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Importance of proper window setting in visual assessment of dopamine transporter imaging: A case of early-onset Parkinsonism related to Park2 gene mutation

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Abstract

In the early stages or atypical manifestation of parkinsonism, dopamine transporter imaging can assist the early diagnosis. We describe a 19 year-old man presenting with progressive gait disturbance, cervical dystonia and head tremor. 18F-FP-CIT PET (FluoroPropyl-Carbomethoxylodopropyl-nor-B-Tropane positron emission tomography) was done and interpreted as normal at other hospital, and his diagnosis remained baffling. He visited our hospital several months later, and the FP-CIT PET image was reviewed by the nuclear medicine physician in our hospital, who also interpreted it as normal. However, we reviewed his FP CIT-PET image because his clinical picture was strongly suggestive of juvenile parkinsonism. After adjusting the window setting of the PET image, we could appreciate the decreased uptake in the bilateral basal ganglia. Thus he was finally diagnosed as juvenile parkinsonism and gene test confirmed Park2 gene mutation. In conclusion, proper window setting is important during visual assessment of dopamine transporter imaging.

INTRODUCTION

Dopamine transporter imaging discriminates patients with Parkinson's disease from healthy individuals, identifying presynaptic dopaminergic deficits in the caudate and putamen with high specificity and sensitivity, even in the early course of the disease, and can be used to differentiate between neurodegenerative parkinsonism and its mimics.[1] Diagnosis of early-onset parkinsonism is often challenging, because rigidity and painful cramps as the predominant initial symptoms are more frequent in the younger group while gait instability as the predominant initial symptoms is more frequent in the older group.[2] In those cases, biomarkers such as dopamine system imaging can assist the diagnosis. However, misinterpretation of dopamine transporter imaging can lead to confusion of diagnosis.

We describe a young man with gait difficulty, painful cramps, dystonia, and tremor. In this case, misreading of 18F-FP-CIT positron emission tomography (PET) resulted in confusion in diagnostic process.

CASE REPORT

A 19 year-old man presented with progressive gait disturbance for 2 years. He often felt painful cramps on his thigh and feet. He also showed cervical dystonia. Besides, he developed resting tremor of bilateral lower extremities when he was 18 years old.

He visited other hospital at first, and FP-CIT PET image was done with the provisional diagnosis of parkinsonism. His FP-CIT PET image was read as normal (Figure 1). He felt better with Sinemet®CR 200mg twice a day, but the degree of subjective improvement diminished over several weeks. As the neurologist in that hospital did not think that the patient had Parkinson's disease because of "normal FP-CIT PET", L-dopa dosage was not increased.

He came to our hospital several months later. On neurologic examination, he had mild rigidity and resting tremor of bilateral lower limbs which was slightly more on the left side. His gait showed short step and wide base. The posture was mildly stooped, but arm swing was decreased bilaterally. The FP-CIT PET image was reviewed by the radiologist in our hospital, who also interpreted it as normal. However, we reviewed his FP CIT-PET again because his clinical picture was highly suggestive of juvenile parkinsonism. After adjusting the window setting of the PET image,

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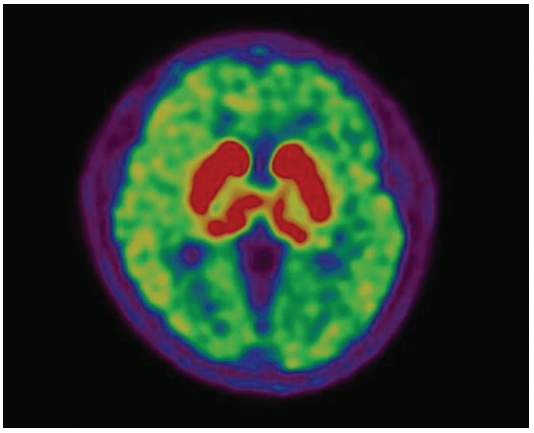

Figure 1. Initial transverse 18FP-CIT PET image does not reveal significant reduction of bilateral striatal uptake.

we could appreciate the decreased uptake in bilateral basal ganglia (Figure 2). Park2 gene was checked and revealed compound heterozygous mutation of exon 3-4 deletion allele and exon 2 deletion allele. He was finally diagnosed as early-onset Parkinson's disease related to Park2 gene mutation. He was started on pramipexole 3mg divided three times a day, which improved his gait difficulty and tremor.

