# Two cases of post-radiation osteosarcoma of the sacrum after pelvic irradiation for uterine cervical cancer

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**Summary**

*Background:* Post-radiation pelvic bone sarcoma can result as a long-term sequela of pelvic irradiation for uterine cervical cancer. *Case:* A 59-year-old woman who had received pelvic irradiation for Stage IIB uterine cervical cancer 16 years before was diagnosed as having post-radiation osteosarcoma of the sacrum. Another 66-year-old woman who had received pelvic irradiation for Stage IIIB uterine cervical cancer seven years previously was also diagnosed as having pleomorphic sarcoma of the sacrum. *Conclusion:* When a bone lesion is observed at a previously irradiated field, post-radiation sarcoma should be considered and differentiated from bone metastases.

*Key words:* Post-radiation; Sarcoma; Cervix.

## Introduction

Secondary malignancies can be induced within or at the margin of radiation fields many years after radiotherapy for a primary cancer. Post-radiation sarcoma is rare but a well-known type of secondary malignancy. It accounts for 0.5-5.5% of all sarcomas [1]; there are several histological types such as osteosarcoma, malignant fibrous histiocytoma and chondrosarcoma [2]. Post-radiation osteosarcoma is one of the most common types of sarcoma and accounts for 17-63% of all post-radiation sarcomas [1].

For the treatment of uterine cervical cancer, whole pelvic radiotherapy is common practice as a definitive or adjuvant treatment modality. Thus, post-radiation sarcoma of the pelvic bone can be induced as a sequela of pelvic irradiation for uterine cervical cancer [2]. Here we report two cases of post-radiation osteosarcoma of the sacrum after pelvic irradiation for uterine cervical cancer.

## Case Reports

*Case 1*

A 59-year-old Korean woman visited the Department of Gynecology at our hospital in October 2004 with complaints of left buttock pain and bilateral radiating thigh pain. She had received pelvic radiotherapy 16 years before for FIGO (International Federation of Gynecology and Obstetrics) Stage IIB squamous cell carcinoma of the uterine cervix. Whole pelvic irradiation was delivered 50 Gy with daily doses of 2 Gy, and low-dose rate brachytherapy was delivered 34.23 Gy to the A point. After she developed the above symptoms, pelvic magnetic resonance imaging (MRI) demonstrated a mass lesion involving S1-2 vertebral bodies and bilateral iliac bone (Figure 1-a). However, because the tissue biopsy for the iliac bone lesion revealed no evidence of malignancy, the patient received no treatment. After one year, the symptoms were worse and the pelvic MRI showed that the bone lesion was larger (Figure 1-b). A tissue biopsy of the sacral lesion confirmed post-radiation osteosarcoma (Figure 2). After histological confirmation, the patient received two cycles of adriamycin and cisplatin combined chemotherapy. However, her symptoms continued to worsen. We provided palliative radiotherapy to the pelvic bone lesion, 30 Gy with daily doses of 3 Gy. However, a follow-up MRI revealed disease progression. The patient received one cycle of VIP (VP-16, ifosfamide, mesna, cisplatin) chemotherapy, which resulted in neutropenic fever and septic shock for two months. After recovering from the septic shock, she has received only conservative management.

*Case 2*

A 66-year-old Korean woman visited our department in June 2005 with complaints of right-sided pelvic pain and ipsilateral lower extremity radiating pain. She was diagnosed with FIGO Stage IIIB squamous cell carcinoma of the uterine cervix with paraaortic lymph node metastasis seven years earlier; at that time she had received whole pelvic irradiation 54 Gy with daily doses of 1.8 Gy (with paraaortic field 45 Gy) and brachytherapy 24 Gy/6 fractions to the A point. After radiotherapy, the patient achieved complete remission and was followed until December 2001. At the time of re-visit, the pelvic MRI revealed a soft-tissue mass at the right side of the sacrum and right posterior ilium; the mass was hypermetabolic by positron emission tomography (PET) scanning (Figure 3). The pathologic result of the computed tomography (CT)-guided needle biopsy revealed a pleomorphic high-grade sarcoma (Figure 4). The lesion was considered inoperable by orthopedic surgery. Palliative radiotherapy or chemotherapy was recommended. However, the patient refused further treatment and has received conservative management with analgesics.

