
A Case Report of Renal Cell Carcinoma Associated with Xp11.2 Translocation/TFE-3 Gene Fusion

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Abstract: Background: Renal cell carcinoma associated with Xp11.2 translocations/TFE3 gene fusion is characterized by the gene fusions between the TFE3, which is located on the chromosome Xp11.2 and a variety of fusion partners. It is a rare renal cancer, which usually has no specific clinical manifestations. The diagnosis mainly depends on imaging, histopathology, and immunohistochemical characteristics. In adults, the disease has a high degree of malignancy. Surgery is the preferred and radical cure for this type of kidney neoplasms. Objective: To further improve the understanding of renal cell carcinoma related to Xp11.2 translocation/TFE-3 gene fusion. Methods: A case of Xp11.2 translocation/TFE-3 gene fusion-related renal cell carcinoma was reviewed, and a systematic review of relevant literature was conducted to summarize and analyze the diagnosis and treatment progress of Xp11.2 translocation/TFE-3 gene fusion-related renal cell carcinoma. Results: Xp11.2 translocation/TFE-3 gene fusion-related renal cell carcinoma is a relatively rare renal malignant tumor. At present, its early diagnosis is still difficult, most of which are found to be advanced, and radiotherapy and chemotherapy are basically ineffective. Surgery is the main treatment method. Conclusion: For Xp11.2 translocation/TFE-3 gene fusion-related renal cell carcinoma, early diagnosis and early treatment are still the main methods to judge the prognosis, and the long-term prognostic effect still needs long-term follow-up.

Keywords: Xp11.2 Translocation/TFE-3 Gene, Kidney Cancer, Diagnosis and Treatment

1. Introduction

Renal cell cancer renal carcinoma associated with Xp11.2 translocations/TFE-3 gene fusions is a tumor that is specific for histopathology, cytogenetics, and molecular immunity. It and t(6;11) translocation/TFEB gene fusion-related kidney cancer together constitute the MIT family translocation kidney cancer, which is relatively rare in clinical practice [1]. In 2004, the World Health Organization (WHO) first classified it as a subtype in the classification of kidney tumors [2]. This type of renal cancer is caused by a break in the TFE-3 gene on the X chromosome site, and at the same time it translocates with the PRC gene, ASPA gene, PSF gene, CLTC gene and other related genes to form a new fusion gene, resulting in the TFE-3 gene protein abnormally elevated expression, therefore, it was named Xp11.2 translocation/TFE-3 gene fusion-related renal cancer. Compared with other types of

kidney cancer, its prognosis is poor [3]. The incidence of this tumor is very low, and it is relatively rare in clinical practice. It is usually diagnosed as advanced, but the disease progresses slowly [4]. Based on relevant literature at home and abroad, a case of translocation renal carcinoma diagnosed in our hospital was reviewed to further improve the understanding of this disease.

The patient, female, 49 years old, was admitted to the hospital due to "physical examination found that the right kidney occupied 13 days". She had no symptoms such as low back pain, frequent urination, urgency, and hematuria; she denied a history of genetic diseases and chemotherapy. On admission, the urine test was negative and there was no obvious positive sign. Color Doppler ultrasound on the abdomen showed that a solid iso-echoic mass of about 5.2 cm×4.0 cm×4.2 cm was visible in the lower pole of the right kidney, the boundary was clear, the envelope was visible, and part of the envelope was continuously interrupted. CDFI: a

little blood flow signal was seen inside. After admission, CT examination suggested that the right kidney was enlarged in volume, and a round low-density shadow could be seen at the lower pole, with a local protrusion out of the renal contour, about 5.2cm × 3.6cm in size. The enhanced scan showed that the CT value of the arterial phase was about 83 Hu, the CT value of the venous phase was about 81 Hu, and the CT value of the delayed phase was about 72 Hu. The surrounding shape of the left kidney was normal; the bilateral ureters and bladder were not abnormal, and the pelvic cavity had no enlarged lymph nodes. (see Figure 1).

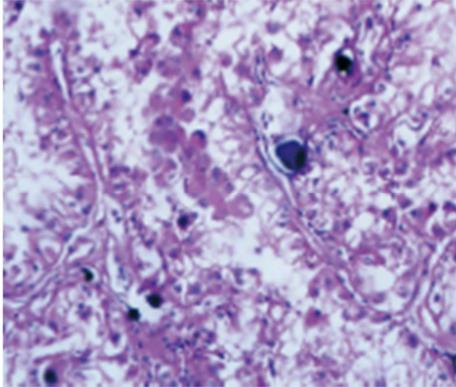


Figure 1. The tumor cells are arranged in an alveolar structure (HE staining, ×200), and some gravel structures can be seen.

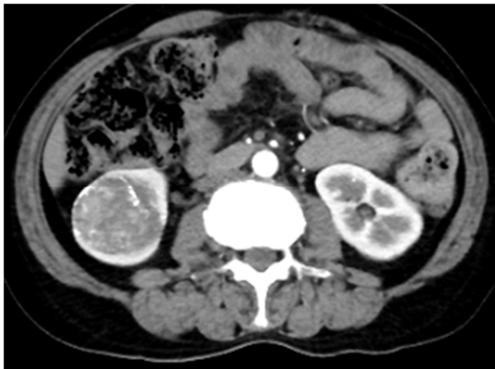


Figure 2. Irregular masses can be seen in the kidney parenchyma, with circular calcifications around, and gravel structures can be seen.

