Chapter II.8
Gynecological Tumors

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Introduction

Gynecological cancers as a group comprise approximately 11% of female cancer.[1] In the United States, it is estimated that nearly 80,720 women will be diagnosed in 2009 with gynecological cancers and that approximately 28,120 women will die as a result of these cancers (accounting for 10% of all cancer-related deaths in women). Gynecological cancers are typically diagnosed by history, physical examination, and selected imaging studies. There has been an increasing use of PET using ^{18}F-fluorodeoxyglucose (FDG) for staging and restaging of these cancers, as well as for assessing response to therapy.[2]

Cervical Cancer

In the United States, cervical cancer is the third most common gynecological cancer, with an estimated 11,270 new cases and 4,070 deaths expected in 2009.[1] Squamous cell carcinomas represent over 90% of cervical cancers. Adenocarcinomas and adenosquamous carcinomas account for most of the remaining cases.

^{18}F-FDG PET/CT in Staging Cervical Cancer

Cervical cancers initially spread locally and then through lymphatic channels before metastasizing to distant organs. Like other gynecological neoplasms, cervical cancer is staged in accordance with the International Federation of Gynecology and Obstetrics (FIGO) system. Lymph node status is not included in this staging system, despite the fact that the status of pelvic and para-aortic lymph nodes is an important determinant of prognosis in patients with locally advanced disease and guides treatment planning in patients undergoing radiation therapy. Since carcinoma of the uterine cervix initially grows locally, the clinical staging of this cancer has relied on careful physical examination (including examination under anesthesia), and traditionally only selective radiological examinations have been used. More recently, ^{18}F-FDG PET has been recognized to improve evaluation of this cancer.

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A systematic review of 15 published studies up through 2003 demonstrated pooled sensitivity and specificity for detection of pelvic nodal metastases of 79 and 99%, respectively, for PET; the corresponding values for MRI were 72 and 96%, respectively.[3] Pooled sensitivity for CT was 47%. The pooled specificity was not available. The pooled sensitivity and specificity of PET for para-aortic lymph node metastases were 84 and 95%, respectively.[3] Based on these promising results, in January 2005, the United States Centers for Medicare and Medicaid Services approved coverage for use of ^{18}F-FDG PET in initial staging of patients with newly diagnosed cervical cancer who have no evidence of extra-pelvic metastatic disease on CT or MRI. More recent studies with ^{18}F-FDG PET/CT have demonstrated further advantages by comparison to PET as a stand-alone modality.[4,5]

Some investigators have found that ^{18}F-FDG PET may not be ideal in evaluating early cervical cancer, in particular for detection of metastases in lymph nodes less than 5 mm in size. Wright and colleagues prospectively studied 59 patients with stages IA–IIA cervical cancer prior to surgery.[6] The patient-based analysis demonstrated a sensitivity of 53%, specificity of 90%, positive predictive value (PPV) of 71%, and negative predictive value (NPV) of 80% for PET detection of pelvic lymph node metastasis. The sensitivity was 25%, specificity 98%, PPV 50%, and NPV 93% for detection of para-aortic lymph node metastases. Chou and colleagues[7] prospectively studied 60 patients with stage IA2–IIA cervical cancer who were MRI negative for lymph node metastases prior to surgery. The sensitivity, specificity, PPV, NPV, and accuracy for detecting metastatic disease in pelvic lymph nodes with PET were 10, 94, 25, 84, and 80%, respectively. In a more recent study employing PET/CT, Sironi and coworkers[8] evaluated 47 patients with stage IA–IB cervical carcinoma prior to surgery. The sensitivity, specificity, PPV, NPV, and accuracy were 72, 99.7, 81, 99.5, and 99.3%, respectively.

^{18}F-FDG PET/CT in Directing Therapy in Cervical Cancer

Treatment of patients with locally advanced cervical cancer includes a combination of radio- and chemotherapy. ^{18}F-FDG PET/CT is increasingly used to delineate the target volume for radiation treatment planning. Fused PET/CT images can be used to differentiate tumor from adjacent normal structures more reliably and, thus, allow for delivery of higher doses of radiation to the tumor while decreasing radiation dose to normal structures. Lin and colleagues[9] recently demonstrated that ^{18}F-FDG PET-based treatment planning allows for improved dose coverage of the tumor without significantly increasing the dose to the bladder and rectum.

^{18}F-FDG PET/CT in Predicting Prognosis in Cervical Cancer

Size of the primary tumor and the presence of lymph node metastases are important prognostic factors in patients with cervical carcinoma.[10,11] Miller and Grigsby[12] demonstrated that tumor volume measured on ^{18}F-FDG PET, using a 40% count threshold, was predictive of survival in cervical cancer. ^{18}F-FDG uptake of the primary tumor at diagnosis is also a sensitive biomarker of prognosis in cervical cancer. Kidd and colleagues[13] studied 287 patients with stage IA2 through IVB cervical cancer who underwent pretreatment ^{18}F-FDG PET. A Cox proportional hazards model for death from cervical cancer was used to evaluate tumor histology, lymph node metastases, tumor volume, and $SUV_{max.}$.

The investigators found the SUV_{max} of the primary tumor to be the only significant independent prognostic factor. The overall survival rates at 5 years were 95% for patients with SUV_{max} of 5.2 or less, 70% for those with SUV_{max} >5.2, and 44% for those with SUV_{max} >13.3. Increasing SUV_{max} was associated with persistent abnormal ^{18}F-FDG uptake in the cervix on 3-month ^{18}F-FDG PET studies in patients who received curative chemoradiation. The extent of lymph node involvement by PET is also highly predictive of prognosis.[14]

^{18}F-FDG PET/CT in Post-therapy Monitoring of Cervical Cancer

Several investigators have demonstrated that ^{18}F-FDG PET after completion of therapy is useful in evaluating clinically asymptomatic patients as well as those with clinically suspected disease. Chung and colleagues[15] demonstrated that the sensitivity, specificity, and accuracy of ^{18}F-FDG PET/CT for detecting disease recurrences were 90.3, 81.0, and 86.5%, respectively. Results of ^{18}F-FDG PET/CT studies changed the management of 12 patients (23%). The 2-year disease-free survival rate of patients with negative PET/CT for recurrence was significantly better than that of patients with positive PET/CT (85.0% vs. 10.9%). Yen and colleagues demonstrated that, in recurrent cervical cancer, the benefits of ^{18}F-FDG PET exceed those of CT/MRI, owing to the ability of PET to identify extra-pelvic metastases with higher sensitivity and specificity.[16]

While the best time interval to perform ^{18}F-FDG PET/CT following therapy is not well established, it has been demonstrated that a study performed at 3 months after completion of therapy is highly accurate in determining long-term survival in patients with advanced cervical cancer treated by chemoradiation.[17,18]

Ovarian Cancer

In the United States ovarian cancer is the second most common gynecological cancer, with an estimated 21,550 new cases and 14,600 deaths expected in 2009.[1] Nearly 90% of ovarian cancers are epithelial in origin and arise from the cells on the surface of the ovary. The remaining 10% are germ cell and stromal tumors. Ovarian cancer typically has vague symptoms that are often ignored, and the disease is therefore usually diagnosed at advanced stage. Prognosis is strongly related to the stage of disease at diagnosis. While early stage disease has a very good prognosis, advanced disease carries poor prognosis. Ovarian cancer spreads early by implantation on both parietal and visceral peritoneum before spreading through lymphatics and involving inguinal, pelvic, para-aortic, and mediastinal lymph nodes. The serum tumor marker CA-125 is elevated in nearly 80% of patients with advanced ovarian cancer and is therefore widely used to assess effectiveness of therapy and to detect tumor recurrence. Abnormal marker levels often precede clinical and radiologic signs of disease recurrence.

^{18}F-FDG PET/CT in Diagnosis and Staging of Ovarian Cancer

Because ovarian cancer typically presents as an adnexal mass, differentiating between their benign or malignant etiology is very important. Adnexal masses go undetected until the patient develops signs and symptoms. Transvaginal ultrasonography (TVUS) has a 90% sensitivity and is considered the imaging method of choice for detecting and evaluating adnexal masses.[19] ^{18}F-FDG PET is limited for evaluating adnexal masses because they are

often cystic in nature and because physiologic uptake of ^{18}F-FDG can occur in normal ovaries in premenopausal patients. Lerman and colleagues[20] reported increased ovarian uptake of ^{18}F-FDG (SUV 5.7 $\pm$ 1.5) in premenopausal women without known ovarian malignancy, including a few patients with oligomenorrhea, while the majority were at the mid-phase of the ovulatory cycle. They reported that a threshold ovarian SUV of 7.9 separated benign from malignant lesions with sensitivity, specificity, accuracy, PPV, and NPV of 57, 95, 85, 80, and 86%, respectively. Whereas earlier studies have demonstrated that ^{18}F-FDG PET is limited in differentiating benign from malignant adnexal masses, more recent reports using PET/CT suggest its possible role in this clinical setting.[21] Castellucci and coworkers demonstrated that the sensitivity, specificity, NPV, PPV, and accuracy of ^{18}F-FDG PET/CT were 87, 100, 81, 100, and 92%, respectively, compared with 90, 61, 78, 80, and 80%, respectively, for TVUS.[23] Ovarian cancer is typically staged by exploratory laparotomy at the time of tumor debulking. CT and/or MRI have been accepted as useful imaging modalities for preoperative staging ovarian cancer. Recent studies have demonstrated that ^{18}F-FDG PET may be useful as an adjunct to diagnostic CT for staging ovarian cancer. Yoshida and colleagues[22] found that ^{18}F-FDG PET has a higher diagnostic accuracy than CT (87% vs. 53%) in preoperative staging of patients with suspected ovarian cancer using histology as the "gold standard" reference. Castellucci and coworkers[23] demonstrated that ^{18}F-FDG PET/CT was concordant with final pathological staging in 69% of patients as compared to 53% for CT alone. More data are needed to better define the role of PET in initial staging of ovarian cancer.

