The positron emission tomography with F18 17β-estradiol has the potential to benefit diagnosis and treatment of endometrial cancer

doi: 10.1016/j.ygyno.2006.10.024

Available online at www.sciencedirect.com
ScienceDirect
Gynecologic Oncology xx (2006) xxx–xxx
Gynecologic Oncology
www.elsevier.com/locate/ygyno

Case Report

The positron emission tomography with F18 17β-estradiol has the potential to benefit diagnosis and treatment of endometrial cancer

Yoshio Yoshida [a,*], Tetsuji Kurokawa [a], Yoko Sawamura [a], Akiko Shinagawa [a], Hidehiko Okazawa [b], Yasuhisa Fujibayashi [b], Fumikazu Kotsuji [a]

[a] Department of Obstetrics and Gynecology, Faculty of Medical Sciences, University of Fukui, Matsuoka-cho, Yoshida-gun, Fukui-ken 910-1193, Japan
[b] Biomedical Imaging Research Center, Faculty of Medical Sciences, University of Fukui, Matsuoka-cho, Yoshida-gun, Fukui-ken 910-1193, Japan

Received 18 July 2006

Abstract

Background. The positron emission tomography (PET) with F18 17β-estradiol (FES) has good imaging for assessment of estrogen receptor in breast cancer.

Case. We report on a 30-year-old woman who desired to preserve her fertility with well-differentiated endometrial adenocarcinoma. Before hormone treatment was started, FES-PET showed increased uptake of endometrium, magnetic resonance imaging (MRI) showed thickness and F-18 fluorodeoxyglucose (FDG)-PET showed increased uptake. FES-PET after 3 months showed remaining FES uptake, but there were no abnormal findings on MRI and FDG-PET. Hysteroscopy showed remaining adenocarcinoma. After additional treatment, FES-PET showed a therapeutic response, and hysteroscopy showed no abnormal finding.

Conclusions. To our knowledge, this is the first report that FES-PET has the potential to provide more useful information than did FDG-PET about the hormone therapy.

Introduction

Endometrial cancer is the most common gynecological malignancy in North American and European women, and the incidence continues to rise. Mortality from endometrial cancer ranks eighth among cancer deaths in North American women, and in Europe nearly 10,000 women die of this disease each year [1]. For young women (under age 40) who desired to preserve their fertility with well-differentiated endometrial adenocarcinoma, conservative treatment with periodic use of progestin is available [2,3]. Present methods to assess tumor responsiveness require a tissue sample obtained by performing a dilatation and curettage (D and C) every 3 months [3]. Sample availability is thus limited by potential morbidity and sampling problems. A noninvasive method to assess tumor responsiveness would avoid unnecessary diagnostic biopsies of the endometrium and permit serial assessments during treatment.

Positron emission tomography (PET) is a highly sensitive, noninvasive technology that is ideally suited for pre-clinical and clinical imaging of cancer biology, in contrast to anatomical approaches. By using radiolabeled tracers, PET can yield cross-sectional images that reflect tissue biochemistry [4]. Two radiolabeled tracers hold promise for the diagnosis and management of endometrial cancer. The most extensively studied of these is F-18 fluorodeoxyglucose (FDG); the other one is F-18 17β-estradiol (FES) [4]. FES-PET has good imaging characteristics in human studies to predict response to endocrine treatment in breast cancer [5]. But there has been no report published on whether FES-PET provides information useful for assessing tumor response to systemic therapy, or whether FES-PET provides more useful information than FDG-PET in endometrial cancer.

Case

We report on an unmarried 30-year-old woman who presented with well-differentiated adenocarcinoma (Fig. 1A)

* Corresponding author. Fax: +81 776 61 8117.
E-mail address: yyoshida@fmsrsa.fukui-med.ac.jp (Y. Yoshida).

