Synchronous Renal, Urinary Bladder, Prostatic and Lung Cancer – Case Report With PD-L1 Status and Review

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SUMMARY

Our aim was to report the case of a patient treated for multiple synchronous primary carcinomas affecting the kidney, urinary bladder, prostate, and lungs.

A 69-year-old man presented with macrohematuria, without any other symptoms. An initial ultrasound examination and cystoscopy revealed a bladder tumor. During a computer tomography scan, a left kidney and lung tumor were incidentally found. The patient underwent transurethral bladder tumor resection, nephrectomy, pulmonic lobectomy, and finally radical cystectomy due to additional evidence of invasive bladder cancer. The pathology report after the last surgery also revealed prostatic cancer. The pathological processing was extended by immunohistochemical analysis. This report showed a rare synchronous appearance of four independent carcinomas in one patient, who was surgically treated. To our knowledge, this is the first case presenting this combination of tumors.

KEYWORDS

Case report; *Multiple primary malignant neoplasms*; *PD-L1*

Introduction

Multiple primary malignant neoplasms (MPMN) are defined as two or more unassociated primary malignant neoplasms that occur synchronously (a second neoplasm occurring within six months of the first one) or metachronously (a second neoplasm occurring more than six months after the first one). Each tumor originates from a different type of tissue or organ, presents as a distinct pathological type, and has to exclude secondary metastatic lesions[1].

We report the case of a patient with four synchronous primary malignant neoplasms, including invasive urothelial carcinoma of the bladder,

papillary renal cell carcinoma, prostate adenocarcinoma, and lung squamous cell carcinoma. Cases of double and triple primary malignant neoplasms are often reported, but quadruple primary malignant neoplasms are rare. To the best of our knowledge, this combination of MPMN has not yet been reported.

Clinical presentation and intervention

A 69-year-old man presented with hematuria without other symptoms. The patient's medical history revealed hypertension and longtime heavy cigarette use. Cystoscopy showed a solid, 3 cm tumor of the urinary bladder. The patient was hospitalized and computer tomography (CT) confirmed a bladder tumor, but incidentally revealed a tumor in the left kidney, measuring 3 cm in diameter (Figure 1A), and possible metastases in the left lung, measuring 2.5 cm (Figure 1B). A transurethral bladder tumor resection (TURBT) and left-sided nephrectomy were performed. Both the procedures and the recovery period were uneventful. A pathological examination showed a muscle invasive urothelial high-grade bladder carcinoma (BC), pT2 (Figure 2A) and papillary renal cell carcinoma (RCC), pT1-G3 (Figure 2B).

During the same hospitalization, a bronchoscopy was performed. The bronchial smear was negative for a tumor, so a CT-guided percutaneous biopsy was indicated. Pathology confirmed a poorly differentiated planocellular carcinoma (Figure 2C). In the period of one month after initial hospitalization, a lung lobectomy was performed (T1cNo). Postoperatively, the patient's general condition deteriorated. Because of the longer recovery period, the patient was not scheduled for radical cystectomy until six months after initial TURBT. Due to the patient's state, cutaneous ureterostomy was performed. The postoperative period was complicated with a mechanical ileus, so a revision with adhesiolysis was performed four days after cystectomy. Pathology confirmed invasive urothelial carcinoma (UC) with spread to fat tissue (T3No), but also prostate cancer (PC) Gleason grade 6 (3+3), (T1-G1), (Figure 2D). Preoperative PSA was 3.5 ng/ml. An additional analysis of PD-L1 expression was performed in all tumors.

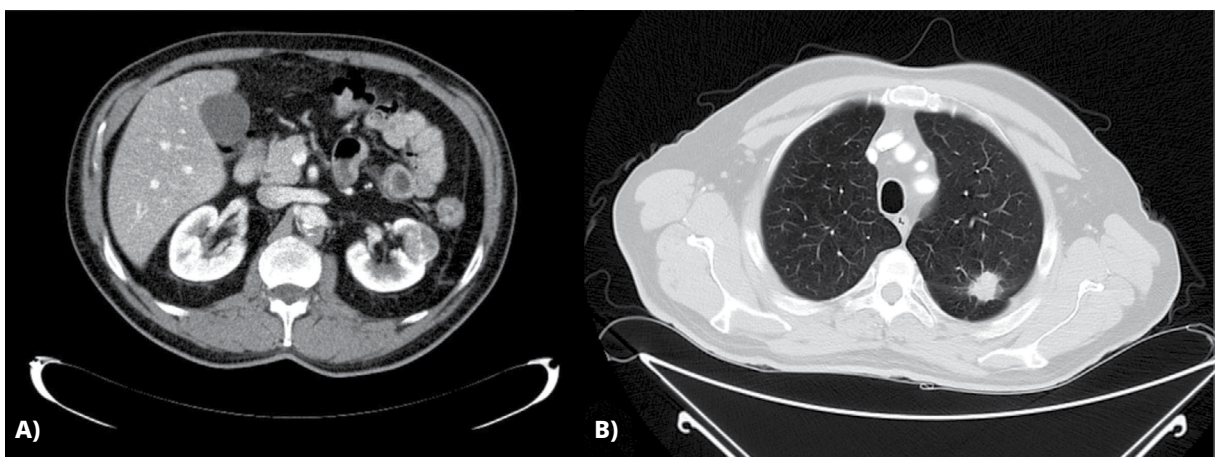

Fig. 1. CT scan, A) of the left kidney tumor and; B) of the pulmonary nodule.

