



Case Report *Genitourinary and Gynecologic Imaging*

TFE3-rearranged renal cell carcinoma with massive calcification: Imaging-pathologic correlation

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ABSTRACT

Transcription Factor E3 (TFE3)-rearranged renal cell carcinoma (RCC) is rare. Radiologically, TFE3-rearranged RCC typically appears as a hyperattenuating mass with calcifications. Calcifications typically appear as small punctate or irregular coarse deposits, which are pathologically associated with granular and collagenous stromal degeneration. Here, we report a case of TFE3-rearranged RCC with extensive calcification in a young female, emphasizing imaging-pathologic correlation to enhance diagnostic accuracy. This case underscores the importance of recognizing atypical radiological features in rare RCC subtypes.

Keywords: Calcification, Computed tomography, Renal cell carcinoma, TFE3-rearranged

INTRODUCTION

TFE3-rearranged renal cell carcinoma (RCC) is rare, exhibits distinct biological behavior and pathological features.^[1-7] Radiologically, TFE3-rearranged RCC typically appears as a hyperattenuating mass with calcifications.^[8-10] Dong *et al.* reported calcification in 50% of cases on CT, typically as small punctate or irregular coarse deposits associated pathologically with granular and collagenous stromal degeneration.^[8] We report a case of TFE3-rearranged RCC with extensive calcification in a young female, emphasizing imaging-pathologic correlation to enhance diagnostic accuracy. This case underscores the importance of recognizing atypical radiological features in rare RCC subtypes.

CASE REPORT

A 20-year-old female patient presented with left-sided lumbar and lower abdominal pain for 1 day without an obvious cause or trigger, accompanied by gross hematuria but without urinary urgency, frequency, dysuria, chills, fever, malaise, or vomiting. Ultrasound demonstrated an enlarged left kidney with loss of normal architecture and a 7.3 cm × 8.5 cm hypoechoic mass in the left renal region, exhibiting heterogeneous internal echogenicity with multiple patchy and confluent echoes. Color Doppler flow imaging showed abundant blood flow signals within the mass.

Imaging

Computed tomography (CT) revealed a significantly enlarged left kidney with morphological abnormalities and a slightly hyperdense soft-tissue mass in the mid-to-lower pole, containing

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diffusely distributed patchy and extensive calcifications – some appearing as dots, stripes, or circular arcs [Figure 1a-b]. Contrast-enhanced CT demonstrated marked heterogeneous enhancement of the lesion, with greater enhancement than the renal cortex and medulla in the cortical phase [Figure 1c-d]; in the medullary phase, the lesion's attenuation was lower than that of the upper pole cortex but higher than that of the medulla [Figure 1e-f]. Intraoperative findings showed a large, grayish-yellow tumor with a homogeneous, softer texture, less glossy margins, only mild adhesion to surrounding tissues, a rich blood supply without obvious hemorrhagic changes on the surface, and an intact left perirenal fascia.

Pathology

Pathological examination revealed a mass on the left kidney immediately adjacent to the renal fascia, measuring approximately 10 cm × 7 cm × 6.5 cm. On gross section, the cut surface was fleshy and grayish-red with a predominantly soft texture, focal areas of firmness, and visible calcifications. The mass did not involve the renal pelvis on gross inspection. After decalcification and routine sectioning, low-power microscopy showed tumor cells arranged in nests with abundant eosinophilic cytoplasm and scattered granulomas. At high power, the cells had round nuclei, some containing small nucleoli; mitotic figures were rare, and the cells were

loosely cohesive [Figure 2a]. Immunohistochemistry demonstrated Cytokeratin pan (CK) (-), CD10 (-), Vimentin (+), CD117 (-), E-Cadherin (+), Epithelial Membrane Antigen (EMA) (-), CK7 (-), RCC marker (-), Paired Box Gene 8 (PAX-8) (+), TFE3 (+), P504S (+), Carbonic Anhydrase IX (CAIX) (-), Ki-67 index 1%, Succinate Dehydrogenase Subunit B (SDHB) (+), and Fumarate Hydratase (FH) (+) [Figure 2b-d]. Special stain: Colloidal iron positive. Fluorescence *in situ* hybridization (FISH) suggested *TFE3* gene rearrangement. These findings support a diagnosis of microphthalmia-associated transcription (MiT) family translocation-associated RCC [Figure 2]. The renal pelvis was not involved; perirenal fat was infiltrated; vascular tumor emboli were identified; there was no perineural invasion; and ureteral and vascular margins were negative. Pathologic stage (AJCC 8th ed.): pT2a Nx Mx.