0090-8258/$ - see front matter © 2006 Published by Elsevier Inc.
doi:10.1016/j.ygyno.2006.10.024

Please cite this article as: Yoshida, Y., et al., The positron emission tomography with F18 17β-estradiol has the potential to benefit diagnosis and treatment of endometrial cancer, Gynecologic Oncology (2006), doi:10.1016/j.ygyno.2006.10.024

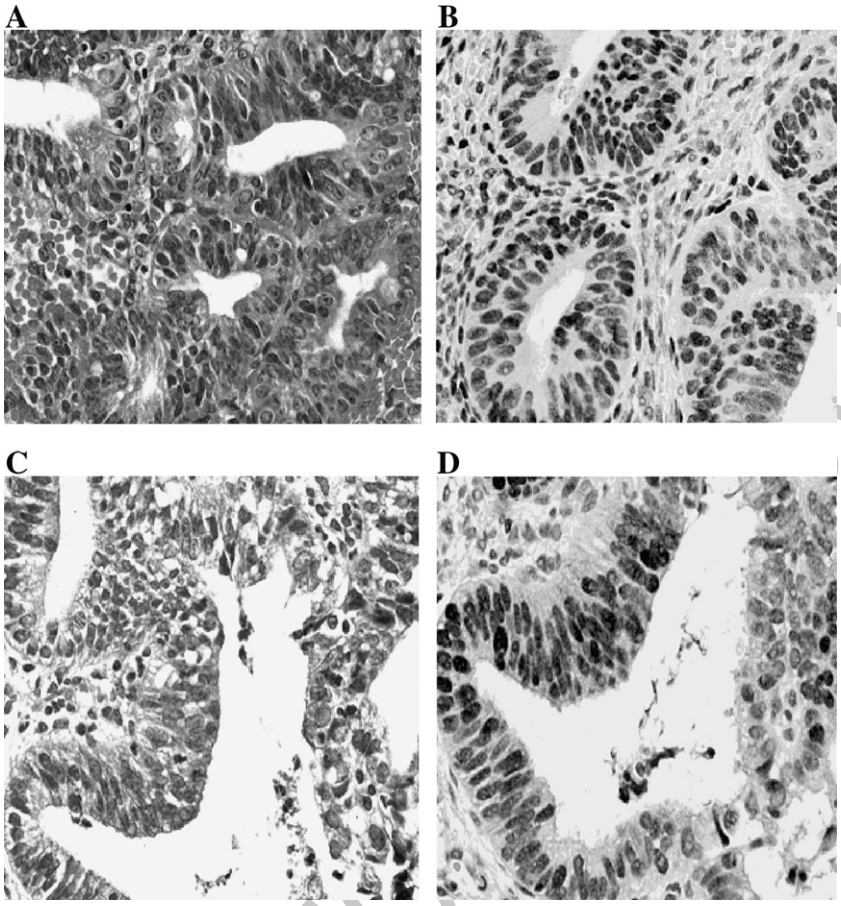

Fig. 1. Histopathology examination of curettaged tissue of endometrium. First curetttaged tissue: (A) hematoxylin and eosin staining showing well-differentiated endometrial adenocarcinoma (magnification ×400), (B) strong positive immunostaining for estrogen receptor (magnification ×400). Second curetttaged tissue: (A) hematoxylin and eosin staining showing remaining focal well-differentiated endometrial adenocarcinoma (magnification ×400), (B) moderate positive immunostaining for estrogen receptor (magnification ×400).

that an endometrial biopsy showed was predominantly estrogen receptor (ER) positive (Fig. 1B). She had a history of polycystic ovary and had received sequential hormone replacement therapy (HRT). Because she desired to preserve her fertility, medical treatment was desirable. In a recent review of women under age 40 with well-differentiated adenocarcinoma, conservative treatment with periodic use of progestin was used [2], and informed consent was obtained from a patient. Before