^{18}F-FDG PET/CT in Assessment of Response to Therapy in Ovarian Cancer

Standard treatment of advanced ovarian cancer includes aggressive cytoreductive surgery followed by platinum/taxane-based chemotherapy. Despite an often initial good response to this therapy, most patients will subsequently die of progressive disease.[24] Recently, neoadjuvant chemotherapy followed by surgical debulking has been used in order to improve outcome. This, however, can only be achieved in patients with complete or nearly complete response to neoadjuvant therapy.[25] CT and MRI are limited in detecting response early after initiation of therapy. Moreover, these modalities are limited in distinguishing residual tumor from necrosis or fibrosis. ^{18}F-FDG PET/CT has been used in a limited fashion in this clinical setting. Avril and colleagues[26] demonstrated that overall survival showed a significant correlation with changes in tumor tracer uptake after the first and third cycles of chemotherapy, but not with conventional clinical or CA-125 response criteria. A higher rate of complete tumor resections was achieved in metabolic responders (defined as 20% reduction in SUV after the first cycle and 50% after the third cycle) compared with non-responders, and macroscopically tumor-free surgery was achieved in 33% of metabolic responders compared with only 13% of non-responders. Metabolic responders had longer median overall survival than non-responders.

^{18}F-FDG PET/CT in Detection of Recurrent Ovarian Cancer

Several studies have shown that ^{18}F-FDG PET/CT is superior to conventional imaging and measurement of CA-125 in detecting recurrent ovarian cancer. A recent systematic review of six published studies that assessed patients with clinical suspicion for recurrent ovarian cancer calculated a pooled sensitivity and specificity of 90 and 86%, respectively, for

^{18}F-FDG PET, 68 and 58%, respectively, for conventional imaging, and 81 and 83%, respectively, for CA-125 measurement.[3] Three studies evaluated ^{18}F-FDG PET in patients with negative conventional imaging and CA-125 measurements in whom surveillance studies were used to detect recurrent or persistent ovarian cancer. The pooled sensitivity and specificity of ^{18}F-FDG PET were 54 and 73%, respectively.[3] Another three studies evaluated patients with rising CA-125 levels and negative or equivocal conventional imaging studies. The pooled sensitivity and specificity of ^{18}F-FDG PET were 96 and 80%, respectively.[3] It appears that ^{18}F-FDG imaging is highly effective as a diagnostic tool in patients with rising CA-125 levels and negative or equivocal CT. ^{18}F-FDG PET/CT has been shown to be very useful in early detection of recurrent disease that is suitable for surgical resection.[27–29]

Endometrial Cancer

Endometrial cancer is the most common gynecologic cancer in the United States, with an estimated 42,160 new cases and 7,780 deaths expected in 2009.[1] Two different clinicopathological subtypes are recognized: the more-common estrogen-related (type I, endometrioid) and the non-estrogen related (type II, non-endometrioid). Endometrial cancer is staged and treated surgically. There are limited reports of the use of ^{18}F-FDG imaging for diagnosis of primary endometrial cancer. One of the potential limitations of ^{18}F-FDG PET is related to ^{18}F-FDG accumulation in benign processes such as menstrual bleeding and leiomyoma.[30,31] Horowitz and colleagues[32] reported that the sensitivity of PET for detection of primary endometrial cancer was 84%. They also reported that the sensitivity and specificity of PET for detection of lymph node metastases were 60 and 98%, respectively. Recently, Suzuki and coworkers demonstrated that PET has a sensitivity of 97% for detection of primary tumor vs. 83% for CT/MRI.[33] The sensitivity, specificity, PPV, and NPV for prediction of pelvic lymph node metastases were 0, 100, 0, and 81%, respectively, for PET and 40, 86, 40, and 86%, respectively, for CT/MRI. For detection of para-aortic lymph node metastases, the sensitivity, specificity, PPV, and NPV were 0, 100, 0, 95%, respectively, for PET and 100, 94.4, 50, and 100%, respectively, for CT/MRI. All the retroperitoneal lymph node metastases were microscopic, and PET was unable to detect any of the involved lymph nodes. The sensitivity of ^{18}F-FDG PET for detection of extrauterine lesions, excluding retroperitoneal lymph nodes, was superior to that of CT/MRI (83% vs. 67%), while there was no difference in the specificity between the modalities (100%). This study demonstrated that the diagnostic ability of ^{18}F-FDG imaging may be limited if PET is used alone while ^{18}F-FDG PET/CT may have a potential role in the preoperative staging of endometrial cancer.

Evaluation of endometrial cancer after therapy typically includes physical examination, evaluation of the serum tumor markers CA-125 or CA-19.9, and selected imaging. All of these methods are limited in early detection of recurrent disease. However, PET has been shown to be beneficial for detection of recurrent endometrial cancer, particularly in asymptomatic patients.[34,35]

Summary

^{18}F-FDG PET/CT is a very useful adjunct to CT/MRI in initial staging of cervical cancer. It not only provides information about the extent of disease, it is also used to direct radiotherapy and predict prognosis. In ovarian cancer, ^{18}F-FDG PET/CT plays an important

role in detecting recurrent disease in patients with rising tumor markers and equivocal or negative CT/MRI. The role of ^{18}F-FDG PET/CT in endometrial cancer is evolving and may be of clinical significance mainly in the post-therapy evaluation of these patients.

Guidelines and Recommendations for the Use of ^{18}F-FDG PET and PET/CT

The National Comprehensive Cancer Network (NCCN) has incorporated ^{18}F-FDG PET and PET/CT in the practice guidelines and management algorithm of a variety of malignancies including cervical cancer.[36] The use of ^{18}F-FDG PET (PET/CT where available) is recommended 1) For initial staging and restaging of cervical cancer; 2) For evaluation of recurrent ovarian cancer in patients with rising CA-125 levels. 3) In uterine cancer, the reported impact of PET on management is not substantial.

Case Presentations

Case II.8.1 (DICOM Images on DVD)

History

This 74-year-old woman presented with FIGO stage IIb squamous cell carcinoma of the cervix. She was referred for initial staging with ^{18}F-FDG PET/CT (Fig. II.8.1A–F).

