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Alpha-methyl CoA racemase expression in renal cell carcinomas

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Summary Alpha-methyl CoA racemase (AMACR), a new molecular marker for prostate cancer, has been recently reported to be one of the most highly expressed genes in papillary renal cell carcinomas (RCCs). We tested the diagnostic usefulness of AMACR antibody in a series of 110 renal tumors: 53 papillary RCCs (33 type 1, 20 type 2); 25 conventional RCCs; 6 chromophobe RCCs; 9 oncocytomas; 5 mucinous tubular and spindle tumors; 2 urothelial carcinomas; 7 angiomyolipomas; and 2 Bellini carcinomas. Immunohistochemical staining was performed on formalin-fixed, paraffin-embedded tissue sections, with a primary prediluted rabbit monoclonal anti-AMACR antibody. Both type 1 and type 2 papillary RCCs exhibited cytoplasmic immunoreactivity for AMACR, with diffuse strong granular staining in 96.4% (53/55) of tumors, without correlation with type or nuclear grade. The 5 mucinous, tubular, and spindle cell carcinomas strongly expressed AMACR, and only 5 of 25 clear cell RCCs and 1 of 9 oncocytomas were focally reactive. The remaining 6 chromophobe RCCs, 5 urothelial carcinomas, and Bellini duct carcinomas showed no immunoreactivity for AMACR. Because high expression of AMACR is found in papillary RCCs (type 1 and 2) and in mucinous, tubular, and spindle cell carcinomas of the kidney, immunostaining for AMACR should be used in conjunction with other markers when histological typing of a renal tumor is difficult.

1. Introduction

Renal cell carcinoma (RCC) is a clinicopathologically heterogeneous disease, subdivided into clear cell, papillary, chromophobe, spindle cell, cystic, and collecting duct carcinoma subtypes based on morphological features according to the World Health Organization international histological classification of kidney tumors [1-6]. Papillary RCC represents the second most frequent RCC and accounts for 10% to 15% [7] of cases. Papillary RCCs are defined by their papillary or tubulopapillary architecture and can be subdivided into two morphological subtypes: type 1 with small cells arranged in a single layer on delicate papilla cores and type 2 with a large eosinophilic cytoplasm and pseudostratified nuclei arranged on broad papillae, which may have different genetic backgrounds [8-15]. Papillary RCCs can display not only papillary but also nonpapillary growth patterns such as trabecular, tubular, and solid patterns. In case of an equivocal diagnosis, immunohisto-

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chemistry may be a useful adjuvant in the diagnosis of papillary RCC [16]. The most relevant markers of papillary RCC are vimentin and CK7 [17]. More recently, alpha-methyl CoA racemase (AMACR), a peroxymal mitochondrial enzyme involved in the β-oxidation of branched-chain fatty acids and fatty acid derivatives, identified as a molecular marker for prostate cancer [18-21] on the basis of complementary (cDNA) microarray technology, has also been reported in epithelial tumors [22-24] and in kidney cancers [16,25]. Complementary DNA microarray study has demonstrated that AMACR overexpression in papillary RCC is one of the top 10 most highly expressed genes [26,27]. The purpose of our study was to assess the usefulness of AMACR (Menarini Diagnostics, Paris, France) in 110 renal tumors.

2. Materials and methods

2.1. Case selection

One hundred ten cases of renal tumors were selected for this study from the pathological databases of the Hôpital Saint Joseph, Paris, France, and the Centre Hospitalier Universitaire, Lausanne, Switzerland.

2.2. Immunohistochemistry

Immunohistochemical staining was performed on 5-μm sections cut from formalin-fixed, paraffin-embedded tissue blocks. Heat-mediated antigen retrieval was performed in 0.1 mol/L pH 6.0 citrate in a water bath for 30 minutes. Immunostaining was performed on a Dako autostainer using a peroxidase-labeled polymer-based detection system (Envision plus, Dako France SAS, Trappes, France) and diaminobenzidine as a chromogen. Rabbit monoclonal prediluted anti-AMACR antibody (p504s, Menarini Diagnostics) was used and incubated for 25 minutes at room temperature. Slides were then counterstained with hematoxylin. Prostatic adenocarcinoma was used as a positive control. Appropriate negative controls were used.

