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Case report

Renal Cell Carcinoma with Concurrent Urothelial Carcinoma of Urinary Bladder and Non-Hodgkin Lymphoma

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A B S T R A C T

We report a case of a 71-year-old male with multiple primary malignancies involving kidney and urinary bladder, combined with synchronous lymphoma. The patient was admitted to the hospital because of painless gross hematuria. Examination revealed tumor of the right kidney and papillary tumor in the urinary bladder and enlarged lymph nodes along aorta and inferior vena cava. Transurethral resection of bladder tumor (TUR), radical nephrectomy of the right kidney and retroperitoneal lymphadenectomy were performed. Pathohistologic evaluation, together with immunohistochemistry, gave the patient the final diagnosis of renal cell carcinoma (RCC), urothelial carcinoma of the urinary bladder and B- small cell Non-Hodgkin lymphoma (B-CLL).

***Key words**: renal carcinoma, transitional cell carcinoma, Non-Hodgkin lymphoma, immunohistochemistry*

Introduction

Multiple primary malignancies are tumors which develop independently either in the same tissue on different localizations or in different tissues. The reason why it happens is unknown, in some cases it can be related to therapy or genetics and in others it can be epigenetic. Epigenetic factors are surely more important in the older group, with factors influencing carcinogenesis such as aging, enviromental carcinogens, viral infection, hormonal factors, gender and underlying genetic alterations[1]. The occurence of multiple neoplasms in a single patient is not a rare phenomenon. The incidence varies from 1–11% of all neoplasms[2]. The incidence increases with age[3].

We present this case to add it to the database, documenting the association of three primary synchronous malignancies – Non Hodgkin lymphoma, renal cell carcinoma and bladder carcinoma.

Case Presentation

A 71-year old Caucasian man was admitted for recurrent episodes of painless hematuria. Abdominal ultrasound showed a lesion in the right kidney measuring 51 × 59 mm and a papillary tumor in the left part of the urinary bladder measuring 27 mm its largest diameter. Computed tomography scan of the abdomen and pelvis confirmed the diagnosis and dimensions of the mentioned tumors in the rignt kidney and urinary bladder (Figure 1). However, lymph node packages along the aorta and vena cava were detected, with largest lymph nodes up to 1 cm in diameter. Blood and biochemical tests were normal and without significant changes.

After cystoscopic confirmation of the papillary tumor mass in the urinary bladder, transuretheral resection under spinal anesthesia was performed in the same act. Postoperative course was uneventful.

* This case was presented in part at »Ljudevit Jurak's« International Symposium in 2005. Afterwards it was published as a conference paper »Renal cell carcinoma with synchronous urothelial carcinoma of urinary bladder and non-Hodgkin lymphoma«, D. Müller, D. Ljubanović, R. Heinzl, I. Savić, Č. Tomasović-Lončarić, G. Aralica, A. Racar, S. Manojlović. Acta Clinica Croatica, Vol. 44, No. 2 p. 230, Zagreb, June 2005. In the meantime, patient passed away, so we decided to make this full case report, as presented above.

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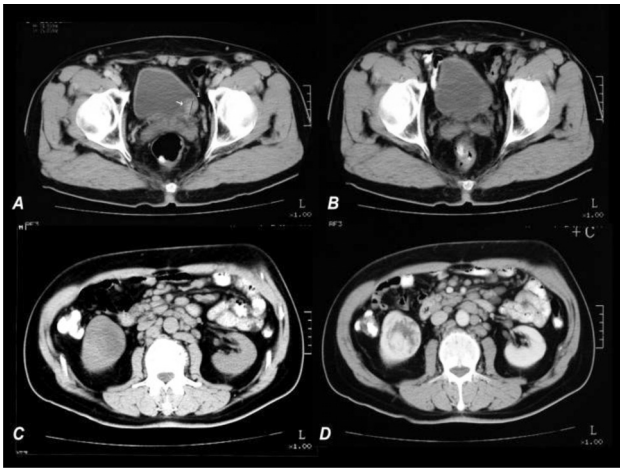

Fig. 1. Computed tomography of the abdomen and pelvis: A – tumor in the urinary bladder with contrast applied (arrow), B – the same tumor without contrast; C – renal tumor without and D – with contrast applied.

