

Atypical features of mixed epithelial and stromal tumour of kidney: a case report with histopathology correlation

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Abstract

Adult cystic nephroma and mixed epithelial stromal tumours (MEST) are classified under the mixed epithelial and stromal tumour (MEST) family, which is a part of the 2016 World Health Organisation (WHO) renal tumour classification. They are rare, benign tumours which have similar imaging appearance as certain types of renal carcinoma. Hence, it is often regarded as malignant pre-operatively and histopathologically confirmed to be benign. We present a case of a 66-year-old lady who complains of gradual abdominal distension for 9 months, associated with loss of appetite, loss of weight and early satiety. Other than clinical findings that point towards ascites, the rest of her physical examination was unremarkable. Blood investigations including tumour markers were normal. Abdominal ultrasound and computed tomography (CT) showed a huge unilocular intra-abdominal cystic mass with enhancing solid component attached to the right kidney which was exerting significant mass effect to the surrounding structures. The patient developed impending abdominal compartment syndrome and underwent right nephrectomy with tumour excision. The final histopathological diagnosis revealed mixed epithelial and stromal tumour (MEST). The patient recovered well. Mixed epithelial stromal tumour (MEST) is a rare clinical entity. Ultrasound and CT imaging are the usual investigating modalities. Histopathological correlation is needed to reach the diagnosis. This case has an unusual and different radiological imaging appearance when compared to past literature and contributes an additional case to our collective knowledge of these lesions.

Keywords: *cystic nephroma, mixed epithelial stromal tumour, renal carcinoma*

Introduction

Adult cystic nephroma and mixed epithelial and stromal tumours (MEST) are classified under the mixed epithelial and stromal

tumour (MEST) family, as defined in the 2016 World Health Organization (WHO) classification of renal tumours. These lesions are rare, predominantly benign neoplasms that are often indistinguishable from certain types of renal carcinoma on diagnostic

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imaging. They typically present as multilocular cystic renal masses with multiple septations on computed tomography (CT). Owing to their overlapping radiological features with malignant renal tumours, MEST is frequently regarded as malignant pre-operatively, resulting in radical surgical management, with the benign nature of the lesion only confirmed on post-operative histopathology. As such, MEST holds important clinical relevance, as misdiagnosis may lead to unnecessary radical or partial nephrectomy. Radical or partial nephrectomy remains the mainstay of treatment, with definitive diagnosis established through histopathology and immunohistochemistry. The present case is significant due to its highly atypical imaging appearance, which does not conform to the usual description in existing literature. To date, only a limited number of cases of unilocular giant MEST presenting with impending abdominal compartment syndrome have been reported worldwide, making this an exceptionally rare presentation.

Case reports

A 66-year-old lady with no underlying comorbidity presented with a 9-month duration of gradual abdominal distension associated with loss of appetite, loss of weight and early satiety. No bleeding per vagina or abnormal discharge. No fever or abdominal pain. Bowel output and urination were regular. She is Para 7 and has attained menopause 20 years ago. Her last childbirth was 27 years ago. No history of surgical intervention or family history of malignancy. Other than generalized abdominal distension up to the xiphisternum with positive fluid thrill, her physical examination was unremarkable. Her infective markers, renal function, and tumour markers (AFP, CEA, CA 19-9, CA 125, CA 15.3, Beta-HCG) were normal.

Bedside abdominal ultrasound (Figure 1) showed a large cystic mass occupying almost the whole abdomen with presence of solid component at the superior aspect of the mass (near to the right hypochondrium).

