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Pathological Analysis of Non-cancerous Lesion in Breast with Abnormal FDG Absorption in 18F-FDG PET/CT Test

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Abstract. 18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) (18F-FDG-PET/CT) is a sensitive molecular imaging modality capable of diagnosing breast cancer by means of increased FDG uptake in growing cancer cells. FDG uptake within cells mainly depends on cellular metabolic activity and the number of glucose transporters. However, this mechanism is not specific to cancer cells, for FDG can accumulate in inflammatory cells and benign processes causing false-positive findings. In this study, we analyzed the non-cancerous lesion diagnosed by histology which showed abnormal absorption of FDG in 18F-FDG PET/CT test and demonstrated the image feature of these cases. We undertook a retrospective review of data from 373 women who had an 18F-FDG PET/CT test and analyzed the false positive results in 48 cases according to final pathological results between January 2016 and April 2018. Among these cases, 296 showed abnormal FDG absorption and were histological diagnosed after surgery. Of 296 patients, who had abnormal FDG absorption, 248 cases were histological diagnosed with breast carcinoma. Fibroadenoma and purulent inflammation accounted for 33.3% and 35.4% of all 48 non-cancerous cases following by intraductal papilloma with the incident of 12.5%. In purulent inflammation cases the max diameter of tumor showed significantly larger than others ($P<0.05$), and the max diameter of lesion in other diseases showed no significantly differences. 18F-FDG PET/CT results showed that the value of SUVmax in purulent inflammation was significantly higher than that in other diseases ($P<0.05$) and adenomyoepithelioma, cyst with ductal ectasia and adenosis were showed with a lower SUVmax ($P<0.05$). In conclusion, despite the low false positive rate 18F-FDG PET/CT is of great value for preoperative evaluation of breast lesion. In the non-cancerous cases which had an indication of carcinoma in 18F-FDG PET/CT test, the most common diagnosis were fibroadenoma, purulent inflammation and intraductal papilloma.

Introduction

Breast cancer is one of the most common malignant tumors in women, which affects women's health seriously and may even be life-threatening[1]. Early detection of breast cancer

is considered to be crucial in determining the choice of therapy, as well as a patient's prognosis and chances for survival[2]. Mammography (MM), ultrasound (US), computed tomography (CT), and magnetic resonance imaging (MRI) are commonly used in clinical practice for detecting primary tumors and staging breast cancer[3]. Besides, with the development of technology in imaging advanced MRI and CT and the introduction of other modalities in breast imaging including optical imaging, single photon emission tomography (SPECT), and positron emission tomography (PET) may help to offer a more accurate and specific diagnosis for breast cancer[4]. 18F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) (18F-FDG-PET/CT) is a sensitive molecular imaging modality capable of diagnosing breast cancer by means of increased FDG uptake in growing cancer cells[5]. FDG is transported by glucose transporters, metabolized by the enzyme hexokinase and builds up in cancer cells. FDG uptake within cells mainly depends on cellular metabolic activity and the number of glucose transporters. However, this mechanism is not specific to cancer cells[6]. FDG can accumulate in inflammatory cells and benign processes, causing false-positive findings [7]. In this study, we analyzed the non-cancerous lesion diagnosed by histology which showed abnormal absorption of FDG in 18F-FDG PET/CT test and demonstrated the image feature of these cases.

Materials and Methods

Patients

The study was conducted with the approval of the ethics committee for clinical research at China-Japan Union Hospital of Jilin University. Written informed consent was waived for each patient for this study. We undertook a retrospective review of patient data for 373 women who had an 18F-FDG PET/CT test and analyzed the false positive results in 48 cases according to final pathological results between January 2016 and April 2018.Among these cases, 296 showed abnormal FDG absorption and were histological diagnosed after surgery. The clinical characteristics of 296 patients were showed in Table 1.

Table 1. Clinical character of 296 patients with abnormal FDG absorption.