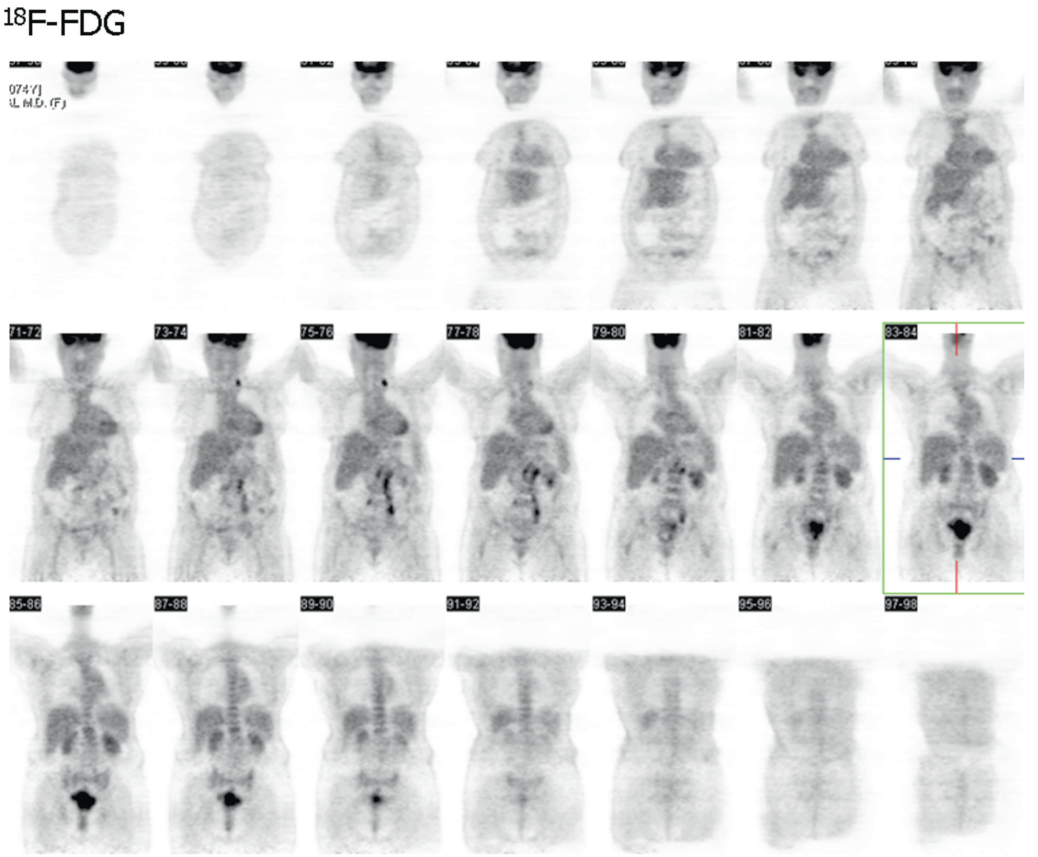

Fig. II.8.1A

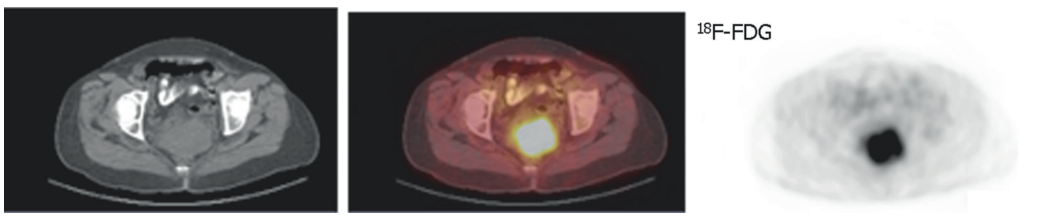

Fig. II.8.1B

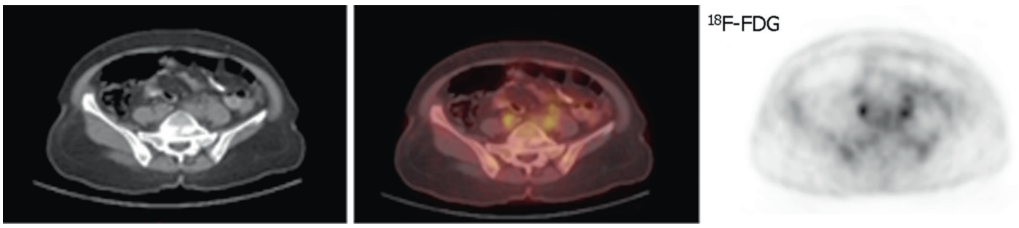

Fig. II.8.1C

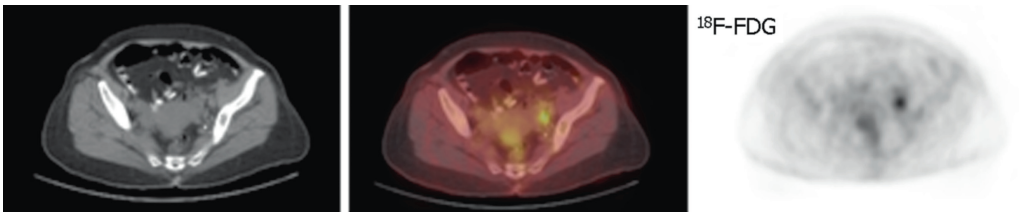

Fig. II.8.1D

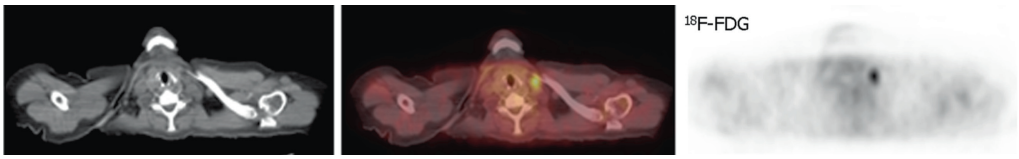

Fig. II.8.1E

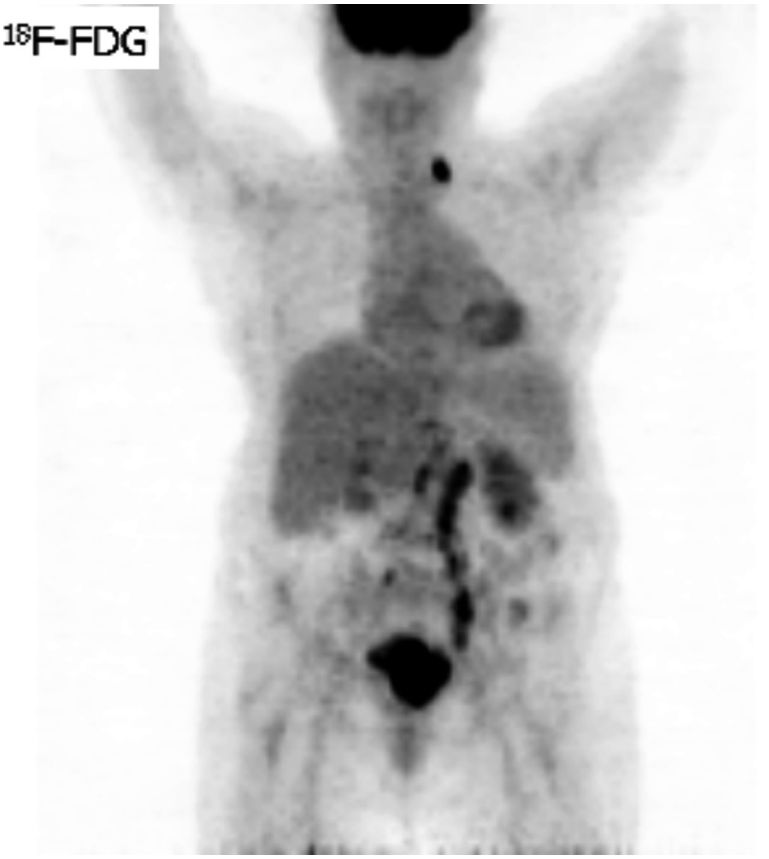

Fig. II.8.1F (MIP image)

Findings

Intense ^{18}F-FDG activity is noted in the cervical mass, most consistent with the known primary cancer (Fig. II.8.1A, B, F). Multiple foci of increased uptake are noted in retroperitoneal para-aortic lymph nodes, predominantly on the left side, with the largest measuring 17 × 14 mm (Fig. II.8.1A, C, F). The lymphadenopathy extends to the aortic bifurcation with increased tracer activity noted in multiple left common iliac and left external iliac lymph nodes (Fig. II.8.1A, D, F). There also is intense ^{18}F-FDG activity in a left supraclavicular lymph node measuring 16 × 13 mm (Fig. II.8.1A, E, F). Additional CT findings are seen on the DICOM images and described in the clinical report.

Discussion

The pattern of lymph node involvement in this patient is typical for metastatic cervical cancer. Lymph node involvement, which is the most common form of metastatic disease in cervical cancer, typically begins in the pelvis extending to the para-aortic and ultimately the left supraclavicular lymph nodes. The extent of lymph node involvement has been shown to be of prognostic significance and is inversely related to survival. Grigsby and colleagues[14] studied 101 patients with newly diagnosed cervical cancer and demonstrated that the lymph

node status determined by ^{18}F-FDG PET is predictive of progression-free and overall survival in patients with cervical cancer. ^{18}F-FDG PET evidence of lymph node involvement was a better predictor of the 2-year disease-free survival than the CT findings. Based on pelvic lymph node status on imaging studies, the 2-year disease-free survival was 84% for CT–/PET–, 64% for CT–/PET+, and 48% for CT+/PET+ patients. Based on the status of the para-aortic nodes on imaging studies, the 2-year disease-free survival was 78% for CT–/PET–, 31% for CT–/PET+, and 14% for CT+/PET+ patients. The finding of PET+ supraclavicular lymph nodes was indicative of dismal prognosis and none of such patients survived 2 years. They also found that the PET-determined status of the para-aortic nodes was the strongest predictor of survival in a multivariate logistic regression analysis.

Diagnosis

Metastatic cervical cancer (regional and distant disease).

Clinical Report: Body ^{18}F-FDG PET/CT (for DVD cases only)

Indication

Initial staging of carcinoma of the cervix.

History

The patient presented with complaint of post-menopausal bleeding. A cervical mass was found, and the biopsy showed moderately to poorly differentiated squamous cell carcinoma of the cervix. The patient stated that the bleeding began about 1 month ago, but she did not require blood transfusion. There was no trouble with her urination including hematuria. She has experienced no lower extremity or groin swelling or pain in her back or pain radiating to her legs. The patient now presents for initial staging.

