Granulosa cell tumor and concurrent endometrial cancer with ^{18}F-FDG uptake

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Abstract
The findings and the role of fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) for the diagnosis of ovarian granulosa cell tumor (OG) are described. *We present the pre-operative findings* of ^{18}F-FDG PET/CT scan of a case of OG concurrent with endometrium cancer and endometrial hyperplasia, which revealed a 48mm mass demonstrating mild increased metabolic activity on the right ovary. Total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed. *Frozen and paraffin-enbeded sections* showed an encapsulated OG. There were few mitoses. There was concurrent atypical endometrial hyperplasia. *In conclusion*, we reported a case of an encapsulated OG, which showed mild uptake of the ^{18}F-FDG with concurrent endometrial cancer. There has been only one report of ^{18}F-FDG findings in primary ovarian granulosa cell tumor, similar to ours.

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Introduction

Ovarian granulosa cell tumors (OG) are the most common sex related cord stromal tumors accounting for about 2%-5% of all ovarian neoplasms [1]. The adult type of OG (ATOG) accounts for 95% of all OG. Estrogen production of these tumors is responsible for most of the non-mass symptoms of these patients. Atypical adenomatous hyperplasia is concurrently found in 42%-55%, and invasive adenocarcinoma in 13%-22% of these cases [2, 3]. The OG are low grade malignancies and with indolent growth. Ninety percent of ATOG are diagnosed at stage I.

Fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) has been broadly used in the diagnosis, staging, response evaluation, and relapse monitoring of various types of gynecologic malignancies [4]. In the differential diagnosis of ovarian cancer from benign tumors, ^{18}F-FDG PET/CT shows high accuracy; sensitivity 87%, specificity 100% [5]. The ATOG have a low level of proliferation and metabolic activity, and ^{18}F-FDG PET/CT may not be diagnostic. We present the preoperative findings of ^{18}F-FDG PET/CT scan of an ATOG tumor concurrent with endometrium cancer and hyperplasia.

Presentation of the case

We report the case of a 40 years old lady presenting with irregular menstural cycles and menorraghia. Her previous medical history was normal; she had no history of serious illnesses or surgical procedures and no family history of malignancies. Her vital signs and gynecologic examination were unremarkable. On ultrasound examination, a 6x5cm unilocular solid mass with regular borders was diagnosed in her right ovary. There was no free fluid in the abdomen, and the left ovary was evaluted as normal. Endometrial thickness was 12mm and myometrium was homogenous. In her laboratory examination, the tumor marker of Ca125 was normal: 7U/mL. Endometrial sampling by dilatation curettage yielded complex atypical endometrial hyperplasia and grade 1 endometrial adenocarcinoma.

A ^{18}F-FDG PET/CT scan was performed for possible detection of the tumor and of metastases. There was a 48mm mass on her right ovary demonstrating mild elevated metabolic activity with maximum standardized uptake value (SUVmax: 3.29). No other abnormality was detected on the ^{18}F-FDG PET scan (Fig. 1A and 1B).

Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. Frozen sections reported a right OG with intact capsule. The number of mitoses was small (Fig. 2A). There was also endometrial atypical hyperplasia-carcinoma. A thorough explo-

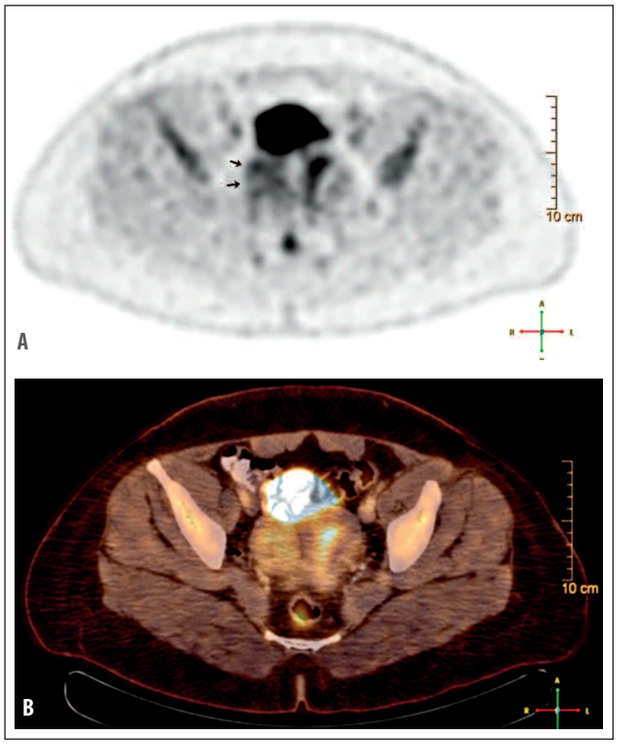

Figure 1. A-B: PET and ^{18}F-FDG PET/CT imaging showing the ovarian mass with mildly increased ^{18}F-FDG uptake on the right (arrows).