		Diagnosed with Cancer	Diagnosed with non-cancer
Cases		248	48
Age		48±6.8	44.7±5.5
Menstruation	menstruation	157	39
	menelipsis	91	9
Clinical TNM stage	I	36	
	II	112	
	III	95	
	IV	5	
Subtype	Luminal A	54	
	Luminal B	127	
	Her-2 overexpression	60	
	Triple negative	7	

FDG PET/CT Protocol and Image Analysis

18F-FDG-PET/CT was performed using a PET/CT scanner (Siemens Biograph Duo LSO, Siemens Medical Solutions USA Inc., Malvern, PA). Noncontrast CT was used for attenuation correction and anatomic coregistration were performed under free breathing. Normal fasting blood glucose levels 150 mg/dL were a standard requirement for imaging in all patients. Whole body scanning was performed 100 minutes after FDG injection. PET data were acquired in 3-D mode on a 128×128 matrix (slice thickness, 5mm). The acquisition time for PET imaging was 2 minutes per table position. PET images were reconstructed using standard vendor- provided reconstruction algorithms. All acquired images were interpreted by 2 radiologists with years of experience in nuclear medicine. Maximum standardized uptake value, a semiquantitative measure of FDG uptake, was most commonly reported.

Statistical Analysis

Sensitivity and specificity were determined on the basis of number of patients, not number of lesions. A Student paired t test was used to compare pre- and post-treatment SUVmax values in the ocular adnexal lesion. These values were reported as mean±standard deviations. Differences were assessed using a 2-sided analysis. P-values<0.05 were considered statistically significant. All statistical analyses were performed using JMP statistical software v 10.0.2 (SAS Institute Inc., Cary, NC).

Results

Of 296 patients, who had abnormal FDG absorption, 248 cases were histological diagnosed with breast carcinoma and 48 cases were non-cancerous disease including fibroadenoma, intraductal papilloma, adenomyoepithelioma, purulent inflammation, cyst with ductal ectasia, adenosis, tuberculosis and fibroadenoma with inflammation. We focused on the 48 cases with false positive FDG absorption, and the pathological results and 18F-FDG PET/CT of these patients were showed in Table 2.

Fibroadenoma and purulent inflammation accounted for 33.3% and 35.4% of all cases following by intraductal papilloma with the incident of 12.5%. In purulent inflammation cases the max diameter of tumor showed significantly larger than other cases (P<0.05).The max diameter of lesion in other diseases showed no significantly differences. 18F-FDG PET/CT results showed that the value of SUVmax in purulent inflammation was significantly higher than that in other diseases (P<0.05), and adenomyoepithelioma, cyst with ductal ectasia and adenosis were showed with a lower SUVmax.

Table 2. Histological results of 48 cases with false positive FDG absorption in PET/CT test.

Pathological result	Number(ratio%)	Max diameter of tumor (X±SD)	SUVmax (X±SD)
Fibroadenoma	16(33.3%)	1.3±0.3	4.2±0.6
Intraductal papilloma	6(12.5%)	1.0±0.2	4.1±0.5
Adenomyoepithelioma	2	1.1	2.1±0.4
purulent inflammation	17(35.4%)	3.2±1.2*	13.2±2.2*
Cyst with ductal ectasia	1	0.7	1.8
adenosis	3	0.8±0.2	2.6±0.7
Tuberculosis	1	1.0	6.6
Fibroadenoma with inflammation	2	1.3	4.6