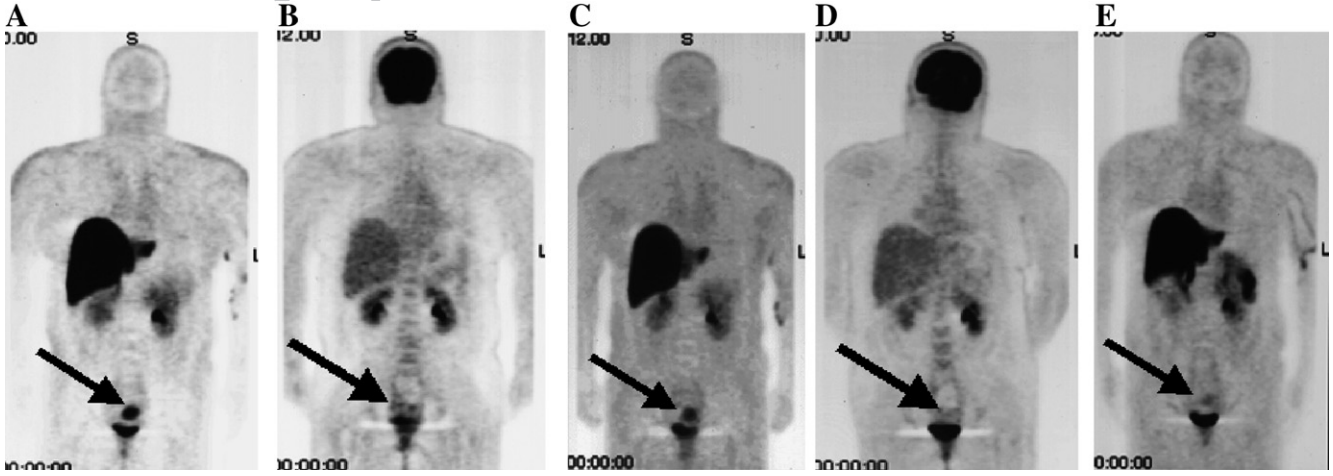

Fig. 2. Endometrial PET during hormonal treatment. Before initiation of treatment: (A) FES-PET showed clearly increased uptake in the endometrium regions and (D) FDG-PET showed slightly increased uptake equivalent to liver uptake. Three months after initiation of treatment, FES-PET showed (B) remaining FES uptake in endometrium site, but (E) FDG-PET showed no abnormal finding. After additional treatment, (C) FES-PET showed no abnormal findings.

Please cite this article as: Yoshida, Y., et al., The positron emission tomography with F18 17β-estradiol has the potential to benefit diagnosis and treatment of endometrial cancer, Gynecologic Oncology (2006), doi:10.1016/j.ygyno.2006.10.024

progestin treatment was started in our patient, FES-PET showed clearly increased uptake in the endometrium regions; the maximum standardized uptake value (SUV) was 12.5 (Fig. 2A) at late pseudo-secretory phase (day 3 before withdraw bleeding), magnetic resonance imaging (MRI) showed slight thickness of endometrium and FDG-PET showed slightly increased uptake equivalent to liver uptake (Fig. 2B). First, the patient was treated with medroxyprogesterone acetate (MPA) 200 mg per day [6,7]. FES-PET after 3 months showed remaining FES uptake in endometrium site (SUV 6.3) (Fig. 2C), but there were no abnormal findings on MRI and FDG-PET (Fig. 2D). Hysteroscopy and endometrial curettage specimens showed remaining focal well-differentiated adenocarcinoma (Fig. 1C) with moderate ER positivity (Fig. 1D). Next, she was treated with MPA 600 mg per day [6,7]. After more than 3 months, FES-PET showed a therapeutic response (Fig. 2E), and there were no abnormal findings on hysteroscopy and endometrial curettage specimens.

Discussion

To our knowledge, this is the first report showing that FES-PET has the potential to provide functional information about the hormone responsiveness of well-differentiated endometrial adenocarcinoma. When we performed serial FES-PET imaging in a woman with well-differentiated adenocarcinoma treated with MPA, a decrease in FES-PET uptake was seen after a therapeutic response. This decrease correlated with the pathological evaluation. Although the pathological evaluation is the "golden" criteria, FES-PET is a new way to evaluate ER activity in endometrial adenocarcinoma.

The standard method of assessing uterine neoplasms is the formal fractional D and C. But to provide sufficient diagnostic information this method requires that patients are anesthetized [3]. At present, FDG-PET is not incorporated in routine clinical practice for diagnosis of gynecologic cancer or assessment of tumor responsiveness to treatment. However, current clinical applications of FDG in gynecologic cancer diagnosis and management have shown many benefits [8]. On the other hand, the limitation of FDG-PET has been shown to provide lower diagnostic accuracy in detecting minimal lesions as well as some pre-forms of cancer and showing no specificity for cancer detection in general. FDG activity can be seen in the gastrointestinal tract, bladder and inflammatory lesions [8,9].