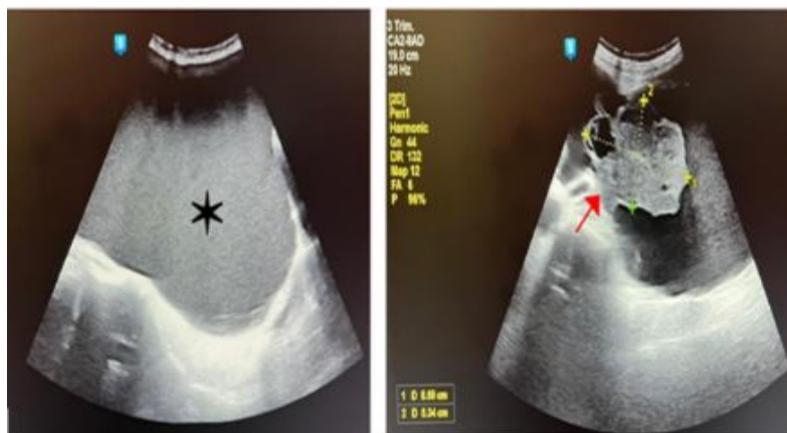


Figure 1. Ultrasound images showing large cystic mass with echogenic material within (*), and a hyperechoic solid component (red arrow) within the mass.

Initial CT scan showed a huge uniloculated cystic mass extending from the mid abdomen until the pelvic region, which measures approximately 18.0 x 25.1 x 33.3 cm. No intralesional calcification. An irregular enhancing solid component is seen at the superior part of the mass, which is attached to the mid-pole of right kidney (Figure 2). The mass displaces the right

kidney superior-medially, and displaces the inferior vena cava (IVC), right adrenal, pancreas and bowel loops to the left side of the abdomen. There is a clear plane of demarcation between the mass and these structures. No enlarged intraabdominal lymph node. The IVC is patent and normal in calibre. A clinical impression of cystic renal tumour was made.

A repeated CT abdomen one month later showed that the cystic mass has increased in size, exerting more mass effect and displacing its surrounding structures (Figure 2). The ratio of maximal

anteroposterior to transverse abdominal diameter is borderline measuring 0.83 (normal <0.8). Hence, impending abdominal compartment syndrome was suspected based on imaging and clinical deterioration.