Procedure

After oral administration of MD-Gastroview^{TM} and intravenous administration of 500 MBq (13.5 mCi) of ^{18}F-FDG, non-contrast CT images were obtained for attenuation correction and fusion. A series of PET images were then obtained beginning approximately 60 min after injection of ^{18}F-FDG. The patient's fasting blood glucose level, measured before injection of ^{18}F-FDG, was 97 mg/dL. The imaged area spanned from the skull base to the upper thighs. The patient was positioned with arms up.

Before administration of ^{18}F-FDG, intravenous access was established for patient hydration. In addition, a 16-French Foley catheter was inserted into the urinary bladder using standard aseptic technique. Furosemide, 20 mg, was administered by slow intravenous injection approximately 20 min after the injection of ^{18}F-FDG. At the conclusion of the procedure, the intravenous line and Foley catheter were removed without incident. The patient tolerated the procedure well, without apparent complications.

Findings

Quality of the study: The quality of this study is good.

Head and neck: There is physiologic distribution of the radiopharmaceutical in the cerebral cortex and lymphoid and glandular tissues of the neck. There is a mucosal retention cyst in the left maxillary sinus. There is intense ^{18}F-FDG uptake within left supraclavicular lymph nodes, with the largest measuring 16 × 13 mm.

Chest: There is mild cardiomegaly with biatrial enlargement. Calcifications of the aorta and coronary arteries are noted. No pulmonary nodule is seen.

Abdomen and pelvis: There is intense ^{18}F-FDG activity within the cervical mass (approximately 81 mm in greatest diameter), consistent with the patient's known primary cancer. There are multiple foci of increased ^{18}F-FDG uptake in retroperitoneal para-aortic lymph nodes, predominantly on the left side with the largest measuring 17 × 14 mm. The lymphadenopathy extends to the aortic bifurcation, with increased ^{18}F-FDG uptake also noted in multiple left common iliac and left external iliac lymph nodes. Multiple diverticula are noted in the sigmoid colon. Multiple anterior body wall collateral vessels are noted.

Musculoskeletal: Extensive degenerative disc disease is noted, more prominent at L1/L2 and L5/S1. Grade 2 anterolisthesis is noted at L5 on S1. Mild T11 and L1 compression deformities are seen. Diffusely increased ^{18}F-FDG uptake is noted intramedullary within the axial and proximal appendicular bones, consistent with bone marrow hyperplasia due to anemia related to bleeding.

Impression

1. Intense ^{18}F-FDG uptake corresponding to the cervical mass, consistent with cervical carcinoma.
2. Intense ^{18}F-FDG uptake within left supraclavicular, para-aortic, and pelvic lymph nodes, consistent with lymph node metastases.

Case II.8.2

History

This 60-year-old woman presented with FIGO stage IIIb squamous cell carcinoma of the cervix. She is referred to ^{18}F-FDG PET/CT for initial staging (Fig. II.8.2A–E).

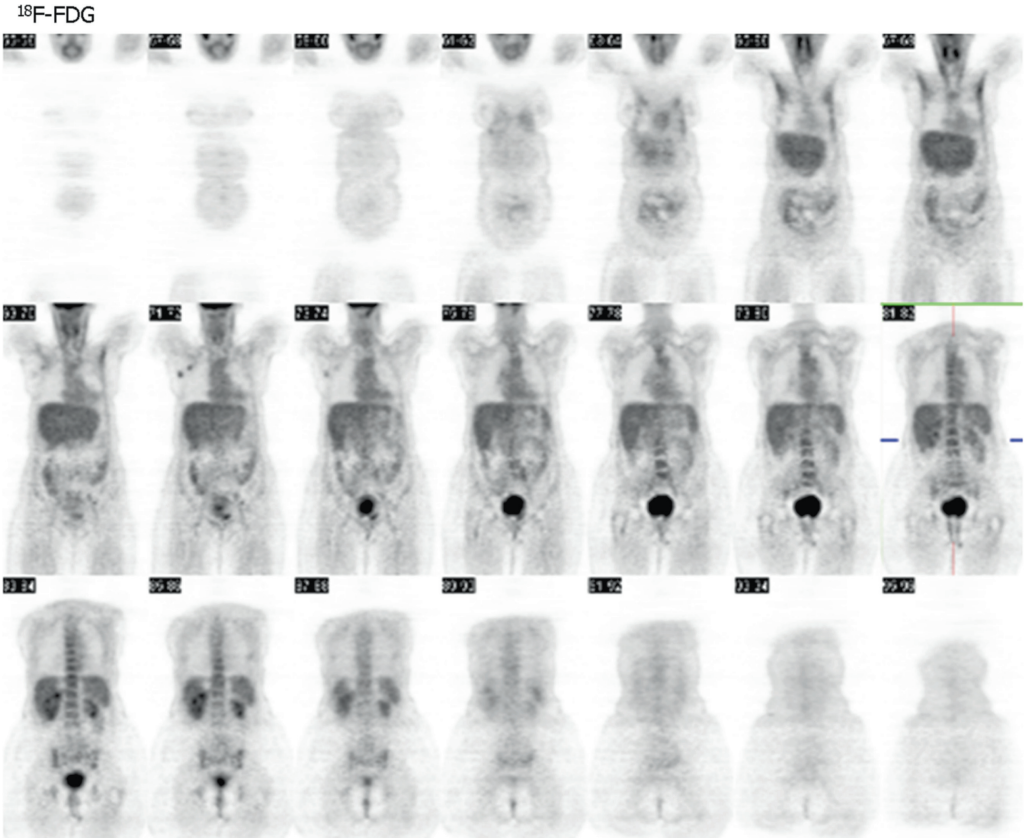

Fig. II.8.2A

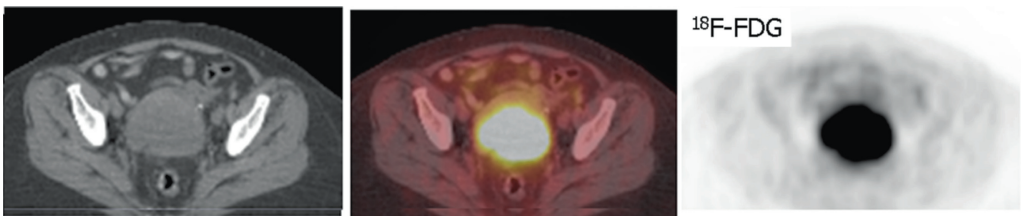

Fig. II.8.2B

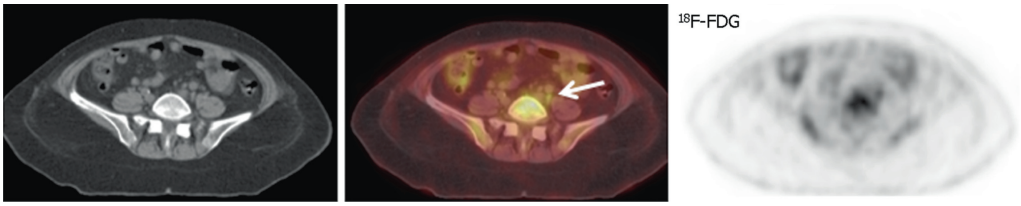

Fig. II.8.2C

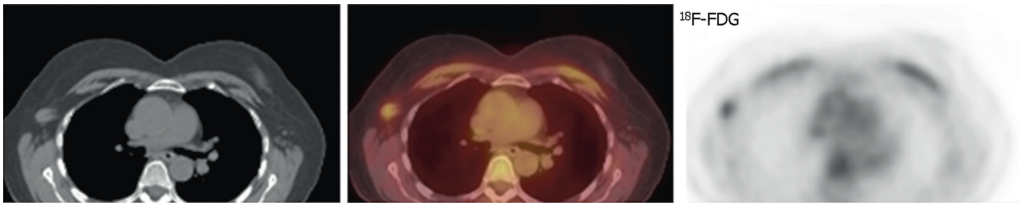

Fig. II.8.2D

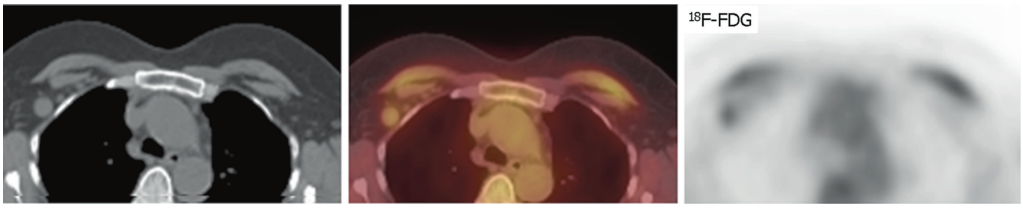

Fig. II.8.2E

Findings

There is intense ^{18}F-FDG uptake within the cervical mass, most consistent with the known primary cancer (Fig. II.8.2A, B). In addition, abnormal ^{18}F-FDG uptake is noted in a 4 mm left common iliac lymph node (arrow, Fig. II.8.2C). Increased tracer uptake is also seen in two enlarged (19 and 15 mm) right axillary lymph nodes (Fig. II.8.2A, D, E).

Discussion

^{18}F-FDG uptake in the cervix is consistent with the known primary cervical cancer. The uptake within the small left common iliac lymph node is highly suspicious for a metastasis.

