Case Report

Differential diagnosis of patients with atypical Parkinsonian syndrome using $^{18}$F-FDG and $^{18}$F-FP CIT PET: A report of five cases

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A B S T R A C T

We describe 5 cases of patients who presented atypical parkinsonian syndrome (APS), including gait disturbance, postural instability, decreasing facial expression, dyskinesia, and subjective cognitive impairment. The patients underwent $^{18}$F-FP-CIT PET and $^{18}$F-FDG PET consecutively for differential diagnosis of APS. Through PET imaging examination, it was possible to offer a suggestive diagnosis and determine individual strategic management for patients with APS.

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Introduction

Parkinsonism is a neurological syndrome characterized by resting tremor, bradykinesia, rigidity, and postural instability [1]. Idiopathic Parkinson’s disease is the most prevalent cause, however, approximately one-third of patients with parkinsonian symptoms have another disease, especially atypical parkinsonian syndrome (APS) including multiple system atrophy (MSA), progressive supranuclear palsy (PSP), corticobasal syndrome (CBS), and dementia with Lewy bodies (DLB) [2]. However, the differential diagnosis of APS remains to be challenging with a high misdiagnosis rate since APS patients exhibit similar symptoms and specific symptoms do not appear in the early stage [3,4].

In complex or doubtful situations, it may be required to complete the clinical assessment with additional imaging tests. In nuclear medicine, $^{18}$F-fluorinated-N-3-fluoropropyl-2β-carboxymethoxy-3 β-(4-iodophenyl)-nortropane (FP-CIT) positron emission tomography (PET) is used to evaluate the presynaptic dopamine transporter (DAT) [5,6]. $^{18}$F-fluorodeoxyglucose (FDG) PET has been widely applied in neurodegenerative diseases to investigate the cerebral glucose metabolism, as a consequence of neuronal destruction or resting, which usually precede morphological atrophy [7]. Here, we would like to report several cases that were able to
Fig. 1 – Case 1. Maximum intensity projection (MIP) and transaxial image at a level of the basal ganglia of ¹⁸F-FP-CIT PET showing severely reduced FP-CIT binding in the bilateral putamen and caudate nuclei (A, B). The transaxial images of ¹⁸F-FDG PET at the levels of the dorsal frontoparietal cortex (C), basal ganglia (D), and cerebellum (E) demonstrated reduced FDG metabolism in bilateral occipital lobes, suggesting DLB. (G) Cingulate island sign of ¹⁸F-FDG PET showing preserved FDG metabolism in the posterior cingulate with surrounding hypometabolism.

Case reports

Case 1

A 76-year-old man arrived at the outpatient room of our medical center presenting stooping posture and postural instability that began 4 years ago and progressed in the past year. He also reported recent visual hallucinations. Physical examination revealed mild cogwheel rigidity in both hands and cognitive impairment. ¹⁸F-FP-CIT PET and ¹⁸F-FDG PET were performed and showed prominently reduced FP-CIT uptake in the bilateral striatum and severe FDG hypometabolism in bilateral occipital lobes (Fig. 1). Considering supportive PET findings, he was diagnosed with DLB, and cholinesterase inhibitors were prescribed for cognitive symptoms along with antipsychotics for neuropsychiatric symptoms and nonpharmacologic management by a corresponding neurologist [8].

Case 2

A 73-year-old man visited our clinic due to aggravating memory impairment, dystonia, slowness in movement, a decline in activities of daily living, visual hallucination, mild resting tremor in the left hand, and autonomic dysfunction such as urinary incontinence in the past 2 years. He recently had presented asymmetric hand clumsiness (left dominant) followed by early bradykinesia and rigidity and noted increasing stiffness in his left arm and tended to hold it flexed at his side. The patient also reported changes in cognition, memory, and mood over the past year. After neurologic examination and interview by the physician, he underwent both ¹⁸F-FP-CIT PET and ¹⁸F-FDG PET for differential diagnosis. The tests showed moderately reduced FP-CIT uptake in bilateral posterior putamen and asymmetric FDG hypometabolism in the right frontal, parietal, and temporal lobes (Fig. 2). According to
the latest consensus diagnostic criteria [9], he has been clinically diagnosed with CBS.

