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Extremely low ^{18}F-fluorodeoxyglucose uptake in the brain of a patient with metastatic neuroblastoma and its recovery after chemotherapy: A case report

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Abstract

Commonly, physiological ^{18}F-fluorodeoxyglucose (FDG) uptake in the brain can be observed in ^{18}F-FDG positron emission tomography. Abnormal uptake of ^{18}F-FDG in the brain suggests disorders of central nervous system. Here, we present a case of extremely low ^{18}F-FDG uptake in the brain of a 4-year-old girl with whole-body metastatic neuroblastoma. Almost missing of physiological ^{18}F-FDG uptake in the brain was ascribed at least partly to the metastatic neuroblastoma. The brain could regain physiological ^{18}F-FDG uptake after chemotherapy.

Keywords

Brain, F-fluorodeoxyglucose, positron emission tomography, I-metaiodobenzylguanidine, neuroblastoma

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Introduction

^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET) is one of functional imaging techniques. ^{18}F-fluorodeoxyglucose, an analog of glucose, accumulates in tissue with high glucose metabolism. ^{18}F-fluorodeoxyglucose positron emission tomography is useful to find metastasis of malignant tumors on the whole body. In the living body, some organs, for example, the brain, show physiological uptake of ^{18}F-FDG. Abnormally low ^{18}F-FDG uptake in the brain suggests disorders of central nervous system (CNS). Here, we present a case of extremely low ^{18}F-FDG uptake in the brain of a 4-year-old girl with whole-body metastatic neuroblastoma.

Case report

A 4-year-old girl presented with a 2-week history of malaise, appetite loss, and pain in both legs. She looked pale with eyelid edema. She had no abnormalities in birth or development. There was no significant family history. Laboratory test showed anemia, thrombocytopenia, high neuron-specific enolase (NSE) level, and increased urinary catecholamine metabolites. Bone marrow aspiration revealed infiltration of tumor cells. Computed tomography (CT) showed a 70-mm right adrenal tumor and some satellite lesions.

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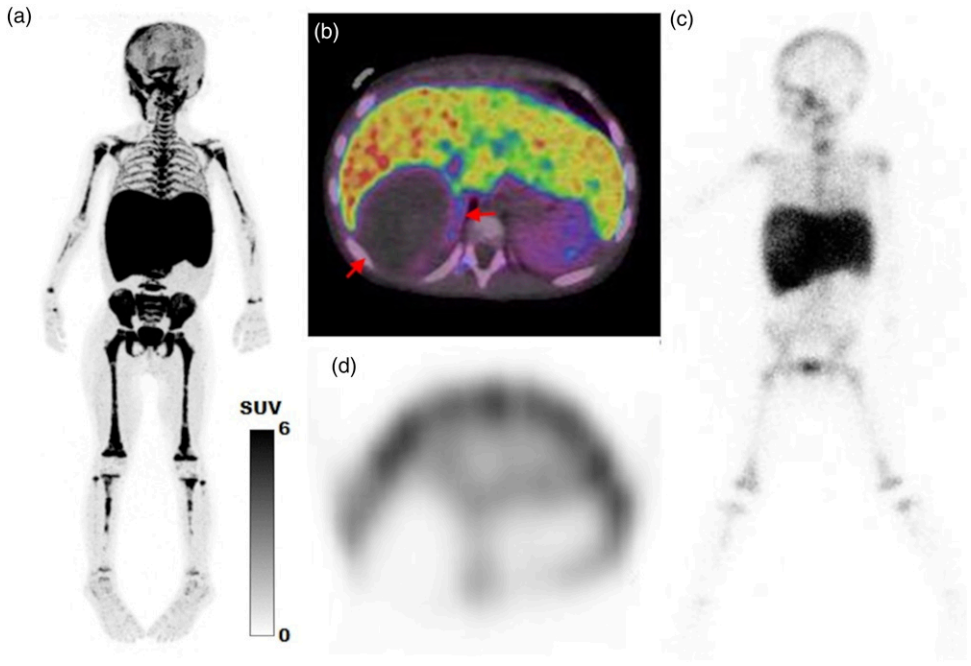

Fig. 1. ^{18}F-FDG PET MIP (a). An axial fusion image of PET and CT and arrows indicate the right adrenal tumor (b). ^{123}I-MIBG scintigraphy's anterior planar image (c) and an axial image (d). Note: ^{18}F-FDG PET MIP: F-fluorodeoxyglucose positron emission tomography maximum intensity projection; ^{123}I-MIBG: I-metaiodobenzylguanidine.

