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Multiple Neoplasms in the Context of Renal Adenomatosis: A Unique Case Report and Literature Review

Ariza-Estepa M[1], Sosa Moreno M[1], Cano-Barbadilla T[2], Torres-Gómez FJ[2*].

[1]Pathology Unit, Virgen de Valme University Hospital, Sevilla, Spain
[2]Pathology Unit, Virgen Macarena University Hospital, Sevilla, Spain

[*]**Corresponding author:** Francisco Javier Torres Gómez, Pathology Unit, Virgen Macarena University Hospital, Sevilla, Spain, Tel: 34+629344869; E-mail: javiertorresgomez@yahoo.es

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Abstract

Renal papillary adenomas, typically benign and under 15 mm, are found more frequently in patients with hereditary renal carcinoma or end-stage renal disease. Renal adenomatosis, the presence of numerous adenomas within one or both kidneys, is rare. We report an unusual case involving simultaneous hybrid carcinomas (papillary type I and clear cell) and multiple adenomas in a patient with renal adenomatosis, contributing to the understanding of the mechanisms of neoplastic progression within this pathological context. A 63-year-old male with a history of benign prostatic hyperplasia presented with incidental findings of multiple cystic and solid renal lesions in both kidneys during an ultrasound examination. Some of these lesions appeared suspicious for malignancy, prompting surgical intervention. Initially, a left partial nephrectomy was performed, followed by a right radical nephrectomy one year later to manage the complex presentation. Comprehensive histopathological and immunohistochemical analyses were conducted on the excised specimens to classify and characterize the tumors. This case illustrates an unusual coexistence of multiple renal neoplasms, including hybrid carcinomas and papillary adenomas, which may indicate an underlying genetic predisposition, potentially involving the *MET* and *VHL* pathways. Such genetic interactions may contribute to the multifocal nature of tumor development in renal adenomatosis. This finding underscores the importance of detailed genetic and histopathological profiling to enhance our understanding of biological behavior and the potential progression of these tumors. Comprehensive profiling in similar cases could also offer valuable insights into personalized treatment approaches and long-term management.

Keywords: ***Renal adenomatosis; Hybrid renal carcinoma; Papillary adenoma***

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1. Introduction

Renal papillary adenomas are small, unencapsulated cortical tumors with papillary, tubular, or tubulopapillary morphology, generally classified as low-grade lesions measuring less than 15 mm in size according to the 5th edition of the World Health Organization's Classification of Tumors of the Urinary and Male Genital Organs. The size criterion for papillary adenoma has historically ranged from 5 mm to 3 cm [1,2], with the latest revision in 2015 setting it at 15 mm due to the minimal metastatic risk. These adenomas are present in approximately 10% of young adults and 40% of elderly patients, often linked to hereditary papillary renal carcinoma [3] or end-stage renal disease. The presence of multiple adenomas within the kidney, known as renal adenomatosis, is an uncommon finding. Multicentricity in renal cell carcinomas is documented in around 5% of cases [4], adding to the uniqueness of cases involving simultaneous multiple tumor types.

2. Materials and Methods

The subject of this case report is a 63-year-old male with a history of benign prostatic hyperplasia. Four years earlier, incidental ultrasound findings revealed multiple cystic and solid renal lesions, some suspicious for malignancy, in both kidneys. The initial intervention involved a left partial nephrectomy, followed by a right radical nephrectomy a year later. Current imaging shows no significant progression in the remaining renal parenchyma, and the patient remains free of metastatic disease.

3. Results

Histopathological evaluation of the left nephrectomy specimen showed an 8 cm hybrid papillary type I and clear cell carcinoma, two smaller papillary type I carcinomas (2 cm and 1.6 cm), and numerous papillary adenomas. The right nephrectomy revealed a 9.5 cm hybrid papillary type I and clear cell carcinoma (FIG. 1 & 2), a 3.2 cm papillary type I carcinoma, and several subcapsular papillary adenomas. Tumor staging and grading followed the WHO/ISUP criteria, with all but one neoplasm classified as grade.