More recent studies with PET/CT have demonstrated the superiority of this imaging modality for detection of lymph node metastases. One study has demonstrated that MRI has a lower sensitivity than ^{18}F-FDG PET/CT for detection of lymph node metastases. The sensitivity, specificity, and accuracy rates for detecting metastatic lymph nodes were 30, 93, and 73%, respectively, for MRI, and 58, 93 and 85%, respectively, for PET/CT.[4] A recent study demonstrated that ^{18}F-FDG PET/CT had a PPV of 75%, NPV of 96%, sensitivity of 75%, and specificity of 96% for detection of pelvic lymph node metastases in 27 patients

who underwent radical surgery.[5] For para-aortic nodal disease in 119 patients, PET/CT showed a PPV of 94%, NPV of 100%, sensitivity of 100%, and specificity of 99%. For distant metastases, ^{18}F-FDG PET/CT had a PPV of 63%, NPV of 100%, sensitivity of 100%, and specificity of 94%.

The uptake within the axillary lymph nodes in this patient is a highly atypical pattern for metastatic cervical cancer. Biopsy of an axillary lymph node demonstrated abundant mixed polymorphous lymphocytes but no evidence of carcinoma. In general, abnormal ^{18}F-FDG PET findings that would potentially lead to a change in management need to be confirmed by biopsy. Although the axillary lymph node foci were highly unlikely to be related to cervical cancer, the physician opted to biopsy one of the lymph nodes. The finding of a probable pelvic lymph node metastasis did not change patient management but affected patient's prognosis, as described in case II.8.1.

Diagnosis

1. Primary cervical squamous cell carcinoma.
2. Metastatic disease in a left pelvic lymph node.
3. Benign hypermetabolic ^{18}F-FDG-avid right axillary lymph nodes.

Case II.8.3

History

This 27-year-old woman presented with a newly diagnosed FIGO stage IIb poorly differentiated squamous cell carcinoma of the cervix. She began to have lower abdominal pain and bleeding approximately a month and a half prior to current examination and was referred to ^{18}F-FDG PET/CT for staging (Fig. II.8.3A–C). Subsequently, chemoradiation treatment was initiated and a follow-up PET/CT study was thereafter performed (Fig. II.8.3D–F).