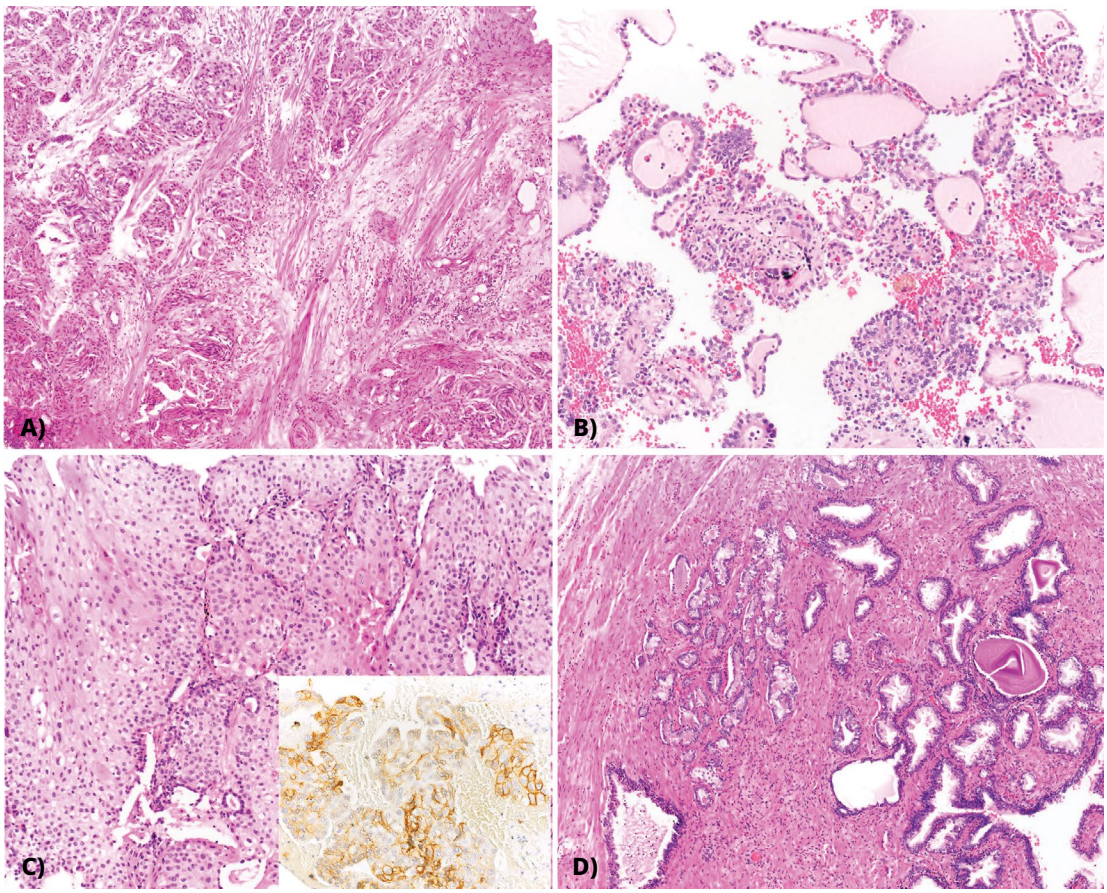

Fig. 2. Histological appearance of the carcinoma (HEx200); A) bladder cancer infiltrating muscle wall; B) papillary renal cell carcinoma; C) squamous lung carcinoma with PD-L1 expression showed in the right lower quadrant (PD-L1x400); D) small foci of prostate cancer.

UC, RCC, and PC showed weak PD-L1 expression, but lung cancer (LC) showed a positive reaction (Figure 2C). One month after hospital release, the patient was treated due to urosepsis. After recovery, the oncologist suggested intensive follow-up without any additional oncological treatment at that point. After three months, the patient had no symptoms and a control CT showed no signs of any residual disease or relapse. CYFRA 21-1 was slightly elevated and periodically controlled. One year after initial presentation, the patient developed pneumonia and died due to multi-organ failure syndrome.

Discussion

Although patients with more than one primary malignant neoplasm have ceased to be a pathological curiosity, they have instead become a practical problem. MPMN incidence has increased over the years because of more frequent oncological follow-ups, as well as due to the routine use of reliable imaging techniques after initial treatment. The incidence rate of MPMN is considered to be around 0.73–11.7%. MPMN cases are mostly seen in the lung, genitourinary, hepatobiliary, and gastrointestinal tracts[2].

