Endocr (2009) 36:385–391
DOI 10.1007/s12020-009-9247-2

ORIGINAL ARTICLE

The role of integrated ^{18}F-FDG PET/CT in identification of ectopic ACTH secretion tumors

Haoping Xu · Min Zhang · Ge Zhai · Miao Zhang · Guang Ning · Biao Li

Received: 8 May 2009 / Accepted: 2 July 2009 / Published online: 6 October 2009

Abstract The role of ^{18}F-Flurodeoxyglucose positron emission tomography (^{18}F-FDG PET) scan in localization of ectopic Cushing's syndrome (EAS) tumor is still controversial. Here, we report on the use of integrated ^{18}F-FDG PET and computed tomography (^{18}F-FDG PET/CT) in localization of EAS tumors in patients with ectopic Cushing's syndrome. Five patients, three men and two women, were reported, whose endocrine investigations and negative pituitary imaging were suggestive of ectopic ACTH secretion. ^{18}F-FDG PET/CT was performed to identify the source of ACTH secretion. Then the patients were suggested to perform pathologic examination. It turned out that all of these five patients have abnormal markedly intense FDG uptake lesions on ^{18}F-FDG PET/CT images. Four of them underwent lesion resection, whose plasma ACTH and serum cortisol levels returned to normal after the surgery. Also, they were at last remission from all the symptoms. Pathologic results showed one thymic carcinoid, one pulmonary carcinoid, one thymoma, and one pulmonary carcinoid with upper mediastinum carcinoid. Unfortunately, one patient died due to severe infection and electrolyte disorders. ^{18}F-FDG PET/CT technology integrates PET and CT imaging in one device so as to increase the accuracy of tumor localization and further improve the prognosis of the patients by curative resection.

Keywords ^{18}F-FDG PET/CT · Cushing's syndrome · Ectopic ACTH secretion · Diagnosis

Introduction

Ectopic ACTH secretion (EAS) is responsible for 10–20% of cases of Cushing's syndrome [1, 2], which is associated with significant morbidity and mortality related to the production of excess cortisol. Unfortunately, it has been reported that no tumor was found in about 12.5% patients despite repeated evaluation and long term follow-up [2]. By reviewing the literatures, the most prevalence of tumors of EAS is thoracic tumors, especially the bronchial carcinoid (>25%) [3, 4], followed by small cell lung cancers (SCLC) (about 20%) which accounted for the most cases of EAS in the past, and thymic tumors (about 20%). Other common benign and malignant tumors have been associated with EAS including abdominal tumors such as islet cell tumors (10%), GI adenocarcinomas (10%) and pheochromocytomas (5%) [4].

Imaging studies are the cornerstone for tumor localization in patients with EAS. Anatomical imaging with computed tomography (CT) and magnetic resonance imaging (MRI) is used most commonly to localize the source of EAS. Most SCLCs are detected using plain chest X-ray, CT, and/or MR imaging. However, bronchial carcinoids can be relatively small and thus be missed by conventional imaging. ^{18}F-Flurodeoxyglucose positron emission tomography (^{18}F-FDG PET) has been proposed as potential imaging techniques for EAS tumor imaging. However, the role of FDG PET scan in localization of EAS tumor is still controversial. ^{18}F-FDG PET/CT technology, which integrates PET and CT imaging, has increased both sensitivity and specificity compared with PET or CT as a

H. Xu · M. Zhang · G. Zhai · M. Zhang · B. Li (✉)
Department of Nuclear Medicine, Rui Jin Hospital, Shanghai Jiao Tong University School of Medicine, No.197, Rui Jin Er Road, Shanghai 200025, People's Republic of China
e-mail: lb10363@rjh.com.cn

G. Ning
Shanghai Institute of Endocrinology and Metabolism, Rui Jin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, People's Republic of China

single modality. We report four patients with ectopic ACTH syndrome to show the usefulness of ^{18}F-FDG PET/CT in the localization diagnosis of EAS.

Materials and methods

Patients

This study was approved by the Ethnics Committee of the Hospital. Five patients, three men and two women, with Cushingoid appearance underwent a whole-body ^{18}F-FDG PET/CT imaging in our PET/CT center for the purpose of EAS tumors identified from June 2007 to March 2009. Their main laboratory data was shown in Tables 1 and 2. And their clinical history was briefly introduces here.