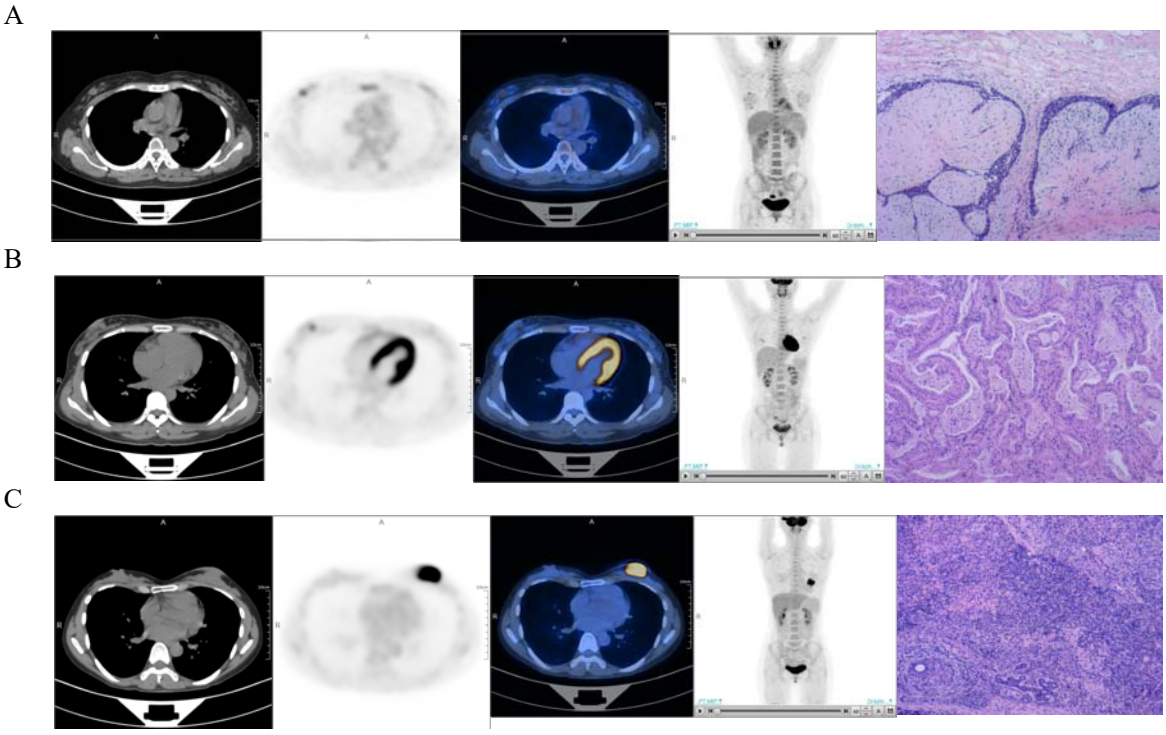

Figure 1. Patients with positive result of 18F-FDG PET/CT and diagnosed with benign lesion pathologically **(A)** a 39-year-old female who has been histological diagnosed with fibroadenoma on her right breast. 18F-FDG PET/CT showed hypermetabolic masses with a max diameter of 1.2cm and a max SUV of 4.55**.(B)** A 35-year-old female who has been histological diagnosed with intraductal papilloma on her right breast. 18F-FDG PET/CT showed hypermetabolic masses with a max diameter of 1.0cm and a max SUV of 4.17. **(C)** A 38-year-old female who has been histological diagnosed with purulent inflammation on her left breast. 18F-FDG PET/CT showed hypermetabolic masses with a max diameter of 2.2 cm and a max SUV of 19.93.

Discussion

Positron emission tomography (PET) is an imaging method that provides insight into the metabolism of glucose in tissues, which is of great help for the imaging of malignant lesions, as such tissues present increased glucose uptake. Fusion of PET and computed tomography (CT) images facilitates the anatomic interpretation and improves the diagnostic accuracy. Nowadays, although 18F-FDG PET/CT has not been recommended for breast cancer screening or diagnosing primary breast cancer, it is of great help for preoperative assessment of breast lesion[8]. In our study, 248(83.8%) of the 296 patients in our study had been histological diagnosed with breast carcinoma. In the detection of malignant lesion on breast 18F-FDG PET/CT test was superior to conventional imaging in terms of both sensitivity and specificity. It has been reported that the 18F-FDG uptake by breast tumors is variable, for example, as invasive lobular breast cancer has a considerably lower 18F-FDG uptake than invasive ductal cancer[9], the latter is much more commonly detected by PET[10]. Therefore, in the following study we analyzed 18F-FDG PET/CT images in different disease with false positive.

Among 48 cases of non-cancerous lesion, the most common diagnoses are purulent inflammation (35.4%), fibroadenoma (33.3%) and intraductal papilloma (12.5%). It has been reported that PET/CT has a high accuracy and sensitivity that reach 100% for inflammatory breast cancer[11]. It is suggested that the skin in the vicinity of the tumor is thickened, with an increased uptake of 18F-FDG in 78% of cases, which is probably caused by inflammatory cell infiltration[12]. In our study, we observed that purulent inflammation tend to have a larger size and higher uptake of FDG while compared with other cases. Besides, uptake of FDG by lymph node usually occurs in these cases. The mean value of SUVmax in purulent inflammation is higher than that in most cases of breast carcinoma in this study.

Conclusion

In conclusion, despite the low false positive rate 18F-FDG PET/CT is of great value for preoperative evaluation of breast lesion. In the non-cancerous cases which had a indication of carcinoma in 18F-FDG PET/CT test, the most common diagnosis were fibroadenoma, purulent inflammation and intraductal papilloma. The characterstics of purulent inflammation in 18F-FDG PET/CT image presented a higher SUVmax value with a longer max diameter in length.

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