

Case report Effective radiotherapy and an abscopal effect for bone metastases of an unknown origin

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Abstract

We report a case that radiotherapy was very effective for a primary unknown bone metastasis, and an abscopal effect was observed.

Although the pelvic bone metastasis was large, a dramatic response to radiotherapy was observed after a radiation dose of 50Gy, and local control lasted two years after the treatment. In addition, spontaneous remission was seen in a portion of the metastatic lesion outside the irradiated field, and it was regarded as an abscopal effect, which is a very rare phenomenon. The immunity of the patient might generate such a good effect in palliative radiotherapy, and an abscopal effect in this patient. CT and FDG-PET did not show a primary lesion of pelvic bone metastases for two years, and the patient enjoyed normal daily life after radiotherapy.

Key words: radiotherapy, bone metastasis, unknown origin, abscopal effect

Introduction

Relief of pain, and prevention of pathological fracture and paralysis are the therapeutic purposes in patients with osseous metastases. Generally, they cannot expect a complete cure by palliative treatment. However, radiotherapy is useful palliative treatment for patients with painful bone metastases. As for the prognosis of patients with osseous metastases, the site of the primary lesion, the degree of bone metastases, and the metastasis of other organs are important. In addition, performance status (PS), and lesions having more than two symptoms are the factors which influence patient outcome¹⁾. In cases of primary unknown carcinoma with onset of bone metastases, it was reported that primary lesions were detected in about 90% of the cases²⁾. We report a case of primary unknown bone metastases that responded well to radiotherapy, and neither the primary site nor any other metastatic lesions were detected two years after the initial treatment.

Case Report

The chief complaint of a 46-year-old male was pain of the left hip joint and the left lower extremity. The patient was referred to our hospital in 2001. Pelvic X-ray showed a large osteolytic lesion at the left side of pelvic bone. The general condition of the patient was ECOG-PS 2, and the patient could not walk by himself on admission. CT of the pelvis showed a massive lesion in the left side of the pelvic bone and bone metastasis in the right ilium (**Fig.1**). Bone scintigraphy revealed mild accumulation in the left ilium (**Fig.2**). Whole body ²⁰¹Tl scintigraphy demonstrated mild accumulation in the metastatic bone tumor, but no other abnormal findings were noted. CT of the chest and abdomen did not detect the primary lesion of bone metastases. The findings of hematology were not abnormal. The tumor marker, CEA, was elevated to 51.0, however, PSA, CA19-9, and AFP were within normal range. CT-guided biopsy was performed in the left ilium, and the specimen was

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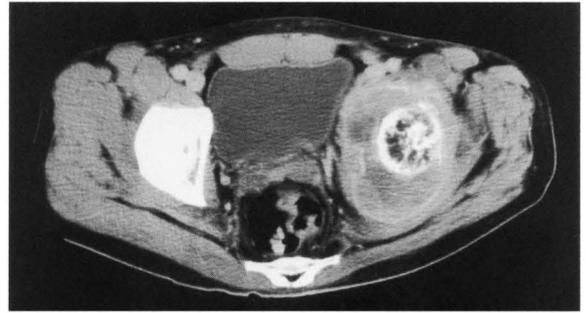
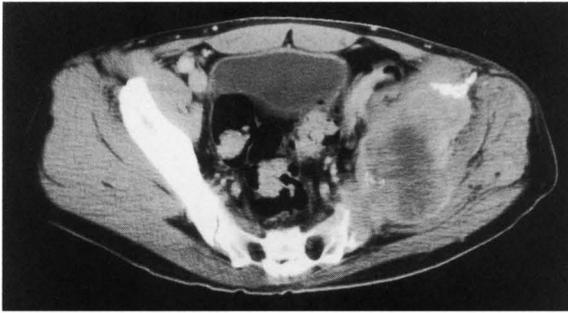


Fig.1. CT of the pelvis showed a massive bone metastasis ,which is from the left ilium (A) to the left acetabulum (B), and bone metastasis in the right ilium (C).

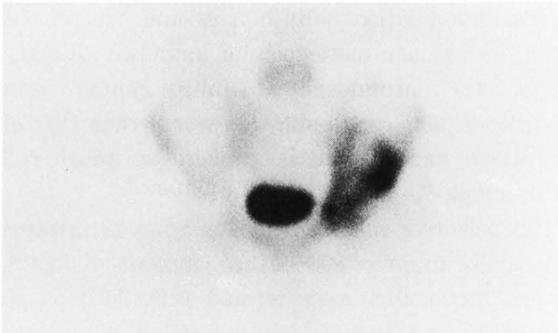
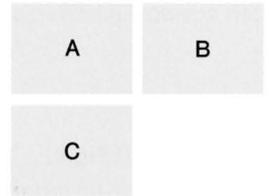


Fig.2. Bone scintigraphy shows abnormal accumulation in the left ilium.

