Extended Abstract

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Does Age Affect the Outcomes of Translocation Renal Cell Carcinoma? A Retrospective Analysis from a Middle Eastern Cohort

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Abstract

Background: The natural history of Translocation renal cell carcinomas (tRCC) is variable from indolent behaviors to aggressive disease that demonstrates lymph node and widespread metastasis. Translocation renal cell carcinomas (TRCC) represent 1% to 5% of all cases of renal cell carcinoma (RCC).

Objectives: We sought to characterize the associations between age at presentation of tRCC patients and stage, grade, survival and recurrence of the disease in Middle Eastern institution. Materials and methods: Retrospective review of clinical and pathological data from a single institution for 23 patients diagnosed with tRCC between 2005 and 2017. Patients were categorized into two group based on age group 1 (>40 years) and group 2 (≤ 40 years). We evaluated the association between tumor grade, gender, disease free survival (DFS), overall survival (OS) and age.

Results: The tumor was on the right kidney in 52.2% of patients and bilateral in one patient. Ten patients (43.5%) were over 40 years of age and 13 patients (56.5%) were less than or equal to 40 years of age in terms of tumor characteristics, the average tumor size was 9 cm; 4 patients (17.3%) had pathological T1, seven patients (30.4%) had pathological T2, 10 patients (43.4%) had pathological T3 or more and two patients (8.7%) n had not had surgery. Eleven patients (47.8%) had lymph node dissection for clinically enlarged lymph nodes and seven (64%) of them had lymph node metastases. Nineteen patients (83%) underwent a radical nephrectomy and two (8%) underwent a partial nephrectomy. Bilateral renal tumors were managed by left and right radical nephrectomy. There was no difference in the DFS in patients over 40 years of age. No statistically significant association between disease-free survival, sex, pathological T-staging, overall survival and age.

Conclusion: tRCC has variable clinical behavior from indolent to aggressive disease. Age may not affect this clinical behavior.

Keywords: Renal cell carcinoma; Translocation renal cell carcinomas; Microphthalmia-associated transcription

Introduction

Renal cell carcinomas (RCC) are a heterogeneous group of tumors that make up about 90% of all renal malignancies in adults. The most common subtypes are clear cells (60 to 75%), followed by papillary (10 to 15%), chromophobic (5%) and collector carcinomas. Recent progress in understanding the molecular alterations involved in the pathogenesis of RCC has led to the development of a new sub-classification of these tumors. Renal cell carcinoma by translocation (tRCC) is a newly recognized subtype of RCC with chromosomal translocations involving TFE3 (Xp11.2) or, less commonly, TFEB (6p21). The transcription family associated with microphthalmia (MiT) tRCC includes Xp11 tRCC and t (6; 11) RCC. Xp11 tRCC and t (6; 11) RCC are also known as rearranged RFE TFE3 and TFEB, respectively. TFE3 and TFEB belong to the MiT family which regulates the differentiation of melanocytes and osteoclasts. The TFE3 and TFEB rearranged RCCs have distinguished clinico-pathological and immunohistochemical characteristics. Xp11 tRCC comprises 20 to 40% of infant RCC and approximately 4% of adult RCC with an average age of 50 at the time of diagnosis. The natural history of Xp11 tRCC is variable, ranging from lazy behaviors to aggressive disease that shows generalized lymph nodes and metastases. TRCC Xp11 has the potential to metastasize up to 20-30 years after diagnosis. The associations between age, stage, grade of disease, survival and recurrence of the disease have not been addressed in the literature. The purpose of this study is to identify if these associations exist.

Materials and Methods

Study settings

The study was conducted at King Hussein Cancer Centre (KHCC), a comprehensive center that serves cancer patients in both inpatient and outpatient settings. RCC patients receive treatment according to KHCC-clinical practice guidelines (CPG). Approval was gained from the KHCC Institutional Review Board and the KHCC ethics committee. Data for all patients who underwent radical or partial nephrectomy and pathology that revealed tRCC between December 2005 and August 2017 were reviewed retrospectively.

Study design

All patients underwent a staging assessment at the time of diagnosis, including clinical examination, blood tests, chest x-ray, and computed tomography (CT) of the abdomen and pelvis. Pathological staging was carried out using the TNM 2010 classification system. Follow-ups were carried out according to the KHCC-CPG, which included laboratory and radiological examinations according to the final TNM stage and the grade of the tumor. Additional imaging was ordered as clinically indicated. For those with metastatic disease, the tumors were evaluated by physical examination and computed tomography at baseline and every 3 to 6 months. Overall responses to the disease were documented using the RECIST criteria. features evoking tRCC, such as papillary architecture and the clear eosinophilic cytoplasm. The diagnosis of Xp11 tRCC was confirmed by immunohistochemistry analysis (IHC) for the nuclear staining TFE3. TRCC Xp11.2 was analyzed by IHC staining to detect TFE3 in each block of tumor and tissue microarrays (catalog no. Sc5958; Santa Cruz Biotechnology, Santa Cruz, CA, USA). Angiogenesis markers IHC analysis of tumor tissue samples was performed using the Ventana XT autoimmuno-dye (Roche, San Francisco, CA, USA) with the Optiview Dab detection kit (Roche) according to the manufacturer's instructions. . The results were independently assessed by two specialist pathologists who were blind to clinical data. The Fuhrman nuclear classification system, which uses a multi-parametric four-point scale based on nuclear characteristics, size, shape, color and nucleolar prominence was used as shown in Figures 1-3. Data including patient characteristics, clinical manifestations, surgical techniques, pathological results, radiology and clinical results were collected. Response to treatment based on cancer specific survival (CCS), overall survival (OS) and progression-free survival (PFS) were analyzed. Patients were classified into two groups according to age group 1 (> 40 years) and group 2 (≤ 40 years) and the association between tumor grade, sex, disease-free survival (DFS) and age.

Results

Clinical characteristics

Twenty-three patients were identified, 15 (65%) of the patients were males. The mean age at diagnosis was 37 years. The majority of the patients (65%) were diagnosed incidentally during abdominal imaging for other indications. The remaining 35% suffered from pain, gross hematuria, metastasis, abdominal distension or weight loss at the time of the first presentation. Patients' characteristics are shown in Table 1.

The tumor was on the right kidney in 52.2% of the patients, and bilateral in one patient. Ten patients (43.5%) were above 40 years of age, and 13 patients (56.5%) were less than or equal to 40 years old. Regarding the tumor characteristics, the mean tumor size was 9 cm; 4 patients (17.3%) had pathologic T1, seven patients (30.4%) had pathologic T2, 10 patients (43.4%) had pathologic T3 or more and two patients (8.7%) had no surgery and thus were not evaluated for pathologic T staging. Eleven patients (47.8%) had lymph node dissection for

clinically enlarged lymph nodes and seven (64%) of them had lymph nodes metastasis. Patients were categorized into two group based on age group 1 (<40 years) and group 2(<=40 years). Tumor T stage distribution among groups are shown in Table 2.

Conclusion

tRCC, is a variant of RCC with unique characteristics. tRCC has variable clinical behavior from indolent to aggressive disease. Age may not affect this clinical behavior. Future studies with larger sample size and a longer follow up period is required.

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