Patient one

A 59-year-old man presented with gradually round face, thin limbs, general fatigue, and hyperglycemia of 2 years duration. He went to a nearby hospital to diagnose and the laboratory studies showed an elevated serum cortisol with loss of the circadian rhythm and 2 mg dexamethasone suppression test failed. The bilateral adrenal was hyperplastic from abdominal enhanced CT scan and the pituitary was normal from magnetic resonance imaging (MRI) scan of brain. Thus, he was diagnosed of Cushing syndrome and referred to our hospital for further diagnosis and treatment. The patient presented with cough and expectoration. A physical examination showed moon-like face, edema in the eyelids and lower extremities. According to the laboratory data, he was diagnosed with ectopic ACTH syndrome and pneumonia.

Patient two

A 53-year-old woman was admitted to our hospital with 1-month duration of gradually round face and fatigue. A physical examination showed moon-like face, subcutaneous ecchymosis in left elbow and right lower limb. The enhanced CT showed hyperplasia of bilateral adrenal gland. And pituitary MRI showed a suspicious microadenoma in the right wing of the pituitary.

Patient three

A 27-year-old man with gradually round face in 1 month, as well as edema in the lower extremities, hairiness and general fatigue visited our hospital for diagnosis and treatment. He had Cushingoid appearance at presentation: moon-like face, hairiness, pigmentation in the chest and the back, ecchymosis in left elbow and blood pressure of 140/90 mmHg.

Table 1 The laboratory data of patients with EAS tumor

No.	WBC (μl)	Neutrophils (%)	Serum potassium (mmol/l)	FBG (mmol/l)	UFC (μg/24 h)	Serum cortisol (7–22 μg/dl)		
						8 a.m.	4 p.m.	12 p.m.
1	15300	90.1	3.11	12.56	1996.6	84.3	78.7	59.5
2	8900	85.6	2.8	8.6	906.6	55.7	33.6	25
3	10300	84.5	2.25	6.4	1235.7	73.1	67.2	65.5
4	11300	89.9	2.2	12.9	1240.4	65.1	69.6	66.3
5	8900	81.7	2.8	4.88	739.7	30.2	29.7	22

WBC white blood count, *FBG* fasting blood glucose, *UFC* urine free cortisol

Table 2 The endocrine tests of patients with EAS tumors

Patients	Cortisol (μg/dl)	ACTH (pg/ml)	DST (μg/dl)		BSIPSS (pg/ml)		
			Post-LDDST	Post-HDDST	Left petrosal	Right petrosal	Peripheral blood
1	84.3	521.9	83.8	89.1	/	/	/
2	55.7	655.3	40.1	28.8	617	500.9	470.5
3	73.1	322.3	67.2	47.2	/	/	/
4	65.1	2240.0	63.5	66.3	/	/	/
5	30.2	365.8	20.9	22.5	296.3	293.7	251.8

DST dexamethasone suppression test, *LDDST* low-dose dexamethasone suppression test, 0.5 mg dexamethasone 6-hourly for 48 h, *HDDST* high-dose dexamethasone suppression test, 2 mg dexamethasone 6-hourly for 48 h, *BSIPSS* bilateral simultaneous inferior petrosal sinus sampling

There was no abnormal in the CT scan or contrast MRI of brain, while the abdominal enhanced CT scan indicated hyperplasia in bilateral adrenal gland.

Patient four

A 64-year-old man went to local hospital for 2-month-duration of general fatigue and edema in both lower extremities. The laboratory data showed decreased serum potassium of 2.7 mmol/l, elevated plasma cortisol and ACTH level. The B ultrasound showed a mass in the right adrenal, and abdominal CT showed thickness of both adrenal, which were pathologically proven to be hyperplasia of adrenal cortex. He came to our hospital for further diagnosis. The physical examination showed plethoric face, ecchymosis in multiply sites, and blood pressure of 160/80 mmHg.

Patient five

A 47-year-old woman presented with amenorrhea, gradually round face and weight gain for 5 months. The laboratory data of the local hospital revealed a high level of serum cortisol and ACTH, a low level of serum potassium and negative results of dexamethasone suppression test. But there was no pituitary or bilateral adrenal lesions scanned by MRI or CT imaging. She was referred to our hospital for further treatment. She had Cushingoid appearance at presentation: central obesity and moon-like face. And physical examination revealed an elevated blood pressure of 150/100 mmHg. She was diagnosed with EAS syndrome after performed necessary endocrinology tests. ^{18}F-FDG PET/CT imaging was suggested to her for identification of the EAS lesion.