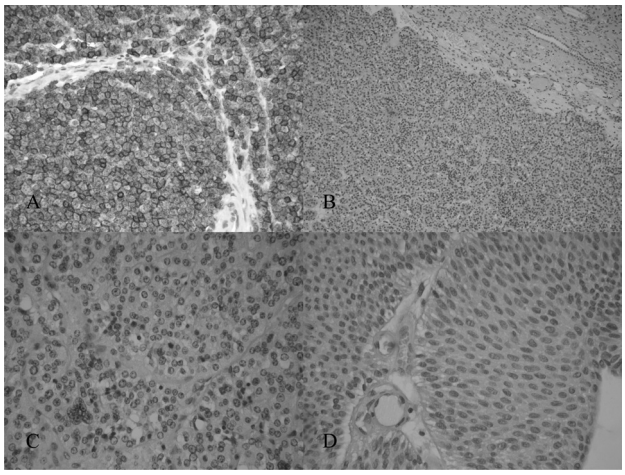

Fig. 2. A – lymphatic tissue CD20 (magnification 400×), B – renal cell tumor HE (magnification 100×), C – renal cell tumor HE (magnification 400×), D – urinary bladder tumor HE (magnification 100×).

Three weeks after TUR, nephrectomy was performed through the 10th intercostal space on the right side in the lumbal area under general anesthesia. In the same act, lymphadenectomy of enlarged paracaval, retrocaval, precaval and interaortocaval lymph nodes from the level of the right suprarenal gland to the right iliac artery was performed. Enlarged lymph nodes existed proximal as well as distal from the spot of surgery.

Gross examination of the resected specimen revealed a normal sized kidney (L:W:T=12×6×5 cm) with perinephric fat tissue and 7.5 cm long part of ureter. At the lower pole of the kidney was a circumscribed tumor mass, 3.5 cm in diameter with solid, soft, yellowish and partly hemorrhagical cut surface. On histological examination we found infiltration to the adjacent renal tissue and to the inner part of renal capsule, but however, there was no invasion to the adjacent fat tissue. Resection margins, together with ureter, renal vein and artery, calyceal and pelvic mucosa, were uninvolved by the tumor. Microscopic morphology revealed solid, tubuloalveolar and pseudopapillary growth pattern of relatively small tumor cells with scanty, mostly eosinophylic and only partly clear cell cytoplasm with large nuclei and conspicious nucleoli, with no significant mitotical activity (up to 2 mitotical figures per 10 HPF), Fuhrman grade 3 (Figure 2B, C). Immunohistochemically, tumor tissue was cytokeratin positive and vimentin negative and hystochemically, coloid iron was negative. According to WHO 2004 classification of renal cell carcinomas[4], this tumor is of clear cell type, and according to TNM classification[5], it corresponds to T1aN0MX.

Gross examination of the resected material from urinary bladder with transuretheral resection method revealed up to ten papillary pieces of tissue up to 2 cm in diameter. Histological finding corresponds to papillary transitional cell carcinoma with more than ten layers of well differentiated atypical urothelium cells with only few mitoses. There was no invasion to subepithelial connective tissue or muscle layer (Figure 2D). According to TNM classification of bladder carcinomas, this tumor corresponds to TaN0MX[5].

Histological analysis of lymph nodes on hematoxylin and eosin sections revealed efacement of lymph node structure with diffuse proliferation of small lymphocytes, some of them with prolymphocyte features and a few blasts. Lymphocytes were immunohistochemically CD79a+, CD20+ (Figure 2A), CD23+, CD5–, CD 43+ and cycline D1–. Therefore the diagnosis of B-cell Non-Hodgkin small lymphocytic lymphoma was made (CLL/SLL).

The patient was released from the hospital eight days after surgical treatment and was advised to take care for his accidentally diagnosed lymphoma. Trephine biopsy was performed two months afterwards and showed the same lymhocytic infiltration concordant with previously diagnosed CLL/SLL. At the same time his peripheral blood count showed normal number of lymphocytes. Patient refused therapy and came back after two years with generalized lymphadenopathy and lymphocytosis. There were 93% of lymphocytes in the bone marrow aspirate. In the meantime he had no sign of recurrence or progression in the urinary bladder and in the left kidney. His general condition rapidly deterriorated and he soon died after refusing therapy.

Discussion

To our knowledge, the present paper is the first one reporting synchronous renal cell carcinoma, bladder carcinoma and Non Hodgkin lymphoma. The only similar case to our one is the case of synchronous renal adenocarcinoma, transitional cell carcinoma of the renal pelvis and metastatic renal lymphoma[6].

As pointed out in the introduction multiple malignancies occuring in a single patient is not a rare event. Renal cell carcinoma has been reported to be associated with

other primary malignancies. According to Rabbani 27.4% patients with RCC had a second primary malignancy in his survey; the five most common being prostate, breast, colon, bladder cancer and NHL[7]. Most of them were antecedent (44.5%), with almost similar frequency synchronous (39.2%) and the rest were subsequent (16.2%)[7]. In the report from Beisland most of them were subsequent (46.7%), followed by antecedent (34.8%) and synchronous (18.7%) to the RCC[1]. In the report from Cheson some other second malignancies are described such as lung carcinomas, Hodgkin's disease, multiple myeloma, some forms of leukemias etc.[8].

