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Clear cell renal cell carcinoma with prominent microvascular hyperplasia: Morphologic, immunohistochemical and molecular-genetic analysis of 7 sporadic cases

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Highlights

- 7 clear cell renal cell RCC (CCRCCs) with microvascular hyperplasia (ccRCCPV) were analyzed.
- Prominent microvascular hyperplasia in CCRCC is a rare phenomenon.
- No significant differences in molecular genetic profile were detected
- ccRCCPV demonstrated similar clinical behaviors, like conventional CCRCC.
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Abstract

Clear cell renal cell carcinoma (CCRCC) is well known for intratumor heterogeneity. An accurate mapping of the tumor is crucial for assessing prognosis, and perhaps this can be linked to potential success/failure of targeted therapies. We assembled a cohort of 7 CCRCCs with prominent vasculature and microvascular hyperplasia (ccRCCPV), resembling those seen in high grade gliomas. A control group of classic CCRCC with no variant morphologies was also included. Both groups were analyzed for clinicopathologic, morphologic, immunohistochemical, and molecular genetic features. No statistically significant differences in mRNA expression of studied genes between the two groups were found. Using NGS panel Trusight Oncology 500 (TSO500), only one clinically significant gene mutation, VHL c.263G > A, p. (Trp88Ter), was found. TMB (Tumor Mutation Burden) and MSI (MicroSatellite Instability) were low, and no copy number variations (CNVs) were detected in the study cohort. Prominent microvascular hyperplasia in CCRCC is a rare phenomenon. From molecular genetic point of view, these tumors do not appear to be different from classic CCRCC. Prognostically, they also demonstrated similar clinical behaviors.

Introduction

Clear cell renal cell carcinoma (CCRCC) is the most common renal cell carcinoma, representing approximately 60–70% of all renal cell carcinomas [1,2]. CCRCC is well known for intratumor heterogeneity, which has extensively been studied [2,3].

In the era of personalized (precision) medicine, surgical treatment combined with targeted therapies, such as tyrosine kinase inhibitors, focusing on the tumor neoangiogenesis and driven by *VHL* mutations, generated a glimpse of hope for the treatment of CCRCC. However, this has resulted in partial success so far, mainly due to intratumor heterogeneity [4,5]. Moreover, no systematic genetic testing is usually performed prior to administration of “targeted” therapy with some patients respond very well, while others unfortunately do not and tumors further progress. We believe that an accurate mapping of each tumor is crucial for assessing prognosis and perhaps it can be linked to potential success/failure of a particular targeted therapy.

We assembled a cohort of 7 CCRCCs with prominent vasculature and microvascular hyperplasia (ccRCCPV), resembling those seen in high grade gliomas, particularly in glioblastomas. We analyzed these cases according to clinicopathologic, morphologic, immunohistochemical, and molecular genetic features.