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Renal cell carcinomas with tubulopapillary architecture and oncocytic cells: Molecular analysis of 39 difficult tumors to classify

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Highlights

- *So-called oncocytic papillary RCC (OPRCC) is a poorly understood and defined entity.*
- *A cohort of 39 "OPRCCa" was divided into 3 distinct CNV groups.*
- *Morphologic and immunohistochemical features were overlapping among all 3 groups.*
- *No particular combination of morphologic and immunohistochemical profile was associated with an aggressive behavior*

Abstract

So-called oncocytic papillary renal cell carcinoma (OPRCC) is a poorly defined variant of papillary renal cell carcinoma. Since its first description, several studies were published with conflicting results, and thus precise definition is lacking. A cohort of 39 PRCCs composed of oncocytic cells were analyzed. Cases were divided into 3 groups based on copy number variation (CNV) pattern. The first group consisted of 23 cases with CNV equal to renal oncocytoma. The second group consisted of 7 cases with polysomy of chromosomes 7 and 17 and the last group of 9 cases included those with variable CNV. Epidemiologic, morphologic and immunohistochemical features varied among the groups. There were not any particular histomorphologic features correlating with any of the genetic subgroups. Further, a combination of morphologic, immunohistochemical, and molecular-genetic features did not allow to precisely predict biologic behavior. Owing to variable CNV pattern in OPRCC, strict adherence to morphology and immunohistochemical profile is recommended,

particularly in limited samples (i.e., core biopsy). Applying CNV pattern as a part of a diagnostic algorithm can be potentially misleading. OPRCC is a highly variable group of tumors, which might be misdiagnosed as renal oncocytoma. Using the term OPRCC as a distinct diagnostic entity is, thanks to its high heterogeneity, questionable.

Introduction

Renal cell carcinomas (RCC) composed of oncocytic cells represents a heterogeneous group of renal neoplasms, which can pose diagnostic challenge in routine practice. Despite the existence of well-established renal tumor entities such as renal oncocytoma (RO) and chromophobe RCC, there are several morphologic variants of “oncocytic” tumors, for which rendering exact diagnosis may be very challenging. Among others, group of papillary RCC with oncocytic cells represents example of such challenging tumors. Papillary renal cell carcinoma (PRCC) has traditionally been divided into two morphologic subgroups – PRCC type 1 and PRCC type 2 [1]. However, in the “histo-molecular” classification era, this does not hold true and remains unsatisfactory as many PRCC cannot be classified as per existing criteria [2].

The WHO classification defines oncocytic PRCC (OPRCC) as a PRCC with voluminous, finely granular, evenly distributed eosinophilic cytoplasm and oncocytoma-like nuclei (usually with low nuclear grade), which are single-layered and linearly aligned [3]. Apparently, “OPRCC” fulfilling these WHO criteria fits well in a subgroup of PRCC recently described as “PRCC with reverse polarity” [4]. However from the reverse perspective, PRCCs composed of oncocytic cells are a part of much broader spectrum, where PRCC with reverse polarity is one of the existing variants/subtypes. The whole group of PRCCs composed of oncocytic cells is so far poorly understood and histologic diagnostic criteria have not yet been determined.

In this study, we analyzed morphological, immunohistochemical, and molecular genetic features of renal tumors showing combined papillary/tubulopapillary/papillary, compressed to solid architecture and oncocytic cells (some of them overlapping with OPRCC as defined by WHO classification/PRCC with reverse polarity) in order to better understand the relationship between morphology and genetic background of these heterogeneous group of RCCs.