Duchateau et al. reported that the third most frequent primary tumor site that synchronizes with LC was uroepithelial tissue[3] and, according to a study by Ventura et al., two out of the four most common tumor sites that synchronize with LC were the prostate and bladder[4]. In a large retrospective study, Antoneli et al. reported that the most common tumor sites associated with RCC were the prostate and bladder[5]. In a single-center retrospective study done by Murray et al., out of 3066 patients with RCC, 267 had a second primary cancer, and three out of the five most common tumor sites in men were the prostate, bladder, and lung[6].

According to Levi et al., the most common synchronous tumor sites, following breasts with breast pairings, were the bladder and ureter with the prostate[7]. The presence of both bladder cancer (BC) and PC in the same patient is common. Chun et al. reported that the rate of BC in patients with PC is eighteen times higher compared to the general population, while the rate of PC in those with BC is nineteen times higher than expected in the general population[8]. Although synchronous BC and PC are commonly found, a third synchronous cancer is rare. There have been only 14 cases of synchronous RCC, BC, and PC reported until now.

Since our case fulfilled the criteria for MPMN, it was classified as synchronous quadruple primary malignant neoplasm. To the best of our knowledge, it is the first one reported in English literature with such a combination of synchronous cancers.

Numerous environmental cancer-causative agents, genetic predispositions, and specific genetic mutations can be understood as an underlying cause connected with MPMN. With the aim to obtain additional prognostic information in our case, we performed immunohistochemistry focused on PD-L1 intensity in all cancer specimens. Our goal was also to establish whether the patient had a predisposition in the cancer microenvironment that favors the development of multiple tumors. The benefit of the immune checkpoint inhibitor therapy is usually expected in patients with a strong immune response in the tumor microenvironment[9]. Two antibody clones were used: sp142 (usually positive in the tumor microenvironment and the inflammatory cells) and 22c3 (marks positivity in epithelial tumor cells). Different clone positivity can suggest changes in treatment approach. RCC and UC in our patient had a negative reaction to 22c3, with positivity for sp142 under 5%, suggesting insufficient levels for immunotherapy application. PC was PD-L1 negative, but LC had a strong positivity in 80% of the tumor cells, suggesting the possibility to apply immunotherapy, which the patient didn't receive due to his deteriorated general condition.

MPMN can represent a therapeutic challenge. Treatment success and follow-up protocols depend on the specific combination of tumors. Considering the low incidence of MPMN, the approach to the patient must be individualized and targeted within a multidisciplinary team. The biggest challenge can be the exact timing and sequence of each treatment modality. Patients with MPMN are characterized by significant morbidity, so planning any additional treatment, such as radiotherapy, adjuvant chemotherapy, or immunotherapy, is challenging. This proved to be the case with regard to our patient as well. Treatment outcome data for MPMN patients vary throughout the literature, but each additional cancer increases morbidity and decreases overall survival[10]. Taking into account the rarity of MPMN, especially cases presenting quadruple synchronous cancers, we hope that our case will contribute to the experiences and understanding of this clinical-pathological category. ■

LIST OF ABBREVIATIONS:

MPMN	Multiple primary malignant neoplasms
CT	Computer Tomography
TURBT	Transurethral bladder tumor resection
RCC	Renal cell carcinoma
UC	Urothelial carcinoma
PC	Prostate cancer
LC	Lung cancer
BC	Bladder cancer

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SAŽETAK

Sinkroni karcinom bubrega, mokraćnog mjehura, prostate i pluća – prikaz slučaja s PD-L1 statusom i pregledom literature

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Cilj nam je bio predstaviti slučaj pacijenta liječenog radi multiplih sinkronih primarnih karcinoma: bubrega, mokraćnog mjehura, prostate i pluća. Muškarac u dobi od 69 godina javio se zbog hematurije bez drugih tegoba. Inicijalni ultrazvučni pregled i cistoskopija pokazali su tumor mokraćnog mjehura. Tijekom obrade kompjuteriziranom tomografijom, tumor lijevog bubrega i pluća incidentalno su otkriveni. Kod pacijenta je izvedena transuretralna resekcija tumora mjehura, nefrektomija, lobektomija pluća i konačno radikalna cistektomija zbog naknadnog dokaza invazivnog karcinoma mokraćnog mjehura. Patološki nalaz iza posljednjeg zahvata dokazao je i karcinom prostate. Patološka obrada proširena je imunohistokemijskom analizom. Ovaj prikaz pokazuje rijetku pojavu četiri neovisna karcinoma u jednog pacijenta, koji je kirurški liječen. Koliko nam je poznato, ovo je prvi slučaj koji prezentira ovu kombinaciju tumora.

KLJUČNE RIJEČI

Multiple primarne maligne neoplazme; *PD-L1*; *prikaz slučaja*