USEFULNESS OF POSITRON EMISSION TOMOGRAPHY (PET) IN A RETROPERITONEAL PRIMARY NON-SEMINOMATOUS GERM CELL TUMOR : A CASE REPORT

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A 32-year-old Japanese man was admitted complaining of palindromic fever and abdominal pain. Computed tomography (CT) revealed retroperitoneal mass and positron emission tomography (PET) demonstrated massive radiotracer uptake in this tumor. Serum levels of alpha-fetoprotein (AFP) and human chorionic gonadotropin (hCG) were 4,760 ng/ml, 6,000 mIU/ml, respectively. Biopsy specimen from the tumor showed non-seminomatous germ cell tumor. The International Germ Cell Cancer Collaborative Group (IGCCCG) staging system indicated this case as an intermediate prognosis group. After three cycles of bleomycin, etoposide and cisplatin (BEP) therapy, CT revealed a degenerated residual mass. Serum levels of tumor markers were normalized completely and PET showed no radiotracer uptake in the retroperitoneal lesion. Although he did not receive further chemotherapy and lymph nodes were not dissected, he was free of disease for two years.

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Key words : Germ cell tumor, Residual mass, FDG-PET

INTRODUCTION

The development of cisplatin-based combination chemotherapy has dramatically improved the prognosis of patients with metastatic non-seminomatous germ cell tumor (NSGCT). After the completion of chemotherapy, residual masses are found in up to 40% of patients with advanced NSGCT, despite the normalization of serum tumor markers[1)]. Computed tomography (CT) and tumor markers profile can not throughly predict the possibility of eradication of viable tumor cells[2)]. The management of these postchemotherapy residual masses has been widely discussed including observation only, lymph node dissection and second line chemotherapy.

2-(^{18}F)-fluoro-2-deoxy-D-glucose (FDG) is trapped into cells as fluoro-deoxyglucose-6-phosphate because of its low rate of dephosphorylation and further metabolism. The association between the grade of malignancy and high uptake of FDG has been established in lymphomas, brain tumors, and musculoskeletal tumors[3)]. FDG-positron emission tomography (PET) is an imaging method that offers the potential to detect residual malignancy after primary curative therapy for germ cell tumors. We present a patient who showed complete remission along with the information of CT, tumor markers and PET study.

CASE REPORT

A 32-year-old man presented with palindromic fever and abdominal pain. CT revealed multiple retroperitoneal lymph node masses, measuring 5cm in the

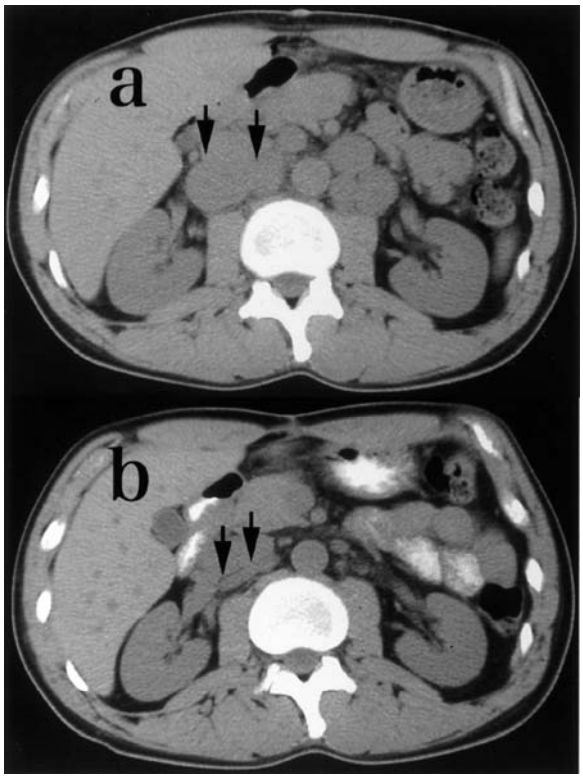

Fig. 1. Computed tomography scans of the abdomen at the level of right renal artery (a) before (b) after three cycles of chemotherapy. Arrows revealing retroperitoneal lymph node mass (a) 5 cm, (b) 2.9 cm in geatest dimension, respectively. These scans revealed approximately 90% reduction in mass size.