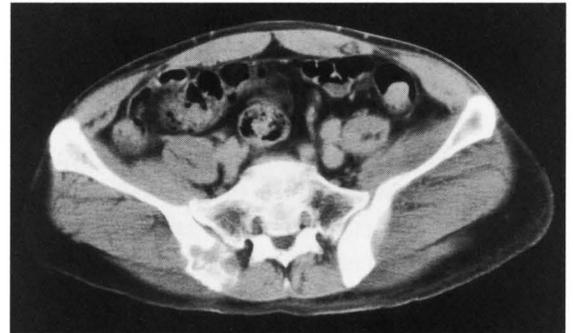


Fig.3. The skeletal metastasis of the right ilium, which is outside the irradiated field, was spontaneously reduced after radiotherapy to the left iliac bone metastasis.

histopathologically diagnosed as adenocarcinoma. The radiation dose was 50Gy to the bone metastasis tumor, which was from the left ilium to the left hip joint, with a fractionated dose of 2 Gy daily.

The irradiation field was wide because the iliac metastasis tumor was very large. Therefore, we did not treat the right ilium metastasis, which was without pain. Radiotherapy palliated the pain of the patient, and walking with a stick gradually became possible two months after radiotherapy.

The serum level of CEA decreased to normal range after radiotherapy. Three months after radiotherapy, pelvic CT showed that the pelvic bone tumor was markedly decreased.

Furthermore, the tumor was spontaneously reduced even if metastases to bone lesion of the right ilium was a lesion outside the irradiated field (Fig.3).

One year after radiotherapy, a pelvic X-ray showed recalcification of the irradiated area, and pelvic CT showed that the tumor had

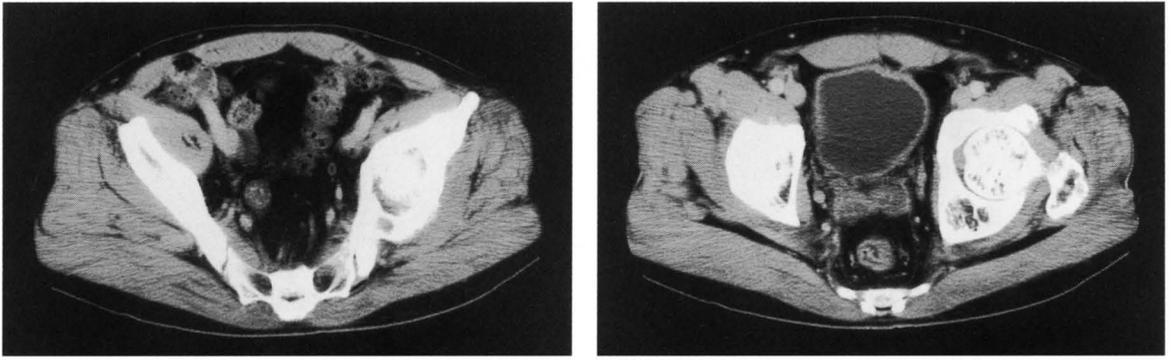


Fig.4. CT of the pelvis shows the metastatic lesion ,which is from the left ilium (A) to the left acetabulum (B) , disappeared one year after radiotherapy.

A

B

disappeared (Fig.4). Neither the primary lesion nor any other metastatic lesion were seen on CT or FDG-PET. At present, normal daily life has been possible for the patient. There was no recurrence in the irradiated area, and a lesion regarded as a new metastatic lesion and the primary site were not detected.

Discussion

Patients were considered to have metastases from an unknown origin if they had clinical and radiological evidence of metastatic cancer, but clinical examinations did not reveal the primary tumor. The frequency of primary unknown carcinoma is about 3% of all malignant tumors³⁾. About fifteen percents of the patients of primary unknown carcinoma (non squamous cell carcinoma) have skeletal metastases⁴⁾. And adenocarcinoma is the most common histologic type⁵⁾. Cases of adenocarcinoma and cervical nodal involvement have poor prognoses in comparison with those of suamous and anaplastic carcinomas⁶⁾. On the other hand, cases of squamous cell carcinoma were found to be the most common histologic type in the long survivors⁵⁾. Lung cancer is the most frequently observed primary lesion in patients with skeletal metastasis of an unknown origin. Other primary lesions are prostatic carcinoma, breast cancer, and hepatocellular carcinoma²⁾. The prognosis of treated patients of primary unknown cancers is better than that of

untreated patients³⁾. Katagiri noted that patients with a long life expectancy should be treated in a manner that is effective for a long period²⁾. In addition, the prognosis of patients with metastases discovered in the lymph nodes was good in comparison with that in other sites⁵⁾. As for the osseous metastasis of unknown primary site, the prognosis of lung cancer and hepatocellular carcinoma was worse than that of prostate cancer, breast cancer, or renal cell carcinoma²⁾.