## Discussion

Therapeutic ionizing irradiation treatment for primary cancers can increase the risk of a second cancer [3, 4]. An international study on women with cervical cancer reported 4,188 patients with second cancers [3]. Very

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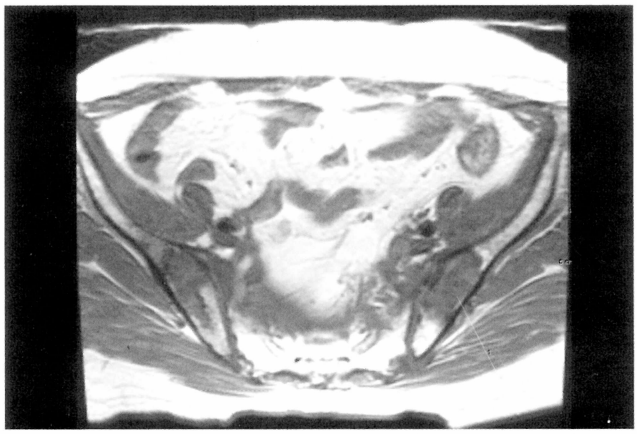
Fig. 1A



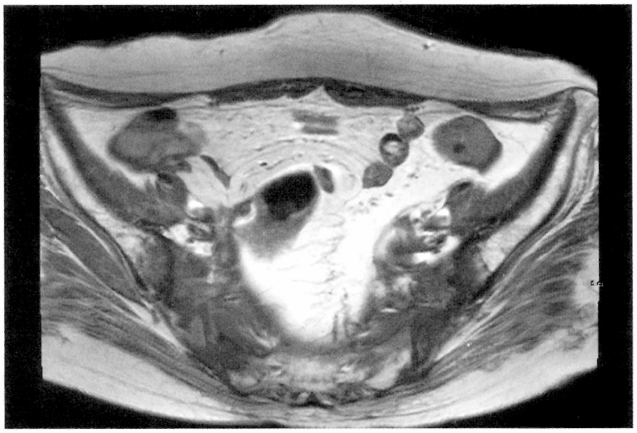


Fig. 1B

Fig. 2

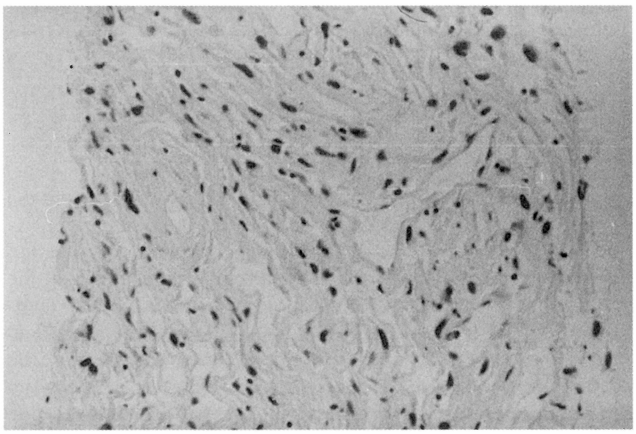
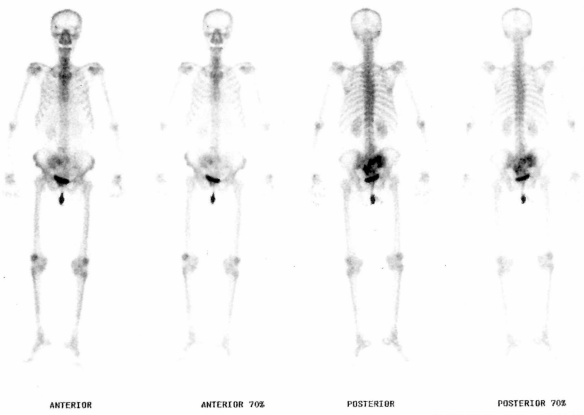


Figure 1. — T1-weighted MRI of case 1. A) In October 2004, there was a bony lesion involving S1-2 and both iliac bones, but tissue biopsy failed to pathologically confirm. B) One year later the bone lesion was much aggravated.

Figure 2. — Histologic examination (x 200) stained with hematoxylin and eosin showed a few pleomorphic atypical tumor cells suggestive of osteosarcoma.