PET/CT imaging

All of the patients fasted for at least 6 h before PET/CT scan except water intake. The blood glucose concentration of each patient was controlled under the level of 7.4 mmol/l before FDG (0.12–0.15 mCi/kg) was injected intravenously. Forty-five to sixty minutes later, the FDG PET/CT scans were performed with a GE Discovery STE[16] integrated PET/CT scanner combining the ability to acquire CT images and PET data of the same patient in one session. The whole-body CT data were acquired first by a continuous spiral technique on a 16-slice helical CT, with the following parameters: gantry rotation speed, 0.8 s per rotation; 140 KV; 17.5 mm per rotation table speed. All CT scans were obtained with 3.75 mm thick axial sections and the axial field of view was 15.6 cm. Subsequently, a positron emission scan was performed from the thigh to the head at a 3 min/bed position speed. Combined with CT data, the attenuation-corrected PET images were reconstructed by an ordered-subset expectation maximization algorithm and then normalized by both injected dose and patients' body weight.

Data analysis

Each report of whole-body ^{18}F-FDG PET/CT imaging was reviewed. These clinical reports were originally generated this way: All the PET/CT images were interpreted by two independent observers and the standardized uptake value (SUV) was calculated as, SUV = (activity in region of interest in mCi/mL)/(injected dose in mCi/weight in kg), and the maximum standardized uptake value (SUV_{max}) was measured on the GE XELERIS workstation. We interpreted the PET/CT images combined intense FDG uptake with the structure information from CT data. Visual analysis was performed with the background liver uptake as a reference. For the regions with a FDG uptake higher than the reference, the maximum FDG uptakes (SUV_{max}) were recorded. Besides, physiologic or nonspecific FDG uptake should be excluded, which may usually occur such as in intestines, pharynx, and muscles.

Laboratory tests and endocrine investigations

All the patients carried out routine examinations including blood and urine routine examination, functions of liver and kidney, and electrolyte. And the endocrine investigations including rhythm of cortisol secretion, ACTH and urine free cortisol at baseline, and dexamethasone suppression test. The bilateral simultaneous inferior petrosal sinus sampling was not performed unless the dexamethasone suppression test was not able to diagnose EAS definitely (patient two) or whenever the patient asked for it (patient five).

Results

In the first case, ^{18}F-FDG PET/CT revealed a mass with elevated-FDG uptake beside the left pulmonary artery in the mediastinum, diameter of about 1.1 cm. The maximum of standard uptake value (SUV_{max}) was 9.4. And it also demonstrated a high-FDG uptake in his lower lobe of the right lung; the SUV_{max} was 8.2, which was proved to be the pneumonia (Fig. 1). The patients underwent the surgery of the thymus and the mediastinum mass resection. According to the surgical findings, the mass was located in the left lobes of thymuses, which was completely removed. The pathologic result was thymoma, type A. All the symptoms including round face, fatigue, and edema relieved after the surgery. The fasting-food blood glucose level and the serum potassium level became normal. And the plasma

