CASE REPORT

AMACR Positive Papillary Renal Adenomatosis and Multifocal Papillary Carcinoma in End Stage Renal Disease

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Abstract Immunomarker α -methylacyl-coenzyme A racemase (AMACR), a protein involved in the metabolism of branched chain fatty acids was initially recognized in the evaluation of prostate cancer. AMACR is also a fairly sensitive marker for papillary renal cell carcinoma. Papillary adenoma associated with papillary renal cell carcinoma are AMACR positive and both represent a continuum of the same biological process. However, the papillary adenomas associated with end-kidney and/or acquired cystic disease are AMACR negative. Herein, we report a case of AMACR positive renal adenomatosis with tiny foci of papillary carcinoma in a background of end stage kidney disease and nephrolithiasis. AMACR staining pattern in renal papillary adenomas needs more evaluation to better understand their pathogenesis under different settings.

Keywords AMACR · End stage kidney disease · Papillary renal cell carcinoma · Renal papillary adenomatosis

Introduction

The current WHO classification of renal epithelial tumors defines papillary adenoma as tumor with papillary

or tubular architecture of low nuclear grade and measures up to 5 mm in diameter. The lesions with clear cells are considered malignant regardless of the size. They are either solitary or multiple. When they are numerous, the condition is known as renal adenomatosis. Majority of the patients remain asymptomatic and the tumors are undetectable radiologically owing to their small size. They are usually well circumscribed, yellow to greyish white nodules occurring just below the renal capsule. The microscopic morphology of papillary adenoma resembles closely with both type 1 and 2 papillary renal cell carcinoma (PRCC) [1, 2].

Papillary adenomas have been reported in 7 % of nephrectomy specimens and 10–40 % of autopsies. There is an association with prolonged hemodialysis and acquired cystic disease. Less than 10 % are present in the setting of other renal diseases including other renal neoplasms and end stage renal disease [3].

It has been proposed that renal papillary adenomas are precursor lesions of PRCC. Papillary adenoma and PRCC represent a continuum of one biologic process as indicated by similar α -methylacyl-coenzyme A racemase (AMACR) positivity in both. In contrast, adenomas associated with acquired polycystic kidney disease and end stage renal disease exhibit distinct morphological and immunohistochemical features and, therefore, may have an entirely different pathogenesis. Latter do not show AMACR expression, suggesting different biological mechanism for these neoplasms [4].

We report a case of multifocal papillary renal cell carcinoma with papillary adenomatosis, detected in a nephrectomy specimen sent with a clinical diagnosis of non functioning kidney, secondary to nephrolithiasis in which strong AMACR positivity was seen.

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Case Report

A 34 year oldman had history of off and on flank pain for the past 8 years. There was no history of diabetes, hypertension or any other systemic disease. General and systemic examination were normal on admission. Urine examination revealed increased WBCs and graveluria. X-Ray KUB showed a staghorn calculus in left kidney. CT scan showed enlarged hydronephrotic left kidney with lower calyceal staghorn calculus and lower ureteric calculi (11.3×9.8 mm) plus VUJ calculus (9.1×7.2 mm). Radionucleotide renography revealed non functional left kidney. Right kidney was normal. Left ureteroscopy revealed three calculi 1×1 cm in lower ureter. Intraoperatively, kidney was enlarged, hydronephrotic and had dense perinephric and periureteric adhesions. Laparoscopic simple nephro-urectomy was done and sent for histopathological examination.

Macroscopically, kidney was enlarged measuring 12×7×4 cm and showed focal scarring. Capsule was adherent. Multiple cortical nodules (>10 in number) were noted on the surface ranging in size from 0.2 cm to largest measuring 1.5 cm in diameter (Fig. 1). Cut surface of some nodules was solid-cystic filled with gelatinous material. The larger nodules (>0.5 cm), were largely solid and were gray-white to yellowish in colour. Cut section of the kidney showed markedly dilated pelvicalyceal system. Ureter was dilated to a diameter of 0.8 cm.

