INCIDENTAL DETECTION OF A NEW SUB-TYPE OF RENAL CELL CARCINOMA « CLEAR CELL PAPILLARY RENAL CELL CARCINOMA»

DÉTECTION ACCIDENTELLE D'UN NOUVEAU SOUS-TYPE DE CARCINOME CELLULAIRE RÉNAL

S. MAKNI[1,3,*]; R. KALLEL [1,3]; A. CHAABOUNI [2,3]; M. TRIKI [1,3]; S. GRAJA[1,3]; S. CHARFI [1,3] ET T. BOUDAWARA [1,3]

1: Department of Pathology, Habib Bourguiba University Hospital, 3029, Sfax, Tunisia.
2: Department of Urology, Habib Bourguiba University Hospital, 3029, Sfax, Tunisia.
3 : Faculty of médecine, University de Sfax-Tunisia.

***e-mail of corresponding author:** *olfa_saadia@yahoo.fr*

Abstract

Clear cell papillary renal cell carcinoma (CCPRCC) is a new entity that was not included in the 2004 World Health Organization (WHO) classification of kidney tumors, but is now an accepted sub-type of renal cell carcinoma in the new 2016 WHO classification. This tumor is characterized by a specific histomorphologic, immunohistochemical and molecular profile, with a good prognosis. We report the case of a 72-year-old man who presented with an incidental finding of a renal mass as part of the staging protocol for lymphocytic lymphoma. This mass was initially misdiagnosed, on kidney biopsy, as clear cell renal cell carcinoma, based on the morphological features. After partial nephrectomy, histological examination confirmed the diagnosis of CCPRCC. The outcome was favorable without recurrence or metastasis after chemotherapy for his lymphoma.

Key words: Clear cell papillary renal cell carcinoma; Immunohistochemistry; Kidney; Lymphocytic lymphoma.

Résumé

Le carcinome papillaire rénal à cellules claires (CCPRCC) est une nouvelle entité qui n'était pas incluse dans la classification de 2004 de l'Organisation mondiale de la santé (OMS) des tumeurs rénales, mais est maintenant un sous-type accepté de carcinome à cellules rénales dans la nouvelle classification de l'OMS de 2016. Cette tumeur se caractérise par un profil histomorphologique, immunohistochimique et moléculaire spécifique, avec un bon pronostic.

Nous rapportons le cas d'un homme de 72 ans qui s'est présenté avec une découverte fortuite d'une masse rénale dans le cadre du protocole de stadification du lymphome lymphocytaire. Cette masse a été initialement diagnostiquée à tort, lors d'une biopsie rénale, comme un carcinome à cellules claires rénales, sur la base des caractéristiques morphologiques. Après néphrectomie partielle, l'examen histologique a confirmé le diagnostic de CCPRCC. Le résultat était favorable sans récidive ni métastase après chimiothérapie pour son lymphome.

Mots clés: Carcinome papillaire rénal à cellules claires; Immunohistochimie; Rein ; Lymphome lymphocytaire.

ملخص

يعد سرطان الخلايا الحليمية الكلوية الصافية (CCPRCC) بمثابة كيان جديد لم يتم إدراجه في تصنيف منظمة الصحة العالمية لعام 2004 لأورام الكلى ، ولكنه يعتبر الآن نوعا فرعيا مصنفا في مادة سرطان الخلايا الكلوية في تصنيف منظمة الصحة العالمية الجديد لعام 2016. يتميز هذا الورم بمظهر نسجي الشكل، المناعي الكيميائي والجزيئي، مع تشخيص جيد.

قمنا بالتبليغ عن حالة رجل يبلغ من العمر 72 عامًا قدم اكتشافًا مصادفة للكتلة الكلوية كجزء من بروتوكول تقصي سرطان الليمفوم اللمفاوية. تم تشخيص هذه الكتلة في البداية بشكل خاطئ، أثناء إجراء خزعة كلوية، باعتبارها سرطان خلايا كلوي صافٍ، بناءً على الخصائص المورفولوجية. بعد استئصال الكلية الجزئي ، أكد الفحص النسيجي تشخيص CCPRCC. وكانت النتيجة ملائمة دون تكرار للمرض أو حصول انتشار خبيث بعد العلاج الكيميائي لهذا السرطان الليمفاوي.