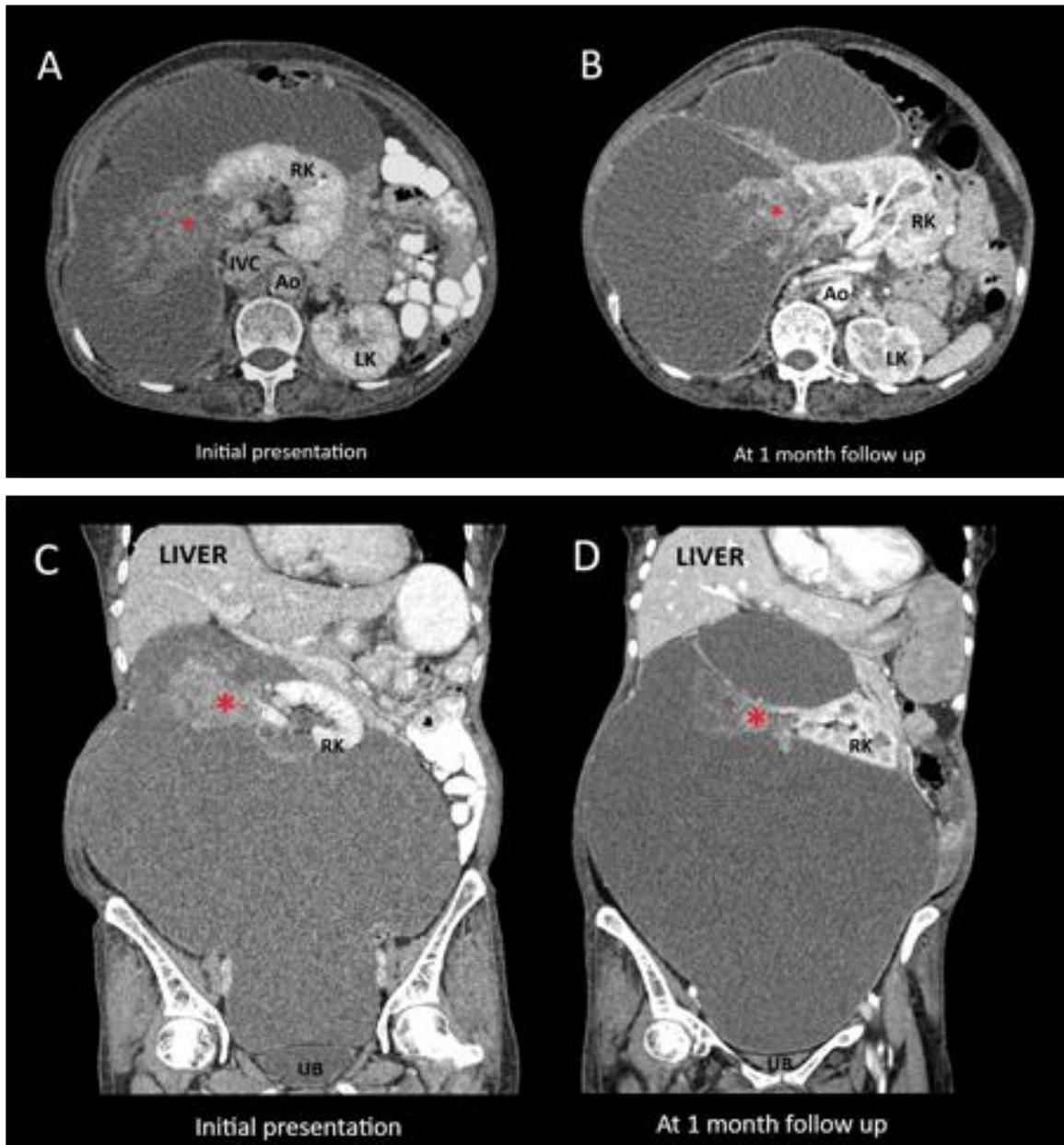


Figure 2. Contrast-enhanced CT Abdomen images demonstrating a large cystic mass occupying the entire abdominal cavity with progressive increase in tumour size and mass effect related to the cystic component at one month follow up. Axial image (A) and coronal image (C) at initial presentation showed a large cystic mass occupying the entire abdominal cavity and displacing the right kidney as well as the other solid organs. Solid enhancing component is seen attached to the mid-pole of the right kidney (red asterisk). Axial image (B) and coronal image (D) at 1 month follow-up illustrating further interval enlargement of the cystic component with increasing mass effect and displacement onto the surrounding structures. Abbreviations: RK - right kidney; LK - left kidney; IVC - inferior vena cava; Ao - aorta; UB - urinary bladder.

A semi-urgent operation for right nephrectomy and tumour excision was planned. Upon entering the abdominal cavity, a huge cystic mass was seen arising from the retroperitoneal region and is continuous with the right kidney. The right ovary, right fallopian tube and right suprarenal gland were adherent to the cystic mass and these organs were removed along with the mass. The patient recovered well post-surgery.

Gross pathology showed a large cystic mass measuring 28 x 23 x 11 cm. The cyst contains haemorrhagic fluid with blood clots. It is uniloculated and the wall thickness ranges between 1-5mm. The kidney is identified on the wall of the cyst. A haemorrhagic solid nodule measuring 7 x 6 x 5 cm was seen at the mid pole with vesicle-like lesion.

Microscopically, it has a fibrous cyst wall, devoid of epithelial lining and replaced by necrotic material, foamy macrophages and haemosiderin-laden macrophages (Figure

3). The cyst wall is infiltrated by dense mixed inflammatory infiltrates, mostly consisting of lymphocytes, plasma cells and histiocytes. There is also granulation tissue with prominent reactive fibroblasts. The vesicle-like lesions are composed of epithelial and stromal components. The epithelial component exhibits flattened to cuboidal cells; some forming glandular structures. The stromal component exhibits variable cellularity and is composed of spindle to epithelioid cells reminiscing ovarian and endometrial stroma. Sections of the mid-pole haemorrhagic nodule also display varying epithelial and stromal elements. No cellular atypia or abnormal mitotic figures seen.