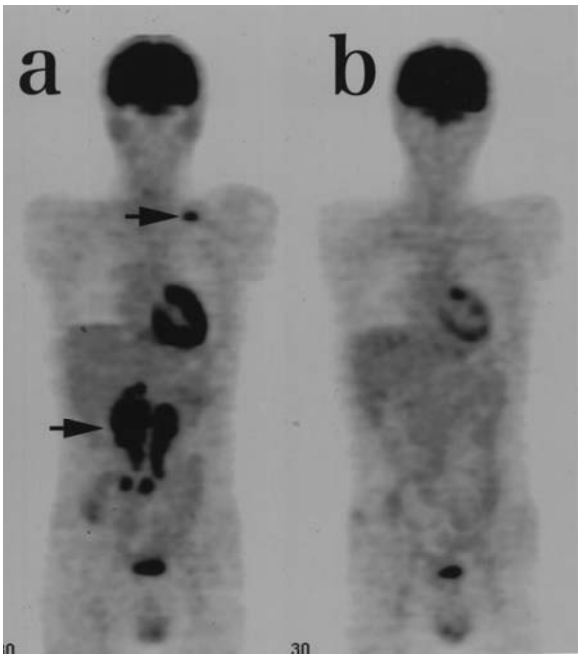

Fig. 2. FDG-PET scans (a) before chemotherapy showed an accumulation in the retroperitoneal and supracravical lesion (arrows). (b) After three cycles of chemotherapy, those lesions are almost disappeared.

greatest dimension at the level of right renal artery (Fig. 1) and FDG-PET showed an accumulation in the retroperitoneal and the left supracravical lesions (Fig. 2). There was not supracravical lymph node mass on CT. Open retroperitoneal lymph node biopsy revealed germ cell tumor consisting yolk sac tumor and embryonal carcinoma. Serum tumor markers were elevated ; hCG 6,000 mIU/ml, β-hCG 76 ng/ml, AFP 4,760 ng/ml, lactate dehydrogenase (LDH) 543 IU/l, respectively. Ultrasonography and physical examination revealed both testes were normal. The diagnosis was non-seminomatous extragonadal germ cell tumor. The stage of the disease was intermediate prognosis group based on the IGCCCG classification. After three courses of bleomycin, etoposide and cisplatin (BEP) therapy, CT revealed residual mass, measuring 2.9×0.9 cm in the geatest dimension at the level of right renal artery with approximately 90% reduction in mass size. Serum tumor markers were normalized (Fig. 3). FDG-PET showed no accumulation in the retroperitoneal and the left supracravical lesions. We thought complete remission had been clinically achieved. The patient is alive with no evidence of recurrence two years after primary chemotherapy.

DISCUSSION

Even metastatic disease can currently be cured in the majority (60–80%) of patients with non-seminomatous germ cell tumor since the introduction of cisplatin-based chemotherapy. After chemotherapy, residual retroperitoneal mass may remain, which harbour residual tumor or totally benign tissues. If tumor markers have normalized, some clinicians recommend that these patients undergo surgical resection of persistent radiographic masses. However, patients who are with necrosis or fibrosis derive no benefit from the surgical procedure. Hendry et al. found that the histologic make-up of primary tumor, pretreatment tumor markers levels and the size of the residual mass indicate the likely pathology of the residual mass[4]. Steyerberg et al. constructed a model to predict the presence of necrosis and fibrosis that included six well-known predictors : residual mass size, the absence of teratoma element in the primary tumor, prechemotherapy levels of the three tumor markers and mass shrinkage during chemotherapy. However this model had a sensitivity of 44% and a specificity of 82%[5].

Recently, there have been some reports that advocate the use of FDG-PET for the evaluation of residual masses in patients with an advanced germ cell tumor. Santis et al. reported that FDG-PET reliably predicts viable tumor in postchemotherapy seminoma residuals. They considered FDG-PET to be a new standard diagnostic tool for clinical decision making in seminoma patients with postchemotherapy residual masses[6].

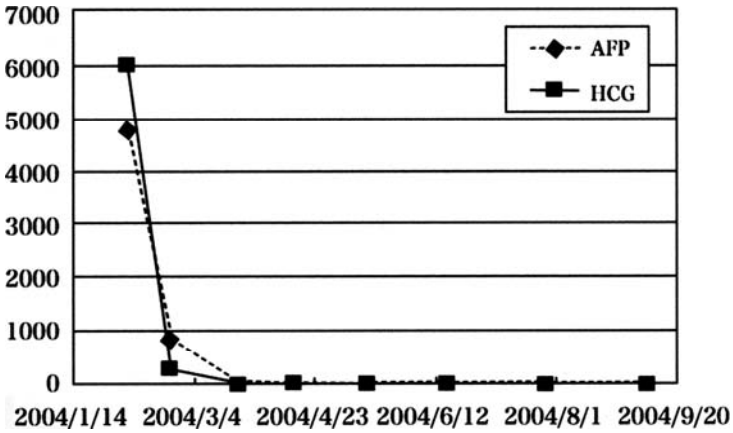

Fig. 3. Effect of chemotherapy on the serum tumor markers. Both alpha-fetoprotein (AFP) and human chorionic gonadotropin (hCG) were normalized with half life of 4.9 days for AFP and 2.9 days for hCG respectively.