Fig. 3A



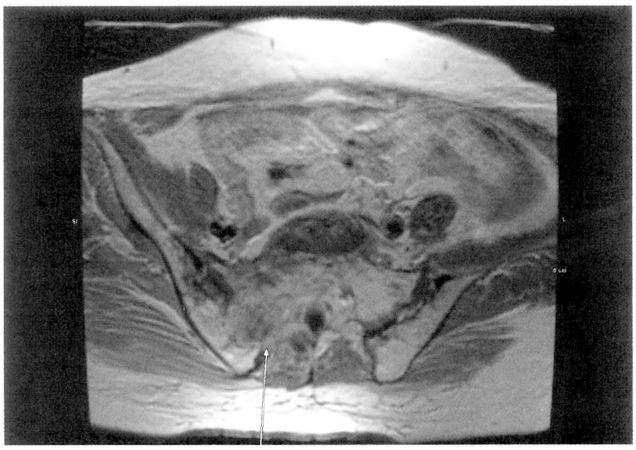



Fig. 3B

Fig. 3C

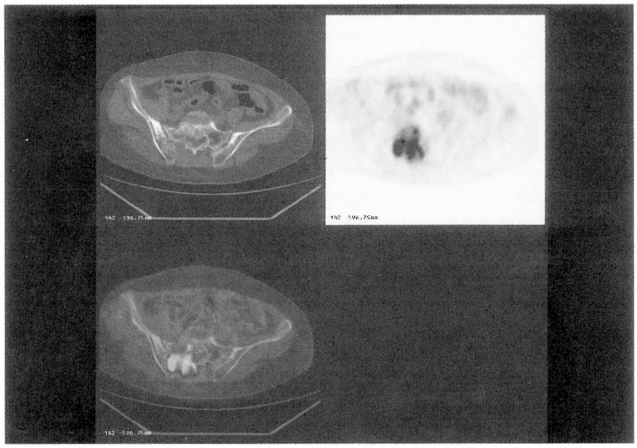


Figure 3. — Imaging studies of case 2. A) Whole body bone scan showed heterogenous radio uptake in the right ilium and sacrum. B) Gadolinium-enhanced T1-weighted pelvic MRI demonstrated an enhanced soft-tissue mass involving the right side sacrum. C) The mass was hypermetabolic on PET.