There are enough reports about coexisting of renal cell carcinoma and transitional cell carcinoma in the pyelon, ureters and urinary bladder to try to connect these two conditions into a relationship[6,9–15]. The risk of bladder and renal cancer was observed in all patients and according to Hisada the risk of developing them was estimated as the ratio of observed to expected number of cases and was 1.16 in all observed patients (n=16367) in their study[16]. Rabbani observed that among patients with RCC those with papillary renal carcinoma were at increased risk of developing subsequnt bladder and prostate cancer[17]. Beisland also found bladder cancer to be the most frequent subsequent malignancy to RCC and not only in the early years after the diagnosis of RCC but also after an interval of more than 10 years[1]. This long interval suggests that the incidence is not related only to surveillance bias but favores a possibility of a common enviromental or genetic causal agent. Smoking was among factors for the high rate of subsequent bladder cancer[18]. Other carcinogens excreted through the kidneys could also influence urothel[19,20]. According to the literature there is also evidence about the connection among some chromosomal aneuploidies in bladder cancer and in chromophilic renal cell carcinoma, showing abnormalities of chromosomes 7 and 17, particularly trisomy and tetrasomy[21].

There are also enough reported cases of coexistent renal cell carcinoma and malignant lymphoma to suggest the possibility of a causal relationship between these two conditons[1,17,21–9]. Most NHL were of B immunophenotype with a slight predominance of extranodal lymphomas. Previous epidemiological studies revealed an increased incidence of RCC in patients with NHL. The basis for the association between RCC and antecedent NHL was attributed mostly to the consequences of the lymphoma treatment[23]. In the report from Hisada et al. the overall risk of developing a second neoplasm is significantly elevated in persons with CLL compared with those in the general population[16]. It seems to be very possible that myelosuppression and consequent immunologic impairment together with some other factors like initial treatment, cigarette smoking etc. plays an important role in pathogenesis of second cancers in such patients. On the other hand population based studies failed to identify an increased risk of renal cancer after NHL. Rabban in his study showed that only white males and females had a significantly increased risk of RCC after NHL and that risk was limited to the first year of follow-up suggesting detection or surveillance bias[17]. This is concordant with other reports where the highest incidence of RCC after NHL was within one year of diagnosis[28]. In some studies the same number of synchronous RCC and NHL as antecedent NHL and RCC was observed while NHL was rare as subsequent case to RCC[17]. Synchronous RCC and NHL as well as subsequent NHL could not be treatement related and no definite etiology, including genetic basis, has been reported linking these tumors[7,23].

The etiology of multiple primary malignant tumors is complex and includes, as previously mentioned, enviromental factors, genetic predisposition, immunologic impairment, previous medical treatment, gender and hormonal factors[1]. The problem is the impact on overall survival by synchronous cancers, which was the case in our patient as well. However, he died sooner because of refusing treatment and neglecting his lymphoma. The treatment of patients with multiple primary tumors should be based on evaluation of the status of each malignant disease. Additional problem is, of course, the mean age of these patients, which is higher than in patients with one neoplasm[3] and thus making the prognosis even worse[30].

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KARCINOM BUBREŽNIH STANICA S ISTOVREMENIM KARCINOMOM PRIJELAZNOG EPITELA MOKRAĆNOG MJEHURA I NON-HODGKIN LIMFOMOM

S A Ž E T A K

Prikazujemo slučaj 71-godišnjeg bolesnika s višestrukim primarnim malignomima, koji uključuju karcinom bubrega i mokraćnog mjehura, zajedno s limfomom. Bolesnik je primljen na liječenje zbog bezbolne hematurije. Pretrage su prikazale tumor desnog bubrega i papilarni tumor u mokraćnom mjehuru, kao i povećane paraaortalne i parakavalne limfne čvorove. U smislu liječenja su učinjeni trasuretralna resekcija tumora mokraćnog mjehura (TUR), radikalna nefrektomija desnog bubrega i retroperitonealna limfadenektomija. Nakon patohistološkog pregleda, zajedno s imunohistokemijskim pretragama, postavljena je konačna dijagnoza karcinoma bubrežnih stanica, karcinoma prijelaznog epitela mokraćnog mjehura te B-sitnostaničnog Non-Hodgkin limfoma.