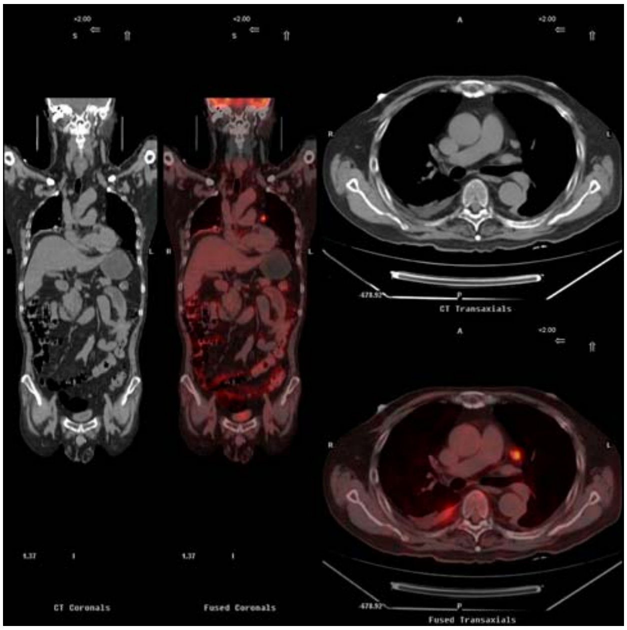

Fig. 1 Integrated whole-body ^{18}F-FDG PET/CT case study of one patient. Coronal images (*left*) and transaxial images of mediastinum window (*right*), CT images and PET/CT fused images. The study revealed a mass with intense FDG uptake beside the left pulmonary artery in the mediastinum. The diameter of the mass was 1.1 cm, and SUV_{max} was 9.4. It also demonstrated a high-FDG uptake of pneumonia in the lower lobe of the right lung, the SUV_{max} was 8.2

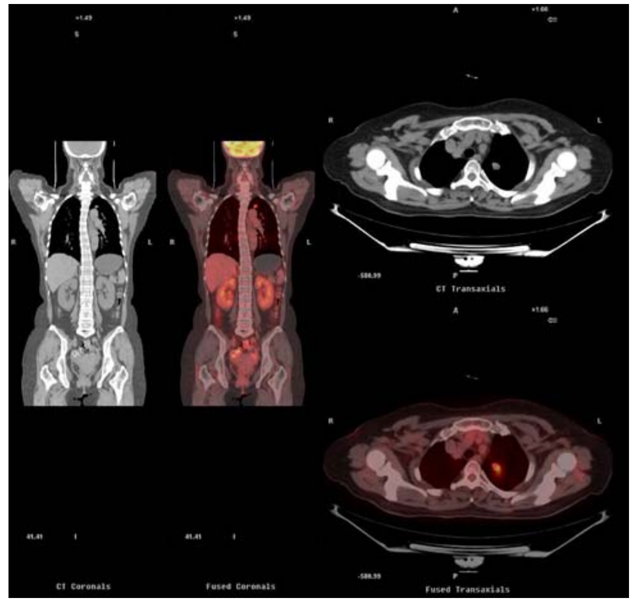

Fig. 2 ^{18}F-FDG PET/CT images of case two patient. Coronal images (*left*) and transaxial images of mediastinum window (*right*), CT images and PET/CT fused images. A round mass was located in the upper lobe of left lung, which was 1.5 cm in diameter. The intense FDG uptake was 6.4 in early imaging and 10.6 in late imaging

ACTH level decreased to 25.2 pg/ml 2 month after the surgery.

In the second case, ^{18}F-FDG PET/CT revealed hyperplasia in bilateral adrenal gland and a round mass located in the upper lobe of left lung, which was 1.5 cm in diameter. The intense FDG uptake was 6.4 in early imaging and 10.6 in late imaging (Fig. 2). According to all the tests above, ectopic ACTH syndrome was diagnosed clinically. And an operative exploration was essential for the lung mass. Thus, the patient underwent left upper lobectomy with thoracoscopy and pathologic test showed typical lung carcinoid with negative lymph node filtrated. The plasma ACTH level decreased to 23.0 pg/ml and serum cortisol decreased to 9.3 µg/dl (8 a.m.) 1 month after the lobectomy.

In the third case, ^{18}F-FDG PET/CT scan revealed a mass behind the sternum with intense FDG uptake. The diameter was 1.6 cm, and SUV_{max} was 12 (Fig. 3). The bilateral adrenal was hyperplasia with intense FDG uptake of 8. The patient underwent resection for the anterior mediastinum mass with thoracoscopy, which showed pathologically a thymic carcinoid. His blood pressure level then decreased to 125/95 mmHg after the surgery. And the serum potassium elevated to a normal level of 4.07 mmol/l. The plasma ACTH level was decreased to 23.3 pg/ml and serum cortisol level was decreased to 18.7 µg/dl at 8 a.m. 1 week after the surgery.