Case 3

For 5 years, a 73-year-old man was followed up due to postural instability, akinesia, and cognitive dysfunction. A local neurologist had previously been evaluated, diagnosed with Parkinsonism, and treated with a dopamine agonist with some subjective symptomatic benefit. Although he has been taking levodopa at our hospital continuously, he has complained of worsening dysphagia and aphasia for the past 6 months. His facial expression was masked on physical examination, gait instability progressed with the onset of falls, and vertical saccades were reduced. For neurologic evaluation, both 18F-FP-CIT and 18F-FDG PET scans were performed. They revealed severely decreased FP-CIT binding in bilateral caudate nuclei and putamen with interval aggravated status compared with a previous study, as well as moderate FDG hypometabolism in bilateral frontal lobes, suggesting PSP (Fig. 3). This patient was further evaluated in the rehabilitation department with a possible diagnosis of PSP [10].

Case 4

He was a 78-year-old patient who presented progressive autonomic failure involving urinary incontinence, orthostatic decrease in blood pressure, poorly levodopa-responsive Parkinsonism, and cerebellar signs such as gait and balance impairment and limb ataxia over the past 4 years. After PET studies (Fig. 4), this patient was diagnosed with MSA with cerebellar feature.

Case 5

This case was a 76-year-old male patient who showed similar symptoms to case 4. On the other hand, he presented with a 2-year history of bradykinesia, rigidity in the right upper extremity, and gait difficulty with recent falls. After PET studies (Fig. 5), this case was diagnosed with MSA with predominant Parkinsonism [11].
Fig. 3 – Case 3. $^{18}$F-FP-CIT PET images of this case showed preferential FP-CIT binding loss in bilateral caudate nuclei as well as putamen (A, B). $^{18}$F-FDG PET images (C–E) showed reduced FDG metabolism in medial, dorso-, and ventrolateral frontal lobes, suggesting PSPS.

Fig. 4 – Case 4. In this case, there was no significant FP-CIT binding abnormality in the bilateral putamen and caudate nuclei (A, B). However, diffuse FDG hypometabolism in the cerebellum via $^{18}$F-FDG PET images (C–E), suggesting MSA with cerebellar feature (MSA-C).
Fig. 5 – Case 5. 18F-FP-CIT PET images showed preferential FP-CIT loss in the ventral putamen as well as in the dorsal posterior putamen (A, B). FDG hypometabolism was noted in bilateral posterior putamen in 18F-FDG PET images (C–E), suggesting MSA with predominant parkinsonism (MSA-P).

**Discussion**

APS comprises MSA, PSP, CBS, and DLB, which is a heterogeneous group of neurodegenerative disorders characterized by cortical involvement (cognitive disorders, aphasia, apraxia, and sensory deficit), pseudo-bulbar signs (dysarthria, dysphagia, and sphincter disorders), pyramidal syndrome, cerebellar syndrome, or oculomotor disorders in addition to motor symptoms [12–15]. Accurate differential diagnosis of APSs is challenging for individual therapeutic and prognostic significance in patients with movement disorders.

Recently, 2 PET radiotracers such as 18F-FP-CIT and 18F-FDG, have been widely utilized to differentiate the diagnosis of APSs [16–20]. 18F-FP-CIT PET can assess dopaminergic neuronal degeneration by determining the density of striatal DAT, while 18F-FDG PET can be used for the evaluation of glucose metabolism. We present 5 cases of APS and the imaging findings of 18F-FP-CIT and 18F-FDG PET. This current case report focuses on some of the most common imaging findings of PET using dual radiotracers and aims to help the clinician determine the possible diagnosis and treatment. In conclusion, PET imaging with dual radiotracers of 18F-FP-CIT and 18F-FDG is useful not only for demonstrating striatal DA loss in neurodegenerative parkinsonism, but also for differentiating APS. It is therefore interesting to perform PET imaging with dual radiotracers in patients with parkinsonian symptoms to optimize the management, with an emphasis on the implementation of clinical practice.

**Patient consent**

Informed written consents were obtained from the patients for publication of these cases and any accompanying images.

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