Cervical cancer coexisting with small lymphocytic lymphoma detected during positron emission tomography/computed tomography simulation: a case report

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Summary

Background: Positron emission tomography (PET)/computed tomography (CT) simulation in cervical cancer may help radiation oncologists to better define the target volumes. It may also detect extrapelvic lesions and incidental second malignancies, leading to significant changes in treatment management. *Case:* A 63-year-old woman who was deemed inoperable due to carcinoma of the cervical stump extending to the parametria and paraaortic lymph nodes detected on MR images presented for extended field radiotherapy. PET/CT simulation revealed an FDG avid mass in the cervical stump, and an enlarged axillary lymphadenopathy showing moderate FDG uptake. The excisional biopsy was consistent with small lymphocytic lymphoma (SLL). *Conclusion:* In our case, PET/CT simulation not only led to changes in treatment management, but also revealed a very rare coexistence of SLL and invasive squamous cell carcinoma of the cervix.

Key words: PET/CT/simulation; SLL; Uterine cervix.

Introduction

Although many cases of multiple malignant neoplasms involving the female genital tract have been reported, synchronous gynecologic and hematologic malignancies are extremely rare [1, 2]. Synchronous malignancies may also be the reason for misdiagnosis and subsequent treatment. In recent years, functional imaging with positron emission tomography (PET) has proved to be superior to computed tomography (CT) or magnetic resonance (MR) imaging in the diagnosis and staging of many types of cancer. PET scanning can result in a change of staging and thus patient management in 20-30% of cases, mainly due to detection of metastatic disease or nodal involvement. Treatment changes occur most frequently in patients with head and neck cancer, lung cancer and gynecologic malignancies [3].

With the recent availability of hybrid PET/CT scanners where anatomic and functional data are acquired simultaneously and fused subsequently, the detection of target volumes during the treatment planning process in radiation oncology can be augmented. Thus, there is a growing interest in PET/CT based treatment planning. In cervical cancer, the incorporation of functional imaging has the ability to more accurately identify viable tumor cells in the primary cervical tumor and in the nodes of the pelvic and paraaortic regions.

We present the case of a patient with cervical cancer in whom PET/CT simulation revealed a second malignancy and totally altered the treatment management.

Case Report

A 63-year-old woman presented to her gynecologist with postmenopausal vaginal bleeding. She had a history of subtotal hysterectomy due to leiomyomas 20 years before. Physical examination revealed an ulcerative mass in the cervical stump with parametrial involvement. Biopsy was consistent with invasive squamous cell carcinoma. To evaluate for metastatic disease an MR scan of the whole abdomen was performed, which demonstrated multiple lymphadenopathies measuring up to 1.5 cm in diameter in the paraaortic, bilateral internal, external, and obturator areas (Figure 1). In the cervical stump a mass lesion measuring 4.5 cm with involvement of the parametrial space posteriorly and laterally was observed. With these findings the patient was deemed inoperable due to Stage IIB disease with paraaortic metastasis and was referred to our department for definitive radiotherapy.

Our initial plan was to treat the patient with intensity modulated radiotherapy (IMRT) using a simultaneous integrated boost technique to escalate the dose at involved lymph node areas while keeping the dose to the surrounding critical structures at acceptable levels. To better define and delineate the primary target volume in the pelvic and paraaortic region we decided to perform PET/CT simulation.

The patient underwent a PET/CT scan in the supine position. The patient's arms were placed over her chest and her pelvis was immobilized using a dual leg positioner (MEDTEC, Orange City, IO, USA). For planning purposes the scan was first acquired from the diaphragm to 3 cm below the ischial

Revised manuscript accepted for publication November 5, 2007

Fig. 1

Figure 1. — MR scan of the pelvis showing enlarged lymph nodes.

Fig. 2

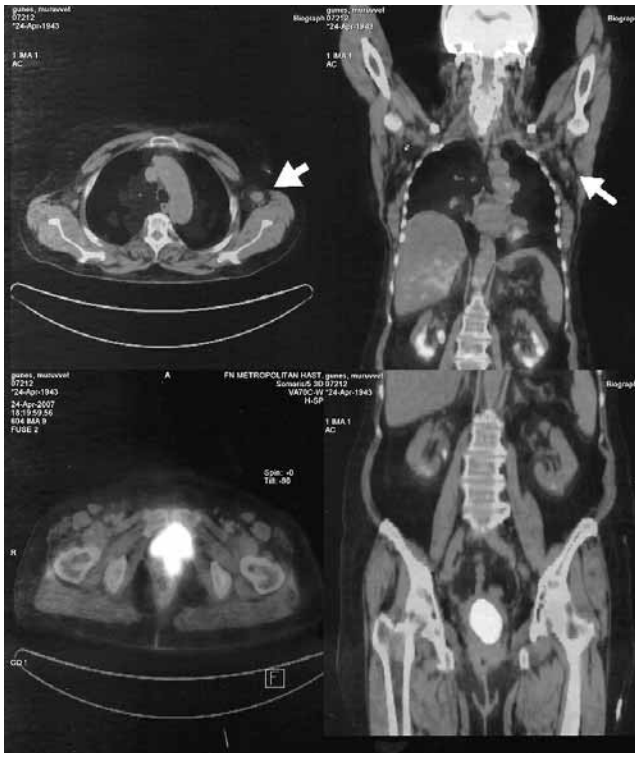

Figure 2. — PET/CT scan of the patient revealed a hypermetabolic mass in the cervical stump, but the pelvic and paraaortic lymph nodes were not FDG avid. In addition, there were enlarged axillary lymph nodes with moderate FDG uptake.

