18F-FDG Positron Emission Tomography/Computed Tomography (PET/CT) for Distinguishing Tuberous Sclerosis Complex Lesions from Colon Cancer Metastases

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Patient: Female, 17-year-old
Final Diagnosis: Tuberous sclerosis complex
Symptoms: No specific symptoms
Medication: —
Clinical Procedure: —
Specialty: Nuclear Medicine

Objective: Rare disease
Background: Tuberous sclerosis complex (TSC; Bourneville-Pringle disease) is a multisystem genetic disorder manifesting as benign tumors that can affect any system. Malignant neoplasm may coexist in patients with TSC. In such cases, there are diagnostic difficulties in distinguishing between metastatic lesions and benign changes. We show the usefulness of positron emission tomography (PET) in resolving these difficulties.

Case Report: The purpose of this article is to present the usefulness of metabolic imaging using 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) in distinguishing benign from neoplastic lesions in a patient with TSC. A 17-year-old female patient with TSC was referred for 18F-FDG PET/CT with suspected lung and bone metastases. The patient underwent a bilateral nephrectomy because of multiple cysts and angiomyolipomas. A colonoscopy – performed in preparation for kidney transplantation – revealed several colon polyps, one of which was found to be cancerous upon histopathologic examination. A diagnosis of adenocarcinoma G3 was made and a CT scan of the chest and abdomen performed afterwards showed multiple pulmonary nodules and sclerotic bone lesions suggestive of metastases. Two 18F-FDG PET/CT scans (performed within 6 months) showed multiple nodules of 7-15 mm in diameter and changes typical of multifocal micronodular pneumocyte hyperplasia in both lungs. In the bones, we found multiple sclerotic lesions. All of the above findings showed FDG uptake at the level of the background activity which contradicted the lesions’ metastatic origin.

Conclusions: Using the example of a 17-year-old patient with TSC, we present the usefulness of metabolic imaging using 18F-FDG PET/CT in distinguishing benign from neoplastic lesions.

Keywords: Hospitals, Pediatric • Molecular Imaging • Tuberous Sclerosis Complex 1 Protein

Abbreviations: TSC – tuberous sclerosis complex; 18F-FDG – fluorodeoxyglucose; PET – positron emission tomography; CT – computed tomography; LAM – lymphangioleiomyomatosis

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Background

Tuberous sclerosis complex (TSC, Bourneville-Pringle disease) is a multisystem genetic disorder with an incidence of 1 per 6800 to 17 300 live births. Worldwide, there are approximately 2 million people living with TSC. The syndrome is caused by a mutation in either the \textit{TSC1} or \textit{TSC2} gene. About 70% of cases are secondary to spontaneous mutations; 30% are inherited in an autosomal dominant manner [1].

TSC typically presents as benign tumors that can affect any system but most often involve the brain, skin, kidneys, heart, eyes, and lungs. The most common pulmonary manifestation of TSC, occurring almost exclusively in women, is lymphangioleiomyomatosis (LAM). In LAM, smooth muscle cells infiltrate various lung structures to form multiple cysts, which usually leads to symptoms such as progressive dyspnea on exertion and recurrent pneumothoraces. Other manifestations of TSC in the lung include multifocal micronodular pneumocyte hyperplasia and clear cell tumor of the lung [2-5]. Malignant

Figure 1. Maximum intensity projection images of 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT) scans performed in June 2020 (A) and December 2020 (B). No FDG-avid lesions suggestive of malignancy were identified in either scan. The high metabolism of the tracer in the brain (green arrows, A, B) and in the heart (red arrow, A) is physiologic. Imaging was conducted using the Advantage Workstation for Diagnostic Imaging (GE; AW4.6_05.003_SLED_11; GIMP 2.10 General Public License).
neoplasm may coexist in patients with TSC. In such cases, there are diagnostic difficulties in distinguishing between metastatic lesions and benign changes. We show the usefulness of PET in solving these difficulties. The aim of this article is to present the usefulness of metabolic imaging using 18F-fluorodeoxyglucose positron emission tomography/computed tomography (18F-FDG PET/CT) in distinguishing benign from neoplastic lesions in a patient with TSC.