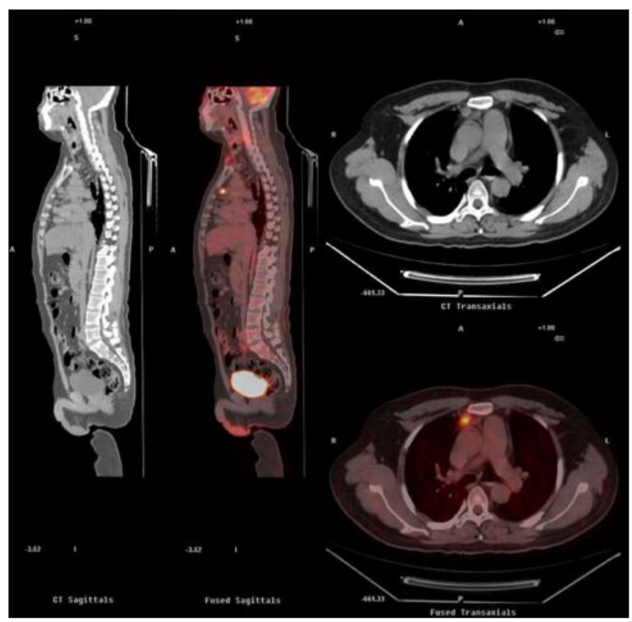

Fig. 3 ^{18}F-FDG PET/CT images of case three patient. Sagittal images (*left*) and transaxial images of mediastinum window (*right*), CT images and PET/CT fused images. A mass behind the sternum was detected with intense FDG uptake. The diameter was 1.6 cm, and SUV_{max} was 12

In the fourth case, ^{18}F-FDG PET/CT revealed a soft-tissue mass in the left parapharyngeal space, which presented with intense FDG uptake of 5.4 (Fig. 4). The

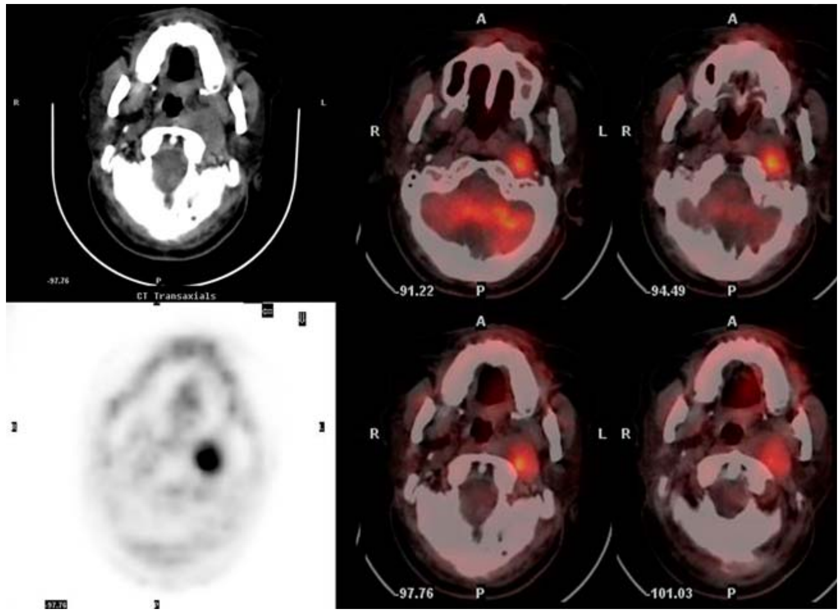

Fig. 4 ^{18}F-FDG PET/CT images of case four patient (*transaxial images*). *Left* CT images (*upper*) and PET images (*low*). *Right* four consecutive layers of CT and PET fused. A soft-tissue mass was detected in the left parapharyngeal space, the SUV_{max} of which was 5.4

cervical MR imaging also revealed a mass there. The bilateral simultaneous inferior petrosal sinus sampling failed because of the mass's compressing to the left internal jugular vein. The mass was clinically diagnosed of EAS tumor considering of all the endocrine tests. But his general condition, uncontrollable blood pressure and electrolyte disturbance deteriorate so that he did not underwent resection, automatically discharge due to the high risk of operation and died 2 months later.

In the fifth case, two elevated-FDG uptake lesions, 2.6 and 1.6 cm in diameters, were detected in the upper lobe of the right lung by ^{18}F-FDG PET/CT imaging. The SUV_{max} was 5.6 and 2.9, respectively. Another positive lesion was detected in the upper mediastinum, 2.3 cm in diameter, SUV_{max} was 6 (Fig. 5). The pathologic results of these lesions after surgery were lung carcinoid and mediastinal carcinoid, with lymph nodes metastases. The serum cortisol level decreased to 8.6 μg/dl at 8 a.m. and ACTH level was decreased to 13.5 pg/ml 1 month after the surgery.