Table 1. Reported articles on Fluorodeoxyglucose Positron Emission Tomography (FDG-PET) sensitivities and specificities for the prediction of residual mass viability following chemotherapy in non-seminomatous germ cell tumor

Authors/year (patient number)	Specificity	Sensitivity
Kollmannsberger et al. (n = 45), 2002	92%	59%
Hain et al. (n=24), 2000	100%	89%
Cremerius et al. (n=18), 1998	92%	67%

Table 2. Reported articles on the pathology or clinical outcome of postchemotherapy residual lesions in patients with tumor markers standardization and negative Fluorodeoxyglucose Positron Emission Tomography (FDG-PET)result

Authors/year	Negative PET lesions	Mature teratoma	Fibrosis/ necrosis	Viable cancer
Stephens et al., 1996	26	15	10	1
Hain et al., 2000	8	6*		2
Putra et al., 2004	12	11*		1

* Number of lesions which consisted of mature teraroma and/or fibrosis/necrosis. These lesions were validated not to contain viable cancer either by histopathological examination or by clinical outcome.

Stephens et al. reported that FDG-PET can be useful for detection of residual viable carcinoma following chemotherapy in non-seminomatous germ cell tumor patients because a significant association between standardized uptake value for the tracer (SUV) and histology was found when comparing viable germ cell tumor versus necrosis/fibrosis or teratoma, and also reported FDG-PET did not differentiate necosis/fibrosis from teratoma[7]. It was also reported that PET sensitivities and specificities for the prediction of residual mass viability following chemotherapy in non-seminomatous germ cell tumor were 59–89%, 92–100%, respectively (Table 1)[2,8,9]. However, there have been no reports about PET sensitivities and specificities for the prediction of residual lesions which showed FDG uptake before chemotherapy and showed the reduction of FDG uptake to normal level after chemotherapy.

As the high PET specificity for the prediction of residual mass viability was observed, Kollmannsberger et al. suggested that a potential benefit of PET was observed in patients with stable disease or with disease in remission on CT, magnetic resonance imaging (MRI) and declining or normalized tumor markers in whom elevated FDG uptake correctly predicted the presence of viable carcinoma or teratoma[2].

On the other hand, relatively low sensitivity for the prediction of residual mass viability was observed. The presence of mature teratoma was the most common cause for false negative PET results in residual lesions from patients with nonseminomatous germ cell tumor[2,7,9]. However, there were also some negative PET residual lesions which contained viable cells (Table 2)[7,8,10]. Low or no FDG uptake lesions such as mature teratoma or viable cancer nest should be evaluated by means of CT/MRI and tumor markers. Kollmansberger et al. reported that persisting or increasing tumor markers as well as progressive disease on CT or MRI during chemotherapy are strong predictors for the presence of viable carcinoma or teratoma, and PET does not provide additional information in these patients. CT/MRI and tumor markers sensitivities and specificities for the prediction of residual mass viability following chemotherapy in nonseminomatous germ cell tumor have been reported to be 42–55% and 86–100%, respectively. The diagnostic efficacies were similar for CT/MRI, tumor markers and PET. Kollmansberger et al. stated that no method in itself appears sufficiently accurate to predict the viability of residual mass, and compared with CT/MRI and tumor markers, PET seems to offer additional information. We thought some benefit of PET also existed in patients with stable disease or disease in remission on CT/MRI and tumor markers in whom negative PET results was observed. We thought PET could play a supplemental role for other imaging modalities and tumor markers in these patients.

The standard management of intermediate risk germ cell tumor in IGCCCG classification has been four cycles of BEP therapy. In our case, with three cycles of chemotherapy, the patient was suspected to have disease in remission because of the rate of mass shrinkage on CT scans and normalized tumor markers with half life of 4.9 days for AFP and 2.9 days for hCG respectively. Additionally, PET study demonstrated completely negative accumulation of radiotracer. We took an unformal decision not to undergo the fourth cycle of chemotherapy and not perform retroperitoneal lymph node dissection.

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和文抄録

Positron Emission Tomography (PET) が有用であった後腹膜原発性腺外胚細胞腫瘍の1例

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症例は間欠的な発熱および腹痛を主訴として入院した32歳，男性．CT上，後腹膜リンパ節の腫大が指摘され，PETにて同部位に著明な集積を認めた．血清AFP，hCGはそれぞれ4,760 ng/ml，6,000 IU/mlと上昇していた．開腹後腹膜リンパ節生検により非セミノーマ性胚細胞腫瘍が検出された．IGCCCG分類ではintermediate prognosis groupであった．3コースのBEP療法により縮小した残存腫瘍が認められるのみとなった．腫瘍マーカー値はいずれも正常化しPETでは後腹膜領域に集積を認めなくなった．4コース目の化学療法や後腹膜リンパ節郭清術を行わず経過を観察したところ，現在まで2年の無再発期間を得ている．

（泌尿紀要 **52**：623-627，2006）