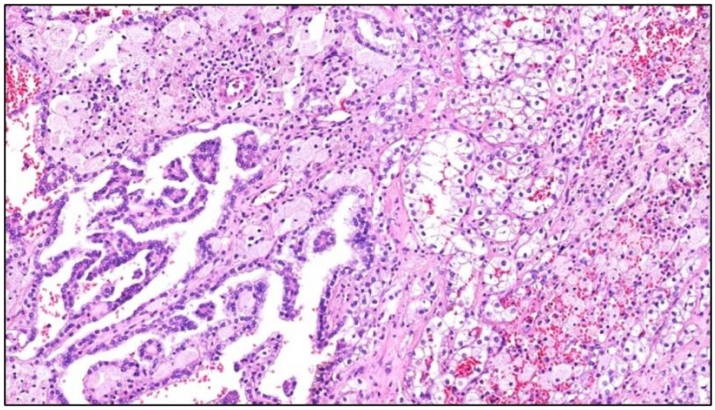

FIG. 1. **HE 10x. Hybrid renal cell carcinoma: type I papillary on the left, and clear cell on the right.**

The largest, a 9.5 cm hybrid carcinoma, received a grade 2 classification. The specimens were sent to the pathology department for further study.

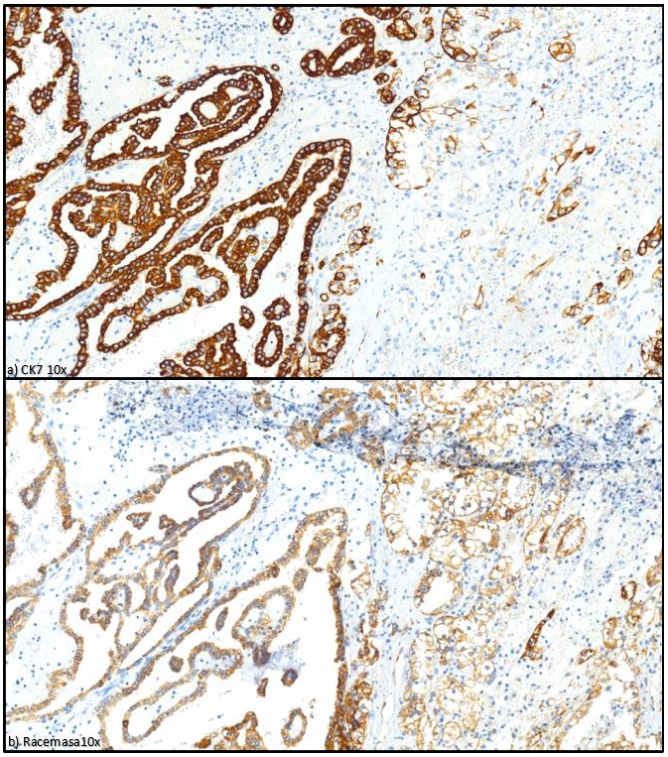

FIG. 2. **a) CK7 10x, positive in the papillary area and negative in the clear cell area. b) AMACR 10x, positive in both.**

On gross examination, papillary adenomas appeared as multiple well-demarcated, gray nodules. The carcinomas appeared heterogeneous in color, ranging from yellowish to brown and gray, with friable consistency and regions of cystic and hemorrhagic changes. Immunohistochemical analysis revealed that the papillary components were positive for PAX8, CD10, CK7, racemase, and vimentin. The clear cell areas, characterized by a large cytoplasmic presence, displayed positivity for PAX8, CD10, and vimentin, but were negative for racemase and CK7. Both carcinoma types exhibited frequent foam cells, without prominent nucleoli. No invasion of the perirenal adipose tissue or vascular structures was observed.

4. Discussion

Although rare, synchronous renal neoplasms in the setting of renal adenomatosis have been reported, such as oncocytic papillary renal cell carcinoma [5], multicentric tubulopapillary carcinoma [6], and multifocal papillary carcinoma, either associated with [7] or independent of terminal nephropathy [8]. However, bilateral hybrid papillary and clear cell carcinomas in this context have not been documented before.

Papillary renal carcinoma is linked to mutations in the MET oncogene on chromosome 7q31, as well as trisomies of chromosomes 7 and 17 and Y chromosome loss. Clear cell carcinoma, by contrast, is associated with mutations in the VHL gene on chromosome 3p25 [9]. A FISH-based study documented focal papillary carcinomas with focal immunohistochemical changes resembling clear cell carcinoma, proposing that hybrid papillary and clear cell carcinomas may have a worse prognosis than classic papillary carcinoma [10]. This case broadens our understanding of renal adenomatosis and highlights the need for comprehensive genetic and immunohistochemical analyses in similar cases. The presence of multiple renal papillary adenomas

alongside hybrid carcinomas (papillary type I and clear cell) in patients with renal adenomatosis may stem from an inherent genetic predisposition or distinct alterations within the renal microenvironment that promote the development of diverse histologic tumor subtypes. Specifically, genetic changes affecting pathways common to both papillary and clear cell carcinomas, such as mutations in MET or loss of the VHL gene, could play a role in facilitating multifocal neoplastic transformation in these cases.

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