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Whole-body PET with FDG is useful for following up an ovarian cancer patient with only rising CA-125 levels within the normal range

Tetsuji KUROKAWA,* Yoshio YOSHIDA,* Kazumi KAWAHARA,* Tatsuro TSUCHIDA,**
Yasuhisa FUJIBAYASHI,*** Yoshiharu YONEKURA*** and Fumikazu KOTSUJI*

*Departments of *Obstetrics and Gynecology, **Radiology and Neurosurgery, Fukui Medical University*
****Biomedical Imaging Research Center, Fukui Medical University*

In April 2000, a 54-year-old woman underwent surgery for ovarian serous cell carcinoma (stage IIb). After initial treatment, the patient underwent a physical examination, ultrasound examination and measurement of serum CA-125 levels every month. Although neither diagnostic imaging (ultrasound and computed tomography) nor physical examination showed any evidence of recurrence, the CA-125 level rose slowly and continuously within the normal range. In March 2001, an increased accumulation of ^{18}F-fluorodeoxyglucose (FDG) in the pelvic cavity was seen on a positron emission tomography (PET) scan obtained 2 weeks before a relapse of a malignant lesion was diagnosed by gadolinium-enhanced MRI (Gd-MRI). It is reasonable to suppose that FDG-PET is clinically useful for detecting an early, small region of relapsed ovarian cancer. Moreover, FDG-PET may be helpful for determining whether a patient who has a continuous rising CA-125 level within the normal range should be treated in the absence of relapse regions detected by conventional methods.

Key words: FDG-PET, ovarian cancers, CA-125

INTRODUCTION

OVARIAN CARCINOMA has the highest mortality rate of all gynecologic malignant tumors. A high incidence of relapse occurs after surgery and radio- or chemotherapy. Indeed, even after negative second-look surgery, relapse occurs in 40–63% of cases.[1,2] For this reason, it is important to accurately assess ovarian cancer patients during follow-up to determine whether a relapse has occurred.

Follow-up procedures for ovarian carcinoma usually rely on gynecologic examination, ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) and measurement of serum tumor markers, particularly CA-125. In most relapse cases, a rise in the CA-125 level can be detected prior to the detection of the relapse region by using CT and/or MRI,[3] but it has been debated whether further treatment should be conducted when the CA-125 level increases continuously even though it is within the normal range and no sign of relapse is seen on CT and/or MRI.

We report a case of an ovarian carcinoma relapse in which a continuous rising CA-125 level was detected even though it was within the normal range. The relapse was detected by positron emission tomography with ^{18}F-fluorodeoxyglucose (FDG-PET); other examinations failed to reveal the lesion as a relapse. We discuss the potential of FDG-PET in the follow-up of patients with ovarian cancer.

CASE

A 54-year-old woman, gravida 2, para 2, had been diagnosed with clinical stage IIb serous cell carcinoma of the ovary according to the International Federation of Gynecology and Obstetrics (FIGO) classification. In addition, she had a high CA-125 level (586 IU/m*l*) (normal range: under 35 IU/m*l*) preoperatively. In April 2000, she underwent complete surgical debulking procedures.

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For reprint contact: Yoshio Yoshida, M.D., Department of Obstetrics and Gynecology, Fukui Medical University, Matsuoka-cho, Yoshida, Fukui 910–1193, JAPAN.
E-mail: yyoshida@fmsrsa.fukui-med.ac.jp

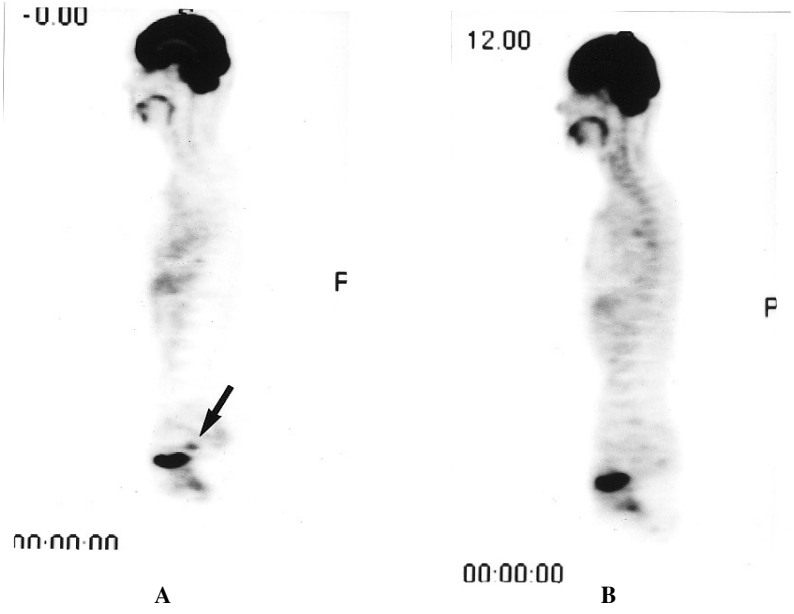

Fig. 1 PET studies with FDG as the tracer. Increased accumulation of fluorine-18-2-deoxyglucose (FDG) (SUV = 3.72) in the pelvic cavity (*arrow*) was seen on a positron emission tomography (PET) scan obtained 2 weeks before a relapse of the malignant lesion was diagnosed by gadolinium-enhanced MRI (Gd-MRI) (Panel A). After 6 weeks of treatment, there was no abnormal uptake of the tracer in the pelvic cavity (Panel B).