DISCUSSION

It is likely that the patient in this case report was strongly suspected to have parkinsonism in the other hospital, since dopamine transporter imaging was ordered and levodopa therapy was initiated even though the CIT-PET was reportedly normal. However, misinterpreted dopamine transporter image resulted in confusion in the diagnosis and delayed the optimal treatment. Our nuclear medicine physician also reported his FP-CIT PET imaging as normal. However, we adjusted the window setting of CIT PET image based on clinical picture, and finally could get the correct diagnosis.

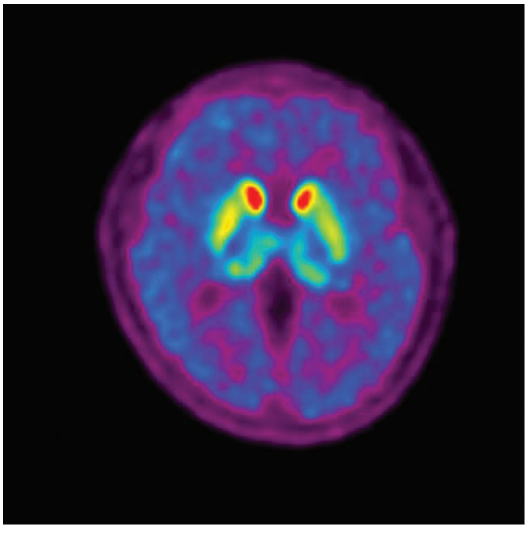

Figure 2. Transverse 18FP-CIT PET image after proper window setting reveals reduced uptake in both basal ganglia.

In usual clinical practice, radiologists commonly analyze 18F-FP-CIT PET based on visual assessment. For quantitative analysis, delineation of volumes of interest (VOI) is required to measure uptake of 18F-FP-CIT in the striatum and reference regions. A VOI can be drawn manually with aid of magnetic resonance imaging (MRI) or semi-automatically using standard VOI.[3] Another method for VOI delineation is normalization of image to a standard brain template.[4] However, these quantitation methods are still laborious and time-consuming for routine clinical practice. When we quantitatively measured the 18F-FP-CIT PET image, the standard uptake value ratio (SUVR) defined as [mean standardized uptake value (SUV) of striatal subregional VOI – mean SUV of occipital VOI]/ mean SUV of occipital VOI was decreased (1.68 on bilateral posterior putamina) to the Parkinson's disease range.[5]

Careful window setting will be needed to assess the specific binding and patterns of radioligand accurately. Dopamine transporter (DAT) density in the striatum is very high relative to other brain regions, which makes DAT imaging a powerful imaging method. Therefore, DAT density in the striatum can be higher than other brain region even with severe reduction of DAT in the striatum. Thus inappropriate adjustment of window setting may saturate the striatal region, which may mask reduction of DAT. In a quantitative study, Schwarz *et al*. reported that reduced striatal binding level of dopamine transporter image reflected severity of parkinsonism. However, there was a significant overlap in the range of striatal IPT (N-(3-iodopropen-2-yl)-2β-carbomethoxy-3β(4-chlorophenyl)-tropane) binding ratio between control group and Hoehn and Yahr I group.[6]

Therefore, simple application of specific striatal binding ratio may not be able to discriminate control and Parkinson's disease. There are other findings other than specific striatal binding of radioligands which can help differential diagnosis in DAT imaging such as progressive reduction of radioligand binding from caudate to posterior putamen and asymmetry in striatal binding

reduction.[7] In this regard, the visual assessment of dopamine transporter image can consider these patterns more easily to make it more practical and as good as quantitative measurement in routine practice.

In conclusion, dopamine transporter image is a powerful tool which can differentiate Parkinson's disease and its mimics. However, it is very important to understand the normal and pathological changes in DAT density in the brain and to adjust window setting properly in order not to be misread.

DISCLOSURE

Conflict of interest: None

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