The patient underwent laparoscopic unilateral nephrectomy with retroperitoneal lymph node dissection. No evidence of recurrence or metastasis was detected on CT imaging at the 12-month follow-up.

DISCUSSION

Xp11.2 translocation RCC was first described by De Jong *et al.* in 1986, with the name reflecting the discovery of an Xp11.2 fusion gene in tumor cells.^[1] In 2016, TFE3-rearranged RCC

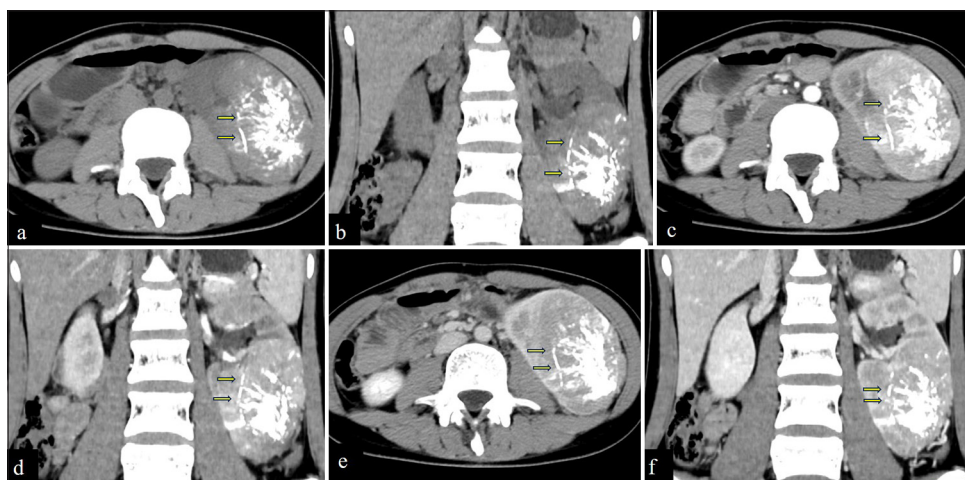


Figure 1: A 20-year-old female patient presented with left-sided lumbar and lower abdominal pain. (a and b) Noncontrast computed tomography (CT) scans show a markedly enlarged, dysmorphic left kidney with a slightly hyperdense soft-tissue mass in the mid-to-lower poles. The lesion contains diffusely distributed patchy and punctate calcifications, solid high-attenuation foci, and intermittent arcuate calcified shadows (yellow arrows). (c and d) Cortical-phase contrast-enhanced CT images demonstrate pronounced heterogeneous enhancement of the lesion's parenchymal component, exceeding the enhancement of the upper pole renal parenchyma. Tortuous intralesional vessels, deep lobulation, and both well-defined and ill-defined margins are visible. The left renal pelvis and collecting system are mildly dilated. Enhancement of the remaining upper-pole parenchyma is significantly lower than that of the tumor and the contralateral kidney (yellow arrows). (e and f) Medullary-phase contrast-enhanced CT images reveal persistent, marked enhancement of the lesion's parenchyma, with attenuation lower than the upper-pole cortex but higher than the medulla (yellow arrows). (The yellow arrows indicate the calcified shadows.)

