989;95(7):423-426.
5. Mahalati K, Sahin A, Ozen H et al. Mesoblastic nephroma in adults: a clinical case. *Bull Cancer* 1994;81(11):928-930.
6. Levin NP, Damjanov I, Depillis VJ. Mesoblastic nephroma in an adult patient: recurrence 21 years after removal of the primary lesion. *Cancer* 1982;49(3):573-577.
7. Van Velden DJ, Schneider JW, Allen FJ. A case of adult mesoblastic nephroma: ultrastructure and discussion of histogenesis. *J Urol* 1990;143(6):1216-1219.
8. Ishibashi K, Ichizjo S, Kameoka H et al. A case of adult mature nephroblastic tumor. *Nippon Hinyokika Gakkai Zasshi* 1994;85(7):1131-1134.
9. Iraqi A, Meziane EM, Sqalli S et al. Histogenetic aspects of mesoblastic nephroma. Apropos of a case in an adult. *Arch Anat Cytol Pathol* 1984;32(4);249-252.
10. Ogawa O, Okumura K, Taniguchi T et al. A case of giant renal hamaroma considered as congenital mesoblastic nephroma of adult. *Hinyokika Kiyo* 1989;35(10):1749-1753.
11. Hara N, Kawaguchi M, Murayama S et al. Mixed epithelial and stromal tumor of the kidney in a 12-year-old girl. *Pathol Inter* 2005;55(10):670-676
12. Sostre G, Johnson JF, Cho M. Ossifying renal cell carcinoma. *Pediatr Radiol* 1998;28(6):458-460.
13. Kabala JE, Shield J, Duncan A. Renal cell carcinoma in childhood. *Pediatr Radiol* 1992;22(3):203-205.
14. Abrams HJ, Buchbinder MI, Sutton AP. Renal cell carcinoma in adolescents. *J Urol* 1979;121(1):92-94.
15. Patterson J, Lohr D, Briscoe C et al. Calcified renal masses. *Urology* 1987;29(4):353-356
16. Krieger, JN, Sniderman KW, Seligson GR et al. Calcified renal cell carcinoma: a clinical, radiographic and pathologic study. *J Urol* 1979;121(5):575-580.
17. Weyman PJ, McClennan BL, Lee JKT et al. CT of calcified renal masses. *Amer J Roentgenol* 1982;138(6):1095-1099.
18. Antic A, Perry KR, Harrison K et al. Mixed epithelial and stromal tumor of the kidney and cystic nephroma share overlapping features. *Arch Pathol Lab Med* 2006;130(1):80-85.
19. Zhou M, Kort E, Hoekstra P et al. Adult cystic nephroma and mixed epithelial and stromal tumor of the kidney are the same disease entity: molecular and histologic evidence. *Am J Surg Pathol* 2009;33(1):72-80.
20. Jevremovic D, Lager D, and Lewin M. Cystic nephroma (multilocular cyst) and mixed epithelial and stromal tumor of the kidney: a spectrum of the same entity? *Ann Diagn Pathol* 2006;10(2):77-82.
21. Fine SW, Reuter VE, Epstein JI et al. Angiomyolipoma with epithelial cysts (AMLEC): a distinct cystic variant of angiomyolipoma. *Am J Surg Pathol* 2006;30:593–599.
22. Sireci AN, Rodriguez, R, Swierczynski SL et al. Fat-predominant mixed epithelial stromal tumor (MEST): report of a unique case mimicking angiomyolipoma. *Int J Surg Pathol* 2008;16(1):73-77.