tuborosities, and then a whole body scan was obtained for metastatic workup. The PET/CT scan revealed no uptake in the pelvic and para-aortic enlarged lymph nodes while showing a hypermetabolic mass at the cervical stump. Additionally, multiple enlarged bilateral axillary lymph nodes were detected on CT scans from which only a left-sided lymph node showed moderate F18-fluoro-2-deoxy-D-glucose (FDG) uptake (Figure 2). Therefore, an excisional biopsy of the left sided enlarged axillary lymph node was performed, which was consistent with diffuse small lymphocytic non-Hodgkin's lymphoma (SLL). Immunohistochemical staining showed positivity for CD 20, CD 5, CD 23, and negativity for CD 3 with a KI 67 index of 20%. Immunophenotyping using blood revealed no abnormal cell clusters, nor any increase in monoclonal antibodies. Her LDH, β2-microglobulin, and complete blood count levels were within normal limits, and she was considered to have Stage IIIA indolent lymphoma. The patient was discussed at the monthly meeting of the Istanbul Lymphoma Group and it was decided that she did not need any further treatment for SLL till symptomatic progression.

We treated her for Stage IIB cervical cancer with pelvic IMRT to 45 Gy in 1.8 Gy fractions with concurrent weekly cisplatin. She tolerated the treatment well and had a good response at the end of treatment. She then received high-dose rate intacavitary treatments. The total dose to point A, including both external beam and brachytherapy, was 75 Gy.

Discussion

In the case presented, PET/CT aided treatment planning revealed a very rare, incidental coexistence of cervical cancer and SLL, and led to changes in the management of the patient.

MR imaging plays an important role in the staging of cervical cancer. Assessment of metastatic lymphadenopathy in patients with endometrial and cervical carcinoma on MRI is based on the size of the lymph nodes. Nodes with a size exceeding 1 cm short axis diameter are considered pathologic [4]. Signal intensity charecteristics have not been useful in differentiating metastatic from hyperplastic lymphadenopathy in the pelvis. Our patient had multiple enlarged lymphadenopathies in the pelvis and paraaortic region with the greatest diameter of 1.5 cm. Therefore, they were considered metastatic and the patient was referred to the Radiation Oncology Department for extended field radiotherapy.

Functional imaging with FDG has been increasingly used for staging purposes in many different tumor sites. FDG is an analog of glucose and is rapidly absorbed by cancer cells that possess an increased glucose need compared with non malignant cells because of greater blood flow, glucose phosphorylation, and cell membrane transporters [5]. Applied in the clinic, PET can be useful for tumor staging, prediction of tumor response, selection and delineation of target volumes in radiotherapy planning, assessment of tumor response to treatment, and for the detection of early recurrences [6]. In cervical cancer the superior specifity of PET support the inclusion of FDG positive nodes into target volumes during the treatment planning process. In addition, its ability to detect extrapelvic lesions may help to determine the appropriate treatment fields and change treatment management [3].

Grigsby *et al*. compared PET/CT and CT in the staging of cervical cancer and demonstrated that PET studies

detected abnormalities in 99% of patients versus 76% imaging these cancers using CT. PET revealed abnormal pelvic/paraaortic nodes in 67%/21% of patients versus 20%/7% using CT scans, respectively. Total-body PET scans were also able to detect occult metastatic disease in the supraclavicular region in 8% of patients [7]. Although based on a limited number of patients, other investigators also reported that PET was much more specific than CT or MRI in detecting paraaortic lymph node metastases [8, 9].

FDG uptake in lymphoma patients is correlated to histologic grade and proliferative activity. There is limited and conflicting data in the literature about the sensitivity of FDG-PET in low-grade SLL. Najjar *et al*. reported sensitivity and specifity for FDG-PET of 87% and 100%, respectively, in 36 indolent lymphoma patients [10]. In contrast, Jerusalem *et al*. studied 36 patients with low-grade NHL [11]. PET detected 40% more abnormal lymph node areas than conventional staging in follicular lymphoma, but was inappropriate for the staging of small lymphocytic lymphoma for which it detected less than 58% of abnormal lymph node areas.