More than 80% of endometrial cancers are usually associated with a history of unopposed estrogen exposure or other hyperestrogenic risk factors such as obesity [1]. And, it has been well documented that the ER level usually is extremely high especially in well-differentiated endometrial adenocarcinoma. An increased response rate to hormonal agents, including progestin, has been associated with positive estrogen or progesterone receptor status. The PR is a product resulting from estrogen binding to the ER. In some studies, the PR appears to be a better predictor of hormone responsiveness than the ER [2]. Yet, the question is whether FES uptake predicts hormone responsiveness more accurately than does the PR. In this case, FES-PET provided functional information about hormone responsiveness in well-differentiated endometrial adenocarcinoma, similar to that of estrogen dependency of breast cancer.

It is important to take into consideration the cyclic changes in estradiol and estrogen receptor when the potential role of FES-PET in premenopausal women is evaluated because estradiol increases and progesterone decreases ER expression. In this case, FES-PET was performed at late pseudo-secretory phase (day 3 before withdraw bleeding) and showed clearly increased uptake in the endometrium regions. During the physiological cycle or during HRT, ER levels are lower in the secretory phase than in other phases of the cycle [10]. Thus, FES-PET has the potential to provide functional information about ER activity in well-differentiated endometrial adenocarcinoma.

In summary, FES-PET showed increased uptake of FES in well-differentiated endometrial adenocarcinoma and provided information for assessing tumor response to hormonal therapy; FES-PET provided more useful information than did FDG-PET. These observations highlight the need for further systemic studies on the utility of FES-PET in gynecologic cancer.

References

[1] Amant F, Neven P, Timmerman D, Van Limbergen E, Vergote I. Endometrial cancer. Lancet 2005;366:491–505.
[2] Curtin JP, Kavanagh JJ, Fox H, Spanos Jr WJ, Corpus. Mesenchymal tumors. In: William JH, Carlos AP, Robert CY, editors. Principles and Practice of Gynecologic Oncology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 1999. p. 961–79.
[3] Pecorelli S, Fallo L, Sartori E, Gastaldi A. Preinvasive lesions of the endometrium. Ann N Y Acad Sci 1991;622:449–62.
[4] Gambhir SS. Molecular imaging of cancer with positron emission tomography. Nat Rev, Cancer 2002;2:683–93.
[5] Linden HM, Stekhova SA, Link JM, Gralow JR, Livingston RB, Ellis GK, et al. Quantitative fluoroestradiol positron emission tomography imaging predicts response to endocrine treatment in breast cancer. J Clin Oncol 2006;24:2793–9.
[6] Randall TC, Kurman RJ. Progestin treatment of atypical hyperplasia and well-differentiated carcinoma of the endometrium in women under age 40. Obstet Gynecol 1997;90:434–40.
[7] Podratz KCO, Brien PC, Malkasian GD, Decker Jr DG, Jefferies JA. Effects of progestational agents in treatment of endometrial carcinoma. Obstet Gynecol 1985;66:106–10.
[8] Kumar R, Alavi A. PET imaging in gynecologic malignancies. Radiol Clin North Am 2004;42:1155–67.
[9] Lerman H, Metser U, Grisaru D, Fishman A, Kievshitz G, Even-Sapir E. Normal and abnormal 18F-FDG endometrial and ovarian uptake in pre- and postmenopausal patients: assessment by PET/CT. J Nucl Med 2004;45:266–71.
[10] Habiba MA, Bell SC, Al-Azzawi F. The effect of hormone replacement therapy on the immunoreactive concentrations in the endometrium of oestrogen and progesterone receptor, heat shock protein 27, and human beta-lactoglobulin. Hum Reprod 2000;15:36–42.

Please cite this article as: Yoshida, Y., et al., The positron emission tomography with F18 17β-estradiol has the potential to benefit diagnosis and treatment of endometrial cancer, Gynecologic Oncology (2006), doi:10.1016/j.ygyno.2006.10.024

Precis

Usefulness of F18 17β- estradiol PET for endometrial cancer.

Please cite this article as: Yoshida, Y., et al., The positron emission tomography with F18 17β-estradiol has the potential to benefit diagnosis and treatment of endometrial cancer, Gynecologic Oncology (2006), doi:10.1016/j.ygyno.2006.10.024