

# Association Of An Urothelial Carcinoma Of The Bladder And A Papillary Carcinoma Of The Kidney: Common Carcinogenesis Or incidental finding?

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## Abstract

The association between renal cell carcinomas and other cancers has been documented in the literature leading to the study of many possible etiopathogenic factors. We report two cases of an association between a high grade urothelial carcinoma of the bladder with a renal papillary carcinoma. These cases have been diagnosed among a retrospective study of 100 patients presenting renal cell carcinomas that were diagnosed between 1994 and 2003. The review of the English literature revealed a high incidence of the cancer of the bladder and the prostate in patients with renal cell carcinoma especially the papillary subtype. The etiopathogenesis of this association remains debated. It seems to be based on genetic alterations that haven't been formally proved. Our study puts emphasis on the possible association of renal cell carcinoma with high grade tumours of the bladder. This finding may be incidental, so that, more clinical trials should be monitored.

## INTRODUCTION

The association of the renal cell carcinoma with other primary tumours has been reported in the literature. A recent study established that these associations were dependent on the histological subtype of the renal tumour (1).

## MATERIAL AND METHODS

A retrospective review of medical records was performed on 100 patients who were treated for renal cell carcinomas diagnosed between 1994 and 2003.

Pathological diagnoses were made on simple nephrectomy or tumorectomy. Macroscopic examination was based on the initial description of the tumour's size, its site, its colour and the presence of foci of necrosis or haemorrhage. All samples were fixed in formalin, embedded in paraffin and stained with hematoxylin and eosin.

The pathological findings were reviewed by the authors in order to ensure that all cases were correctly characterized.

## RESULTS

The mean age of our patients was 58 years (range, 28 to 83 years) with an equal distribution between men and women (sex ratio=1). Papillary renal cell carcinoma was diagnosed in 20 patients (20%). No patient had a particular past

medical history. Among these 20 patients, two ones were men aged 62 and 83 years and presented an urothelial carcinoma of the bladder. In the first case, the two tumours were synchronized. In the second one, the cancer of the bladder was diagnosed 3 years after the renal tumour. Morphologic examination showed papillary renal cell carcinoma grade 2 of Furhman stage PT2 and an urothelial carcinoma grade 3 PT1 in both cases.

## DISCUSSION

The association of many primary cancers accounts for 2,6 to 3,9% [1,2]. Some genetic mutations are reported to be responsible for this phenomenon [3]. These familial cases are well known and their management is clear. Hereditary forms of renal cell carcinomas such as the Von Hippel-Lindau syndrome aren't known to be associated with urothelial cancer of the bladder, besides; the hereditary forms of cancer of the bladder aren't associated with renal tumours. The etiopathogenic factors implicated in the primary tumours' associations should be searched and assessed in order to reduce their mortality and morbidity.

The association of the renal cell carcinomas with other primary tumours including the bladder, the prostate, the rectum and the lung has been described in the literature.

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Many authors reported the higher incidence of the association of renal cell carcinoma with cancer of the bladder [4, 5, 6]. Kantor and coworkers reported that the patients treated for a renal cell carcinoma have a high risk of developing a cancer of the bladder after a follow up period ranging between 1 to 4 years [4]. Reciprocally, the risk of occurrence of a renal cell carcinoma is higher in patients presenting cancer of the bladder [5, 6, 7, 8, 9, 10]. Neuzillet et al and Rabbani and colleagues reported that the association of cancer of the bladder or the prostate with a renal cell carcinoma was essentially observed in papillary subtypes [6, 8].

Some authors supposed that the pathogenesis of the association of many primary cancers may be due to the existence of similar risk factors. They reported that the chemotherapy and the radiation therapy indicated for one cancer may induce the second [11, 12]. However, the treatment of the renal cell carcinoma isn't based on chemotherapy or radiation therapy; so, this hypothesis couldn't explain the occurrence of a cancer of the bladder secondary to a renal cell carcinoma. In the other hand, a renal cell carcinoma may be induced by an anterior chemotherapy used in the treatment of an anterior carcinoma of the bladder [13]. Other studies reported many risk factors implicated in this association like smoking, drinking alcohol or other oncogenic substances. In fact, the tobacco and some oncogenic substances are implicated in the pathogenesis of both renal cell carcinoma and cancer of the bladder but their implication in this association haven't been demonstrated [5, 10, 14]. Our 2 patients haven't any risk factor but this finding couldn't be interpreted because we have few patients.

Palmedo and his coworkers reported a study about 673 patients with renal cell carcinoma with identification of 17 patients with bladder cancer, which was significant ( $p=0,038$ ). The incidence was 2,8/100 patients. In our study, the finding of 2 patients presenting this association may seem similar but we can't assess the incidence because we report a retrospective study and not a trial so that, we can't compare our findings with those of Palmedo and colleagues.

The carcinogenesis is a local phenomenon determined by a clonal selection, thus, the association of primary cancers affecting different tissues necessitates the coexistence of genetic alterations. This coexistence is only explained by a genetic predisposition or a multifocal action of a common carcinogenetic factor. Similar chromosomal alterations are

observed in the papillary renal cell carcinoma and the cancer of the prostate [15, 16, 17, 18]. But, the coexistence of these changes in the association bladder cancer and renal cell carcinoma hasn't been proved yet. Palmedo et al described allelic duplications at 7q31-33 in 64 % of the renal cell carcinoma, 17q12-22 in 70 % of the cases, 16q24-qter in 55 % of the cases, 12q12-14 in 42 % of the cases, 8p21 in 25 % of the cases, 3q22-24 of 24 % of the cases, 20q13 in 48 % of the cases and allelic losses at chromosome Y in 74 % of the cases [15]. The same alterations were reported in the cancers of the bladder and the prostate. The association of the papillary renal carcinoma with other malignant tumours is usually based upon the same chromosomal imbalances such as the allelic losses at chromosome Y that are observed in the association between the papillary renal cell carcinoma and the cancer of the prostate [18]. It is mandatory to establish whether this association is due to common genetic alterations or it is only incidental and in this case it could be explained by the frequency of the cancer of the bladder which remains the first urologic cancer in Tunisia.

### **CONCLUSION**

Our study report 2 cases of association between renal cell carcinoma and bladder carcinoma. This finding may be incidental but further trials that will prospectively follow patients with renal cell carcinoma are necessary to establish the true incidence of this association. This could be necessary to show that there's a benefit to finding these tumours by screening.

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