A case of renal cell carcinoma in the contralateral kidney with TFE3 gene translocation following successful treatment of nephroblastoma

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Key clinical message

Renal cell carcinoma as a secondary malignant neoplasm is relatively rare; however, the possibility of secondary renal cell carcinoma following chemoradiotherapy for nephroblastoma should be considered.

Keywords: translocation renal cell carcinoma; nephroblastoma; secondary malignant neoplasm; robot-assisted partial nephrectomy

Abstract

The occurrence of secondary renal cell carcinoma following chemoradiotherapy for nephroblastoma is relatively rare, especially microphthalmia transcription factor family translocation renal cell carcinoma (RCC). A 13-year-old Japanese male was referred to our department for treatment of a right kidney mass. The patient had undergone open left nephrectomy and adjuvant chemotherapy for nephroblastoma, 12 years before. Diagnostic imaging revealed a tumor in the right kidney and a lesion suspected to be metastasis in the left eighth rib. Partial nephrectomy by robot-assisted surgery for the right renal tumor and resection of the left eighth rib were performed. Pathologically, the renal tumor was diagnosed as translocation RCC, and the rib lesion demonstrated no evidence of malignancy. In this study, we present a rare case of secondary translocation RCC after successful treatment of nephroblastoma.

Introduction

The occurrence of secondary malignant neoplasm (SMN) in association with chemoradiotherapy for nephroblastoma is well-established; however, the incidence of secondary RCC is relatively uncommon.[1]Furthermore, only a limited number of case reports have detailed the development of translocation RCC following nephroblastoma treatment. In this study, we present a rare case of secondary RCC following open nephrectomy and postoperative chemoradiotherapy for nephroblastoma.

Case presentation

A 13-year-old Japanese male was referred to our department for treatment of a right renal tumor that had been detected by abdominal ultrasound in a related pediatric clinic. The patient had been diagnosed with a large right kidney mass at the age of 11 months, and subsequently underwent an open left nephrectomy, resulting in a pathological diagnosis of nephroblastoma. The surgical and pathological findings indicated that the tumor was stage III, and adjuvant chemoradiotherapy was administered, including total abdominal irradiation of 10.5 Gy and DD4A (a multi-drug chemotherapy: vincristine/dactinomycin/doxorubicin). In addition to the nephroblastoma, the patient was also diagnosed with two other urogenital malformations: hypospadias and right cryptorchidism. Following treatment for the nephroblastoma, urethroplasty and right orchiopexy were performed.

Enhanced computed tomography (CT) imaging revealed a 30-mm-sized mass in the right kidney. The imaging pattern indicated chromophobe RCC or translocation RCC in the right kidney. The R.E.N.A.L. nephrometry score, which is a scoring system that categorizes the complexity of kidney tumors, was 8 points (1-3-3-×-1). Bone scintigraphy and positron emission tomography-CT demonstrated an accumulation in the left eighth rib (Figure 1). The clinical diagnosis was right RCC with suspected single bone metastasis. It was hypothesized as being a secondary malignant neoplasm following nephroblastoma treatment. The patient's serum creatinine

level at the time of initial consultation was 0.72 mg/dL. We decided to perform partial nephrectomy by robot-assisted surgery of the renal tumor for preservation of renal function and tumor resection of the left eighth rib. Given the patient's history of abdominal surgery, the procedure was performed via a retroperitoneal approach. A partial clamp of the renal artery associated with the tumor was performed during resection of the tumor, and the warm ischemic time was 21 minutes. The patient was discharged on postoperative day 8 without any complications. One month post-surgery, the patient's serum creatinine concentration was 0.80 mg/dL. Pathological examination revealed that the tumor exhibited clear cell RCC characteristics on hematoxylin–eosin staining. However, carbonic anhydrase 9 staining was negative, which is atypical for clear cell RCC. Additional immunohistochemistry revealed positive transcription factor E3 (TFE3) staining, while *TFE3* fluorescence in situ hybridization (FISH) revealed a split signal (Figure2). These examinations led to a definitive diagnosis of microphthalmia transcription factor family (MiT-family) translocation RCC, Fuhrman nuclear grade 3, with no sarcomatous change, no lymphovascular invasion, and negative surgical margins. Resection of the left eighth rib was performed 3 months after partial nephrectomy. Histopathological findings demonstrated no evidence of malignancy (fibrotic lesion, lib). The patient is currently undergoing imaging follow-up and has sustained no recurrence for 15 months.