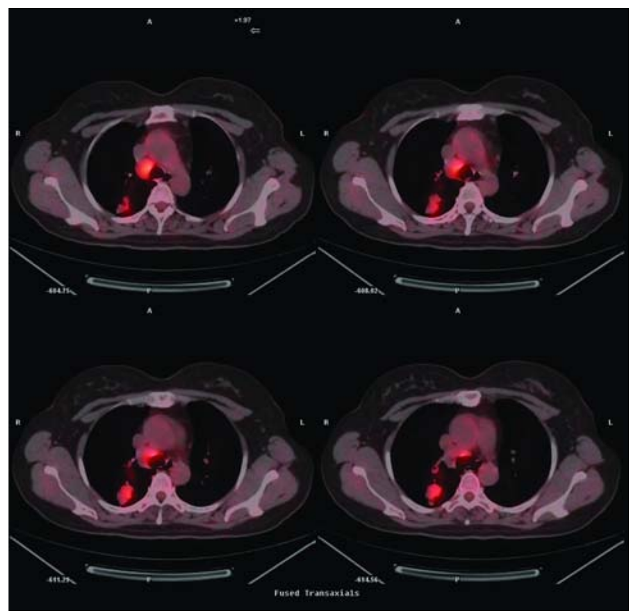

Fig. 5 ^{18}F-FDG PET/CT images of case five patient (transaxial images). The four continuous layers of the PET/CT fused images of the patient. The two elevated-FDG uptake lesions, 2.6 cm and 1.6 cm in diameters, were detected in the upper lobe of the right lung. The SUV_{max} was 5.6 and 2.9, respectively. Another lesion was detected in the upper mediastinum, 2.3 cm in diameter, SUV_{max} was 6

Discussion

Generally speaking, early diagnosis of EAS and curative tumor resection may lead to a favorable prognosis, because the optimal treatment of EAS tumors is surgical resection of the corticotrophin-secreting tumor [5, 6]. Our patients underwent EAS tumor resection, all of them showed symptom remission but one patient died unfortunately due to untreated hypercortisolism. Thus, the qualitative and localization diagnosis of EAS correctly are challenging as well as crucial clinical problems for decreasing the risk from infections, venous thrombosis and any other life-threatening complications of hypercortisolism. All of our reported patients presented with hypokalemia and signs of infection, elevated neutrophils, and pneumonia for example. The infection and life-threatening electrolyte disorder make the disease progress rapidly. Thus, the accurate diagnosis of EAS tumors becomes particularly important.

Integrated ^{18}F-FDG PET/CT combines anatomic and metabolic information in a single device, which has both increased sensitivity and specificity compared with ^{18}F-FDG PET or CT alone. Up till now, relatively few EAS tumors were reported identified by ^{18}F-FDG PET/CT scan.

In this study, FDG was markedly taken up in all of our reported cases. Several researches have showed ^{18}F-FDG PET can be used in localization of the EAS tumors. Thymic carcinoid tumor was reported [7, 8] to have intense FDG uptake so as to be localized in FDG PET imaging. Biering et al. [9] reported an ectopic ACTH-secreting bronchial carcinoid tumor detected by ^{18}F-FDG PET imaging but not detected by MRI, CT or octreotide scintigraphy initially. Athina et al. [10] also illustrated the usefulness of functional imaging with ^{18}F-FDG PET in the diagnosis, management, and follow-up of neuroendocrine tumors through reporting a case of Cushing's syndrome. In our study, the abdominal CT and brain MR imaging of all the five patients before PET/CT scan detected nothing abnormal definitely except the hyperplasia of the bilateral adrenal. As a whole-body imaging, ^{18}F-FDG PET/CT scan is more likely to identify the EAS tumors than other imaging examinations. While other examinations such as ultrasound, CT, and MR imaging provide more information about the regional sites. Some researches concluded that, in circumstances where the source of the ACTH remains occult or a suspect lesion is present in conventional radiology studies but there still remain any diagnostic uncertainty, FDG PET may be a useful addition to conventional imaging [11, 12].