Microscopically, pelvicalyceal lining was largely ulcerated. Renal parenchyma showed features of chronic pyelonephritis. Sections from the subcapsular nodules showed tumor with tubulopapillary architecture. The tubules and papillae were lined by cuboidal to columnar cells showing mild nuclear pleomorphism, inconspicuous nucleoli and focal longitudinal nuclear grooves (Fig. 2). Cells had scant pale to moderate amount of finely granular cytoplasm. Many of the papillary structures contained foamy macrophages within their

fibrovascular cores. Tumor size ranged from 0.2 to 1.5 cm. The tumor cells were positive for CK7 and AMACR.

Based on the macroscopic, microscopic and immunohistochemical findings, a diagnosis of multiple subcortical papillary adenoma and papillary carcinoma with nephrolithiasis leading to hydronephrosis and chronic pyelonephritis was made.

Discussion

The concept of renal papillary adenoma is controversial and has evolved over the past 3 decades [5, 6]. Reliable criteria for differentiating adenoma from carcinoma remain elusive.

In 1950, Bell classified all tumors less than 3 cm in diameter as adenoma [6]. Since Bell's description, it is well known that some of the small tumors, especially clear cell type have metastasis. Therefore, currently the existence of an adenoma of clear cells is not accepted. Later various authors defined papillary adenomas on the basis of histological features [7, 8].

At present, WHO defines papillary adenomas as tumors with papillary or tubular architecture of low nuclear grade and 5 mm in diameter or smaller. However, clear cell morphology excludes the diagnosis of papillary adenoma irrespective of size [1, 2].

The papillary adenoma-carcinoma sequence has continued for a reasonable period of time. Increase in size of small benign lesions is associated with greater amount of chromosomal alterations and therefore the possible transformation in papillary carcinomas. For this reason, the WHO 2004 renal cell tumours classification considered tumors with a maximum diameter of 5 mm as papillary adenomas [1].

WHO also suggests that it is not possible to distinguish adenomas and carcinomas by genetic changes, because many carcinomas show only few genetic alterations [1].

Fig. 1 Multiple subcapsular nodules (arrows) ranging from 0.2 to 1.5 cm in a nephrectomy specimen

Fig. 2 Papillary tumors of varying size (adenoma and carcinoma)—H&E and AMACR positivity in corresponding tumors

Hence, size (≤ 5 mm) and tubulopapillary architecture along with absence of clear cells are the only criteria to define papillary adenomas currently [1].

AMACR diffusely labels PRCC in a granular cytoplasmic fashion [9]. It is now recognized that AMACR can show positivity in several different types of renal tumors, including

most acquired cystic disease–associated renal cell carcinomas, and some high-grade urothelial carcinomas of the renal pelvis [10].

It has been proposed that renal papillary adenomas are precursor lesions of papillary renal cell carcinoma because of its association with PRCC and similar

immunohistochemical expression of AMACR [4]. Papillary adenoma are also often seen in kidneys scarred from chronic pyelonephritis or renal vascular disease, long term hemodialysis, acquired renal cystic disease and in children with von Hippel-Lindau syndrome [8].

Wang et al. [4] in their study observed that papillary adenomas associated with APKD/ESRD stain negative with AMACR whereas those seen in other settings show positive staining in a fashion similar to PRCC.

Algaba also suggested that papillary adenoma and papillary renal cell carcinoma represent a continuum of the same biological process (both being AMACR positive). However, the papillary adenomas associated with end-kidney and/or acquired cystic disease may have a different pathogenesis (AMACR negative) [11].

In contrast to the above studies by Wang et al. [4] and Algaba [11] our case showed AMACR positivity in the multiple foci of papillary adenoma and carcinoma, even though our case was associated with nephrolithiasis and end stage renal disease. It suggests that AMACR staining pattern in papillary adenomas does not necessarily differ in the two conditions as indicated by the previous studies. However, occurrence of multiple pathology in same nephrectomy specimen cannot be ruled out.

The status of AMACR in papillary adenoma has not been studied much as per the literature reviewed by us. AMACR staining pattern in renal papillary adenomas needs more evaluation to better understand their pathogenesis under different settings.

Conflict of Interest Authors declare they have no conflict of interest.

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