Clinical, pathological and ^{18}F-FDG PET/CT findings in synchronous primary vaginal and endometrial cancers

Burcak Yilmaz Gunes[1] **MD,**
Ozgur Akbayır[2] **MD,**
Emre Demirci[1] **MD,**
Ipek Ozaydin[3] **MD**

1. Istanbul Sisli Hamidiye Etfal Research and Training Hospital, Nuclear Medicine Department, Istanbul, Turkey
2. Istanbul Kanuni Sultan Suleyman Research and Training Hospital, Obstetrics and Gynecology Department, Istanbul, Turkey
3. Istanbul Kanuni Sultan Suleyman Research and Training Hospital, Pathology Department, Istanbul, Turkey

Keywords: - Vaginal carcinoma
- Endometrial carcinoma
- ^{18}F-FDG PET/CT

Corresponding author:
Burcak Yilmaz Gunes MD
Halaskargazi Cad. Etfal Sk.
34371 Şişli / İstanbul
Phone: +902123735223
Fax: +90 212 224 07 72
drburcak@gmail.com

Received:
28 March 2016
Accepted revised:
1 May 2016

Abstract
Synchronous primary gynecologic malignancies are infrequently seen. In this report, we describe the clinical, pathological and fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) findings of a patient with synchronous primary vaginal and endometrial cancers. To our knowledge, this is the first such case described in the literature.

Hell J Nucl Med 2016; 19(2): 170-172 *Epub ahead of print: 22 June 2016* *Published online: 2 August 2016*

Introduction

Multiple primary malignant neoplasms (MPMN) are described as two or more different malignancies in the same patient [1, 2]. Different detection time help to classify these cancers in two categories: synchronous or metachronous malignacies [3]. Two or more primary malignacies diagnosed within 6 months are synchronous whereas if detected within a period of >6 months, are metachronous [4]. Synchronous MPMN are less frequent than metachronous MPMN [3]. The incidence of multiple primary malignant neoplasms has been reported between 0.73%-11.7% [5]. It has also been reported that, 13.5% of MPMN are genitourinary tumors [6]. Synchronous primary female genital tract malignancies are not frequent and 50%-70% of them arise from the endometrium and the ovaries [7]. It is usually difficult to evaluate the stage of each cancer and to decide for the optimal treatment strategy for each one of them. In developing countries the most common gynecological malignancy is endometrial carcinoma [8]. On the other hand, only about 3% of female genital tract cancers are vaginal cancers [9]. In the diagnosis, in staging therapy response and in relapse detection of female genital tract malignancies, fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) has been widely and preferably used [10]. Here we report a unique case of synchronous endometrial and vaginal cancers, with its clinical, pathological and ^{18}F-FDG PET/CT findings showing multiple metastases.

Case Report

A 62 years old woman (155cm height and 85kg body weight) was admitted to our hospital with a history of postmenopausal bleeding and a pelvic mass. From her previous medical history she reported hypertension and hypothyroidism. She had no history of surgical procedures and no family history of malignancies. Her vital signs were unremarkable. On gynecologic examination, a vegetative tumor of 3cm diameter in the distal anterior vaginal wall was detected extending to the vulva. Cervical examination by speculum was normal. Uterus and ovaries by ultrasonographic examination had no abnormality, except endometrial ECO was thick (15mm). Endometrial sampling by dilatation curettage diagnosed endometrial adenocarcinoma with stromal invasion and vaginal excision biopsy showed squamous cell carcinoma with lympho vascular invasion (Figure 1).

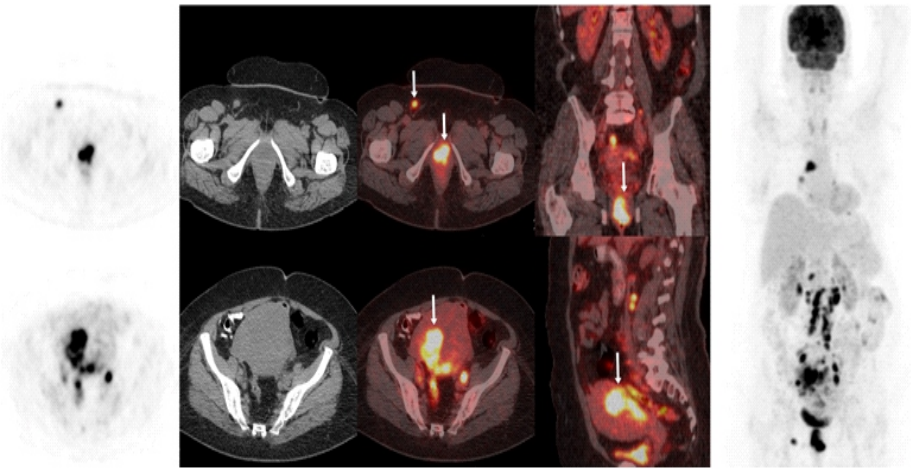

Figure 2. Fluorine-18-FDG PET/CT examination with highly increased ^{18}F-FDG uptake in the vagina and the uterine cavity with multiple metastases, easily visible on the MIP image (arrows).