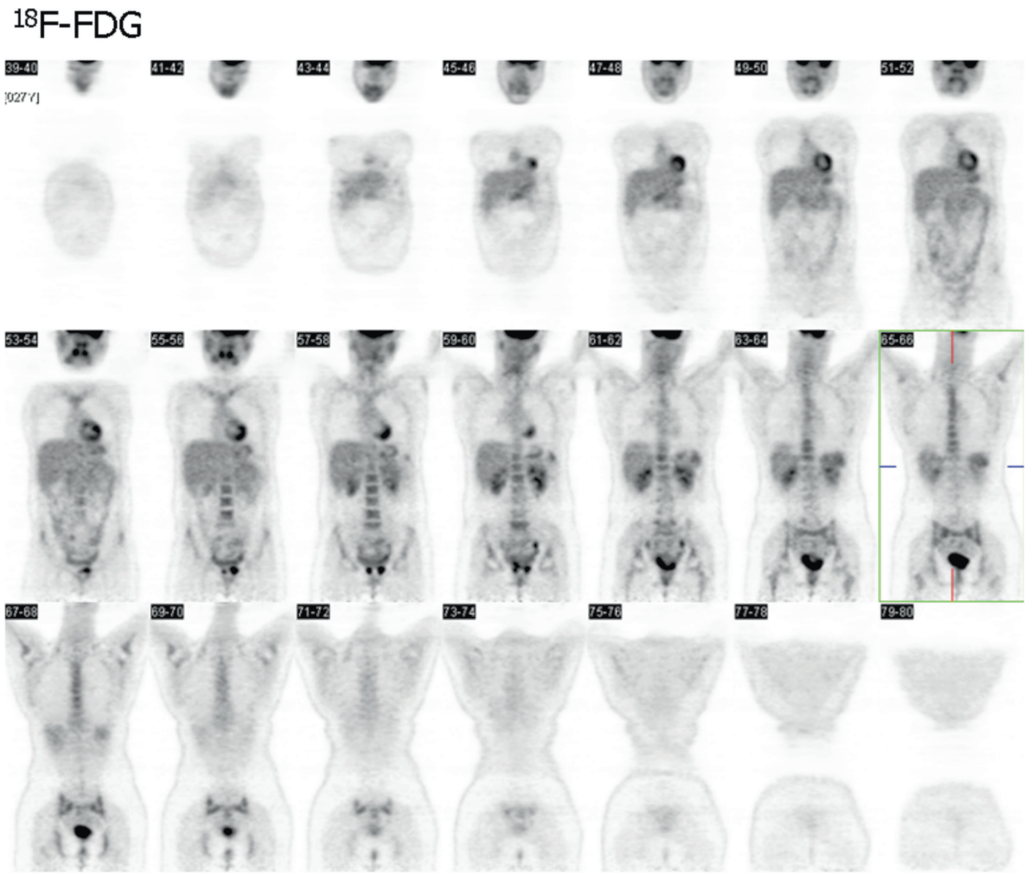

Fig. II.8.3A

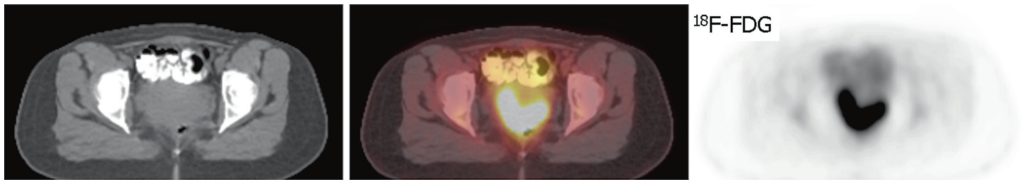

Fig. II.8.3B

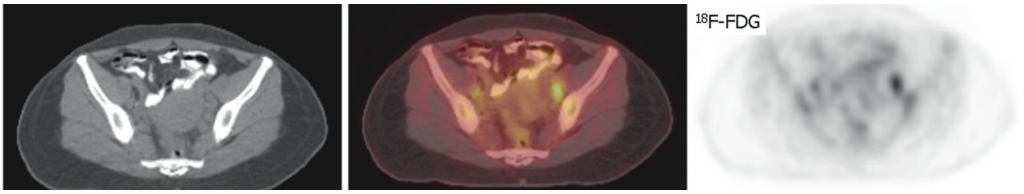

Fig. II.8.3C

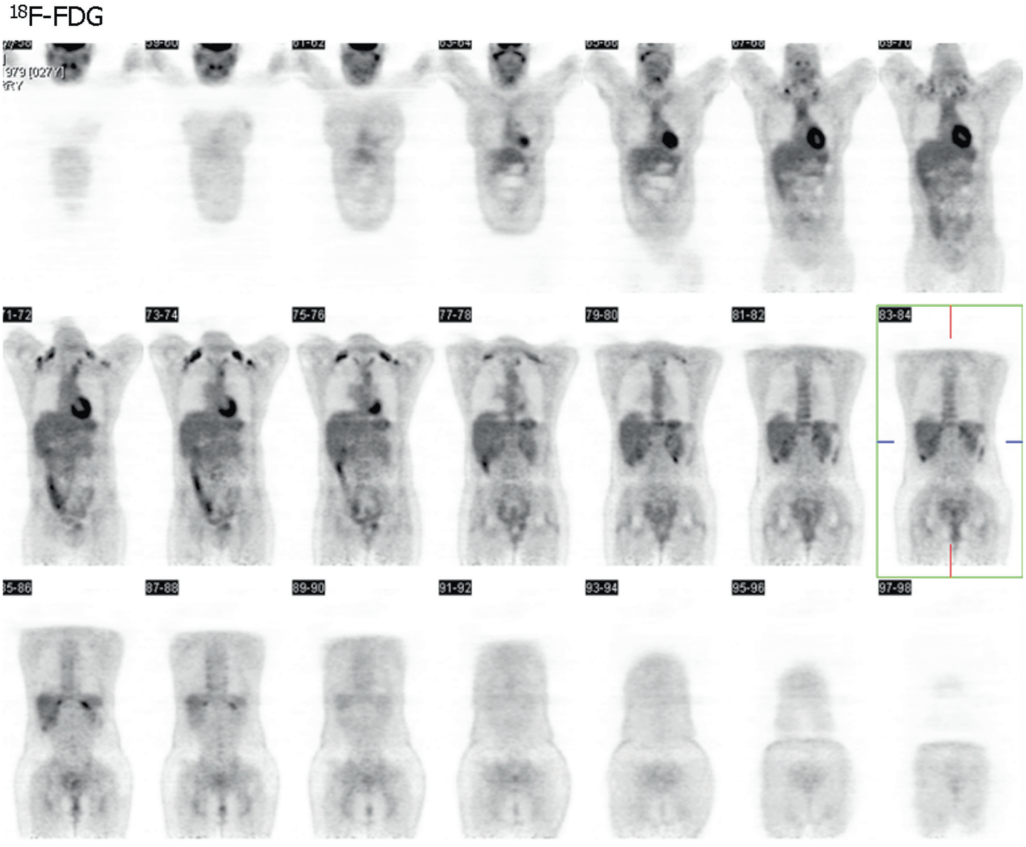

Fig. II.8.3D

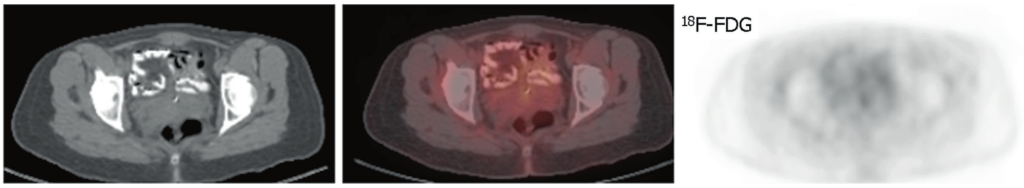

Fig. II.8.3E

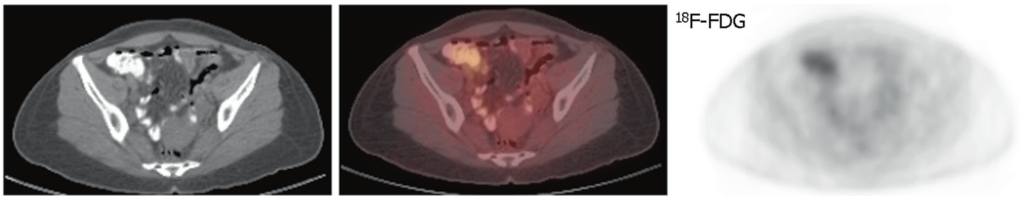

Fig. II.8.3F

Findings

In the pretherapy PET/CT study, there is marked ^{18}F-FDG uptake within a large (approximately 50 × 50 mm) soft tissue mass originating in the cervix. Additional focally increased ^{18}F-FDG uptake is seen within external iliac lymph nodes bilaterally. The left external iliac lymph node measures 18 × 9 mm and the right measures 14 × 5 mm (Fig. II.8.3A–C).

The post-therapy PET/CT study performed approximately 3 months after completion of chemoradiation demonstrates minimal diffusely increased tracer uptake in the cervix, most probably related to post-radiation changes. There is a marked decrease in the size of the cervix as compared to the baseline study. There is also interval resolution of the ^{18}F-FDG uptake in the external iliac lymph nodes. There is decreased tracer activity in the lumbar spine and pelvic bones, due to the intervening radiation. Increased physiologic tracer activity is seen in the brown adipose tissue in the lower neck (Fig. II.8.3D–F).

Discussion

Three-month post-therapy ^{18}F-FDG PET/CT demonstrates complete resolution of abnormal tracer uptake within the cervical mass and the pelvic lymph nodes. This is highly predictive of good prognosis.

Grigsby and colleagues[17] demonstrated that ^{18}F-FDG PET performed 3 months after completion of therapy is highly accurate in predicting long-term survival in patients with advanced cervical cancer treated with chemoradiation. A normal ^{18}F-FDG PET 3 months after therapy was indicative of an excellent prognosis, with a 5-year survival rate of 90% in patients with cervical cancer. In contrast, 5-year survival was only 45% in patients with persistent tracer uptake in the primary tumor or the nodal metastases seen before therapy. If the post-therapy PET study demonstrated new metastatic lesions, prognosis of the patients was poor with a 15% 5-year survival. These results were recently validated prospectively in 92 patients with cervical carcinoma treated with external irradiation, brachytherapy, and concurrent chemotherapy.[18] These patients underwent post-therapy PET 2–4 months after completion of therapy. ^{18}F-FDG PET showed a complete metabolic response in 71% of patients, partial metabolic response in 16%, and progressive disease in 13% of patients, with a significant difference in the 3-year progression-free survival of 78, 35, and 0%, respectively. The 3-year cause-specific survivals were 100, 51, and 0%, respectively. Multivariate analysis demonstrated that the post-therapy metabolic response was more predictive of survival than all known pretreatment prognostic factors. Thus, 3-month post-therapy ^{18}F-FDG uptake can be considered to represent a metabolic biomarker of tumor response and is a robust surrogate for prolonged follow-up to determine prognosis in cervical cancer.

Diagnosis

1. Primary cervical squamous cell carcinoma.
2. Metastatic disease in external iliac lymph nodes bilaterally.
3. Metabolic response to chemoradiation.

Case II.8.4 (DICOM Images on DVD)

History

This 52-year-old woman with ovarian cancer was initially treated with total abdominal hysterectomy and bilateral salpingo-ophorectomy as well as omentectomy and chemotherapy. She presents with an elevated CA-125, and ^{18}F-FDG PET/CT was performed for suspected recurrence (Fig. II.8.4A–F).

