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# 6p21 translocation renal cell carcinoma: A case report

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ABSTRACT

6p21 translocation renal cell carcinoma (RCC) was newly classified in the WHO 2016 classification as a subtype of microphthalmia-associated transcription factor (MIT) family translocation RCC.A 42-year-old man was referred to our hospital with an asymptomatic solid mass in the right kidney identified during routine medical checkup. Computed tomography (CT) revealed a 14-mm buried-type solid mass accompanied by punctate calcification. CT-guided biopsy suggested clear-cell carcinoma. He underwent robotic-assisted partial nephrectomy. Pathological findings revealed 6p21 translocation RCC based on diffuse nuclear immunoreactivity for TFEB and TFEB gene rearrangement in tumor cells by FISH analysis.

## Introduction

Renal cell carcinoma (RCC) subtypes are discerned by their molecular characteristics. Translocation RCC is a newly recognized subtype of RCC characterized by chromosomal translocations involving *TFE3* (Xp11.2) or, less frequently, *TFEB* (6p21). We present a case of 6p21 RCC.

### *Case presentation*

A 42-year-old man was referred to our hospital with an asymptomatic solid mass in the right kidney detected during a medical checkup. He had no surgical history and no family history of cancer. Non-contrast computed tomography (CT) revealed a 14-mm buried-type solid mass accompanied by punctate calcification. Contrast-enhanced CT demonstrated intense contrast uptake in the corticomedullary phase and early washout in the nephrographic phase. Neither lymph node metastasis nor distant metastasis was recognized (Fig. 1).

To distinguish RCC from a benign mass such as angiomyolipoma (AML), CT-guided biopsy was performed. The biopsy sample contained 10% clear-cell lesions, with positive CD10 and negative HMB45 expression by immunohistochemistry (IHC), suggesting RCC rather than AML. These results led to a diagnosis of RCC, cT1aN0M0.

The patient underwent robot-assisted partial nephrectomy. Surgery was successful, with no intraoperative complications. Total operative time, warm ischemia time, and estimated blood loss were 152 minutes, 10 minutes, and 10 mL, respectively. He was discharged on the tenth post-operative day without postoperative complications.

Gross examination of the resected specimen showed a well-circumscribed, light brown, solid, 1.3 × 1.2 × 1.0-cm tumor, without hemorrhage or necrosis. Pathological examination showed a negative surgical margin and basement membrane-like materials surrounded by small tumor cells, resulting in rosette-like structures (Fig. 2). IHC results were focally positive for CD10 and HMB-45 expression, and with diffuse nuclear immunoreactivity for *TFEB;* FISH analysis confirmed *TFEB* gene rearrangement in tumor cells (Fig. 3). These results led to a final diagnosis of 6p21 translocation RCC. He received no adjuvant chemotherapy and has not experienced any recurrence nor distant metastasis for 3 years since surgery.

## Discussion

Since the early 1990s, the histologic classification of RCC has undergone several major revisions. The most recent revision, the 2016 WHO classification, incorporated several RCC subtypes with characteristic genetic aberrations, including XP11.2 translocations/*TFE3* gene fusions and 6p21 translocation/*TFEB* gene fusions.

To the best of our knowledge, 6p21 translocation RCC is very rare, with about 57 cases reported in the literature thus far.[1–5] It occurs more frequently in young adults, with a median age at diagnosis of 34. There

