Radiation-Induced Urothelial Carcinoma

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<th>Masahiko</th>
<th>Saito a</th>
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<tbody>
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<td>A.</td>
<td>Atsuo</td>
<td>Kondo a</td>
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<td>T.</td>
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<td>Miyake a</td>
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</tbody>
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Key Words
Bladder tumor
Ureter tumor
Pelvic irradiation
Uterine cancer
Radiation-induced tumor

Abstract
Four cases of urothelial carcinoma following pelvic irradiation for carcinomas of the cervix uteri (n = 3) and the ovary (n = 1) are reported. The urothelial carcinomas developed 26.8 (mean) years after radiotherapy and invaded the bladder in 3 patients and the ureter in 1. Despite radical surgery, the patients died of metastatic cancer.

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Introduction
Pelvic irradiation with or without surgery for uterine cancer is known to produce many years later such severe adverse effects as hemorrhagic cystitis, contracted bladder, dermal ulcer, carcinomas of bladder and rectum, pelvic girdle sarcoma, and leukemia [1–4].

Case Reports
Case 1
A 73-year-old female had undergone total hysterectomy followed by irradiation for uterine cervical cancer in 1959. Although the total dose was unknown, it was large enough to result in an intractable ulcer of the soft tissue of the buttock in 1977. In 1989, 30 years after prior irradiation, a right nephroureterectomy with a cuff excision of the bladder wall was performed for a carcinoma of the distal part of the right ureter. Pathology was transitional cell carcinoma of grade II and stage T2, with no evidence of metastatic lesions. Six months after surgery, however, the patient died of general metastases of the transitional cell carcinoma.

Case 2
A 63-year-old female has been operated on for carcinoma of the cervix uteri and had received cobalt irradiation (60 Gy) postoperatively in 1963. A bilateral ureterocutaneostomy was performed for severe hematuria and urinary incontinence in 1975. Twenty-six years later a radical cystectomy was necessary for a transitional cell carcinoma (grade III, stage T1) in the unused bladder. The patient died of
multiple metastases of bladder cancer 18 months after the cystectomy. Autopsy confirmed disseminated metastases of carcinoma of the bladder.

Case 3
A 66-year-old female had undergone total hysterectomy and 60Co irradiation for uterine cervical carcinoma in 1967. Twenty-one years later radical cystectomy and Rocks’ operation were performed for bladder malignancy consisting of transitional cell carcinoma and squamous cell carcinoma of grade III and stage T3B. Despite two courses of chemotherapy (M-VAC + pepleomycin), the bladder carcinoma recurred at the genital skin. She died of multiple metastases 9 months after the cystectomy.

Case 4
A 42-year-old female had undergone bilateral ovariectomy and pelvic irradiation for ovarian tumor at the age of 10 years. She had colostomy for radiation proctitis in 1989, 28 years later. Thirty-one years later acute renal failure developed because the bladder carcinoma invaded the ureters. Cystectomy and ileal conduit were performed. The tumor comprised transitional cell carcinoma and adenocarcinoma of grade III and stage T3B. Seventeen months after the cystectomy the patient died of multiple lung metastases of the bladder cancer.

Discussion
Although irradiation is highly effective in treating malignant tumors, it has the potential to induce neoplastic transformation. It is likely that pelvic irradiation could be involved in the initiation and/or the promotion of urothelial tumors. Radiation-induced neoplasia itself is difficult to be properly identified, because its histology is indistinguishable from that of naturally occurring tumors [1–3]. The diagnosis should be based on the facts that the organs are different, the pathohistological findings are not the same, the latency period exceeds 5 years, and the organ in which the secondary malignancy developed is located within the area irradiated [3]. Our 4 cases met these criteria. Ulceration of the buttocks (case 1), contracted bladder (case 2), and intractable radiation proctitis which resulted in colostomy (case 4) are other adverse effects of irradiation. Urothelial carcinoma developed insidiously and slowly, on average 27 years later, in our 4 patients who then survived only 16 months after radical surgery.

Dunkan et al. [2] found 8 patients with bladder carcinomas among 2,674 women who had received radiotherapy of the cervix uteri. This incidence (0.29%) is 58 times that observed among females in the general population. Quilty and Kerr [4] pointed out that the prognosis of radiation-induced bladder tumors is less favorable than that of naturally occurring cancer (i.e., 1-year survival rate 32%) because such tumors tend to be poorly differentiated and to deeply invade the muscle coat. Our present experience and the results described by Dunkan et al. [2] and Quilty and Kerr [4] should alert urologists and gynecologists to the need to examine with great care a patient who has previously received pelvic irradiation for a possible urothelial malignancy.

References

R. Radiation-Induced Urothelial Tumor