Brain ^{18}F -FDG, ^{18}F -Florbetaben PET/CT, ^{123}I -FP-CIT SPECT and Cardiac ^{123}I -MIBG Imaging for Diagnosis of a "Cerebral Type" of Lewy Body Disease

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Abstract A 67-year-old man was referred for fluctuating neuropsychiatric symptoms, featuring depression, delirious episodes, recurrent visual hallucinations and catatonic syndrome associated with cognitive decline. No parkinsonism was found clinically even under neuroleptic treatment. ^{18}F -FDG PET/CT showed hypometabolism in the posterior associative cortex including the occipital cortex, suggesting Lewy body dementia, but ^{123}I -FP-CIT SPECT was normal and cardiac ^{123}I -MIBG imaging showed no signs of sympathetic denervation. Alzheimer's disease was excluded by a normal ^{18}F -florbetaben PET/CT. This report suggests a rare case of α -synucleinopathy without brainstem involvement, referred to as "cerebral type" of Lewy body disease.

Keywords Brain imaging · ^{18}F -FDG · ^{18}F -florbetaben · ^{123}I -FP-CIT · Lewy body disease · (MeSH terms) · MIBG

Introduction

Dementia with Lewy bodies (DLB), the second most common type of neurodegenerative dementia after Alzheimer's disease (AD) [1] causes a progressive decline in mental abilities characterized by recurrent visual hallucinations, cognitive fluctuations and spontaneous motor parkinsonism [2]. The main histopathological findings are the presence of variable regional density of Lewy bodies (LB) associated with Lewy neurites

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Fig. 1 Multi-tracer imaging. ^{18}F -FDG PET/CT (**a**, **b**) showed hypometabolism in the posterior associative cortex including the occipital cortex (white arrows), while amygdalo-hippocampal complexes and posterior cingulate cortex (cingulate island sign) were preserved (black arrows). ^{18}F -FDG PET abnormalities were not

explained by a cortical atrophy on CT scan (**b**). Alzheimer's disease was ruled out by a normal ^{18}F -florbetaben PET/CT, showing no β -amyloid deposition in the grey-matter (**c**). ^{123}I -FP-CIT SPECT (**d**) was normal and cardiac ^{123}I -MIBG showed no signs of sympathetic denervation (**e**, heart-to-mediastinum ratio H/M = 1.86)

and neuronal loss. The main involved areas of LB are brainstem, subcortical nuclei, limbic cortex and neocortex. Based on the regional distribution of these lesions, according to the pathologic diagnostic criteria described in the third report of the DLB consortium, DLB is classified into three pathological categories: the brainstem-predominant type, transitional type and diffuse neocortical type [2]. We present clinical data and multi-tracer images of a probable case of α -synucleinopathy without brainstem involvement, referred to as "cerebral type" of DLB.

Case Report

A 67-year-old man was referred to the psychiatry unit for fluctuating neuropsychiatric symptoms, featuring depression, delirious episodes, recurrent visual hallucinations and catatonic syndrome associated with cognitive decline. No parkinsonism was found clinically, even after neuroleptic treatment. The patient was transferred to the neurology unit for differential diagnosis between DLB and AD. Cerebrospinal fluid analysis of $\text{A}\beta_{42}$ and Tau proteins was inconclusive and brain MRI was normal, except for diffuse and moderate cortical atrophy. As part of the work-up, a brain ^{18}F -fluorodeoxyglucose (^{18}F -FDG) PET/CT, a

brain ^{18}F -florbetaben PET/CT, a ^{123}I - N - ω -fluoropropyl-2 β -carbomethoxy-3 β -(4-iodophenyl)nortropane (^{123}I -FP-CIT) SPECT and a cardiac ^{123}I -meta iodobenzylguanidine (^{123}I -MIBG) imaging were performed. Both PET acquisitions were performed on a Gemini GXL PET/CT camera (Philips, Da Best, The Netherlands). ^{18}F -FDG imaging was performed 30 min after intravenous injection of 134 MBq ^{18}F -FDG (diagnostic CT 120 kV 220 mAs over the head, followed by 1 step emission scan of 15 min). Amyloid imaging was performed 90 min after injection of 307 MBq ^{18}F -florbetaben using the same acquisition. ^{18}F -FDG PET/CT (Fig. 1-a, b) showed hypometabolism in the posterior associative cortex including the occipital cortex (white arrows), while amygdalo-hippocampal complexes and posterior cingulate cortex were preserved (black

Table 1 Binding potentials of ^{123}I -FP-CIT

	Right	Left	Normal limits*
Caudate	2.45	2.51	>2.00
Anterior putamen	2.11	2.22	>1.80
Posterior putamen	1.30	1.61	>1.10

* calculated from 10 normal controls (mean—2 standard deviations)

arrows), a pattern suggesting DLB [3, 4]. AD was ruled out by a normal ^{18}F -florbetaben PET/CT, showing no β -amyloid deposition in the grey-matter (Fig. 1-c). The ^{123}I -FP-CIT SPECT (Fig. 1-d) was normal (Table 1) showing preserved binding potential indexes (BPI). BPI are calculated as ratio of uptake between striatal structures (caudate, anterior putamen, posterior putamen) and occipital cortex as the reference background [5, 6]. Finally, the cardiac ^{123}I -MIBG planar image acquired 4 h after injection of 111 MBq MIBG showed no signs of sympathetic denervation (heart-to-mediastinum ratio = 1.86) (Fig. 1-e).

Discussion

This report suggests a rare case of α -synucleinopathy without brainstem involvement, referred to as a "cerebral type" of DLB. Indeed, DLB is probable here because the patient showed two of the three core features of DLB: fluctuating cognition and alertness, recurrent visual hallucinations, but no parkinsonism [2]. The preservation of metabolic activity in the cingulate gyrus (cingulate island sign) has been described as being characteristic for DLB (100 % specific; sensitivity 62–82 %) [4]. ^{123}I -FP-CIT imaging is usually useful in this setting because it improves both the sensitivity and specificity of clinical assessment (from 75 to 88 % and from 42 to 100 %, respectively) [7]. However, ^{123}I -FP-CIT imaging was negative in our case; a small number of false-negative scans has been reported in patients with a pathology-proven diagnosis of DLB, probably due to the expression of cortical and striatal LB pathology without significant striatal neuronal loss [8]. Another explanation is that our patient presented a "cerebral type" of DLB, a 4th type of DLB with no LB deposition in the brainstem first described by Kosaka et al. [9]. The absence of subcortical involvement is further supported in our case by a normal MIBG scan showing no sympathetic denervation. The existence of a cerebral type of DLB suggests that LB formation can occur in the cerebral cortex prior to its appearance in the substantia nigra and locus ceruleus. Multi-tracer imaging suggests in the present case that the development of cortical dementia can precede parkinsonism in DLB. Although no pathological proof can be obtained at this time, this diagnosis was finally retained by the multidisciplinary committee.

Compliance with Ethical Standards

Conflict of Interest Axel Van Der Gucht, Laurent Cleret de Langavant, Ophélie Bélissant, Corentin Rabu, Anne-Ségolène Cottureau, Eva Evangelista, Julia Chalaye, Sophie Bonnot-Lours, Gilles Fénelon, and Emmanuel Itti declare that they have no financial or other relation that could lead to a conflict of interest.

Ethical Statement All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

The manuscript has not been published before or is not under consideration for publication anywhere else and has been approved by all co-authors.

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