2.3. Evaluation of immunohistochemistry

Immunoreactivity was evaluated in a semiquantitative manner that assessed both staining intensity and percentage of positive cells. Positive AMACR staining was defined as

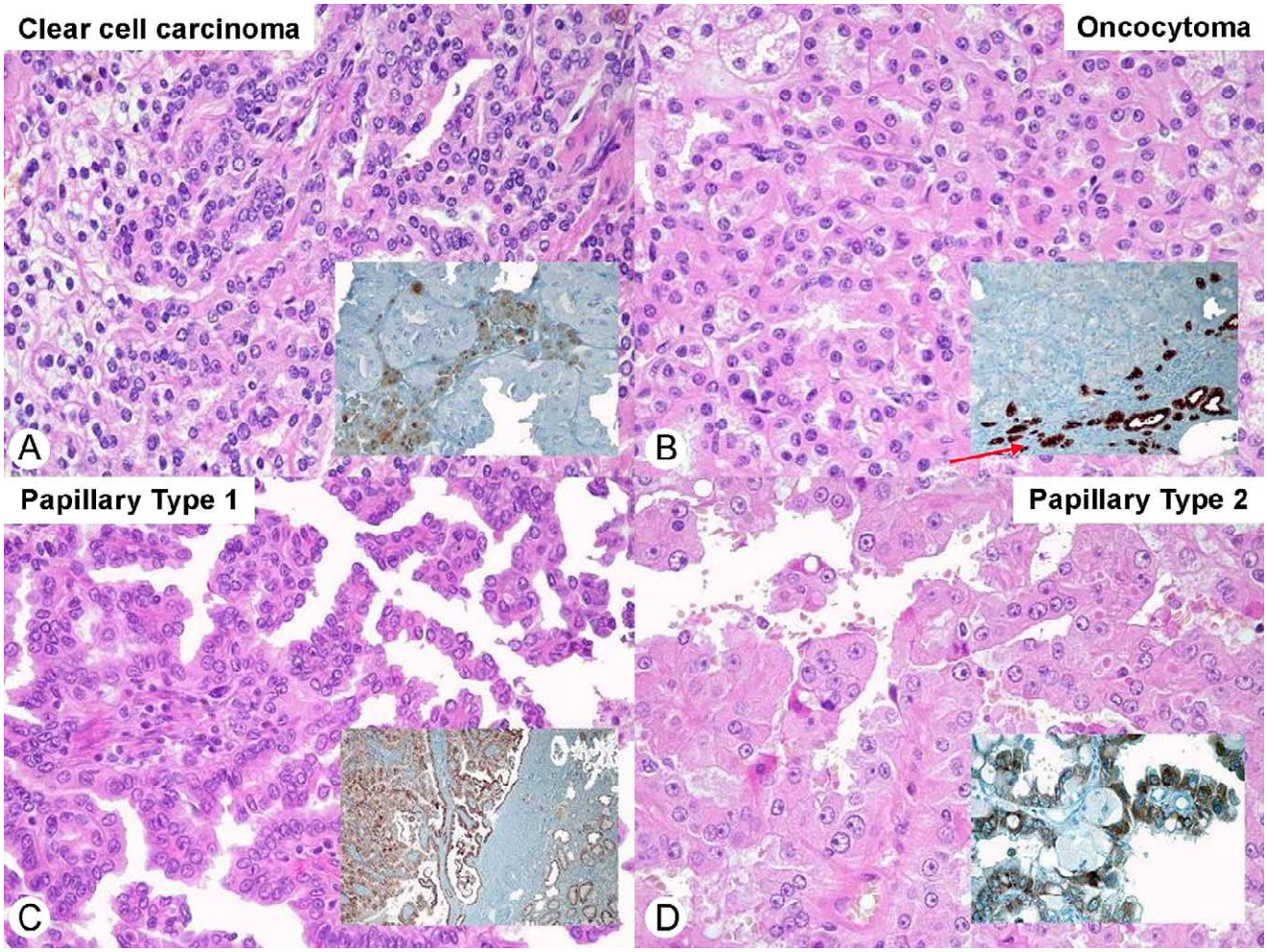

Fig. 1 A-D, Different renal subtype tumors and p504s expression.