The palliative radiotherapy for bone metastases generally improves 80% of the symptoms of pain¹⁾. Most metastases were treated with 30Gy in 10 fractions or 40 to 50Gy with a fractionated dose of 2Gy. The patient received 50Gy in 25 fractions, because the metastatic lesion was very large. Although the size of the tumor was over 10cm, a very good response to radiotherapy, including the disappearance of the tumor, was achieved in this case. Radiosensitivity is not commonly high for adenocarcinoma. However, in this case, a large tumor regressed markedly, and local control in the irradiated area was achieved for two years. Arcangeli reported that the response of bone metastasis to radiotherapy was independent from the primary sites and the histologic types⁷⁾. In addition, the other osseous metastatic lesion outside the irradiated field spontaneously reduced, and it is attributable to abscopal effect. Abscopal regression of tumors results from the

irradiation effect on a tumor in remote non-irradiated tissue. The abscopal effect is a very rare phenomenon. Ohba reported spontaneous regression of hepatocellular carcinoma after radiotherapy for vertebral bone metastasis⁸⁾. Pathophysiology and mechanism of the abscopal effect have not been well defined. Konoeda described that the abscopal effect was often observed in patients who had infiltrating lymphocytes around the degenerated cancer cells in the irradiated primary tumor nests⁹⁾. Ohba described that the abscopal related regression might be associated with the host immune response⁸⁾.

Our patient with a very large metastatic lesion responded well to radiation, and an abscopal effect was observed after radiotherapy. Therefore, it is suggested that immunological mechanisms might have played an important role in the response.

It is needed to detect the primary lesion with skeletal metastases of an unknown origin as soon as possible. Katagiri reported that chest CT and abdominal CT were useful, but examination of the gastrointestinal tract and pelvic CT seldom revealed the primary lesion, and should not be performed as an initial routine study in the absence of abdominal symptoms²⁾. The primary lesion did not appear on either chest or abdominal CT, or gastrointestinal tract examination in this patient. In recent years, it is reported that FDG-PET is useful for detecting primary lesions, or metastatic lesions, and as influencing in selecting appropriate therapeutic management¹⁰⁾. Lassen noted that 18F-FDG PET was useful in unknown primary tumors¹¹⁾. Our patient underwent FDG-PET to detect the primary lesion two years after radiotherapy. However, the primary site of osseous metastases has not been detected.

References

1. Snee MP, Vyrarnuthu N: Metastatic carcinoma from unknown primary site: the experience of a large oncology center. *Br J Radiol* 58;1985:1091-1095.
2. Katagiri H, Takahashi M, Inagaki J, Sugiura H, Ito S, Iwata H: Determining the site of the primary cancer in patients with skeletal metastasis of unknown origin: a retrospective study. *Cancer* 86; 1999:533-537.
3. Altman E, Cadman E: An analysis of 1539 patients with cancer of unknown primary site. *Cancer* 57;1986:120-124.
4. Nystrom JS, Weiner JM, Heffelfinger-Juttner J, Irwin LE, Bateman JR, Wolf RM: Metastatic and histologic presentations in unknown primary cancer. *Semin Oncol* 4;1977: 53-58.
5. Greager JA, Wood D, Gupta TKD: Metastatic cancer from an undetermined primary site. *J Surg Oncol* 23; 1983:73-76.
6. Glynne-Jones RGT, Anand AK, Young TE et al: Metastatic adenocarcinoma in the cervical lymph nodes from an occult primary. *Clin Oncol* 1;1989: 19-21.
7. Arcangeli G, Micheli A, Arcangeli G, et al: The responsiveness of bone metastases to radiotherapy: The effect of site, histology and radiation dose on pain relief. *Radiother Oncol* 14; 1989:95-101.
8. Ohba K, Omagari K, Nakamura T, Ikuno N, Saeki S, Matsuo I, Kinoshita H, Masuda J, Hazama H, Sakamoto I, Kohno S: Abscopal regression of hepatocellular carcinoma after radiotherapy for bone metastasis. *Gut* 43;1998:575-577.
9. Konoeda K: Therapeutic efficacy of pre-operative radiotherapy on breast carcinoma: in special reference to its abscopal effect on metastatic lymph-nodes. *J Jpn Soc Cancer Ther* 25; 1990: 1204-1214.
10. Trampal C, Sörensen J, Engler H, Langström B: 6.18F-FDG whole body positron emission tomography (PET) in the detection of unknown primary tumors. *Clin Positron Imaging* 3; 2000; 160.
11. Lassen U, Daugaard G, Eigtved A, Damgaard K, Friberg L: 18F-FDG whole body positron emission tomography (PET) in patients with unknown primary tumours (UPT). *Eur J Cancer* 35; 1999:1076-1082.

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