Discussion

MiT-family translocation RCC has *TFE3* on chromosome Xp11.2 and the transcription factor *EB* gene on chromosome 6p21 as the major translocated genes. It was also reported that approximately 15% of these cases have a history of chemotherapy in childhood.[1] Our case was suspected of being associated with prior chemoradiotherapy. SMN after nephroblastoma treatment is widely known; for example, brain tumors, single retinoblastoma, and basal cell carcinoma. RCC is relatively rare as a SMN after nephroblastoma treatment, and only 4 of 13,351 patients were found to have RCC in a recent multi-institutional report.[2] In our review of 11 previously reported cases of secondary RCC after nephroblastoma treatment as well as our own study (Table 1), only 2 cases, including our own study, were diagnosed as translocation RCC.[1] Eight cases were clear cell RCC[3–9], one case was papillary cell RCC[10], and one case had an unspecified histologic type. Our review included only two cases of translocation RCC, although this number might be underestimated. This is because translocation RCC was first classified in the 2004 World Health Organization classification of renal tumors; prior cases were impossible to diagnose, and diagnosis of *TFE3* translocation RCC may be inaccurate in facilities that cannot perform the *TFE3* break-apart FISH technique.[11]

The appropriate course of action for this clinical case was difficult to determine because of suspected metastasis. For a single metastatic RCC suspected in the left eighth rib, cytoreductive partial nephrectomy and resection of the metastases, or systemic therapy after tissue diagnosis by renal biopsy, are viable treatment options. However, given that this is a single kidney case, needle renal biopsy is a high-risk option. Additionally, there is insufficient evidence supporting the efficacy of immune checkpoint inhibitors or tyrosine kinase inhibitors for metastatic translocation RCC. In our review, the longest recurrence-free period of RCC after surgery was 22 months.[4]Considering the need to preserve renal function, enhance the precision and safety of histological analysis, and ensure curative potential, partial nephrectomy was deemed the preferable option.

In our review (Table 1), six cases underwent partial nephrectomy as surgical treatment. No reports of severe acute renal failure were observed during the operative period. These findings suggest that partial nephrectomy is also valuable in treating secondary RCC after nephroblastoma treatment with regards to preservation of renal function.

Conclusion

We report a case of contralateral translocation RCC after treatment of nephroblastoma with radical resection by partial nephrectomy. RCC is a rare SMN following nephroblastoma treatment, with only two reported cases of translocation RCC. This case implies that the prospect of translocation RCC should be considered as a secondary renal neoplasm post-chemoradiotherapy. Moreover, if the case is operable, partial nephrectomy can be considered for functional and oncological outcomes.

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Figure legends

Figure 1 . (a,b,c,d) Contrast-enhanced CT showed a well-defined 30×25 mm-sized mass in the lower pole of the right kidney in the early phase, with a weak contrast effect below the renal cortex in the equilibrium phase and washout in the drainage phase. (e,f) Bone scintigraphy and positron emission tomography-CT showed an accumulation in the left eighth rib, which was suspected of metastasis.

Figure 2. (a) The cells were eosinophilic, pale, and proliferating in a focal- and cord-like structure, similar to clear cell RCC (×400 magnification). (b) Diffuse positive findings of TFE3 staining (×400 magnification). (c) Split signal pattern of *TFE3*break-apart FISH.