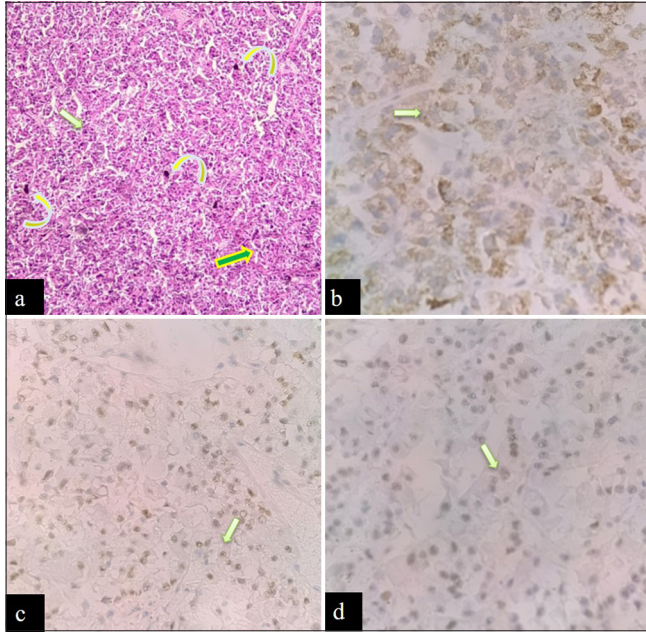


Figure 2: (a) At low-power microscopy (Hematoxylin and eosin stain, $\times 10$), the tumor cells were arranged in a vesicular, nested mass (yellow arrow), with slender fibrovascular interstitial segregation seen between the cancer nests (green arrow), as well as abundant eosinophilic cytoplasm. Scattered distribution of grit bodies was also observed (curved arrows). (b) P504S immunohistochemistry ($\times 400$) reveals strong brown cytoplasmic staining in tumor cells (yellow arrow). (c) PAX-8 immunohistochemistry ($\times 400$) highlights brown nuclear staining in tumor cells (yellow arrow). (d) TFE3 immunohistochemistry ($\times 400$) shows tan nuclear staining in tumor cells (yellow arrow).

was classified alongside Transcription Factor EB (TFEB)-rearranged tumors within the Mit factor family, reflecting their unique biological and pathological characteristics.^[2] The gold standard for diagnosis is FISH.^[3]

In the fifth edition of the World Health Organization 2022 Renal Tumor Classification, several molecularly defined RCC entities are listed, including TFE3-rearranged RCC, TFEB-rearranged RCC, (ELOC, Elongin C) ELOC-mutant RCC, FH-deficient RCC, succinate dehydrogenase-deficient RCC, and Anaplastic Lymphoma Kinase (ALK)-rearranged RCC.^[4] TFE3-rearranged RCC is rare, particularly in adults. Argani *et al.*^[5] reported that it is more common in children and adolescents—constituting 40% of pediatric kidney cancers. However, RCC constitutes <5% of all childhood kidney tumors.^[5] TFE3-rearranged RCC demonstrates a female predominance, possibly because gene translocations more frequently involve the active X chromosome.^[6,7] Our patient, a 20-year-old female, fits this demographic profile. Clinically, this tumor often presents asymptotically; when symptoms occur, hematuria and pain are the most common.^[7,8] Our patient's presentation with 1 day of left-sided lumbar pain and hematuria aligns with previously reported cases.

TFE3-rearranged RCC usually arises in the renal medulla but can also occur in the renal cortex. The tumor demonstrates infiltrative growth and can be surrounded by a pseudocapsule; on gross section, it appears predominantly brownish-yellow or grayish-yellow with a soft texture. Necrosis, hemorrhage, and calcification may be present.^[7,9] In this case, although the tumor was large, it demonstrated well-defined margins without clearly protruding beyond the kidney's contour and was mainly located in the renal medulla.

