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Original Article

Malignancies arising in allograft kidneys, with a first reported translocation RCC post-transplantation: A case series

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ABSTRACT

Background: The increased risk of malignancy in the post-renal transplant population has been well documented. Renal carcinoma is more common in this population, usually arising in native kidneys. Rarely, tumors arise in the transplanted kidney. Our case series reports four cases of malignancy in allograft kidneys, one of which is a first reported case of translocation RCC in a transplanted kidney.
Methods: The renal transplantation database (1584 patients) at St. Michael's Hospital was reviewed for malignancies arising in allograft kidneys: reports and pathology slides were reviewed.
Results: Four cases of malignancies arising in the allograft kidney were identified among our kidney transplant population. One patient developed a high grade urothelial carcinoma in the donor kidney post BK virus infection. The other 3 cases were renal cell carcinomas: one clear cell renal cell carcinoma, one translocation renal cell carcinoma, and one papillary renal cell carcinoma. The translocation renal cell cancer had confirmed TFE3 protein over-expression by immunohistochemistry. Molecular testing of the tumors in all 4 cases identified two separate genetic profiles, favored to represent tumors arising from donor tissues along with infiltrating recipient lymphocytes.
Discussion: Previous reports suggested that epithelial malignancies in allograft kidneys are rare. We identified 4 such tumors in 1584 transplant patients. Further, we identified the first reported case of translocation RCC in an allograft kidney. While the rate of malignancy in allograft kidneys is low, screening of the donor kidneys by ultrasound and/or urine cytology may be of use in detecting these lesions.

Introduction

Cancer in the post transplant population has been a constant concern [1–4], raising the possibility of the need for increased post transplant surveillance for the types of cancer with most significantly increased risk of development. Renal malignancies in particular are one of the most common cancers to occur in this population; however these tumors arise almost exclusively in the native, end stage kidneys – development of renal cell carcinomas, particularly the papillary subtype, is well-recognized in the native diseased kidneys in this population. Tumors in the transplant kidney have been uncommon, though increasingly reported [5–8]. Although these kidneys lack the risk factor of end stage kidney disease, they still experience the on-going damage of rejection and the increased risks of chronic immunosuppression with the corresponding potential for infections that increase the risk of malignancy (i.e. BK virus infection).

To assess the risk of tumor development in allograft kidneys, we reviewed the renal tumor database of St. Michael's Hospital, Toronto, to determine the number and types of renal malignancies in our patient cohort.

Methods

Approval for review of the renal transplant database was received from the Research Ethics Board at St. Michael's Hospital. This database has been kept since the initiation of renal transplants at St. Michael's Hospital, and tracks the clinical information for the 1584 patients who have had renal transplants and are followed at this hospital to date. The hospital clinical database and the pathology laboratory information system were utilized to search for any

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Table 1
Clinical and pathologic details of malignancies in allograft kidneys.

Patient	Age/sex	Duration of renal transplant	Type of malignancy	Immunohistochemistry/molecular studies
1	66/F	9 years	High grade papillary urothelial carcinoma in allograft kidney and bladder, kidney stage pT3, pNX	BK viral genome present in tumor by PCR
2	49/F	16 years	Papillary RCC, Fuhrman grade G1, stage pT1a, pN0	Cytokeratin (CK)7 +, racemase +, CD 10 –
3	56/F	9 years	Translocation renal cell carcinoma, Fuhrman grade G3, stage pT1b, pNX	TFE3 +ve, CK 7 +, racemase +, CD 10 weak +
4	31/M	1 year	Renal cell carcinoma, clear cell phenotype, Fuhrman grade G3, stage pT1a, pNX	Vimentin +, pankeratin +, CD 10 +, RCC +

pathology reports for any of these patients where malignancies were identified in the donor/allograft kidney. The pathology reports and slides were reviewed and correlated with patient history.

Results

Of the 1584 patients in the renal transplant database, four cases of malignancies arising in the allograft kidney were identified among our kidney transplant population (Table 1); this is a significant proportion (3.8%) of all post-transplant malignancies, as a total of 106 patients with dysplasia or malignancies were identified in the 1584 patients of our group.

One patient, a 66-year-old woman, developed a high grade urothelial carcinoma in the pelvis of the donor kidney 9 years post transplant and 6 years post BK virus infection – this was a high stage tumor (pT3) with involvement of the renal vein margin (Fig. 1). Immunohistochemistry for SV-40, a marker of polyomavirus infection, was positive in the tumor cells, and the viral genome was identified in the tumor cells by polymerase chain Reaction (PCR). The patient was well 24 months after resection of the allograft kidney for the tumor.