Immunohistochemical studies showed the epithelial cells are positive for CKAE1/AE3, EMA and PAX8 (Figure 3). The stromal cells exhibit CD10, ER, PR, WT1, SMA, and vimentin positivity. Final histopathological interpretation is mixed epithelial and stroma tumour of the kidney (MEST).

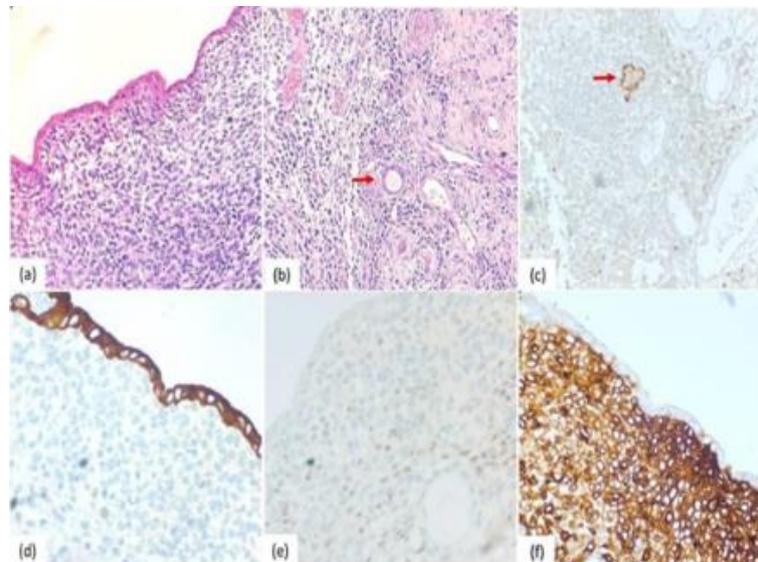


Figure 3. Morphological and immunohistochemical features of mixed epithelial and stromal tumour (MEST). All images were obtained from whole-slide digital scans (original magnification 200×). (a) The cyst is lined by simple flattened to cuboidal epithelial cell with bland nuclei and eosinophilic cytoplasm. The stroma consists of fibrous tissue resembling ovarian stroma (H&E, 200×). (b) Scattered small cysts (red arrows) are seen in the solid areas (H&E, 200×). (c–f) Immunohistochemical analysis using the immunoperoxidase method with DAB chromogen visualisation. (c) The epithelial cells exhibit strong nuclear positivity for PAX8 (red arrow) and (d) diffuse cytoplasmic positivity for CKAE1/AE3 (200×). (e) The stromal cells are positive for ER and (f) CD10 (200×).

Discussion

Mixed epithelial stromal tumours (MEST) were previously radiologically categorised into two patterns: cystic renal masses with septa and nodular components (type A) and solid masses with cystic areas (type B) (Wang *et al.*, 2013). This historical distinction has largely been superseded by the World Health Organization (WHO) classification of kidney tumours 2016, which recognises these entities as part of a single MEST family with a morphological spectrum ranging from the predominantly cystic adult cystic nephroma (ACN) to more solid tumours classified as MEST. They account for 0.2% of all renal tumours as well as distinctive neoplasms with biphasic epithelial and stromal component (DeFanti & Nodit, 2013; Karasavvidou *et al.*, 2022). Despite their benign biological behaviour, these tumours pose a significant diagnostic challenge due to their close radiological resemblance to malignant renal neoplasms, often resulting in aggressive surgical management.