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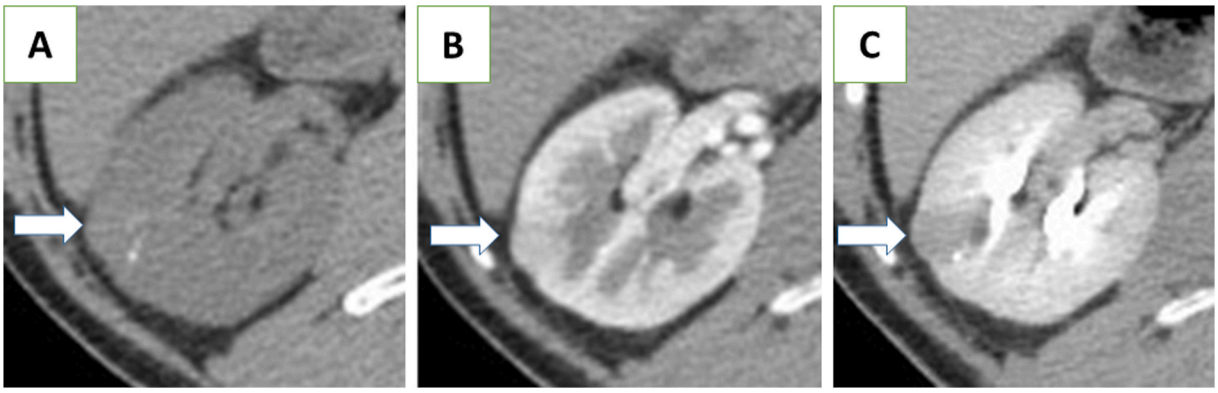


**Fig. 1.** Computed tomography (CT) revealed a buried solid mass accompanied by punctate calcification at the tumor periphery, indicated by the arrow (A). Contrast-enhanced CT demonstrated intense contrast uptake in the corticomedullary phase (B) and early washout in the nephrographic phase (C).

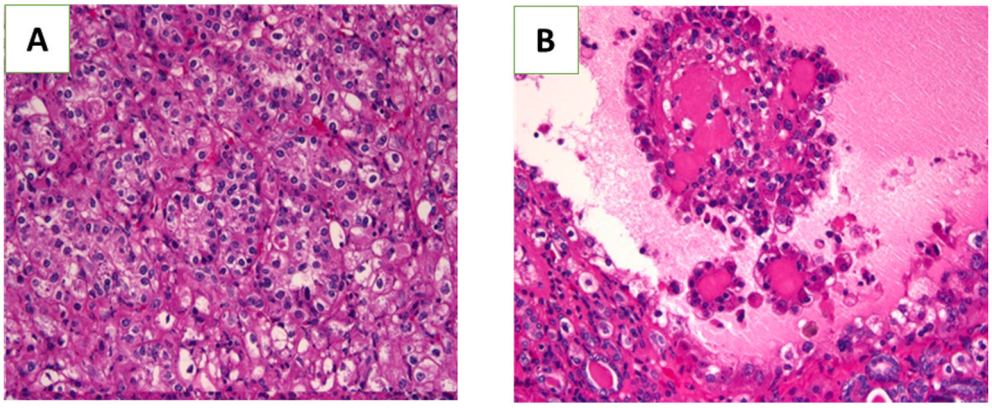


**Fig. 2.** Hematoxylin and eosin staining show epithelioid cell nests in the tumor with an admixture of clear and eosinophilic cells (A), and at the tumor periphery, basement membrane-like materials surrounded by small tumor cells, resulting in rosette-like structures (B).