الكلمات المفاتيح: سرطان الخلايا الحليمية الكلويةالصافية ;المناعية الكيميائية ; الكلية ; سرطان الليمفومات اللمفاوية.

INTRODUCTION

Clear cell papillary renal cell carcinoma (CCPRCC) is a new entity, recently described, it is reported for the first time in the setting of end-stage renal disease [1], but many cases, now, have been described in healthy kidneys [2]. This entity is now recognized in the new 2016 World Health Organization (WHO) classification system, it has a unique morphological, immunohistochemical and molecular profile that differentiates it from other renal cell carcinomas (RCCs) especially clear cell RCC and papillary RCC [3-5]. In this article we report a new case of CCPRCC in a patient with lymphocytic lymphoma and we identify its distinct pathological features.

OBSERVATION

A 72-year-old man, without a significant past medical history, especially without chronic renal failure, presented with fever and right inguinal lymphadenopathy. Biological analysis and histological examination confirmed the diagnosis of lymphocytic lymphoma. As part of the staging protocol for his lymphoma, a Computed Tomography (CT) was performed and revealed a round,well-defined, hypodense, lesion in the lower pole of the right kidney.

A kidney biopsy was recommended and on histological examination was thought to be clear cell renal cell carcinoma, based on the morphological features (immunohistochemistry was inconclusive by exhaustion of biopsy material). The patient underwent partial nephrectomy. Macroscopic examination revealed a well circumscribed tumor mesuring 2.0×1.5×1.2 cm. The cut surface was beige and homogeneous. The tumor was located at a distance of 0,1 cm from the surgical margin, without capsular involvement. Histologically, it consisted of papillary structures lined by columnar cells with clear cytoplasm and low grade apically aligned nuclei. Führman nuclear grade was 2. No necrosis or vascular invasion was seen (Fig. 1). Immunohistochemical study showed strong and diffuse cytokeratin 7 (CK7) reactivity, but no labelling for α-methylacyl-coA racemase (AMACR), CD10 and vimentin (Fig. 2).

The patient was well with no recurrence or metastasis at the 6-month follow up evaluation after chemotherapy for his lymphoma.

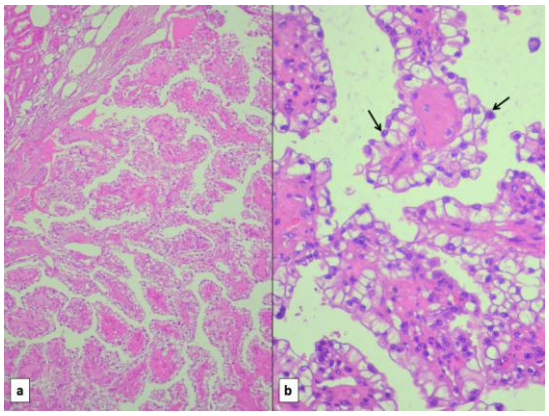

Figure 1 : a : Tumor is composed of tubulo-papillary structures (HE×100), **b :** Tumor cells have abundant and clear cytoplasm with low grade nuclei, located away from the basement membrane (↘) (HE×400)

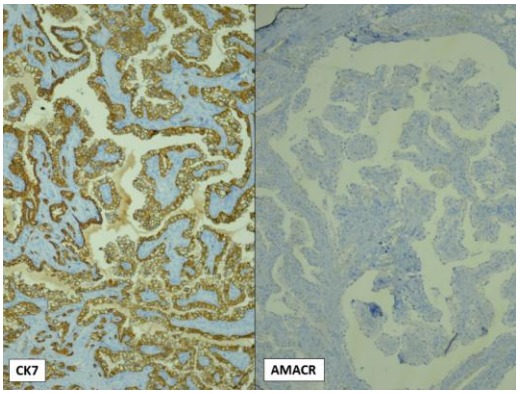

Figure 2 : Strong and diffuse CK7 positivity, and negative staining for AMACR (HE×200)

DISCUSSION

CCPRCC also named « renal angiomyoadenomatous tumor » and « clear cell tubulopapillary renal cell carcinoma », composed of cells with clear cytoplasm lining cystic, tubular and papillary components [1, 2, 6].

Tumor incidence varies, according to studies, from 1,2% to 4,3% of all adult renal cell carcinoma [7-10]. There is a slight male predominance with an age of diagnosis arround 60 years [11]. These tumors are usually asymptomatic and discovered incidentally [11], as in our case.