Case Report

A 17-year-old female patient with TSC was referred for 18F-FDG PET/CT with suspected lung and bone metastases. The patient and her legal representative signed a written informed consent form to participate in this study. The diagnosis of TSC was made in accordance with clinical criteria, Roach’s criteria, and Goetz’s criteria [2,3]. The patient was not treated with mTOR inhibitors. In the course of the disease, the patient underwent a bilateral nephrectomy because of multiple cysts and angiomylipomas. A colonoscopy – performed in preparation for kidney transplantation – revealed several colon polyps, one of which was found to be cancerous upon histopathologic examination. A diagnosis of adenocarcinoma G3 was made and a CT scan of the chest and abdomen performed afterwards showed multiple pulmonary nodules and sclerotic bone lesions suggestive of metastases. However, 18F-FDG PET/CT (Figure 1) revealed multiple nodules, 7-15 mm in diameter (Figures 2, 3, left columns), and changes typical of LAM (Figure 2, left column) in both lungs. In the bones, we found multiple sclerotic lesions (Figure 4, left column). All of the above findings showed FDG uptake at the level of the background activity, which contradicted their metastatic origin. We did not identify lesions indicative of metastases in other regions of the body. In followup
PET/CT performed 6 months later (Figures 1-4, right columns), the lesions in the lungs and bones were stable. Again, we found no FDG-avid lesions indicative of malignancy.

Discussion

In the presented case, we show the utility of 18F-FDG PET/CT in discriminating between benign and malignant lesions in a patient with TSC and colorectal cancer. Anatomical imaging (CT) proved insufficient in this setting as colorectal cancer metastases and benign TSC lesions may look alike. However, colorectal adenocarcinoma and its metastases generally show high glucose metabolism; this was the rationale for performing PET/CT with the glucose analogue, 18F-FDG, which is rapidly absorbed and trapped in most cancerous cells, in contrast to benign lesions where the uptake is low or absent [6].

In the reported case, PET/CT was performed to identify FDG-avid lesions (suggestive of malignancy) that would be suitable for biopsy. However, both the pulmonary and the bone lesions showed minimal tracer uptake. This led to the conclusion that all of them were of TSC origin. Followup PET/CT showed a lack of lesion progression (which would be the natural course for malignancy) and hence supported the benign character of the findings.

TSC has many clinical manifestations and potential complications. For this reason, a group of doctors composed of pediatricians, neurologists, surgeons, radiologists, and nuclear medicine doctors is involved in the treatment of TSC patients in our Centre. The use of such a multidisciplinary team has been shown to be beneficial in treating TSC by other authors [7,8].

Figure 3. Transaxial scans of computed tomography (CT) and fused 18F-fluorodeoxyglucose (FDG) positron emission tomography/CT (PET/CT) performed in June 2020 (left column, images A, C) and in December 2020 (right column, images B, D). Yellow arrows show pulmonary nodules (with no FDG uptake). No progression was seen between the 2 scans. Imaging was conducted using the Advantage Workstation for Diagnostic Imaging (GE; AW4.6_05.003_SLED_11; GIMP 2.10 General Public License).
Figure 4. Transaxial scans of computed tomography (CT) and fused 18F-fluorodeoxyglucose (FDG) positron emission tomography/CT (PET/CT) performed in June 2020 (left column; images A, C) and in December 2020 (right column; images B, D). Yellow arrows indicate sclerotic lesions in the body of the L3 vertebra, with no FDG uptake. The lesions did not progress in the time between the 2 scans. Imaging was conducted using the Advantage Workstation for Diagnostic Imaging (GE; AW4.6_05.003_SLED_11; GIMP 2.10 General Public License).

Conclusions

We believe that metabolic imaging such as 18F-FDG PET/CT might be helpful in discriminating benign from malignant lesions in patients with tuberous sclerosis complex.

Declaration of Figures Authenticity

All figures submitted have been created by the authors, who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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