The clinical diagnosis was a space-occupying lesion of the right kidney, and the LA right kidney CA radical operation was performed. Postoperative pathology report: One kidney (right kidney) has been cut open for examination, the size is 11.0 cm×6.5 cm×4.0 cm, The ureter is 9.5 cm long and 0.5 cm in diameter. A 5.1 cm×4.1cm×4.1 cm gray-yellow nodule can be seen in the lower pole of the kidney. The cut surface is crisp and gray-yellow, and the boundary with the surrounding is still clear. Pathological diagnosis: (Right kidney) compliant with Xp 11.2 translocation/TFE-3 gene fusion-related renal cancer (papillary renal cell-TFE-3 carcinoma). The size of the mass was about 5.1 cm×4.1 cm×4.1 cm. The renal capsule was invaded. No intravascular tumor thrombus or nerve invasion was found. Immunohistochemical results: CD10 (+), PAX8 (2+), CD117 (-), EMA (-), CK7 (-), TFE-3 (2+0), Ki-67 (+ about 5%), RCC (-), CK (+). The ureter was severed, the renal

hilar blood vessels, and the perrenal fat sac were all negative. Interstitial hyperemia of surrounding kidney tissue. Pathological stage: pT1bN0 (see Figure 2).

2. Discussion

Kidney cancer is the most common renal malignant tumor, accounting for 85% of malignant tumors and 3% to 6% of all adult malignant tumors [5]. The common histological subtypes are clear cells (60% to 75%), papillary cells (10% to 15%), chromophobe cells (5%) and collecting duct carcinoma. Each pathological type has different histopathological and genetic characteristics. Xp11.2 translocation/TFE-3 gene fusion-related renal cancer is a relatively rare subtype. It was first added to the histopathological classification of kidney cancer as a new subtype by the WHO in 2004. Ellati RT, et al. [6] discovered this rare cancer for the first time (12 cases). It has unique genetic characteristics: chromosomal translocation including Xp11.2, resulting in gene fusion including TFE-3 transcription factor gene. At least five RCCs of TFE-3 gene fusion have been discovered, including ASPL-TFE-3, PSF-TFE-3, CLTC-TFE-3, PRCC-TFE-3 and Nono-TFE-3. Its chromosomal translocations include: t (p11.2; q25), t (X; 1) (p11.2; p34), t (X; 17) (p11.2; q23), t (X; 1) (p11.2; q21) and inv (X) (p11.2; q12). Translocated renal cell carcinoma has similar morphological features and clinical manifestations to clear cell renal cell carcinoma and papillary renal cell carcinoma. Macroscopic observation of tumors is mostly solid or cystic. The cut surface can be gray-yellow, gray-brown, gray-red, etc., with some signs of hemorrhage and necrosis. Typical morphological features include papillary structures composed of clear cells, nested structures composed of eosinophilic granular cytoplasmic tumor cells, and occasional grit-like bodies in the interstitium. Rao et al. [7] studied 17 cases of Xp11.2 translocation /TFE-3 gene fusion-related renal carcinoma and found that the structure of the renal carcinoma was characterized by nests and papillae, among which the nests accounted for 47% and the papillae accounted for 12%, and both accounted for about 35%. The characteristics of tumor cells are mainly clear cells, accounting for about 53%, eosinophils are less, only 6%, and both account for 41%. Clinically, Xp11.2 translocation/TFE-3 gene fusion-related renal cell carcinoma usually presents as asymptomatic masses, which are usually found accidentally during physical examination or abdominal examination [8]. CT plain scan may show low-density, iso-density or high-density, and a small number of patients can see calcification. Enhanced scan can show uneven enhancement, which is weaker than renal clear cell carcinoma [9]. The MRI plain scan showed uneven signal, and the enhancement scan showed enhancement in each phase, but it was lower than the normal renal cortex enhancement in the same period. Fluorescence in situ hybridization is considered to be the gold standard for diagnosing the disease, especially when immunohistochemistry is not clear. However, it may not be detected for special types of fusions, and methods such as DNA sequencing are needed to further clarify [10].

The treatment of Xp11.2 RCC is currently mainly based on surgery. In addition, immunotherapy and biological targeted therapy also have certain effects, but radiotherapy and chemotherapy are basically ineffective. If the size of the tumor is less than 7 cm, nephron-sparing surgery is considered a treatment option [11]. Immunotherapy is of great value to patients with hematological metastases, including interleukin 2 and interferon alpha. Recent studies have shown that the mammalian target of the rapamycin suppressor gene may be effective for Xp11.2 translocation type renal cell carcinoma [6, 12]. In addition, molecular targeted drugs such as sorafenib and everolimus also have a certain effect on the treatment of this tumor [13, 14]. The prognosis of Xp11.2 translocation renal cell carcinoma is currently controversial and lack of big data follow-up. Klatte et al. [15] reported that the average survival time of the disease in adults can reach 2 years, while the average survival time of children is 6.3 years. There are many factors affecting the prognosis of this tumor patient, such as race, age, clinical stage, and even treatment options. Large-scale and systematic research should be established, and unified diagnosis and treatment standards should be formulated. The disease stage of this patient is T1bN0M0. After 24 months of follow-up, the patient is basically in good condition, with no symptoms and signs of recurrence or metastasis. However, the long-term prognostic effect still needs long-term follow-up.

3. Conclusion

Xp11.2 translocation/TFE3 gene fusion-related renal cell carcinoma is a rare new type of renal cell carcinoma. Preoperative enhanced CT has an important prompting role in diagnosis. Traditional immune tissue can be used as the main screening method, Fish examination is the gold standard for diagnosis of the disease. Through early treatment, the tumor has good therapeutic effect. Surgical treatment is the main treatment, radiotherapy and chemotherapy are basically ineffective. If there are metastases, targeted therapy may be effective, but the prognostic factors require long-term follow-up.

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