Carbon beam therapy in recurrent ovarian cancer

Ovarian cancer results in more deaths than any other gynecologic malignancy. In the United States and Japan, there are >15,000 and 4,000 deaths from ovarian cancer per year, respectively [1]. This high mortality rate can be attributed to ~75% of patients who are diagnosed with stage III and IV disease with i.p. carcinomatosis [2]. Although the 5-year survival rate of patients in whom lymph nodes are the only site of metastasis, the so-called 'retroperitoneal stage IIIc', ranges from 84% to 96%, higher than the 20%–30% of i.p. stage IIIc patients [3], we have sometimes encountered cases of ovarian cancer with local recurrence in the lymph nodes which was completely unresectable at surgery and chemo-resistant, resulting in salvage chemotherapy. Therefore, a more potent treatment should be introduced for this situation to achieve either disease-free survival or local control.

High linear energy transfer (LET) particle therapy has various advantages in terms of radiobiological effects as well as
dose distribution and has been expected to offer a therapeutic advantage over conventional photon therapy. The biological advantages of high LET radiation, including 'carbon beam therapy', are summarized as a decreased oxygen enhancement ratio, diminished capacity for sublethal and potentially lethal damage repair and diminished cell cycle-dependent radiosensitivity [4]. Thus, these advantages prompted us to use carbon beam therapy for bulky recurrent ovarian tumor, which is considered to have a large fraction of hypoxic tumor.

The patient was a 68-year-old woman with ovarian cancer who was optimally treated by hysterectomy, bilateral salpingo-oophorectomy, omentectomy and pelvic and para-aortic lymphadenectomy in February 2003, followed by three courses of paclitaxel and carboplatin (TJ) for right ovarian cancer, endometrioid type, grade 2, pT1cN0M0. Since local recurrence of ovarian cancer at the site of the right internal-iliac artery lymph node was detected in November 2004, six more courses of TJ were carried out. The recurrent tumor had grown to a maximum of 8 cm in diameter despite several protocols of chemotherapy, including platinum, taxane, CPT-11 and gemcitabine. After we had confirmed no metastasis besides the recurrence site with positron emission tomography using 2-[fluorine-18]fluoro-2-deoxy-D-glucose/computed tomography, we decided to treat the lesion with carbon beam therapy. Before the therapy, the patient gave written informed consent, and the study was approved by the local ethics committee and institutional review board of our hospital. Moreover, the patient underwent an operation in which a Goretex sheet was inserted, the lesion was partially excised and an artificial anus was constructed to protect the intestine and rectum adjacent to the tumor from injury by high LET particles. The heavy ion medical accelerator in Chiba is the first heavy ion accelerator specially dedicated to medicine in the world, and its design variables are on the basis of the radiological requirements [5]. The ‘carbon beam’ energy used was 350–400 MeV. As shown in Figure 1A and B, anteroposterior, posteroanterior and lateral opposing ports were used for 16 fractions >4 weeks with four fractions weekly; consequently, the total dose was a 57.6-Gy equivalent dose. Through out the treatment, no severe side-effects were observed. At 10 months after treatment, the pelvic tumor had drastically shrunk (Figure 1C), and the patient has continued clinical disease free for 2 years.

This is the first report, to our knowledge, showing that carbon beam therapy was effective for recurrent ovarian cancer. The result is sufficiently encouraging to continue the therapy in patients with metastatic, anticancer drug-resistant ovarian cancer as well as other types of gynecologic cancer.

funding

Ministry of Education, Culture, Sports, Science and Technology of Japan (No.15591791).

A. Nawa1*, K. Suzuki1, S. Kato1, S. Fujiwara1, H. Kajiyama1, K. Shibata1, K. Ino1, S. Nakamura2 & F. Kikkawa1

1Department of Obstetrics and Gynecology, 2Department of Pathology and Clinical Laboratories, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, 3Research Center Hospital of Charged Particle Therapy, National Institute of Radiological Science, 4-9-1 Anakawa, Inage-ku, Chiba 263-8555, Japan

(*E-mail: nawa2005@med.nagoya-u.ac.jp)

references


Figure 1. Dose distribution curve in axial section (A) and sagittal section (B) before treatment with ‘carbon beam therapy’. Red, green and purple lines show the regions of 95%, 50% and 10% of the dose, respectively. (C) The pelvic lesion at 10 months after treatment. A white arrow shows a regressed tumor. (D) Histopathological finding from the recurrent ovarian cancer lesion excised from the patient, endometrioid grade 3 (stained with hematoxylin and eosin).


doi:10.1093/annonc/mdm553