Case Report

Triple malignancy: A rare occurrence

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ABSTRACT

During the long-term follow-up of patients with renal cell carcinoma (RCC), the incidence of subsequent second primary malignancies increases with each passing year. The incidence of more than one second primary malignancy in these patients is very rare. We are presenting a case report where one of our patients developed metachronous malignancy with papillary cell carcinoma in kidney, transitional cell carcinoma in the urinary bladder, and squamous cell carcinoma in the skin.

Keywords: Renal cell carcinoma, multiple primary malignancies, urinary bladder.

INTRODUCTION

Cancer patients are at an increased risk for developing additional subsequent primary tumors. One recent study using Surveillance Epidemiology and End Results (SEER) data found that of the cancer patients alive as of January 1, 2001, nearly 8% were diagnosed with more than one primary malignant tumor between 1975 and 2001. This statistic underscores the pervasive nature of multiple malignancies and raises important questions regarding etiology, treatment decisions, demographics, and outcomes. The development of multiple malignancies in an individual has been reported after successful treatment of primary tumors.

In the follow-up of patients with successful treatment of kidney cancer, second malignancies have been reported. Most commonly involved sites with second primary malignancies include urothelial, lung, breast, colon, and skin. We are presenting a case report in which one of our patients developed three malignancies metachronously, which involved right kidney, urinary bladder, and skin with successful treatment in all three cancers, and, presently, the patient is disease-free and is on follow-up on a regular basis.

CASE REPORT

A 45-year-old male smoker presented with painless hematuria in December 1998. He had no other symptom and there was no other significant positive history. Routine baseline investigations including complete blood count, liver and kidney functions, and chest X-ray were normal. Ultrasound of the abdomen revealed right renal mass suggestive of renal cell carcinoma (RCC). Contrast computed tomography (CT) scan showed right renal mass limited to kidney. Bone scan was normal. A clinical impression of RCC was made and right nephrectomy was done. Histopathology revealed transitional cell carcinoma papillary type with capsular and renal pelvis infiltration [Figure 1]. Postoperatively, the patient was treated with adjuvant radiotherapy of 45 Grays by an external beam telecobalt unit to renal bed.

He was put on follow-up and was disease-free up to February 2000, when he started with hematuria,
dysuria, and difficulty in micturition. The patient was evaluated and ultrasound of the abdomen revealed a urinary bladder mass and normal left kidney. Levels of NMP22 was 12 U/mL. Transurethral resection of the bladder tumor was done. Histopathology of the tumor showed transitional cell carcinoma with no muscle invasion (T1N0M0) [Figure 2]. Level of NMP22 normalized. The patient was put on follow-up, but, in 2002, the patient developed bladder mass in lateral wall. He was again subjected to transurethral resection of the bladder tumor with histology of transitional cell carcinoma, grade 4 with muscle invasion and infiltration into surrounding adipose tissue with focal areas showing necrosis. He refused radical surgical treatment and received external beam radiotherapy of 45 Grays to pelvis, followed by boost radiotherapy with reduced portals to the tumor site in June 2002. The patient was on follow-up and presented in the outpatient department with an ulcerative lesion in the right thigh in June 2009. Excision of the lesion was done and histopathology revealed well-differentiated squamous cell carcinoma (Stage was T2 N0 M0). The patient had no regional lymphadenopathy. The patient received postoperative radiotherapy to the scar area and prophylactic radiation to the draining lymph nodes. The patient is presently disease-free and is on a regular follow-up.

**DISCUSSION**

Multiple primary malignant tumors are a well-known phenomenon. RCC has been linked to numerous secondary malignancies. Reports have showed that other primary malignant tumors associated with kidney cancer include cancer of the bladder, prostate, colorectal, and lung. Malignant melanoma and Non-Hodgkin's lymphomas are also associated with kidney cancer. Squamous cell carcinoma of skin is extremely rare in these patients.

The aetiology of multiple primary malignant tumors is complex and includes environmental factors, genetic predisposition, previous medical treatment, gender-specific factors, hormonal factors, and interactions of these factors. Multiple malignancies most often involve two sites. The occurrence of the third malignancy is exceedingly rare. In our patient, a common risk factor was smoking that is an established factor for both kidney and bladder carcinoma. However, the patient developed an invasive skin cancer in the medial aspect of the thigh. All cancers in the patient developed as metachronous lesions and were treated successfully.

While several investigations have focused on assessing risk factors for developing subsequent primary malignancies, long-term outcome data on patients with multiple malignancies are lacking. Multiple malignancies may have better overall prognosis as compared with their single
malignancy counterparts. Aside from clinical observations, this hypothesis stemmed, in part, from the question: if a patient survives one malignancy, is there perhaps something inherently different in their immune system or other genetic surveillance mechanisms that might confer improved survival? The case in reference has survived all three cancers and is presently disease-free.

It is well-known that cancer therapy may result in other primary cancers, but these usually appear after 10 years. As the standard treatment of RCC does not include chemotherapy or radiation, this is probably not a major contributory cause to the increased risk of second primary cancers. In our patient, the time gap for the occurrence of bladder cancer was 14 months and 10.5 years for skin cancer from the onset of RCC. Both bladder and skin were outside the treatment field of radiation for RCC.

The study by Czene and Hemminki[6] clearly indicates that patients with RCC have a greater risk of other cancers not only in the first year after the primary diagnosis but also after more than 10 years. Beisland et al. conducted a major study in diagnosed cases of RCC to evaluate the incidence of other primary malignancies and found that of the 1425 patients diagnosed with RCC, 228 (16%) had one, 23 (1.6%) had two, three (0.2%) had three, and one (0.07%) had four other primary malignancies. They found that bladder cancer was one of the most common (28 cases) second primary in these patients.[3] The RCC was of papillary type in our patient. The patients with this histology are more likely to have a second malignancy and multiple malignancies as compared with patients with clear cell RCC.[10] Bladder cancer has been found to be more common in this histological subtype.

To conclude, we would recommend every patient of malignancy to be screened for second malignancy during follow-up.

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REFERENCES