Postoperatively, four cycles of chemotherapy with carboplatin and paclitaxel were given from April 2000 to July 2000. After the initial treatments, the patient underwent physical examination, ultrasound examination and measurement of serum CA-125 levels every month.

From January to March 2001, the serum CA-125 levels continuously rose from 14 IU/m*l* to 25 IU/m*l*. However, a whole-body CT scan, transvaginal and transabdominal ultrasound and physical examination did not show any evidence of malignant lesions. She also underwent whole-body FDG-PET in March 2001.

The whole-body PET was conducted with FDG produced by means of the NKK synthesis system (NKK, Tokyo, Japan) with a small cyclotron (OSCAR3; Oxford Instruments, Oxford, UK).[4] PET scanning was performed with a GE advanced system (General Electric, Milwaukee, WI, USA). The patient fasted for 4 h before the PET scan. The whole-body emission scan was performed 40 min after the patient was injected with 370 MBq of FDG. Thereafter, post-injection transmission with a ^{68}Ge rod source was performed for attenuation correction. To quantitatively evaluate regional radioactivity in static PET images, a region of interest (3.5-mm diameter area) was selected in the most radioactive area of the lesion. The tissue radioactivity was corrected for the injected dose and the patient's body weight to calculate the standardized uptake value (SUV) by using the formula of Strauss et al.[5]

An increased accumulation of FDG in the pelvic cavity (SUV = 3.72) was seen on a PET scan (Fig. 1A) obtained

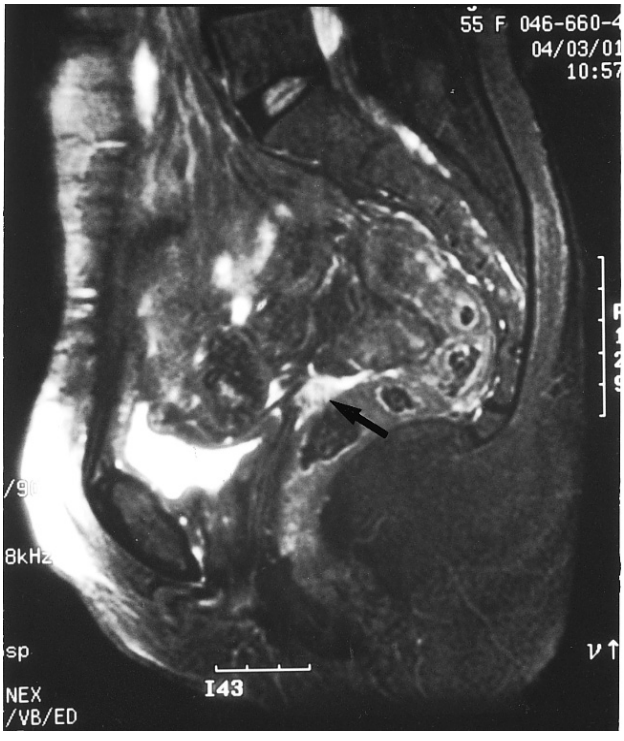

Fig. 2 Transsagittal gadolinium-enhanced T1-weighted MRI studies of the pelvic cavity. A relapse lesion was present in the pelvic cavity. Contrast enhancement of the relapse lesion (*arrow*) was heterogeneous, with strong enhancement at the periphery in the pelvic cavity.

2 weeks before a relapse of the malignant lesion was diagnosed by gadolinium-enhanced MRI (Gd-MRI). On the Gd-MRI, contrast enhancement of the relapse lesion was heterogeneous, with strong enhancement at the periphery in the pelvic cavity (Fig. 2). The patient had received 6 weeks of paclitaxel treatment under the clinical diagnosis of a relapse of ovarian carcinoma. The level of serum CA-125 was 46 IU/m*l* just prior to treatment. After chemotherapy, it decreased to 9 IU/m*l*. No enhancement was seen on Gd-MRI scans obtained after treatment. On a PET scan obtained after treatment, no abnormal uptake of FDG was seen in the pelvic cavity (Fig. 1B).