Fig. 4A

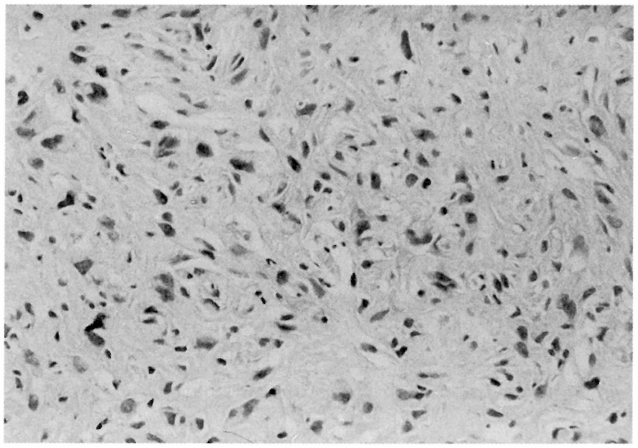


Fig. 4B

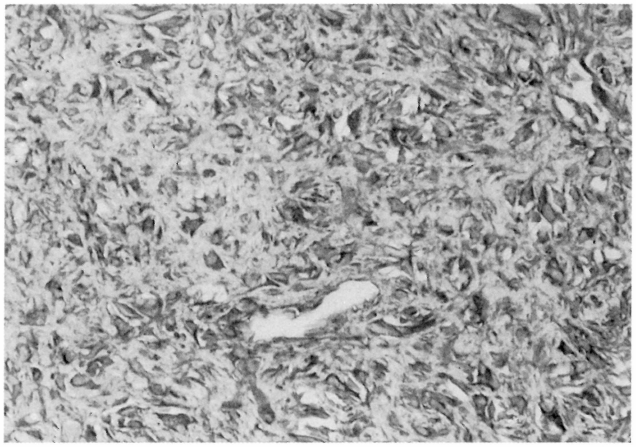


Fig. 4C

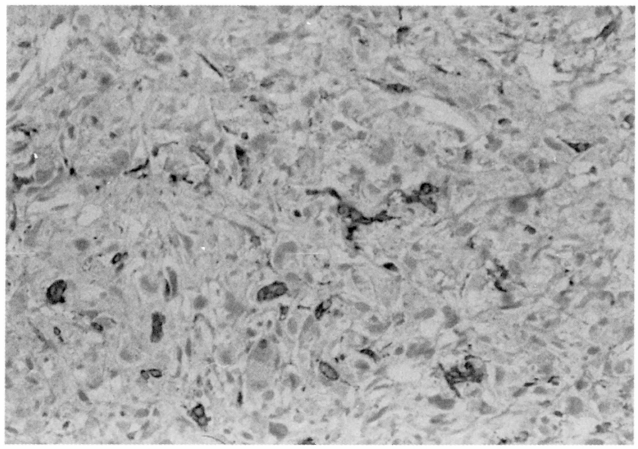


Figure 4. — Histological examinations (x 200) of case 2. A) There were lots of atypical tumor cells (stained with hematoxylin and eosin). B) Immunostain showed positivity for vimentin in tumor cells. C) Some tumor cells showed positivity for CD 68.

high doses were found to increase the risk of second cancers of the bladder, rectum, vagina, and possibly bone, uterine corpus, cecum as well as non-Hodgkin's lymphoma. Among the patients, there were 16 women with bone cancer including nine (56%) cancers of the pelvic bone. When compared with matched controls, an overall relative risk (RR) of 1.3 was observed, increasing to a three-fold risk for bone radiation doses greater than 10 Gy.

Post-radiation sarcoma is a serious long-term complication of radiotherapy. Tountas *et al.* [5] reported that the incidence of post-radiation sarcoma of bone was 0.035% of all irradiated five-year survivors. Because of such a low incidence and the long latent period (mean 8~15.5 years [1, 2, 6-9]), this complication is not widely recognized by clinicians. Mistaken diagnoses such as skeletal metastasis may be treated palliatively even if there is a curative potential. If a patient complains of pain in the pelvic bone area, within the previously irradiated fields, a physician should consider the possibility of post-radiation sarcoma of the bone.

In 1948, Cahan *et al.* [10] reported on post-radiation sarcoma in irradiated bone and used the following criteria for at-risk case selection: For the diagnosis of post-radiation bone sarcoma, the criteria (below) has been the important basis for determination. "1. There must have been microscopic or roentgenographic evidence of the nonmalignant nature of the initial bone condition. 2. Irradiation must have been given and the sarcoma that subsequently developed must have arisen in the area included within the radiotherapeutic beam. 3. A relatively long, asymptomatic period must have elapsed after irradiation before the clinical appearance of the bone sarcoma. In these cases, this has been longer than the so-called five-year-cure-period. 4. All sarcoma must have been proved histologically."

The radiological findings of post-radiation bone sarcoma include: a soft tissue mass, bone destruction, tumor matrix mineralization and periosteal reaction [1]. Nakanishi *et al.* [2] suggested that when a round or oval mass, largely extending into the soft tissue, develops within the irradiated field, post-radiation sarcoma should be considered. In the series reported by Nakanishi *et al.*, all five cases developed sarcoma at the margin of the irradiated field including the sacroiliac joint, mid-ilium and acetabulum, where the distribution of the radiation dose is relatively low to medium and inhomogeneous. Therefore, the radiation dose at the edge of the radiation field may be insufficient to kill all viable cells, but may be sufficient to cause cell damage and genetic mutations. Although not pathognomic, these findings provide radiological and geometric characteristics that can be clues for the diagnosis of post-radiation bone sarcoma.

The treatment of these tumors is difficult and the prognosis is generally poor. Mean survival ranges from

8~13.5 months from the time of diagnosis [7, 11, 12]. The role of chemotherapy or radiotherapy is limited. When feasible, only surgery can provide a curative potential. Tabone *et al.* [8] reported 23 cases of post-radiation osteosaroma, and their overall and event-free-survival rates were 50% and 41% at eight years, respectively. Among the cases in this series, complete surgical resection was an important prognostic factor. However, resectability is often related to the site of the tumor. Central trunk and limb girdle lesions have a poorer prognosis than extremity or craniofacial lesions [7, 9]. Thus, sacral lesions such as those present in our two cases are difficult to treat.

In summary, we report here two cases of post-radiation osteosarcoma of the irradiated pelvis seven and 16 years after primary treatment of cervical cancer. Post-radiation bone sarcoma is a rare and serious long-term sequela of therapeutic radiation. A heightened awareness of post-radiation sarcoma is essential for early diagnosis, and wide surgical excision should be considered for patients where cure is still possible.

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