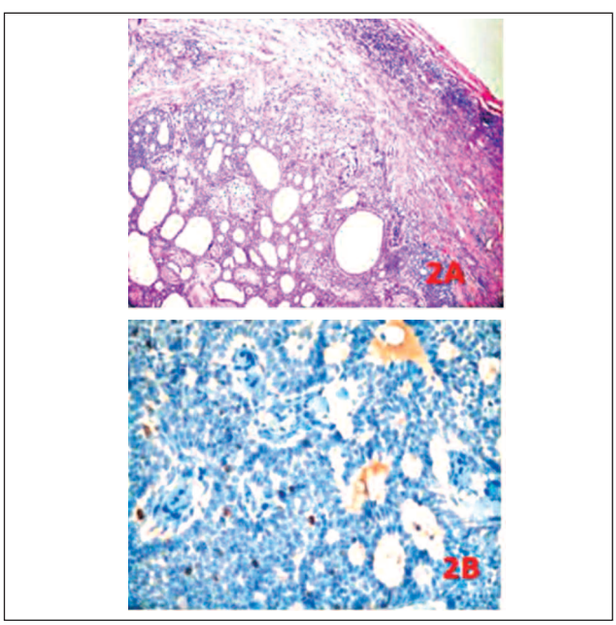

Figure 2. Pathological examination of the OG cell tumor. Although there were few mitoses and the grade of OG was low, there was high SUVmax uptake in the ^{18}F-FDG PET/CT scan. A: Granulosa cell tumor, well differentiated with an intact capsule (H&E, x100). B: Low proliferative activity in the OG tumor with immunohistochemical Ki-67 staining (Ki-67, x200).

ration of the upper abdomen, pelvis and retroperitoneum found no suspicious lymph nodes or lesions. Omental biopsy, peritoneal biopsies and cytological evaluation were performed for staging. Paraffin-embedded and frozen sections were examined.

In order to evaluate the moderate to high SUV of the tumor, Ki-67 was tested. Immunohistochemical analysis of Ki-67 revealed a low proliferation index (Fig. 2B).

Discussion

The OG tumors have the tendency for late recurrence, usually after 5 years. The ^{18}F-FDG PET/CT imaging technique offers an opportunity to detect ovarian tumors [6-8] and specifically to detect active metabolic processes and morphological features of the OG tumors [9-12].

The distribution by others of SUVmax in malignant, borderline malignant, and benign ovarian tumors studied in 160 patients, showed only one incidentally diagnosed OG tumor [7]. In this study, positive ^{18}F-FDG uptake values were higher in malignant ovarian tumors, in serous adenocarcinoma subtype, and in endometroid adenocarcinomas. However, in clear cell and mucinous adenocarcinomas, ^{18}F-FDG uptake values were low. Positive ^{18}F-FDG uptake (SUVmax>2.9) was seen in OG tumors [7]. In our case, positive ^{18}F-FDG uptake (SUVmax: 3.29) was seen in the OG tumor (Fig. 2). In recurrent OG tumors, studies have shown a higher ^{18}F-FDG uptake [8]. The tumor biology and activity may be different in recurrent OG than in the primary tumor and these discrepancies between primary and recurrent tumor might explain the different ^{18}F-FDG PET findings in some studies.

Ki-67 is assessed as a proliferation index. Higher levels of Ki-67 are related with high uptake in ^{18}F-FDG PET/CT [12]. Ki-67 proliferation index is reported to be higher in recurrent OG. Ki-67 proliferation index in our case was found to be at low levels. Thus, OG may present as a solid or cystic tumor in preoperative ultrasonography and the SUVmax might be different for each type of the tumor. The relation of SUVmax with tumor grading is yet to be defined. Currently, the most important prognostic factor for OG is the stage of the disease. Patients at high risk, stage IC disease are usually associated with a large tumor (≥10-15cm) and a poorly differentiated tumor, high mitotic index, or even tumor rupture. Ii seems that in stage I disease SUVmax levels in ^{18}F-FDG PET/CT should be further assessed as a prognostic factor.

In conclusion, we reported a case of an ovarian encapsulated granulose cell tumor, which showed mild uptake of the ^{18}F-FDG with concurrent endometrial carcinoma. There has been only one report of ^{18}F-FDG findings in incidentally found primary ovarian granulosa cell tumor, similar to ours.

The authors declare that they have no conflicts of interest.

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Painting on a ceramic vessel by ancient Greek painter Douris (485-480 BC), now in Antikenmuseum, Berlin. A rare scene from an ancient teaching school in Athens. In the middle sits the teacher, who corrects with a stylus the homework-book roll of a young student standing in front of him. On the right sits the "paedagogue". On the left sits another teacher, playing and teaching the flute to a student. Above him are hanging a lyra, a book roll and a cross.