Some literatures reported that increased uptake of FDG is most likely in less well differentiated neuroendocrine tumors with high proliferative activity [13–15]. And it is recognized that thymic carcinoids are more aggressive than carcinoids originating elsewhere [16], which agrees to our reported case of thymic carcinoid with the most marked FDG uptake of 12 in all the four cases with pathological result. According to the results of some researches [17, 18], ^{18}F-FDG PET seems less useful in identifying tumors with low proliferative activity. However, the fact is that most of the high-FDG uptake lesions in our study were proven to be carcinoid tumors pathologically. And the typical pulmonary carcinoid in our report, which was recognized less invasive than atypical carcinoids, presented with increased FDG uptake of 6.4, even higher than the SUV_{max} of carcinoid with lymph nodes metastases (the fifth patients). Also, the type A thymoma in our study, which is considered an low grade malignancy, and represents less invasive than other types of thymomas according to WHO classification [19], presented a high value of SUV_{max} of 9.4. Thus, we think the increased FDG uptake is not absolutely correlated with the malignant behavior of ACTH-secreting tumor. The EAS tumor possesses a higher rate of metabolic activity than normal tissue, thus it will be detected by ^{18}F-FDG PET scan due to the elevated glucose metabolism. In a larger series [20], the authors concluded that ^{18}F-FDG PET added little to conventional techniques in localizing ACTH-secreting neuroendocrine tumors with a high number of false-negative results. We have realized that the shortcoming of PET imaging is the limited spatial resolution with PET scanners. Potentially, lesions less than 7 mm (GE medical system, different medical system may have different standard) may be resolved by the scanner due to partial volume effect. And it may be the most likely reason for the false-negative uptake in FDG PET imaging. Besides, there potentially exist but not be proved presently a low enzymatic activity of hexokinase, a high level of glucose-6-phosphatase in these kinds of cells or even decreased expression of GLUT-1 receptor (the most important transporter of glucose into the cell), which needs further research and exploration.

Integrated ^{18}F-FDG PET/CT may compensate the limited spatial resolution of PET scan alone by combining CT imaging in one device so as to reduce the false-negative rate in diagnosis. Besides, CT scan may localize the source of ectopic ACTH tumor better so as to reduce false positive rate, especially some physiological uptake. PET imaging provides metabolic information and may reveal the high-FDG uptake lesions which potentially mislead by CT scan due to the similar appearance with surrounding tissue. ^{18}F-FDG PET/CT is a refinement in imaging technology and improves the localization of EAS tumors.

Acknowledgment This work was supported by Shanghai Leading Academic Discipline Project S30203.

References

1. A.M. Isidori, G.A. Kaltsas, S. Mohammed, D.G. Morris, P. Jenkins, S.L. Chew et al., Discriminatory value of the low-dose dexamethasone suppression test in establishing the diagnosis and differential diagnosis of Cushing's syndrome. J. Clin. Endocrinol. Metab. **88**, 5299–5306 (2003)
2. A.M. Isidori, G.A. Kaltsas, C. Pozza, V. Frajese, J. Newell-Price, R.H. Reznek et al., The ectopic adrenocorticotropin syndrome: clinical features, diagnosis, management and long-term follow-up. J. Clin. Endocrinol. Metab. **91**, 371–377 (2006)
3. A.M. Isidori, A. Lenzi, Ectopic ACTH syndrome. Arq. Bras. Endocrinol. Metabol. **51**(8), 1217–1225 (2007)
4. J.P. Aniszewski, W.F. Young Jr, G.B. Thompson, C.S. Grant, J.A. van Heerden, Cushing syndrome due to ectopic adrenocorticotropic hormone secretion. World J. Surg. **25**(7), 934–940 (2001)
5. I. Ilias, D.J. Torpy, K. Pacak, N. Mullen, R.A. Wesley, L.K. Nieman, Cushing's syndrome due to ectopic corticotropin secretion: twenty years' experience at the National Institutes of Health. J. Clin. Endocrinol. Metab. **90**, 4955–4962 (2005)
6. B.M. Biller, A.B. Grossman, P.M. Stewart, S. Melmed, X. Bertagna, J. Bertherat et al., Treatment of adrenocorticotropin-dependent Cushing's syndrome: a consensus statement. J. Clin. Endocrinol. Metab. **93**(7), 2454–2462 (2008)
7. A.M. Groves, H.K. Mohan, E.A. Wegner, S.F. Ham, S.B. Bingham, S.E. Clarke, PET with FDG to show thymic carcinoid. Am. J. Roentgenol. **82**, 511–513 (2004)
8. E. Gomard-Mennesson, P. Sève, E. De La Roche, S. Collardeau-Frachon, C. Lombard-Bohas, C. Broussolle, Thymic carcinoid