The largest known tumour in the MEST spectrum reported by Sawant *et al.* (2017) measured 31 × 19 × 19.6 cm and demonstrated a multilocular architecture. In contrast, the tumour in our patient measured 28 × 23 × 11 cm and represents, to our knowledge, it is the largest reported unilocular MEST. This architectural distinction is clinically relevant, as unilocular morphology is exceedingly rare within the MEST spectrum and further complicates pre-operative radiological characterisation. Furthermore, our case is unique in that the tumour progressed rapidly and resulted in impending abdominal compartment syndrome, a complication that has only rarely been described in association with renal tumours and has not been well documented in MEST within existing literature. To our knowledge, there has been no previously published case

of a giant, predominantly cystic, unilocular MEST causing impending abdominal compartment syndrome identified in international literature to date in PubMed and Google Scholar.

There is a marked female predominance with a reported ratio of approximately 10:1 (Sharma *et al.*, 2017), and patients are typically peri-menopausal women (Tsakiris *et al.*, 2024). Hormonal influences have been implicated, including associations with gonadotropin-releasing hormone agonists and oestrogen therapy (Verma *et al.*, 2024). Our patient's demographic profile aligns with these observations. While many patients are asymptomatic, with tumours detected incidentally, symptomatic cases may present with flank pain, haematuria, or a palpable abdominal mass (Tatsuya *et al.*, 2021).

Both ACN and MEST are typically solitary, unilateral, well circumscribed, and unencapsulated, with reported sizes ranging from 2 cm to 24 cm (Picken *et al.*, 2018). Classical descriptions of MEST on contrast-enhanced computed tomography (CECT) include multiloculated, multiseptated cystic masses with delayed enhancement of septa or solid components (Sharma *et al.*, 2017). ACNs typically present as multiloculated cystic lesions with thin septations and without a significant solid component. Septal enhancement may be present. Haemorrhage, calcification and fat may be seen in both, but these features are not consistently observed. In our case, CECT demonstrated a large, unilocular, almost entirely cystic renal mass with minimal solid enhancing component. The lesion was devoid of septations. It deviates markedly from the expected radiological appearance of both adult cystic nephroma and MEST. Table 1 compares the classical radiological features of ACN and MEST reported in the literature with those of the present case, while Figure 4 depicts the corresponding imaging differences.

Table 1. Radiological comparison between classical MEST, Adult Cystic Nephroma (ACN), and the present case.

Feature	Classical MEST	Classical ACN	Present Case
Typical Morphology	Predominantly solid mass with multiple cystic components	Predominantly cystic, multiloculated mass	Predominantly cystic, unilocular mass
Loculation	Multiloculated	Multiloculated	Unilocular
Septations	Common, often thick	Common, thin fibrous septa	Absent
Solid Component	Common, variable size	Minimal or absent	Small focal solid component
Contrast-Enhanced CT Appearance	Delayed enhancement of solid components and septa	Septal enhancement may be present	Enhancing solid component without septations
Bosniak Classification	Usually Bosniak III–IV	Usually Bosniak III	Bosniak IV–like appearance due to solid enhancement
Calcification	Rare	Rare	Absent
Growth Behaviour	Slow-growing	Slow-growing	Rapid interval growth
Mass Effect	Usually limited	Usually limited	Severe mass effect with impending abdominal compartment syndrome
Typical Pre-Operative Diagnosis	Renal cell carcinoma	Multilocular cystic renal neoplasm	Cystic renal malignancy



Figure 4. Contrast-enhanced axial CT images illustrating the radiological spectrum of cystic renal lesions: (A) Adult cystic nephroma (ACN) demonstrating a well-circumscribed multiloculated cystic mass with thin enhancing septations and no solid enhancing component (red outline). *Adapted from Kakish (2026).* (B) Mixed epithelial and stromal tumour (MEST) showing a complex right renal mass with both cystic and enhancing solid components (red outline). *Adapted from Sheldon (2026).* (C) Imaging from the present case demonstrating a unilocular cyst with a minimal enhancing solid component and no internal septations (circled outline). Abbreviations: RK - right kidney; LK - left kidney; IVC - inferior vena cava.