In the present case the pathologic paraaortic and pelvic lymph nodes which were revealed by MR imaging were not found FDG avid during the PET/CT planning process. However, the whole body PET/CT scan showed additional bilateral axillary lymphadenopathies from which a left-sided scan showed moderate FDG uptake. The excisional biopsy was consistent with indolent lymphoma. Because of the high node specifity of FDG-PET in cervical cancer, and low specificity in detecting abdominal and pelvic lymph nodes in small lymphocytic lymphoma we decided that the pelvic and paraaortic lymphadenopathies originated from lymphoma, rather than cervical cancer. The patient had two primaries, a locally advanced cervical stump cancer and indolent lymphoma involving supra-and infradiaphragmatic sites.

Patients with SLL have been reported to have an increased risk of developing a secondary malignant tumor due to immunosuppression which may be related to B-cell dysfunction or to chemotherapeutic agents. The most frequent sites of secondary malignancy are the lung, gastrointestinal tract and prostate. Uterine tumors account for about 1% of secondary tumors associated with SLL. Our literature search resulted in two case reports of the synchronous appearance of uterine tumors and SLL, one in the international and the other one in the national database. Mikami *et al*. [1] reported the case of a woman who was followed for stage 0 SLL who developed invasive squamous cell carcinoma of the uterine cervix. The microscopic evaluation of the hysterectomy specimen established the diagnosis of invasive squamous carcinoma of the cervix and monotonous populations of small lymphoid cells with proliferative centers, which were consistent with SLL, in the cervix as well as parametrium. The prognosis was dismal, and the patient died of disseminated squamous cell carcinoma. In our patient the cervical stump was involved by a pure squamous cell carcinoma. Öksüz *et al*. [2] described a patient with the diagnosis of endometrial adenocarcinoma, in whom the CT scan of the abdomen revealed multiple lymphadenopathies. It was the detection of multiple, mobile, peripheral lymphadenopathies on physical examination which led the authors to excisional biopsy and the diagnosis of concomittant SLL. The prognosis was also dismal, and the patient died of disseminated disease 23 months after the initial diagnosis.

In conclusion, the use of PET/CT aided treatment planning is a hot topic in radiation oncology. Although it is recommended to select the target volumes for tumor types like non-small cell lung cancer and esophageal cancer where FDG-PET shows superior specificity to CT, for other sites the data are still immature. For cervical cancer, especially with involved pelvic and paraaortic lymph nodes, PET/CT simulation may help in directing more focused external beam irradiation to these nodes. PET/CT scanning during the treatment planning process may also detect extrapelvic abnormalities and incidental secondary primaries leading to significant changes in treatment management, as was the case in our patient.

References

[1] Mikami Y., Maehata K., Fujiwara K., Sasano H.: "Squamous cell carcinoma of the uterine cervix in association with stage 0 chronic lymphocytic leukemia/small lymphocytic lymphoma". *Gynecol. Oncol.,* 2004, *92,* 974.

[2] Öksüz D.Ç., Şahinler İ., Atkovar G., Ferhanoğlu B, Okkan S.: "Synchronous endometrium cancer and chronic lymphocytic leukemia: a case report" (in Turkish). *Türk. Onkoloji Dergisi,* 2003, *18,* 118.

[3] Gregoire V., Haustermans K., Geets X., Roels S, Lonneux M.: "PET based treatment planning in radiotherapy: A new standard?". *J. Nucl. Med.,* 2007, *48,* 68S.

[4] Brown M.A., Kubik-Huch R.A., Reinhold C., Semelka R.C.: "Uterus and Cervix". In: Semelka R.C. (ed.). Abdominal-Pelvic MRI, second edition. New Jersey: John Wiley and Sons, Inc., 2006, 1251.

[5] Smith T.: "FDG uptake, tumor characteristics, and response to therapy: A review". *Nucl. Med. Commun*., 1998, *19,* 97.

[6] Rohren E.M., Turkington T.G., Coleman R.E.: "Clinical application of PET in oncology". *Radiology,* 2004, *231*, 305.

[7] Grigsby P.W., Siegel B.A., Dehadashti F.: "Lymph node staging by positron emission tomography in patients with carcinoma of the cervix". *J. Clin. Oncol.,* 2001, *19*, 3745.

[8] Reinhardt M.J., Ehritt-Braun C., Vogelgesang D., Ihling C., Högerle C., Mix M. *et al*.: "Metastatic lymph nodes in patients with cervical cancer: Detection with MR imaging and FDG PET". *Radiology*, 2001, *218*, 776.

[9] Sugawara Y., Eisbruch A., Kosuda S., Recker B.E., Kison P.V., Wahl R.L.: "Evaluation of FDG PET in patients with cervical cancer". *J. Nucl. Med.,* 1999, *40*, 1125.

[10] Najjar F., Hustinx R., Jerusalem G., Filet G., Rigo P.: "PET for staging low grade NHL". *Cancer Biother Radiopharm.,* 2001, *16,* 297.

[11] Jerusalem G., Beguin Y., Najjar F., Hustinx R., Fassotte M.F., Rigo P. *et al*.: "Positron emission tomography (PET) with 18F-Fluorodeoxyglucose (18F-FDG) fort he staging of low grade non-Hodgkin's lymphoma (NHL)". *Ann. Oncol.,* 2001, *12,* 825.

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