^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (Philips Vereos digital scanner[1] with high spatial resolution by a semiconductor detector) was performed, providing some interesting images (Figure 1). A maximum intensity projection (MIP) image showed an impactful appearance like a skeleton. Strong uptake was seen in the bone marrow (SUVmax 7.6 at sacrum) and in the liver (SUVmax 10.0). However, the right adrenal tumor had only a slight accumulation on the margin. A surprising finding is almost missing of physiological ^{18}F-FDG uptake in the brain (Figure 2, SUVmax 1.8), mimicking brain death.[2] She did not present with disturbance of consciousness nor neurological signs during the procedure. Magnetic resonance imaging (MRI) revealed no abnormal findings in the brain (Figure 2). ^{123}I-metaiodobenzylguanidine (MIBG) scintigraphy showed unclear uptake of the adrenal tumor but remarkable uptake in the bone marrow and in the liver (Figure 1). Final diagnosis by a biopsy of the right adrenal lesion was neuroblastoma.

We initiated induction chemotherapy.[3] The next day she developed multiple organ failure due to tumor lysis–related bleeding from the liver. After she had been cared for 1 month in an intensive care unit, she resumed chemotherapy. Some laboratory tests and image inspections (Figure 3) were done to confirm the therapeutic effect. Significant reductions in serum NSE and urinary catecholamine metabolites were revealed. ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (Siemens Biograph 64 TruePoint scanner) demonstrated the disappearance of most of the metastasis. The brain regained its physiological uptake of ^{18}F-FDG (SUVmax 9.5). ^{123}I-metaiodobenzylguanidine scintigraphy and bone marrow biopsy also confirmed complete remission of the disease.

Discussion

^{18}F-fluorodeoxyglucose positron emission tomography is one of the functional imaging techniques. ^{18}F-fluorodeoxyglucose, an analog of glucose, is taken up into cells by glucose transporters.[4] Subsequently, ^{18}F-FDG is converted to ^{18}F-FDG-6-phosphate by the enzyme hexokinase and is trapped inside cells. ^{18}F-fluorodeoxyglucose positron emission tomography can be used to assess regional glucose metabolism in the human body. Major usage of ^{18}F-FDG PET is to find metastasis of malignant tumors on the whole body.

When it comes to neuroblastoma, ^{123}I-MIBG scintigraphy is generally used as a disease-specific imaging modality. In addition, ^{18}F-FDG PET is combined to it because better sensitivity and specificity are achieved.[5] In this case, the accumulation of ^{123}I-MIBG to the right adrenal tumor was unclear due to most necrosis inside the tumor. However, ^{18}F-FDG PET with high spatial resolution revealed slight accumulation on the margin of the tumor and whole-body metastasis including a tiny lesion on the cranium.