tumor revealed by a Cushing's syndrome: usefulness of positron emission tomography. Rev. Med. Interne **29**(9), 751–753 (2008). (Epub 2008 Mar 4)
9. H. Biering, M. Pirlich, J. Bauditz, D. Sandrock, H. Lochs, H. Gerl, PET scan in occult ectopic ACTH syndrome: a useful tool? Clin. Endocrinol. **59**, 404–405 (2003)
10. A. Markou, P. Manning, B. Kaya, S.N. Datta, J.B. Bomanji, G.S. Conway, [18F] Fluoro-2-deoxy-D-glucose ([18F]FDG) positron emission tomography imaging of thymic carcinoid tumor presenting with recurrent Cushing's syndrome. Eur. J. Endocrinol. **152**, 521–525 (2005)
11. J. Kumar, M. Spring, P.V. Carroll, S.F. Barrington, J.K. Powrie, 18Flurodeoxyglucose positron emission tomography in the localization of ectopic ACTH-secreting neuroendocrine tumours. Clin. Endocrinol. **64**, 371–374 (2006)
12. A.B. Moraes, G.F. Taboada, M.P. Carneiro, L.V. Neto, L.E. Wildemberg, K. Madi et al., Utility of [18F] fluoro-2-deoxy-D-glucose positron emission tomography in the localization of ectopic ACTH-secreting tumors. Pituitary, 2008 May 6. (Epub ahead of print)
13. S. Adams, R. Baum, T. Rink, P.M. Schumm-Dräger, K.H. Usadel, G. Hör, Limited value of fluorine-18 fluorodeoxyglucose positron emission tomography for the imaging of neuroendocrine tumours. Eur. J. Nucl. Med. **25**(1), 79–83 (1998)
14. J.J. Erasmus, H.P. McAdams, E.F. Patz Jr, R.E. Coleman, V. Ahuja, P.C. Goodman, Evaluation of primary pulmonary carcinoid tumors using FDG PET. Am. J. Roentgenol. **170**, 1369–1373 (1998)
15. C. Le Rest, J.B. Bomanji, D.C. Costa, C.E. Townsend, D. Visvikis, P.J. Ell, Functional imaging of malignant paragangliomas and carcinoid tumours. Eur. J. Nucl. Med. **28**, 478–482 (2001)
16. V.T. de Montpreville, P. Macchiarini, E. Dulmet, Thymic neuroendocrine carcinoma (carcinoid): a clinicopathologic study of fourteen cases. J. Thorac. Cardiovasc. Surg. **111**, 134–141 (1996)
17. S. Adams, R.P. Baum, A. Hertel, P.M. Schumm-Drager, K.H. Usadel, G. Hor, Metabolic (PET) and receptor (SPET) imaging of well- and less well-differentiated tumours: comparison with the expression of the Ki-67 antigen. Nucl. Med. Commun. **19**, 641–647 (1998)
18. C. Pasquali, D. Rubello, C. Sperti, P. Gasparoni, G. Liessi, F. Chierichetti, G. Ferlin, S. Pedrazzoli, Neuroendocrine tumor imaging: can 18F-fluorodeoxyglucose positron emission tomography detect tumors with poor prognosis and aggressive behavior? World J. Surg. **22**, 588–592 (1998)
19. M. Okumura, M. Ohta, H. Tateyama et al., The World Health Organization histologic classification system reflects the oncologic behavior of thymoma: a clinical study of 273 patients. Cancer **94**(3), 624–632 (2002)
20. K. Pacak, I. Ilias, C.C. Chen, J.A. Carrasquillo, M. Whatley, L.K. Nieman, The role of 18F flourodeoxyglucose positron emission tomography and 111In–diethylenetriaminepentaacetate-D-phepentreotide scintigraphy in the localisation of ectopic adrenocorticotropin-secreting tumours causing Cushing's syndrome. J. Clin. Endocrinol. Metab. **89**, 2214–2221 (2004)