They are in general unique and small (<5 cm), Williamson et al [8]. and Zhou et al [10]. reported two cases of tumor size more than 5 cm, respectively mesuring 7,5 and 6 cm. Multifocality can be present especially in the setting of end-stage renal disease, and association, concurrently, with other renal tumors can be, also, present [8,12], but

we did not found, in the English literature, any case of CCPRCC associated with lymphocytic lymphoma or any other hematological malignancies.

Grossly, CCPRCC are well circumscribed and have a thick capsule with tan-pink to tan-red cystic cut surfaces [12,13].

Histologically, the dominant architecture is tubulopapillary or cystic and the papillae are lined by medium sized cuboidal or columnar cells with abondant clear cytoplasm and low Führman nuclear grade. The nuclei are arranged toward the luminal surface, which is a characteristic feature of CCPRCC. Neither mitotic figures, nor foamy macrophages, calcifications, necrosis, lymphovascular or renal sinus invasion are identified [11-13]. The stroma varies from being minimal to occasionally prominent, myxoid to hyalinized and rarely with organized amianthoid fibres or well-defined smooth muscle bundles presenting an angiomyomatous appearance without prominent capillary network [11-13].

CCPRCC has a distinctive immunoprofile, most studies found that tumors show strong and diffuse immunohistochemical staining for CK7 and Carbonic Anhydrase IX (CA IX), these tumors are negative for AMACR, CD10 and Transcription Factor E3 (TFE3) [2,6,11,13,14]. Another study reported that CD10 can be focally positive at the apical pole of cells lining cystic structures [8].

In our case report, tumor cells were strongly and diffusely positive for CK7 and negative for AMACR and CD10.

Cytogenetically, CCPRCC lacks typical abnormalities seen in either clear cell RCC or papillary RCC, no 3p deletion, loss of y chromosome or trisomy 7/17, VHL gene mutation is also absent [12-14].

The major differential diagnostic consideration are clear cell RCC, papillary RCC, multilocular cystic RCC and Xp11.2 translocation RCC [4, 5, 8, 12, 14]. The distinction between CCPRCC and these tumors is important because prognosis is different, Table 1 summarize the principale differences between these entities (Table 1).

In conclusion, CCPRCC is a new distinct epithelial tumor characterized by prominent papillary architecture, clear cell cytology, low nuclear grade and typical immunohistochemical pattern. This tumor is indolent and aggressive behavior, recurrence or metastasis have not been reported, surgical excision (partial or total nephrectomy) seems to be curative [8]. We report this case because of its rarity and good prognosis and to avoid a misdiagnosis as other papillary renal tumors with clear cells, and because to our knowledge, this is the first case of CCPRCC, in the literature, associated with lymphocytic lymphoma.

Table 1: Principale differences between CCPRCC and other RCC with clear cells and papillary architecture

RCC Type	Histology	IHC					Genetics
		CK 7	AMACR	CA IX	CD10	TEF3	
Clear Cell RCC	Solid or acinar architecture, clear cells separeted by hypervascular thin septa	–	+	+	+	–	3p deletion
Papillary RCC	Papillary architecture, fibrovascular cores, foamy histiocytes, cells with amphophilic cytoplasm and nuclei arranged in a single layer (type 1), cells with abondant eosinophilic cytoplasm and pseudostratified nuclei (type 2)	+	+	– or focal	–	–	Trisomy 7,17 Loss of Y
Multilocular Cystic RCC	Cysts lined by clear cells and separeted by fibrous septa that may contains aggregates of clear cells with low Führman grade	+	– or focal	+	+ or focal	–	3p deletion
Xp11.2 translocation RCC	Papillary or cystic architecture, cells with voluminous cytoplasm clear or granular and eosinophilic, high grade nuclei, stroma with psommoma bodies	– or focal	+	+ or focal		+	Xp11 translocation
Clear Cell Papillary RCC	Papillary or cystic architecture, cells with abundant clear cytoplasm and low Führman grade, nuclei polarized away from the basement membrane	+	–	+	–	–	Neither 3p deletion nor trisomy 7, 17

IHC: immunohistochemistry, RCC: renal cell carcinoma, AMACR: α-methylacyl-coA racemase, CA IX: Carbonic Anhydrase IX, TFE3: Transcription Factor E3

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