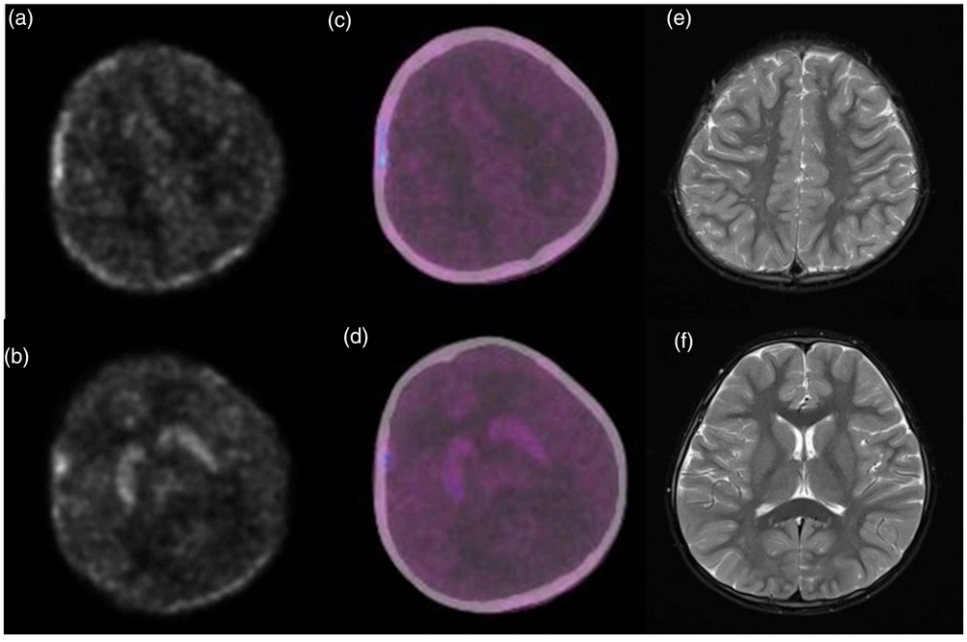

Fig. 2. Axial images of the brain. PET with small accumulation on cranium might be metastasis (a,b). Fusion images of PET and CT (c,d). T2-weighted images of MRI (e,f). Note: PET: positron emission tomography; MRI: magnetic resonance imaging.

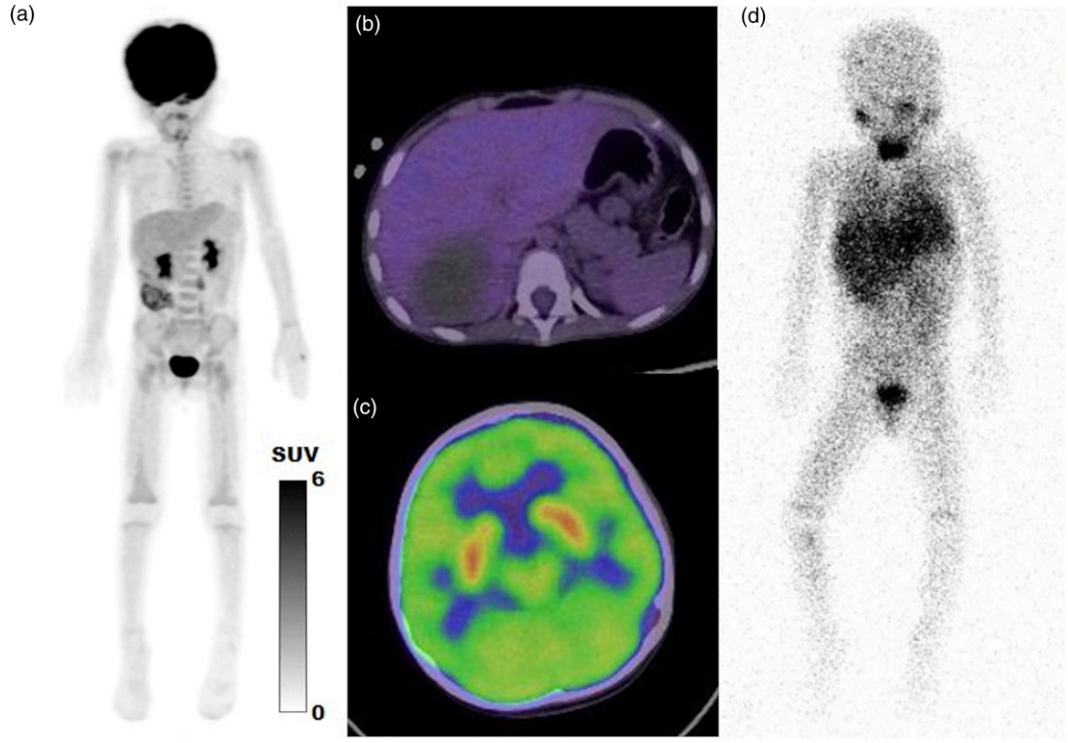

Fig. 3. Images after chemotherapy. ^{18}F-FDG PET/CT MIP (a) and axial fusion images of PET and CT (b,c). ^{123}I-MIBG scintigraphy's anterior planar image (d). Note: F-FDG PET/CT MIP: F-fluorodeoxyglucose positron emission tomography/computed tomography maximum intensity projection; PET: positron emission tomography; CT: computed tomography; I-MIBG: I-metaiodobenzylguanidine.