Radiologically, MESTs are almost always indistinguishable from malignant cystic renal tumours (Tsakiris *et al.*, 2024), and many reported cases carry a pre-operative diagnosis of renal cell carcinoma, with the benign nature of the lesion only established after surgical excision (Stamatiou *et al.*, 2008). This diagnostic dilemma was particularly pronounced in our patient as the extreme size due to rapid tumour growth, unilocular configuration, and aggressive mass effect culminating in impending abdominal compartment syndrome clearly distinguish this case from the majority of previously reported MESTs. Percutaneous biopsy was not feasible because of bleeding risk and concern for tumour seeding. As such, radical nephrectomy served as both a diagnostic and therapeutic intervention in this case.

Gross pathological examination of MEST typically reveals mixed solid and cystic components, with cysts commonly containing clear serous fluid (Michal *et al.*, 2004; Turbiner *et al.*, 2007). In our case, the cyst contained haemorrhagic fluid with blood clots and areas of necrosis, features that are atypical and infrequently reported in benign MEST. Haemorrhagic MESTs have only rarely been mentioned in the literature, including reports by Sukov *et al.* (2007), Wang *et al.* (2015) and Varghese *et al.* (2023)

reinforcing the unusual nature of this presentation. These pathological features likely contributed to the aggressive radiological appearance and heightened clinical suspicion for malignancy.

Microscopically, ACN and MEST have some overlapping histological features. MEST has a solid-cystic architecture which is made up of stromal and epithelial components (Verma *et al.*, 2024). The stromal component can be paucicellular to hypercellular and have a wide spectrum of morphology (Adsay *et al.*, 2000; Antic *et al.*, 2006; Caliò *et al.*, 2016; Michal *et al.*, 2004; Turbiner *et al.*, 2007). It can be fibrous and oedematous, dense and collagenous, have slender to plump spindle cells, have focal areas of smooth muscle differentiation or have ovarian type stroma with luteinisation. Sometimes, adipose tissue can be present. The epithelial component of MEST has clustered or scattered cysts and glands of varying sizes and architecture. The cells lining the cysts and glands have a broad spectrum of morphology such as flat, cuboidal, columnar, hobnail, urothelial like, clear cell and ciliated. Its cytoplasm can be eosinophilic, amphophilic or vacuolated. Occasionally, the small cysts contain eosinophilic material reminiscent of thyroid follicles. Cellular atypia, calcification, mitotic figures, necrosis, and haemorrhage are rare

(DeFanti & Nodit, 2013; Tatsuya *et al.*, 2021; Verma *et al.*, 2024; Wang *et al.*, 2013). ACN histologically consists of multilocular cysts lined by flat to cuboidal epithelium and separated by fibrous septae. Mature tubules may also be seen in the fibrous septa (Picken *et al.*, 2018; Sharma *et al.*, 2017; Tatsuya *et al.*, 2021; Verma *et al.*, 2024). According to Turbiner *et al.* (2007), the diagnosis of ACN was defined as a tumour composed of large cysts, microcysts and tubules with stroma consisting of variable spindle cells as well as dividing septa less than 5 mm in size. If any lesion within the MEST family spectrum does not fulfil these criteria, it is classified as MEST.

On immunohistochemistry studies, the epithelium stains strongly for renal lineage markers PAX8, cytokeratins AE1/AE3 and for CK7 (Karasavvidou *et al.*, 2022). The stromal component express positive CD10, ER, PR, SMA and WT1 (DeFanti & Nodit, 2013; Demir *et al.*, 2022; Karasavvidou *et al.*, 2022; Sharma *et al.*, 2017; Tinguria & Chorneyko, 2023; Wang *et al.*, 2013). Table 2 compares the histopathological and immunohistochemical features of classical MEST and ACN reported in the literature with those observed in this case.

Table 2. Histopathological comparison between classical MEST, Adult Cystic Nephroma (ACN), and the present case.