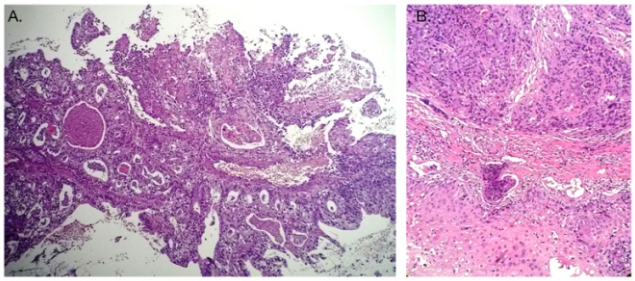

Figure 1. Pathological examination. A): Endometrioid adenocarcinoma with stromal invasion findings. B): Squamous cell carcinoma of the anterior vaginal wall.

For further evaluation contrast enhanced magnetic resonance imaging (MRI) with T1 weighted and T2 weighted fat saturated images were performed on the whole abdomen and showed a vaginal mass on the anterior wall with hypointensity on T1 weighted and hyperintensity on T2 weighted images with partial contrast enhancement, without any evidence of invasion throughout the fornix and uterine collum. On the anterior myometrium an intramural myoma and on the uterine fundus a polipoid formation were found. Many lymph nodes on the para-aorta-caval lymphatic chain up to 1cm diameter were reported.

For further evaluation a ^{18}F-FDG PET/CT scan was performed. In the uterine cavity highly elevated metabolic activity with a maximum standardized uptake value (SUVmax) up to 21.8 and a mass lesion of 38mm diameter on the anterior wall of the vagina with highly elevated metabolic activity (SUVmax: 22.0) were observed. Multiple hypermetabolic metastatic lymph nodes with SUVmax up to 16.0 on para-aorto-caval, bilateral iliac chain, bilateral inguinal region and bilateral parametrial areas were reported. Some skeletal metastases in the T4 vertebra with SUVmax: 13.6, in bilateral hilar hypermetabolic lymph nodes with SUVmax: 7.0, in bilateral mildly hypermetabolic subsantimetric lung nodules with SUVmax: 2.1 and some focally elevated metabolic activities with SUVmax: 4.8 in the liver were seen. Palliative chemotherapy was subsequently started (Figure 2).

Discussion

At the time of diagnosis it is important to differentiate two synchronous tumors from metastatic disease. It is better for clinicians to keep in mind that although it is very rare, synchronous tumors can be detected and if any suspicion arises, as in our case, histopathological verification must be performed.

Dubeau L. (2008) suggested that the epithelia of the peritoneal surface, uterus, cervix, Fallopian tubes and ovaries share molecular receptors (secondary Mullerian system) responding to carcinogenic stimulus and may lead to the development of synchronous primary tumors [11]. This could only be explained if synchronous tumors are of similar and not of dissimilar histology [12].

For optimal primary therapy, in the pretreatment work-up it is better to perform both MRI, in which parametral extension and tumor size can be best detected and ^{18}F-FDG PET/CT imaging, in which lymphadenopathy and distant metastases can be seen [13, 14].

Vaginal cancer is a very rare gynecological cancer. Lymph node metastases, histology, size and age are important prognostic factors influencing the choice of treatment. The most often reported histopathology type is squamous cell carcinoma, similar to our case. Human papilloma virus is the most common risk factor. For advanced cancers radiation therapy with simultaneous combined chemotherapy is the treatment of choice [15].

Endometrial cancer is the most common gynecological malignancy detected in developing countries like Turkey [16]. During planning surgery, pretreatment imaging is preferred [13]. The most important risk factors for overall survival are surgical stage, histology, depth of myometrial

invasion, cervical involvement, lymph-node metastases, and lymphovascular space invasion [17]. Fluorine-18-FDG PET/CT is reported to be more sensitive than CT or MRI for the detection of nodal metastases [18-19]. Furthermore, ^{18}F-FDG PET/CT is used to identify unsuspected distant metastases of endometrial cancer [20]. Walentowicz-Sadlecka M et al. (2014) reported that in more advanced stages of endometrial cancer according to the international Federation of Gynecology and Obstetrics-FIGO, higher SUVmax values similar to our case were observed [21].

In conclusion, we have reported a case with synchronous primary vaginal and endometrial cancer in a 61 years old woman, the first such case reported, and described its clinical, imaging and pathology findings.