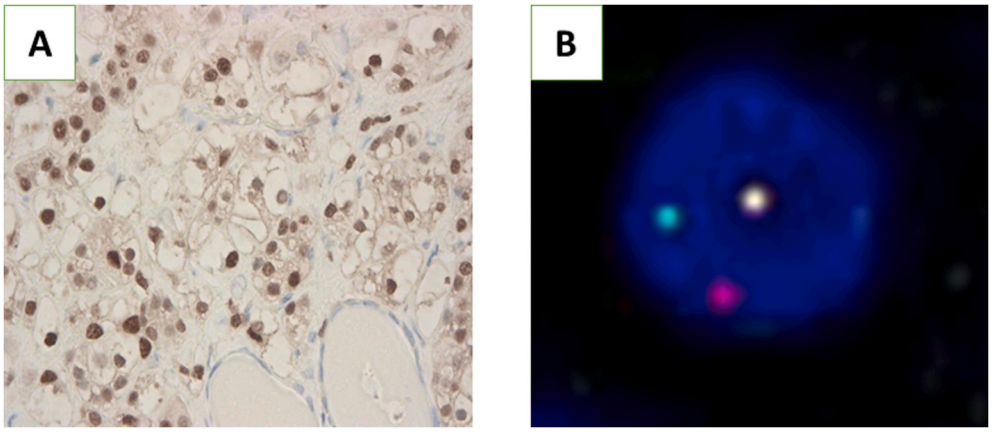


**Fig. 3.** Immunohistochemical examination showed diffuse nuclear immunoreactivity for *TFEB* (A), and FISH analysis showed *TFEB* gene rearrangement in tumor cells (B).

is no male predominance. It is often observed during routine medical check-ups or during evaluations for other diseases.

6p21 translocation RCC tumor size has been reported to be 1–20 cm in diameter (median, 7.0 cm). The masses are generally well-circumscribed, and daughter nodules are occasionally observed around the main tumor.[1,3] Histologically, these tumors are characterized by a "bipolar pattern of growth," consisting of rosette-like or pseudopapillary structures in solid tissues resembling clear-cell carcinoma. 6p21 translocation RCC often involves punctate calcifications, called psammoma bodies, at the tumor periphery.[3,5]

Differential diagnoses for 6p21 translocation RCC include AML and other common types of RCC. Among these, ruling out AML preoperatively is most challenging in clinical practice. AML is generally positive for HMB45 and negative for CD10 expression, while clear-cell RCC is positive for CD10 expression. In the present case, HMB45 was negative in a CT-guided biopsy sample, which implied clear-cell RCC rather than AML. According to a report that summarized 19 cases of 6p21 translocation RCC, HMB45 expression was positive in all cases, while in a

clinicopathological study of 5 Japanese cases of 6p21 translocation RCC, HMB45 was focally positive in 2 of the 5 cases.[4] In the present case, scant rosette structures consisting of small tumor cells at the tumor periphery were observed, in which HMB-45 expression was focally positive. Thus, it was difficult to make a preoperative diagnosis of 6p21 translocation RCC in this case.

Genetically, t (6; 11) (p21; q12) results in fusion of the *Alpha (MALAT1)* gene on *11q12* with the transcription factor-encoding gene *TFEB* on 6p21. The *Alpha-TFEB* gene fusion results in overexpression of TFEB protein. TFEB is a member of the MIT family, to which TFE3 expressed in Xp11 translocation RCC also belongs. Nuclear labeling for *TFEB* and *TFE3* is a highly sensitive and specific marker for 6p21 and Xp11 translocation RCC, respectively. In the present study, IHC analysis of TFEB expression provided conclusive evidence for 6p21 RCC, and *TFEB* gene rearrangement by fluorescence in situ hybridization (FISH) confirmed the diagnosis.

According to a review that summarized 6p21 translocation RCC, it generally has an indolent clinical course, while several cases display aggressive behavior. Larger masses and older age appear to be parameters correlated with aggressiveness. Furthermore, *TFEB* amplification is associated with a more aggressive clinical course. In our case, *TFEB* amplification was not observed on FISH.

In previous reports, all 3 cases with tumors <4 cm in size underwent partial nephrectomy, while 16 other cases initially underwent radical nephrectomy. Retrospectively, partial nephrectomy was optimal for the present case because the tumor was small (14 mm) without metastasis. The pathological results showed the mass to be well-circumscribed with a negative margin, suggesting that complete resection was achieved.

## Conclusion

6p21 translocation RCC is a very rare tumor, but urologists must consider it during differential diagnosis for young patients with RCC. IHC and FISH for *TFEB* and *TFEB* gene rearrangement are required for diagnosis.

## Declaration of competing interest

The authors declare no conflicts of interest.

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