DISCUSSION

Many patients with ovarian carcinoma who entered clinically complete remission have been followed up with a combination of pelvic examinations, CT[6] and monitoring of serum CA-125 levels. In about 70% of patients, a rise in the CA-125 level may be the first sign of relapse, predating clinical recurrence,[3] but the appropriate management of an asymptomatic patient, after the first treatment, for only a continuous rise in the CA-125 level within the normal range remains undetermined. Some clinicians routinely perform CA-125 measurements and treat asymptomatic patients on the basis of a rising CA-125 level alone, whereas others ignore a rising level until symptoms warrant treatment.[3] Theoretically, it is advantageous to restart chemotherapy at the time of lowest tumor volume, but there is no evidence that starting chemotherapy for only a rising CA-125 level within the normal range is effective for the management of ovarian carcinoma.[1]

Ultrasonography, CT and MRI are helpful in diagnosing recurring lesions only when a tumor has attained a size of 10 mm–15 mm.[5] Many reports indicate that these conventional imaging methods lack sensitivity and specificity.[6–8] It has been demonstrated that FDG-PET is sensitive enough to detect ovarian carcinoma, particularly in patients with a relapse.[9–10] Yuan et al. stated that PET has the potential to detect metastases in normal-sized lymph nodes and can verify malignant tissue in enlarged nodes,[11] but Nakamoto et al. stated that PET has the potential to miss a poorly localized microscopic spread of the disease and lesions smaller than 1 cm in diameter.[9]

In this patient's case, FDG-PET imaging showed the relapse of ovarian cancer even though it was not detected by ultrasound and CT. Serum CA-125 had been slowly and continuously increasing within the normal range. Two weeks after the FDG-PET, the relapse region was detected by Gd-MRI in the same region that had appeared as a hot spot in the FDG-PET imaging. Moreover, after additional chemotherapy, the region could not be detected by either Gd-MRI or FDG-PET imaging. The serum CA-125 level, which had risen to a maximum of 46 IU/m*l*, went down to 9 IU/m*l* after the additional chemotherapy. In light of these points, the hot spot was diagnosed as a malignant lesion.

CONCLUSION

This case suggests that FDG-PET is clinically useful for the detection of a relapse of ovarian cancer. It is important to note that the serum CA-125 had been slowly and continuously increasing within the normal range in the absence of relapse regions detected by conventional methods.

REFERENCES

1. Ozols RF, Rubin SC, Thomas GM, Robboy SJ. Epithelial ovarian cancer. In: *Principles and Practice of Gynecologic Oncology*, 3rd ed. William JH, Carlos AP, Robert CY (eds), Philadelphia; Lippincott Williams & Wilkins, 1999: 841–918.
2. Munkarah A, Levenback C, Wolf JK, Bodurka-Bevers D, Tortolero-Luna G, Morris RT, et al. Secondary cytoreductive surgery for localized intra-abdominal recurrences in epithelial ovarian cancer. *Gynecol Oncol* 2001; 81: 237–241.
3. Meyer T, Rustin GJ. Role of tumour markers in monitoring epithelial ovarian cancer. *Br J Cancer* 2000; 82: 1535–1538.
4. Kitagawa Y, Sadato N, Azuma H, Ogasawara T, Yoshida M, Ishii Y, et al. FDG PET to evaluate combined intra-arterial chemotherapy and radiotherapy of head and neck neoplasms. *I Nucl Med* 1999; 40: 1132–1137.
5. Strauss LG, Conti PS. The applications of PET in clinical oncology. *J Nucl Med* 1991; 32: 623–645.
6. Prayer L, Kainz C, Kramer J, Stiglbauer R, Schurawitzki H, Baldt M, et al. CT and MR accuracy in the detection of tumor recurrence in patients treated for ovarian cancer. *J Comput Assist Tomogr* 1993; 17: 626–632.
7. Kurtz AB, Tsimikas JV, Tempany CM, Hamper UM, Arger PH, Bree RL, et al. Diagnosis and staging of ovarian cancer: comparative values of Doppler and conventional US, CT, and MR imaging correlated with surgery and histopathologic analysis—report of the Radiology Diagnostic Oncology Group. *Radiology* 1999; 212: 19–27.
8. Hamm B, Kubik-Huch RA, Fleige BX. MR imaging and CT of the female pelvis: radiologic-pathologic correlation. *Eur Radiol* 1999; 3: 3–15.
9. Nakamoto Y, Saga T, Ishimori T, Mamede M, Togashi K, Higuchi T, et al. Clinical value of positron emission tomography with FDG for recurrent ovarian cancer. *Am J Roentgenol* 2001; 176: 1449–1454.
10. Schroder W, Zimny M, Rudlowski C, Bull U, Rath W. The role of ^{18}F-fluoro-deoxyglucose positron emission tomography (^{18}F-FDG-PET) in diagnosis of ovarian cancer. *Int J Gynecol Cancer* 1999; 9: 117–122.
11. Yuan CC, Liu RS, Wang PH, Ng HT, Yeh SH. Whole-body PET with (fluorine-18)-2-deoxyglucose for detecting recurrent ovarian carcinoma. Initial report. *J Reprod Med* 1999; 44: 775–778.