Bibliography

1. Da M, Peng L, Zhang Y et al. Synchronous double primary gastric and endometrial cancer: a case report and literature review. *Intern J Clin Experiment Pathol* 2015; 8(7): 8573-8.
2. Warren S, Gates O: Multiple primary malignant tumors: A survey of the literature and a statistical study. *Am J Cancer* 1932; 16: 1358-14.
3. Pastore AL, Palleschi G, Leto A et al. A novel combination of triple metachronous malignancies of the kidney, oropharynx and prostate: A case report. *Oncol Lett* 2015 Aug; 10(2): 917-20.
4. Moertel CG. Multiple primary malignant neoplasms: Historical perspectives. *Cancer* 1977; 40(Suppl): 1786-92. 5. Demandante CG, Troyer DA, Miles TP. Multiple primary malignant neoplasms: case report and a comprehensive review of. *Am J Clin Oncol* 2003; 26: 79-83.
6. Ray P, Sharifi R, Ortolano V et al. Involvement of the genitourinary system in multiple primary malignant neoplasms: A review. *J Clin Oncol* 1983; 1: 574-81.
7. Gutiérrez-Palomino L, de los Reyesa JMR, Pareja-Megíaby MJ et al. Tumores triple sincrónicos ginecológicos. Reporte de un caso. *Cirugía y Cirujanos* doi:10.1016/j.circir.2015.06.015.
8. Kara T, Kara PO, Gedik GK et al. Splenic and multiple abdominal metastases of endometrial carcinoma detected with FDG-PET/CT. *Rev Esp Med Nucl Imagen Mol* 2012 Jan-Feb; 31(1): 31-3. doi: 10.1016/j.remn.2011.04.005.
9. Rajaram S, Maheshwari A, Srivastava A. Staging for vaginal cancer. *Best Pract Res Clin Obstet Gynaecol*. 2015 Aug; 29(6): 822-32. doi:10.1016/j.bpobgyn.2015.01.006.
10. Maldona A, Gonzalez-Alenda FJ, Alonso M et al. PET/CT in clinical oncology. *Clin Transl Oncol* 2007; 9: 494-505.
11. Dubeau L. The cell of origin of ovarian epithelial tumors. *Lancet Oncol* 2008; 9: 1191-7.
12. Lim YK, Padma R, Foo L et al. Survival outcome of women with synchronous cancers of endometrium and ovary: a 10 year retrospective cohort study. *J Gynecol Oncol* 2011 Dec; 22(4): 239-43. doi: 10.3802/jgo.2011.22.4.239.
13. Lee SI, Catalano OA, Dehdashti F. Evaluation of gynecologic cancer with MR imaging, ^{18}F-FDG PET/CT, and PET/MR imaging. *J Nucl Med*. 2015 Mar; 56(3): 436-43.doi: 10.2967/jnumed.114. 145011. Epub 2015 Jan 29. Review.
14. Pandharipande PV, Choy G, del Carmen MG et al. MRI and PET/CT for triaging stage IB clinically operable cervical cancer to appropriate therapy: decision analysis to assess patient outcomes. *Amer J Radiol* 2009; 192: 802-14.
15. Shrivastava S, Agrawal G, Mittal M et al. Management of Vaginal Cancer. *Rev Recent Clin Trials* 2015; 10(4): 289-97
16. Gultekin M, Boztaş G. *Türkiye Kanser İstatistikleri. T.C Sağlık Bakanlığı Türkiye Halk Sağlığı kurumu*. January 2014; 19.
17. Quick CM, May T, Horowitz NS et al. "Low grade, low-stage endometrioid endometrial adenocarcinoma: a clinicopathologic analysis of 324 cases focusing on frequency and pattern of myoinvasion" *Inter J Gynecol Pathol* 2012; 31(4): 337-43.
18. Antonsen SL, Jensen LN, Loft A et al. MRI, PET/CT and ultrasound in the preoperative staging of endometrial cancer: a multicenter prospective comparative study. *Gynecol Onco*l 2013; 128: 300-8. 21.
19. Signorelli M, Guerra L, Buda A et al. Role of the integrated FDG PET/CT in the surgical management of patients with high risk clinical early stage endometrial cancer: detection of pelvic nodal metastases. *Gynecol Oncol*. 2009; 115(22): 231-5.
20. Picchio M, Mangili G, SamanesGajate AM et al. High-grade endometrial cancer: value of ^{18}F-FDG PET/CT in preoperative staging. *Nucl Med Commun* 2010; 31: 506-12.
21. Walentowicz-Sadlecka M, Malkowski B, Walentowicz P et al. The preoperative maximum standardized uptake value measured by ^{18}F-FDG PET/CT as an independent prognostic factor of overall survival in endometrial cancer patients. *Biomed Res Int* 2014; 2014: 234813. doi:10.1155/2014/234813.