A case of synchronous double malignancy: Invasive bladder cancer and Leiomyosarcoma of extremity and review of literature

Dear Editor,

Incidence of multiple primaries is not uncommon. The incidence of association of urinary bladder cancer with prostate cancer is 2.5-70%. Also, invasive bladder cancer has been described with other second malignancies such as lung cancer and renal cell cancer. Here, we have reported a rare and possibly first case of synchronous double malignancy- invasive urinary bladder cancer and soft tissue sarcoma of the extremity.

A 45-year-old male farmer was evaluated with pain abdomen, hematuria, and dysuria of 4-months duration and swelling of the left thigh of 2-months duration. He was a chronic smoker and an occasional alcoholic. His general physical and abdominal examination was normal, except for the left thigh swelling. Left thigh examination revealed a 15 x 10 cm, hard, non-tender, and non-inflamed mass on the posterior aspect of left mid-thigh [Figure 1a].

Routine hemogram and other blood tests were normal. Renal profile revealed normal blood urea nitrogen (BUN) and raised serum creatinine of 1.3 mg/dL (normal 0.5-1.2 mg/dL). Decreased glomerular filtration rate (GFR) with Tc 99 isotope of left kidney 31.1 mL/min and right kidney 17.1 mL/min with a total GFR of 18.2 mL/min (normal 80-120 mL/min), probably because of post renal causes.

Left thigh computed tomography (CT) scan [Figure 1b, black arrow] showed large, well-defined irregular, lobulated soft tissue mass lesion in the posterior aspect of thigh and inhomogenous moderate peripheral contrast enhancement with central necrosis along with infiltration of the semimembranous muscle. CT scan of the abdomen [Figure 1c, black arrow] showed an irregular, asymmetric nodular thickening of the urinary bladder wall (more on the right side) and a moderate inhomogeneous central enhancement with hypo dense non-enhancing necrotic areas. In addition perivesicular fat stranding was noted.

**Pathological findings**

Bladder biopsy specimen showed invasive bladder cancer [Figure 2a and b]. Immunohistochemistry (IHC) of the left thigh lesion was negative for SK, S100, and Myo-D1 and positive for Desmin and smooth muscle antigen (SMA) with grade 3 tumors [Figure 2c-e] consistent with leiomyosarcoma. Bone scan and CT scan of the chest were normal. A diagnosis of synchronous invasive bladder carcinoma cT2a/2bNxM0, stage II, and leiomyosarcoma cT2aN0M0 stage III was made.

**Treatment and outcome**

Surgical oncology and radiotherapy consultations were obtained and the patient was deemed inoperable for both malignancies in view of the advanced nature of both the cancers. The case was discussed in tumor board and considered for chemotherapy, which works in both tumors. The patient received platinum-based chemotherapy IAP (consisting of ifosfamide 1500 mg/m² on days 1-5 with MESNA, Adriamycin 60 mg/m² on day 1 only, and cisplatin 20 mg/m² on days 1-5) for three cycles with prophylactic growth factors. This treatment had more than partial response for leiomyosarcoma and partial response for the urinary bladder tumor. He underwent complete excision of leiomyosarcoma. However, the patient refused cystectomy and hence received palliative radiotherapy. Following radiotherapy, the patient had excellent response and was disease-free for 8 months. Later, he had progressive disease in the form of abdominal lymphadenopathy and vertebral metastasis and died after 1 year of radiotherapy.

Incidence of cancers is increasing in developing countries like India.[1] Newer diagnostic tools have helped detect these at the earliest. Also, multiple primaries in a single individual are being increasingly diagnosed due to the availability of newer imaging modalities, newer histopathological markers, better follow-up and understanding of second malignancies. [2]

The association of genitourinary malignancy with second cancer diagnosed either synchronously or metachronously is well described. However, these multiple tumors had no common genetic etiology or any specific genetic abnormality.[3] Our case does not belong to any of the syndromes associated either with invasive bladder cancer or leiomyosarcoma.

According to Ray et al., incidence of second or multiple malignancies among cancer patients is 5-8%, and genitourinary system constitutes nearly 13.5% of these second or multiple primaries. [4] Various authors have reported the incidence of urological cancer with other second primaries ranging 1.2-26.9%.[5] However, this rare association of invasive bladder cancer with leiomyosarcoma of extremity is not described to the best of our knowledge.

