Occult Renal Cell Carcinoma of Eosinophilic Morphology Detected within Renal Angiomyolipoma Mass in a Patient with Tuberous Sclerosis Complex

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Key words: Angiomyolipoma; Collision Tumor; Renal Cell Carcinoma; Tuberous Sclerosis Complex

The kidney is affected in about 80–85% of tuberous sclerosis complex (TSC) patients. Renal manifestations in TSC patients include an increased incidence of epithelial cysts and tumors, such as multiple renal angiomyolipomas (AMLs), renal cell carcinoma (RCC), and oncocytoma.¹² The coexistence of RCC and renal AML within same tumor masses, namely collision tumor, is very rare, and about six cases have been reported.³ Here, we present a case of a young male with TSC and multiple AMLs, containing RCC with eosinophilic morphology.

A 26-year-old male was diagnosed with TSC at the age of 11. Bilateral renal lesions were found by ultrasound and computerized tomography (CT) in 2008 and had never been cured. He was referred to Ningbo Clinical and Pathological Diagnosis Center in December 2013. The patient felt general weakness. Physical examinations revealed multiple cutaneous nodules on the face and hypopigmented skin lesions in the abdominal wall region. His biochemical values were as follows: uric acid, 597 µmol/L; total cholesterol, 5.60 mmol/L; and homocysteine, 13.5 µmol/L.

The abdominal ultrasound showed multiple masses in the bilateral kidney. CT with contrast enhancement confirmed these findings [Figure 1a]. He underwent nephrectomy on the left-side kidney.

Fragmented tissues of the postoperative specimens were 7.0 cm × 6.0 cm × 2.5 cm and weighed 117 g. The cut surface of the tumor had a soft, white to yellow appearance. There was a well-circumscribed, unencapsulated, tan-colored tumor-like lesion, with 2.0 cm in diameter and without necrosis.

Under light microscopy, the tumors showed AMLs with predominant lipomatous and myomatous components, without nuclear pleomorphism and mitotic activity. Thick-walled vessels were present. The tumor cells were positive for HMB45, SMA, Melan-A (A103), vimentin and negative for CD117, CK7, CK8, CD10, and RCC. One section of the tumors showed a well-circumscribed lesion composed of cells with abundant granular eosinophilic cytoplasm growing in a tubular or small solid nest manner, which was surrounded by AML tumor [Figure 1b and 1c]. The nuclei were small and round, with obvious nucleolus [Figure 1d]. Despite the lack of mitotic figures, focal nuclear pleomorphism was visible. There was no papillary structure, areas of clear cell carcinoma, or sarcomatoid pattern. Immunohistochemistry revealed positivity of tumor for CD117, CK8 [Figure 1e], CD10, EMA, Pax-8, CK AE1/3, CK AE1/3, CK cocktail and negative for HMB45, SMA [Figure 1f], Melan-A (A103), TFE3, vimentin, CK7, and Cathepsin K. The diagnosis of multiple renal AMLs and RCC with eosinophilic morphology was established.

AML is a common finding in TSC patients, reported in about 80% of patients with TSC.² However, the coexistence of AML and RCC is uncommon. The two primary tumors can happen synchronously or heterochronously. The coexistence of neoplasms was found more frequently in women and at a younger age.² The literature reported that RCCs that coexisted with AMLs mostly were double...
primary tumors, and more rarely collision tumor. There are only six case reports about AML and RCC coexisting in the same tumor mass. TSC-associated RCCS showed different histological types, including TSC-associated papillary RCC, hybrid eosinophilic/chromophobe tumor, and unclassified RCC. Eosinophilic morphology of TSC-associated RCCs is reported in 48–61% of cases and described as chromophobe, granular-eosinophilic, or hybrid oncocylic tumors.

The association between AML and RCC is still unclear. Inomoto et al. had reported one case of RCC originated in a previously existing AML and considered that RCC arose in the AML from the clinical and pathological point of view. However, other researchers suggested that AML and RCC were coincidentally present in the same tumor mass. The presented case provides another case of occult RCC detected within renal AML mass, mimicking a collision tumor.

If AML and RCC in the same kidney are two or more separate masses, the diagnosis is not difficult. However, if AML and RCC form collision tumor and two kinds of histological morphology mixed, we should carefully identify the diagnosis. When AML is given priority to fat composition, few of smooth muscle and blood vessels, the fat ingredient is easily mistaken for RCC tumor invasion in renal surrounding or internal fat. Furthermore, RCC with admixed smooth muscle predominant AML may cause diagnostic problems because this may be misdiagnosed as sarcomatoid RCC. These will directly affect the pathological staging and prognosis of the tumor.

Our patient was followed up for 38 months, and is alive with neither recurrence nor metastasis. It is still unclear whether there are differences in clinical outcomes between collision tumor and isolated renal neoplasia because of lack of large sample statistics. In general, the prognosis mainly relies on the pathological staging of RCC and tumor effects on kidney function.

In conclusion, TSC patients should be regularly examined, including radiological examination, assessment of TSC status, and possible tumor progression. Accurate and timely diagnosis, as well as proper treatment, plays a key role in the prognosis of the patients.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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