On CT imaging, the solid portion of TFE3-rearranged RCC exhibits higher attenuation than the renal cortex, likely reflecting abundant protein content and increased cellular density.^[8,9] In our patient, the lesion's non-contrast CT density exceeded that of the adjacent cortex, consistent with the literature. The tumor parenchyma in this case was relatively homogeneous in density, without obvious hemorrhagic or cystic degeneration and necrosis, differing from the findings of Dong *et al.*^[8]

In this case, the tumor demonstrated marked enhancement in the cortical phase of contrast-enhanced CT, and the enhancement of the residual renal parenchyma at the upper pole of the left kidney was significantly lower than that of both the tumor and the contralateral kidney. This finding likely reflects compression of the upper-pole parenchyma by the large tumor mass, together with concomitant dilation of the left calyx and renal pelvis with hydronephrosis, which further compromised renal perfusion. Both cortical- and medullary-phase scans showed pronounced enhancement, with a slight decrease on delayed imaging that nonetheless remained at approximately 100 HU. Although TFE3-rearranged RCC cells are characteristically rich in eosinophilic cytoplasm, the degree of tumor enhancement in this case exceeded prior reports^[8-10] likely due to an abundance of thick, tortuous, and dilated intratumoral vessels.

Calcification is a relatively distinctive feature of TFE3-rearranged RCC, and the presence of calcific or hyperdense foci within the primary tumor or its metastases strongly suggests this diagnosis.^[10] Dong *et al.* reported calcification in 50% of cases on CT, typically as small punctate or irregular coarse deposits associated pathologically with granular and collagenous stromal degeneration.^[8] In our patient's lesion, numerous calcified foci of varied morphology—patchy, clustered, and dotted—were observed throughout the mid- and lower-pole mass, with some calcifications forming arcuate, intermittent arcs. The CT attenuation of these calcifications ranged from 155 HU to 468 HU (mean, 330 HU). Such extensive and morphologically diverse calcification has not been previously reported; whether this presentation is specific to TFE3-rearranged RCC will require analysis of additional cases in the future.

TFE3-rearranged RCC can metastasize to retroperitoneal lymph nodes and distant sites, and may form tumor thrombi in the inferior vena cava.^[9,10] Ma *et al.*^[11] found that TFE3-rearranged RCC is more aggressive in adults than in children

and adolescents. In our case, the tumor demonstrated only minimal adhesion to surrounding tissues, with no obvious invasion. Firm adhesion was noted only at the renal hilum adjacent to the peritoneum, but there was no invasion of the left renal artery or vein, no vascular tumor thrombus, no enlarged retroperitoneal lymph nodes, and no metastases in the chest or abdomen. At 12 months postoperatively, chest and abdominal CT revealed no recurrence or metastasis, which differs from prior reports.

Magnetic resonance imaging reveals that TFE3-rearranged RCC is isointense to the renal parenchyma on T1-weighted imaging, heterogeneous or hypointense on T2-weighted imaging, and exhibits relatively high signal intensity on diffusion-weighted imaging. In addition, it demonstrates heterogeneous enhancement on contrast-enhanced imaging.^[9] Fludeoxyglucose positron emission tomography-CT shows an increased standardized uptake value in the tumor, which suggests that TFE3-rearranged RCC may be highly malignant.^[9]

The imaging features of TFE3-rearranged RCC often overlap with those of other RCC subtypes, necessitating correlation of imaging and clinical findings for accurate differentiation: (1) Clear cell RCC is the most common subtype, characterized by high-grade malignancy, frequent cystic necrosis, and hemorrhage; calcification is rare. It typically shows strong enhancement in the cortical phase and washout in the parenchymal phase, aiding distinction from TFE3-rearranged RCC. However, differentiation can be challenging when TFE3-rearranged RCC exhibits clear-cell morphology, as both demonstrate intense enhancement, though calcifications are uncommon in clear-cell RCC. (2) Papillary RCC is the second-most common subtype and often presents with hemorrhage, low-level enhancement, and may be associated with hilar lymphadenopathy and distant metastasis. Papillary RCC lesions are generally smaller, more homogeneous in density or signal intensity, exhibit less enhancement than TFE3-rearranged RCC, and display fewer papillary-specific enhancement patterns.^[8-10]

CONCLUSION

Some imaging features of TFE3-rearranged RCC correlate closely with the underlying pathology. On CT, these tumors typically appear as large, well-defined, mildly hyperdense, rounded masses surrounded by a pseudo-capsule, with possible hemorrhage and calcification. Enhancement is usually mild to moderate, occasionally marked. When these imaging findings are present, TFE3-rearranged RCC should be suspected and treated as early as possible.

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