^{18}F-fluorodeoxyglucose positron emission tomography is a helpful imaging modality when ^{123}I-MIBG scintigraphy cannot indicate distribution of neuroblastoma.

Physiological accumulation of ^{18}F-FDG in some organs is one of the pitfalls when interpreting acquired images of ^{18}F-FDG PET.[6] For example, the liver or the heart shows high uptake of ^{18}F-FDG, which reflects its physiologically high glucose metabolism. The urinary tract (renal pelvis, ureter, and urinary bladder) exhibits high accumulation because of excretion of ^{18}F-FDG into urine. The brain also highly metabolizes glucose due to almost limited energy source to glucose for neuron and glial cells.

Deviation from physiological uptake pattern of ^{18}F-FDG suggests some abnormality. ^{18}F-fluorodeoxyglucose positron emission tomography imaging of the brain is used for assessment of CNS disorders with glucose metabolic changes related to neuronal and synaptic activity. Brain death is indicated by absence of ^{18}F-FDG uptake in the brain.[2] Neurodegeneration diseases, such as Alzheimer's disease or other dementias, present specific hypometabolic patterns.[7] Central nervous system tumors show hypo- or hypermetabolism depending on the malignancy of the tumor in the localized lesions.[8] Infectious or autoimmune encephalitis demonstrates abnormal glucose metabolism reflecting brain inflammation.[9,10] In epilepsy, a scan is performed in the seizure-free interval and can detect low metabolic area corresponding to the focus of epilepsy.[11] In other literature, anomalies of ^{18}F-FDG uptake in the brain were reported in some neurological or psychiatric disorder.[12,13]

Here, we experienced a case of extremely low ^{18}F-FDG uptake in the brain of a 4-year-old girl with whole-body metastatic neuroblastoma. Almost missing of physiological uptake of ^{18}F-FDG first suggested an error of pre-inspection conditions about blood glucose level.[14] She had no history of diabetes. The fasting time before ^{18}F-FDG injection was 20 h and no uptake elevation in the skeletal muscle was observed. Next, some CNS disorder was suspected. However, she was clearly conscious and exhibited no neurological signs during the procedure. MRI did not reveal brain atrophy or other anomalies except small metastasis on the cranium. CNS metastasis was not recognized at diagnosis and possibility of CNS relapse during the course was thought to be low because lumbar puncture, one of risk factors, was not done although MYCN amplification, another risk factor, was not inspected.

Injected dosage of ^{18}F-FDG was about 4.5 MBq/kg. A loss of dosage is negligible when a small lesion exists. However, a larger volume of the lesion possibly effects the distribution. For example, running promoted glucose metabolism in the large skeletal muscle of the lower extremities. Increased accumulation of ^{18}F-FDG in the skeletal muscle was balanced by reduction of uptake in the abdominal organs.[15] However, brain uptake did not show statistically significant change because biological homeostasis regulated blood flow and preserved brain function. In recent studies for malignancy, metabolic tumor volume or total lesion glycolysis (TLG) was used to evaluate malignant tumors.[16–18] Total lesion glycolysis is a product of mean SUV and tumor volume. A study reported that TLG was negatively correlated with a^{18}F-FDG uptake in the brain.[19] Higher TLG means that a significant part of injected ^{18}F-FDG is caught to tumor and a less portion of the tracer is distributed to whole-body organs.

Regarding this case, an outstanding picture of ^{18}F-FDG PET/CT MIP reflected large volume of metastatic neuroblastoma and strong accumulation of ^{18}F-FDG with high SUV value. Pathologically, the worse condition of the disease was confirmed because of poorly differentiated subtype and high mitosis-karyorrhexis index in a pathological diagnosis[20] and high-risk group as International Neuroblastoma Risk Group.[21] A large amount of tumor with high SUV value was thought to affect extremely low uptake of ^{18}F-FDG in the brain. Regaining physiological uptake after chemotherapy could prove the normal CNS and support this idea.

In conclusion, we present a rare case of extremely low uptake of ^{18}F-FDG in the brain. We thought that this phenomenon was ascribed at least partly to the elevated metabolism in the metastatic neuroblastoma. Our finding can provide an idea to avoid one of the pitfalls in oncological imaging.

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Informed consent

The authors obtained verbal and written informed consent by the patient about his/her condition being presented in a case report.

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