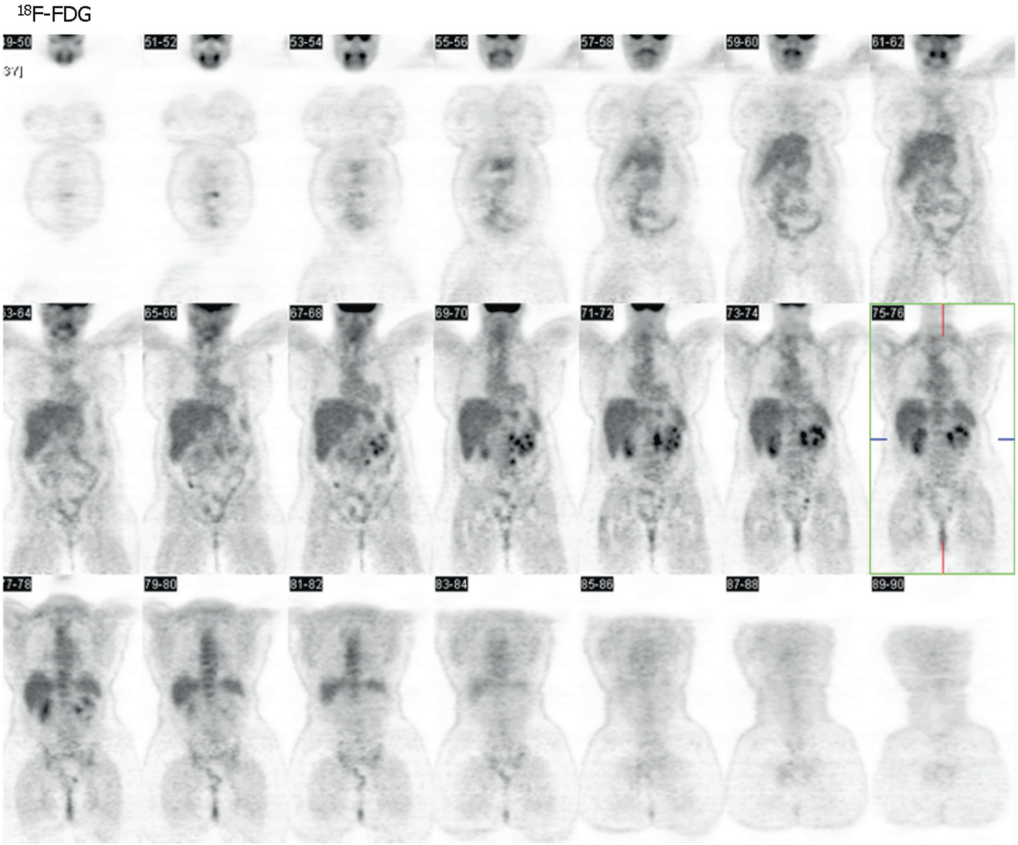

Fig. II.8.4A

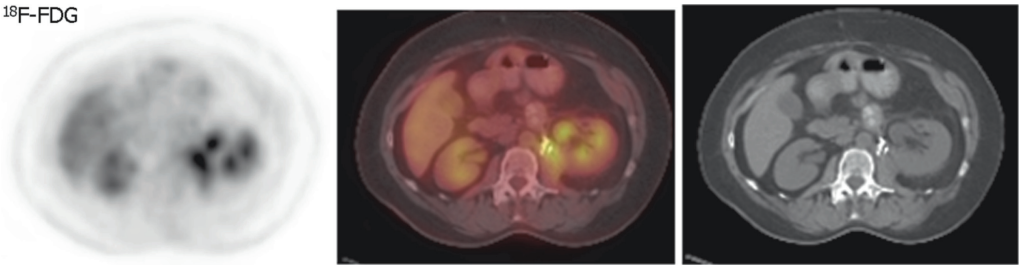

Fig. II.8.4B

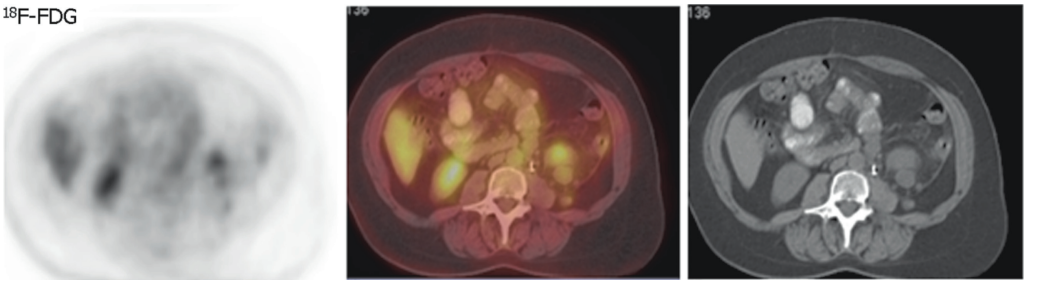

Fig. II.8.4C

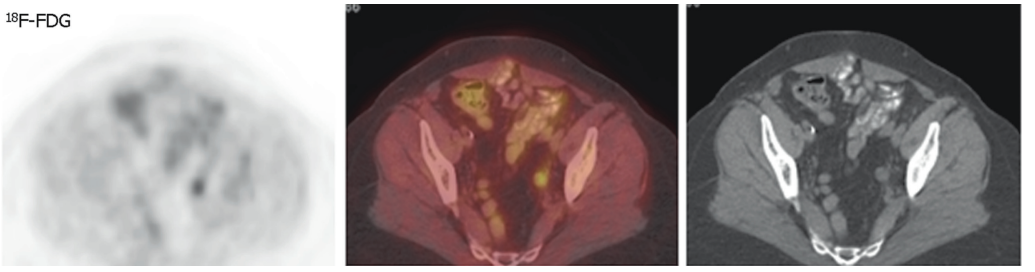

Fig. II.8.4D

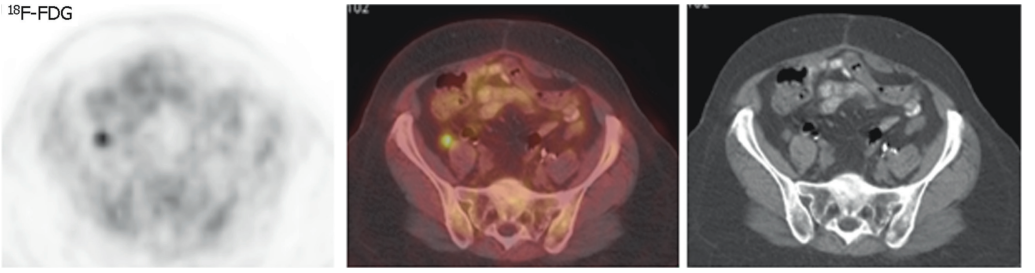

Fig. II.8.4E

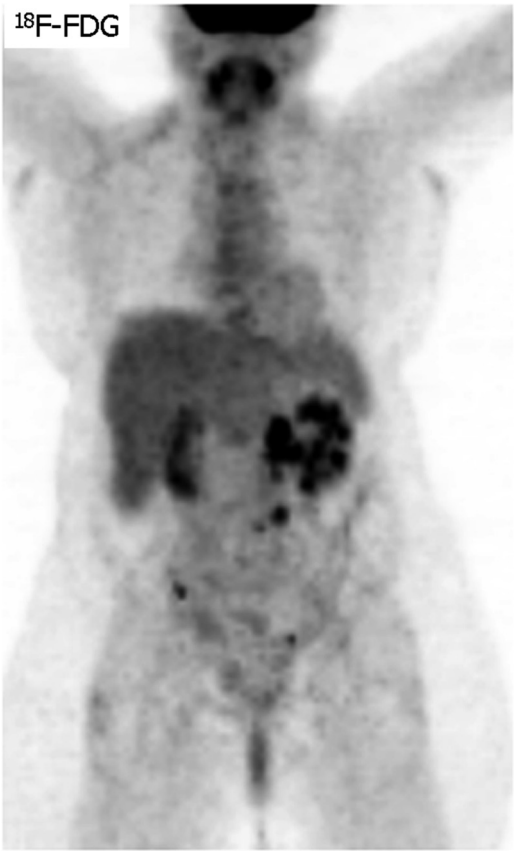

Fig. II.8.4F (MIP image)

Findings

Intense ^{18}F-FDG uptake is noted in multiple soft tissue nodules scattered throughout the abdomen and pelvis, consistent with recurrent disease (Fig. II.8.4A–F). There are multiple foci of markedly abnormal ^{18}F-FDG uptake in the left para-aortic region adjacent to surgical clips (Fig. II.8.4A, B, F), and multiple soft tissue nodules in the left perinephric space demonstrating mildly increased tracer activity (Fig. II.8.4A, C, F). Additionally, there is increased ^{18}F-FDG uptake within a 15 mm soft tissue nodule in the left pelvis, in a 9 mm nodule anterior to the right psoas muscle (Fig. II.8.4A, D–F), and in a small soft tissue nodule in the anterior abdomen in the region of the umbilicus (Fig. II.8.4A). Additional CT findings are seen on the DICOM images and described in the clinical report (see DVD).

Discussion

The pattern of peritoneal involvement in this patient is typical for recurrent ovarian cancer. This pattern is associated with an unfavorable prognosis in comparison with recurrent disease presenting with discrete lesions.[37] Thus, early detection of localized recurrent

disease may be beneficial. ^{18}F-FDG PET/CT has proven to be very useful in early detection of recurrent disease that is suitable for surgical resection.[27] Bristow and colleagues[27] demonstrated that in patients with rising CA-125 and negative or equivocal CT, ^{18}F-FDG PET has a sensitivity of 83% and PPV of 94% for detecting recurrent disease of at least 10 mm. Complete cytoreduction of the tumor was accomplished in 72% of patients with recurrent ovarian cancer larger than 10 mm. Some investigators have suggested that ^{18}F-FDG PET/CT is a sensitive post-therapy surveillance modality for detection of recurrent ovarian cancer. It assists in selecting the most appropriate treatment for individual patients. Chung and colleagues[28] studied 77 patients and demonstrated that the overall sensitivity, specificity, accuracy, PPV, and NPV of ^{18}F-FDG PET/CT were 93, 97, 95, 98, and 91%, respectively, for detection of recurrent ovarian cancer. PET/CT resulted in alteration of the management plan in 25% of patients by either avoiding previously planned diagnostic procedures or indicating the need for previously unplanned therapeutic procedures. Simcock and coworkers[29] demonstrated that ^{18}F-FDG PET/CT improves assessment of recurrent disease and provides prognostic information. In patients with rising CA-125, PET/CT results led to change in the distribution of known disease in 64% of patients and resulted in a major change in planned management in 58%. ^{18}F-FDG PET/CT identified a subgroup of women with apparently localized or no definite evidence of disease who had improved survival as compared with those patients with proven systemic disease.

Diagnosis

Recurrent ovarian cancer – diffuse abdominal carcinomatosis.

Clinical Report: Body ^{18}F-FDG PET/CT (for DVD cases only)

Indication

Localization of recurrent ovarian cancer.

History

This 52-year-old woman with ovarian cancer was initially treated with total abdominal hysterectomy, bilateral salpingo-ophorectomy and omentectomy, followed by chemotherapy. She also underwent bilateral pelvic lymphadenectomy. Approximately a year prior to current examination, she had recurrence in her left para-aortic region for which she underwent surgery and cisplatin washing. Subsequent ^{18}F-FDG PET/CT showed resolution of disease. She now presents with a suspicion of recurrence due to elevated CA-125.

Procedure

After oral administration of MD-Gastroview^{TM} and intravenous administration of 555 MBq (15 mCi) ^{18}F-FDG, non-contrast CT images were obtained for attenuation correction and for fusion with PET images. PET was then obtained beginning approximately 87 min after injection of ^{18}F-FDG. The patient's fasting blood glucose level, measured before injection of ^{18}F-FDG, was 103 mg/dL. The area imaged spanned from the skull base to the upper thighs. The patient was positioned with arms up.

Before administration of ^{18}F-FDG, intravenous access was established for patient hydration. In addition, a 16-French Foley catheter was inserted into the urinary bladder using standard aseptic technique. Furosemide, 20 mg, was administered by slow

intravenous injection approximately 20 min after the injection of ^{18}F-FDG. At the conclusion of the procedure, the intravenous line and Foley catheter were removed without incident. The patient tolerated the procedure well, without apparent complications.

Findings

Quality of the study: The quality of this study is good.

Head and neck: There is physiologic distribution of the radiopharmaceutical in the cerebral cortex and lymphoid and glandular tissues of the neck.

Chest: The heart is normal. No pulmonary nodule is seen.