The other three cases were renal cell carcinomas; these developed 1 year, 16 years, and 9 years post transplant (average 8.7 years) (Figs. 2–4). Histologic evaluation of the tumors showed one renal cell carcinoma of pure clear cell type and one papillary renal cell carcinoma. The third case, on histologic evaluation, was a renal cell carcinoma with both clear and papillary architecture, initially diagnosed as a renal cell carcinoma, unclassifiable.

The renal cell carcinoma clear cell type (ccRCC) arose in a 31-year-old male patient. The tumor was 3.5 cm in maximum dimension, with Fuhrman Grade 3 and stage pT1a. The tumor was immunoreactive to vimentin, pancytokeratin, CD10 and RCC. On follow-up, the patient was well 30 months post removal of the allograft kidney, with no evidence of recurrence/metastasis.

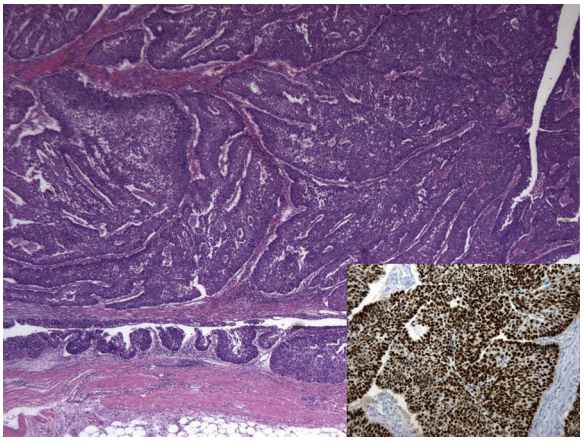

Fig. 1. Urothelial carcinoma in allograft kidney, H&E 16×, with inset of immunohistochemistry for SV-40 virus.

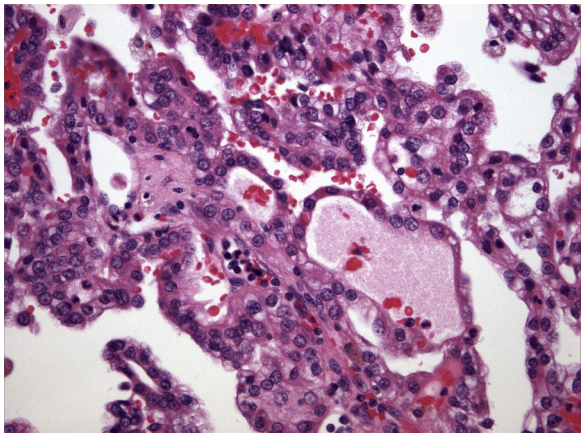

Fig. 2. Papillary renal cell carcinoma in allograft kidney, H&E 200×.

A 49-year-old female patient was diagnosed with papillary renal cell carcinoma (pRCC) in the allograft kidney; the tumor was 3.9 cm in maximum dimension, Fuhrman Grade 1, stage pT1a. The patient was well with no evidence of metastasis 12 months after diagnosis and transplant nephrectomy.

The third case of renal cell carcinoma, originally diagnosed as unclassified type, arose in a 56-year-old female patient. The lesion was 5.7 cm in maximum dimension. Fuhrman Grade 3, stage pT1b. Initial immunohistochemical staining performed demonstrated patchy staining with racemase with cytokeratin 7 staining in the papillary areas. On histologic review for this case, the mixed pattern was particularly noted, and the possibility of a translocation carcinoma was raised. Immunohistochemistry for TFE3 showed diffuse moderate staining. Taken together, the morphology and immunohistochemical pattern was considered to be sufficient for a diagnosis of Xp11 Translocation RCC. The patient was well with no evidence of malignancy 17 months after tumor removal.

Tumor and benign renal tissue from the four kidneys were submitted for DNA analysis; in all four cases, both tumor and benign tissues showed two distinct profiles. Histologic evaluation of the blocks sent for molecular testing showed a significant lymphocytic infiltrate in both tumor and non-tumor tissues. The presence of two different profiles suggests that the tumors were of donor origin and the second profile was from the lymphocytes present in the tumor of recipient origin.

Discussion

Increased risk of malignancy is a well documented complication after solid organ transplant, due to improved long-term survival and the consequent chronic immunosuppression [2–4,13–15]. After renal transplant, the risk of developing renal cell carcinoma (RCC) of the native kidney is 15-fold compared to the normal population, due to increased incidence (up to 70–90%) of cystic renal