The largest series of double malignancy study in urothelial cancers was by Salminen et al., who followed up 10,014 patients with bladder cancer from 1953 to 1989. In this group, 652 developed metachronous lesions, 195 developed lung cancer, and 35 developed renal cell carcinoma.[6] A report from Japan described association of bladder cancer with stomach, prostate, cervix, pharynx, oesophagus, stomach, colon, rectum, and liver. In most cases of bladder cancer associated with other urological cancers (85.2%), the two were synchronous.[7] Temple University, USA authors found that 22 out of
Viveka, et al.: Double malignancy, bladder cancer, leiomyosarcoma

515 (4.3%) urological malignancy patients had multiple tumors like prostate cancer with bladder and the remaining 18 patients (3.5%) had another nonurologic primary malignancy. In a study by Bergfeldt et al., among 4815 women who were treated for uterine cancer, an increased incidence of cancer of the colon, ovary, vulva, bladder, and leukemia was found.

Contrary to the above described associations, a study by Isaacs et al., examining the risk of associated malignancies in patients with prostate cancer, found no higher incidence of other tumors. Furthermore, Miller et al., reported a low incidence of coexistent disease as determined by pre-treatment CT scanning for radiation therapy in patients with prostate carcinoma.

The interaction between the occupational hazards, smoking, dietary causes, ageing, and genetic susceptibility all play an important role in the multifactorial process of these multiple malignancies, and our patient was a chronic smoker.

Molecular mechanisms have been suggested for multiple cancers in a single individual like faulty DNA repair mechanisms and expression of p53 and the pRb and N-acetyltransferase genotypes. Conventional cytogenetic study of our patient did not show any abnormality and molecular studies were not conducted.

Our case is a rare combination of invasive urinary bladder cancer and leiomyosarcoma, not associated with any known syndromes. This requires multidisciplinary approach and timely interventions. Patients need psychological support as burden of two malignancies is difficult to bear. It is a challenge to treat two different malignancies together without any known standard of care. Some evidence for management of this type of condition needs to be available in literature to help treat patients in situation like ours. Bladder cancer directed treatment like cystectomy, and additional treatment probably would have resulted in longer survival of our patient.

Acknowledgment

We acknowledge the services of the Department of Radiology and Radiotherapy for their help in treating this patient.

B. K. Viveka, Usha Amirtham1, Vijaya M. Kumar2, Govind K. Babu
Departments of Medical Oncology, Pathology, Surgical Oncology, Kidwai Memorial Institute of Oncology, Bangalore, Karnataka, India

Correspondence to: Dr. Viveka BK, E-mail: vivekquest@gmail.com

References

1. Mudur G. India has some of the highest cancer rates in the world. BMJ 2005;330:215.
2. Vainrib M, Leibovitch I. Urological implications of concurrent bladder and lung cancer. Isr Med Assoc J 2007;9:732-5.
3. Bergfeldt K, Einhorn S, Rosendahl I, Hall P. Increased risk of second primary malignancies in patients with gynecological cancer. A Swedish record-linkage study. Acta Oncol 1995;34:771-7.
4. Ray P, Sharifi R, Ortolano V, Guinan P. Involvement of genitourinary system in multiple primary malignant neoplasms: A review. J Clin Oncol 1983;1:574-81.
5. Mydlo JH, Gerstein M. Patients with urological cancer and other neurological malignancies: Analysis of a sample and review of the literature. Urology 2001;58:864-9.
6. Salminen E, Pukkala E, Teppo L, Pyhönen S. Risk of second cancers among lung cancer patients. Acta Oncol 1995;34:165-9.
7. Kotake T, Kiyohara H. Multiple primary cancers (MPC) associated with bladder cancer: An analysis of the clinical and autopsy cases in Japan. Jpn J Clin Oncol 1985;15:201-10.
8. Isaacs SD, Kiemeney LA, Baffoe-Bonnie A, Beatty TH, Walsh PC. Risk
of cancer in relatives of prostate cancer probands. J Natl Cancer Inst 1995;87:991-6.
9. Miller JS, Puckett ML, Johnstone PA. Frequency of coexistent disease at CT in patients with prostate carcinoma selected for definitive radiation therapy: Is limited treatment-planning CT adequate? Radiology 2000;215:41-4.
10. Mydlo JH, Agins JA, Donohoe J, Grob BM. A review of urologic cancer patients with multiple primary malignancies. World J Urol 2001;19:240-3.
11. Smith AH, Goycolea M, Haque R, Biggs ML. Marked increase in bladder and lung cancer mortality in a region of Northern Chile due to arsenic in drinking water. Am J Epidemiol 1998;147:660-9.
12. Singh A, Jones RF, Friedman H, Hathir S, Soos G, Zabo A, et al. Expression of p53 and pRb in bladder and prostate cancers of patients having both cancers. Anticancer Res 1999;19:5415-7.
13. Wang CY, Jones RF, Debiec-Rychter M, Soos G, Haas GP. Correlation of the genotypes for N-acetyltransferases 1 and 2 with double bladder and prostate cancers in a case-comparison study. Anticancer Res 2002;22:3529-35.