Feature	Classical MEST	Classical ACN	Present Case
Overall Architecture	Mixed solid–cystic	Predominantly cystic	Predominantly cystic with focal solid nodule
Cyst Configuration	Multiple cysts of varying size	Multiloculated cysts	Single large unilocular cyst
Epithelial Lining	Variable (flat, cuboidal, hobnail, glandular)	Flat to cuboidal epithelium	Flattened to cuboidal epithelium
Stromal Component	Prominent, often ovarian-type	Fibrous septa with mature tubules and minimal stroma containing spindle cells	Prominent stromal component resembling ovarian/endometrial stroma
Septa	Present	Present (<5 mm thick)	Absent
Haemorrhage	Rare	Rare	Present (haemorrhagic fluid and blood clots)
Necrosis	Rare	Rare	Present
Cellular Atypia	Absent	Absent	Absent
Mitotic Activity	Absent or rare	Absent	Absent
Immunohistochemistry – Epithelium	PAX8+, CK AE1/AE3+, EMA+	PAX8+, CK+	PAX8+, CK AE1/AE3+, EMA+
Immunohistochemistry – Stroma	CD10+, ER+, PR+, SMA+, WT1+	Usually ER/PR negative or weak	CD10+, ER+, PR+, SMA+, WT1+
Final Diagnosis	MEST	ACN	MEST (despite ACN-like architecture)

In short, adult cystic nephroma and MEST share overlapping microscopic features, with MEST demonstrating a solid-cystic architecture composed of epithelial and stromal components (Verma *et al.*, 2024). Although necrosis and haemorrhage are considered rare histological findings in MEST, both were present in this case, further underscoring its atypical nature. Immunohistochemical staining confirmed the diagnosis, with epithelial markers positive for PAX8 and cytokeratins, and stromal components expressing CD10, ER, PR, SMA, and WT1, consistent with previously reported profiles (DeFanti & Nodit, 2013; Karasavvidou *et al.*, 2022).

The differential diagnosis for a large cystic renal mass is broad and includes malignant cystic renal cell carcinoma, cystic nephroblastoma, angiomyolipoma with cysts, and other rare entities (Joshi & Beckwith, 1989; Sun *et al.*, 2014).

Furthermore, the unusual constellation of features observed raises the question of whether further refinement or sub-classification within the MEST spectrum may eventually be warranted, a hypothesis that would require validation through larger case series or registry-based studies rather than isolated case reports. At present, neither advanced imaging modalities nor urinary biomarkers permit a confident pre-operative diagnosis of MEST. These tools may provide supportive information but lack sufficient specificity to distinguish MEST from other complex cystic renal lesions. Histopathological examination continues to represent the diagnostic gold standard. Pre-operative biopsy may be considered in selected cases with appropriate precautions, though bleeding risk and tumour seeding remain concerns.

Although MEST lesions are almost always benign, rare cases of malignant transformation, recurrence, and peritoneal seeding have been reported (DeFanti & Nodit, 2013; Sun *et al.*, 2014; Tatsuya *et al.*, 2021; Verma *et al.*, 2024). Certain signs such as an absence of lymphadenopathy and distant metastases as well as normal tumour marker levels, are the usual guides for the

clinician to suspect a benign entity. But in cases like ours, these signs may not be reliable as both MEST family and multilocular cystic renal neoplasm of low malignant potential (MCRNLMP) which are indistinguishable from the other, have a low incidence of recurrence and metastasis. Given the atypical and aggressive presentation in our patient, this case underscores the importance of post-operative surveillance, even in histologically benign MEST, particularly when unusual features such as massive size, haemorrhage, necrosis, and rapid growth are present.

Conclusion

This case highlights that MEST may present with highly atypical features such as a unilocular giant cystic mass and rapid progression leading to abdominal compartment syndrome. Radiology alone is insufficient, histopathology and immunohistochemistry remains gold standard for diagnosis. Surgical excision is almost always the treatment of choice as there is radiological diagnostic dilemma given their similar presentation and appearance to malignancy, a high number of differential diagnoses and difficulty in obtaining biopsy. Active surveillance post-resection is recommended given rare reports of recurrence and malignant transformation.

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