Abdomen and pelvis: There is increased ^{18}F-FDG uptake in multiple soft tissue nodules scattered throughout the abdomen and pelvis, consistent with recurrent disease. There are multiple soft tissue nodules in the perinephric region of the left kidney, the larger nodules demonstrate increased ^{18}F-FDG uptake, with the largest measuring 23 mm in maximum dimension. There are multiple left para-aortic soft tissue lymph nodes in the region of surgical clips demonstrating markedly abnormal tracer uptake. An additional soft tissue nodule is seen adjacent to the left diaphragmatic crus just above the origin of the renal arteries. There also is increased ^{18}F-FDG uptake within a 15-mm soft tissue nodule in the left pelvis and a 9-mm nodule anterior to the right psoas muscle. There is a small umbilical hernia containing a portion of normal appearing bowel, with an adjacent ^{18}F-FDG-avid soft tissue nodule.

The CT images demonstrate multiple soft tissue nodules scattered throughout the abdomen and pelvis. Multiple surgical clips are seen scattered throughout the abdomen and pelvis. There is mild anterior displacement of the left kidney secondary to posterior perinephric nodules. There is a small left extrarenal pelvis. The liver, pancreas, spleen, and bilateral adrenal glands are normal. There is a small hiatal hernia. The stomach and small and large bowels demonstrate normal wall thickness and caliber. A Foley catheter is seen within a decompressed urinary bladder. There are surgical clips adjacent to a small umbilical hernia containing a portion of normal appearing bowel.

Musculoskeletal: Evaluation of the osseous structures demonstrates no suspicious lytic or sclerotic lesions.

Impression

Multifocal ^{18}F-FDG uptake in the abdomen and pelvis, consistent with recurrent ovarian carcinoma.

Case II.8.5

History

This 56-year-old woman with endometrioid adenocarcinoma of the uterus initially treated with total abdominal hysterectomy and bilateral salpingo-ophorectomy as well as pelvic and abdominal lymphadenectomy presented to ^{18}F-FDG PET/CT for further evaluation of a nodule in the anterior abdomen (Fig. II.8.5A–D).

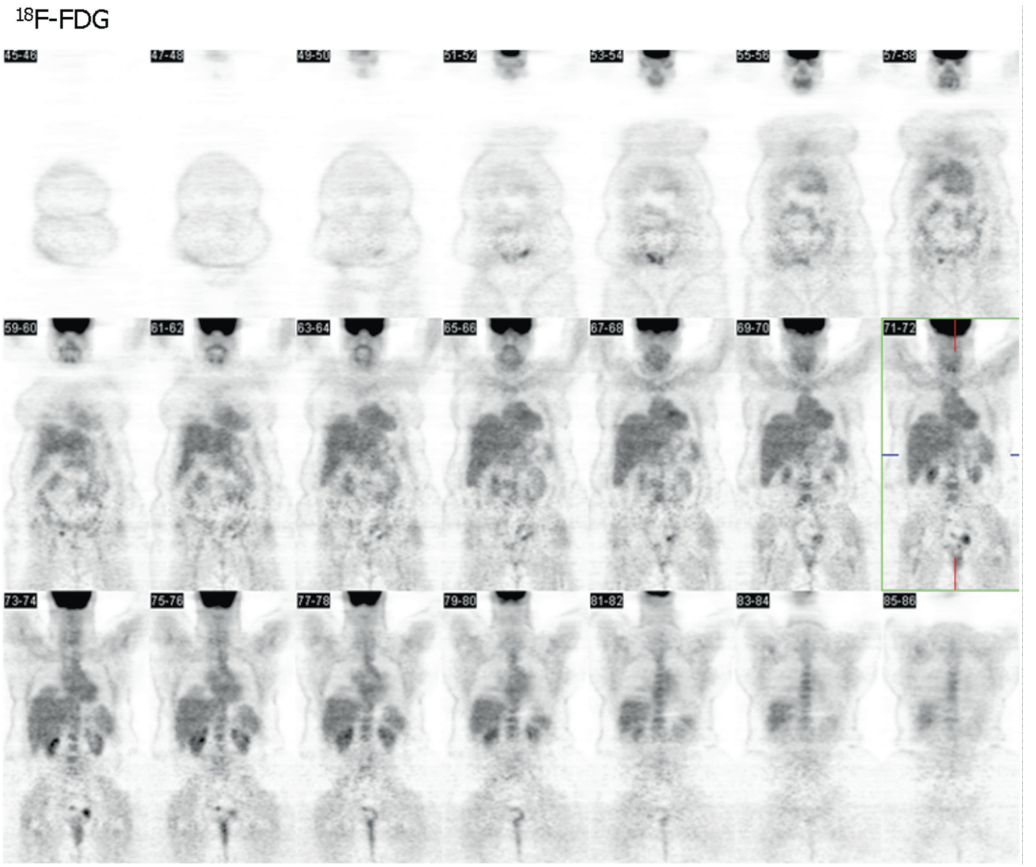

Fig. II.8.5A

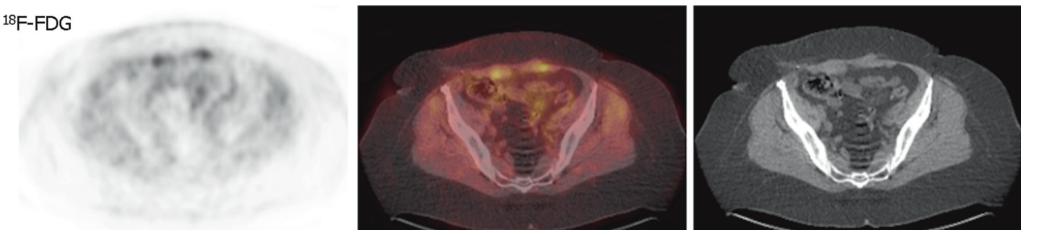

Fig. II.8.5B

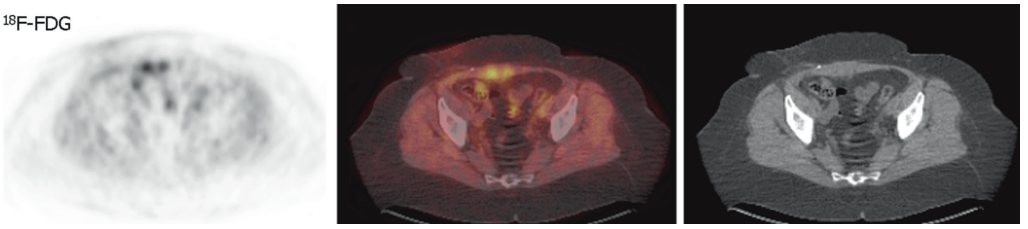

Fig. II.8.5C

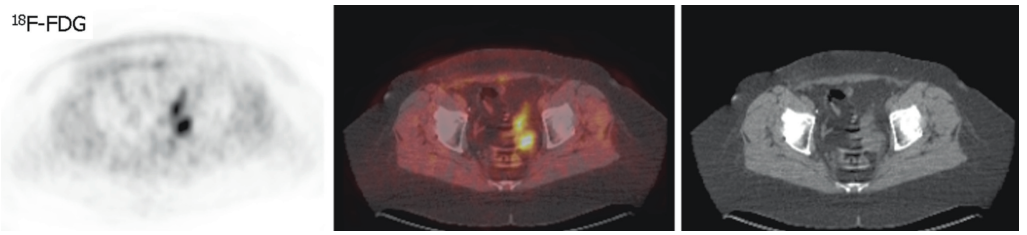

Fig. II.8.5D

Findings

There are multiple foci of increased ^{18}F-FDG activity along the anterior abdominal wall corresponding to slight thickening of the lower rectus muscle (Fig. II.8.5A–C). There is increased ^{18}F-FDG uptake within a soft tissue mass measuring 20 × 33 mm in the left pelvis, localized to the left iliac nodal chain (Fig. II.8.5D).

Discussion

In patients with endometrial cancer, a significantly better prognosis has been noted when recurrences were detected during asymptomatic follow-up, supporting the benefit of surveillance programs in high-risk patients, whereas it seems to be of limited benefit for patients at low risk for recurrent disease.[38] Among patients with asymptomatic recurrent endometrial cancer, pelvic examination and conventional imaging can detect a large number of relapses.[38] Belhocine and colleagues[34] demonstrated that ^{18}F-FDG imaging has a sensitivity, specificity, diagnostic accuracy, PPV, and NPV of 96, 78, 90, 89, and 91%, respectively, for detection of residual or recurrent disease. PET confirmed recurrence initially suspected based on results of other tests in 88% of cases, but detected asymptomatic recurrences in an additional 12% of patients. In 35% of cases, PET significantly altered treatment decisions by detecting otherwise unsuspected distant metastases. Saga and colleagues[35] studied patients with endometrial cancer following therapy for detection of disease recurrence or to assess response to treatment. ^{18}F-FDG imaging had a sensitivity of 100%, specificity of 88%, and accuracy of 93% when evaluated in conjunction with CT/MRI. PET detected unsuspected metastatic disease in 19% of patients and changed the management of 33%. No false-negative result was noted for PET after a minimal follow-up of 5 months, thus suggesting a high NPV for this modality.

Diagnosis

Recurrent endometrial cancer in abdominal wall and metastatic lymphadenopathy in pelvis.

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