Table 1. A review of patients with secondary renal cell carcinoma after treatment for nephroblastoma

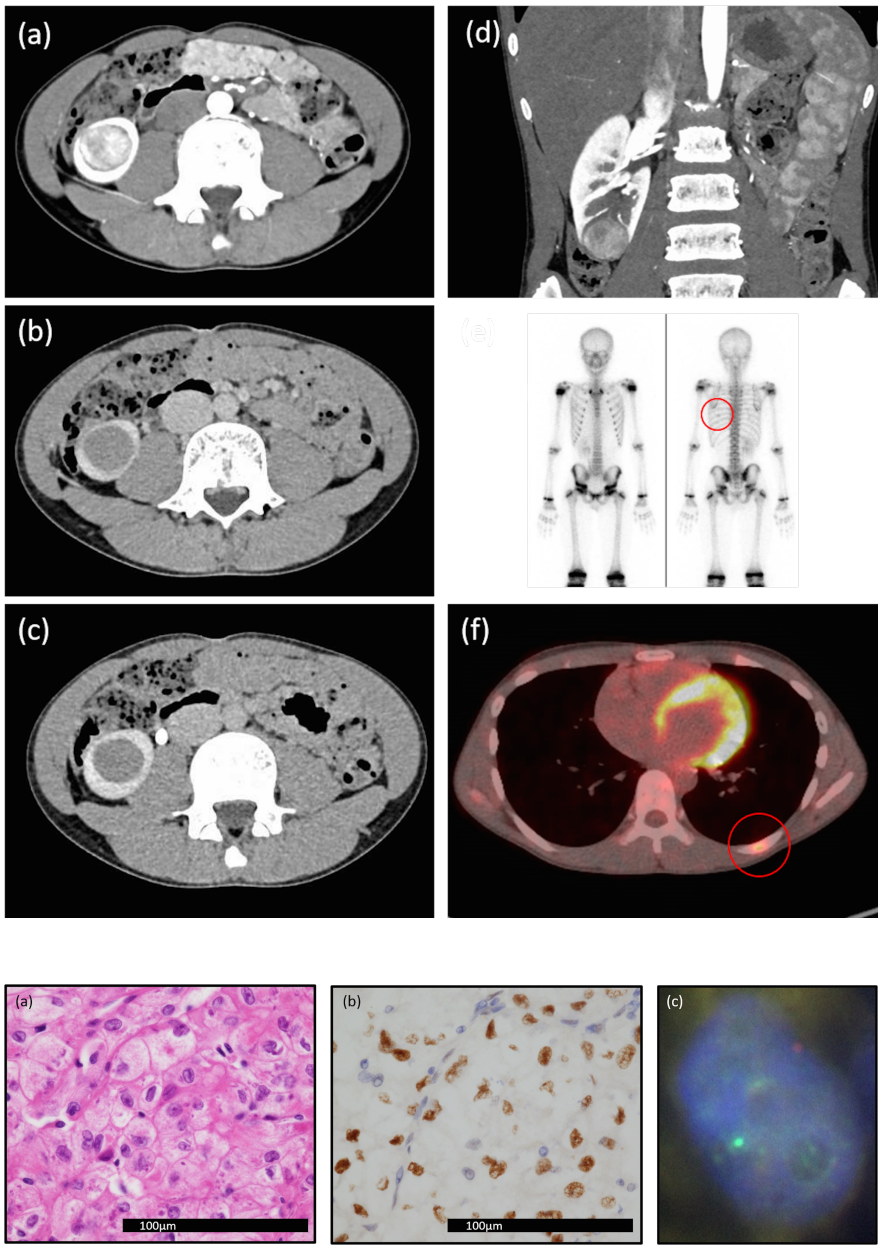

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Table1.pptx available at https://authorea.com/users/598310/articles/630952-a-case-of-renal-cell-carcinoma-in-the-contralateral-kidney-with-tfe3-gene-translocation-following-successful-treatment-of-nephroblastoma