

Case Report

Young-Onset Dementia with Lewy Bodies

Yosuke Aiba^a Ryuji Sakakibara^a Tsuyoshi Ogata^a Ayako Iimura^a
Keiichiro Terayama^a Keiko Suzuki^b Shuichi Katsuragawa^b Yuuki Kato^b
Fuyuki Tateno^a Hitoshi Terada^c Tsutomu Inaoka^c Tomoya Nakatsuka^c

^aDementia Support Team, Neurology, Internal Medicine, Sakura Medical Center, Toho University, Sakura, Japan; ^bDementia Support Team, Psychiatry, Sakura Medical Center, Toho University, Sakura, Japan; ^cRadiology, Sakura Medical Center, Toho University, Sakura, Japan

Keywords

Young onset · Dementia with Lewy bodies · Mild cognitive impairment · MIBG myocardial scintigraphy · Dopamine transporter scan

Abstract

Young-onset (<65 years) dementia is a challenging clinical problem. A 61-year-old man visited our clinic because of a 2-year history of mild cognitive impairment of the executive disorder type. He was initially suspected of having young-onset Alzheimer's disease due to the lack of motor signs or hippocampal atrophy by conventional brain MRI. However, he proved to have anosmia, erectile dysfunction, hypersexuality, constipation, REM sleep behavior disorder, and emotional lability; imaging findings included positive brain perfusion SPECT, nigrosome MRI, DAT scan, and MIBG myocardial scintigraphy. All these clinical imaging features led to the correct diagnosis of young-onset dementia with Lewy bodies (YOD-DLB). It is hoped that this case report will help facilitate a future prospective study to diagnose and follow YOD-DLB patients with the aim of determining appropriate management and care.

© 2018 The Author(s)
Published by S. Karger AG, Basel

Introduction

Young-onset (<65 years) dementia (YOD) is a challenging clinical problem with potentially devastating medical and social consequences. The differential diagnosis is wide. According to Sampson et al. in London [1], YOD comprises Alzheimer's disease in 30%, vascular dementia in 15%, frontotemporal lobar dementia in 13%, alcohol-related dementia in 12%, and dementia with Lewy bodies (DLB) in 4% of patients, with these frequencies being almost constant worldwide [2–4]. Arriving at the correct diagnosis is not always easy, particularly for DLB. This is because DLB is not reflected on conventional magnetic resonance imaging (MRI). We herein report the case of a man who presented with YOD (starting at age 59) without motor signs throughout the course of disease, simulating Alzheimer's disease. He lacked hippocampal atrophy. However, his autonomic/sleep signs and other neuroimaging findings helped diagnose him as having YOD-DLB in situ.

Case Report

A 61-year-old man, the manager of a facilities division in the city government, was referred to our memory clinic by a local general physician because of his 2-year history of mild memory disorder starting at age 59. He had become unable to deliver presentations at the city council without difficulty and made small mistakes in calculations. He underwent memory tests and showed mild cognitive impairment (MCI) with executive disorder predominance, i.e., 22/30 on the Mini-Mental State Examination (MMSE; 0–30 scale, normal >24), 11/70 on the Alzheimer's Disease Assessment Scale-Cognitive Behavior Section (ADAS-cog; 0–70 scale, normal <10), 11/18 on the Frontal Assessment Battery (FAB; 0–18 scale, normal >16), and general <50, verbal 51, and visual <50 on the Wechsler Memory Scale Revised (WMS-R). A detailed history taken from him and his spouse revealed that he had started to have erectile dysfunction and anosmia (he later tested positive on an intravenous anosmia test) at age 58, followed by the MCI described above, which dominated throughout the course of disease with some fluctuations in symptoms. He had no history of hallucinations. These symptoms were followed by hypersexuality toward his spouse, constipation (infrequent bowel movements [2 times per week, normal >3] and defecation difficulty [colonic transit time 24 h under laxative [normal <39 h]), and reported REM sleep behavior disorder (at age 60) and emotional lability (at age 61). He did not show motor signs (Hoehn-Yahr grade 0; no resting tremor, rigidity, akinesia, or postural instability), postural hypotension, sleep apnea (apnea-hypopnea index 9.4 [normal <10]), or bladder dysfunction (no detrusor overactivity or post-void residual by urodynamics). His brain MRI scan showed no hippocampal atrophy, and the z-value of the parahippocampus by a voxel-based specific regional analysis system for Alzheimer's disease ver. 2 (VSRAD2) was normal (0.66, normal <2.0). Indeed, the complete lack of motor signs had initially suggested young-onset Alzheimer's disease.

However, he was diagnosed with YOD-DLB [5] based on the neurological symptoms/signs and positive brain perfusion SPECT with voxel-based analysis (occipital hypoperfusion), nigrosome MRI (parallel dopaminergic depletion [6]), ioflupane (N- ω -89 fluoropropyl-2 β -carboxymethoxy-3 β -[4-iodophenyl] nortropine, i.e., FP-CIT) dopamine transporter (DAT) scan (low specific binding ratio in the striatum on the right side [–0.16] and the left side [–0.79,

normal >3.0], indicating dopaminergic depletion, with 85–90% sensitivity and specificity [7]) and ¹²³I-metaiodo-benzylguanidine (MIBG) myocardial scintigraphy (low heart-to-mediastinum ratio on delayed imaging [1.24, normal >2.0], indicating noradrenergic depletion, with approx. 90% sensitivity and specificity [8, 9]) (Fig. 1). He did not have cardiac disease (cardiomyopathy, cardiac ischemia, etc.), and he was not being treated with drugs that might affect DAT scan or MIBG test.

He was started on oral memantine 20 mg/day, which ameliorated his emotional lability and facilitated concentration at work. However, his cognitive/mental status gradually deteriorated. Three years later, at age 64, he quit his work. At age 67, his MMSE scored zero (Table 1), he could not communicate at all, had apathy/loss of initiative, and became totally dependent on his spouse for daily living, using disposable briefs for incontinence. However, his motor function was preserved (Hoehn-Yahr grading 0; no resting tremor, rigidity, or postural instability; able to walk without cane; but with mild mask-like face), apart from apraxia when sitting on a chair. At this stage, his brain MRI scan showed only mild hippocampal atrophy on the left side. He was transferred to an institution for care.

Discussion

Our patient started with anosmia and erectile dysfunction (at age 58), followed by MCI of executive disorder type (at age 59). These features are in accordance with those seen in the MCI stage of DLB [10]. He next experienced hypersexuality, constipation, REM sleep behavior disorder (at age 60), and emotional lability (at age 61). He had no motor signs, which at first suggested young-onset Alzheimer's disease. However, he showed positive brain perfusion SPECT, nigrosome MRI, DAT scan, and MIBG myocardial scintigraphy. His autonomic/sleep sign, along with neuroimaging, helped to diagnose him as having YOD-DLB in situ. The obvious question arises: what explains the lack of motor signs despite the clear presence of abnormal dopaminergic imaging? We do not have an answer. However, pathology and clinical studies have shown that at least initially, DLB patients may present with cognitive/psychiatric signs alone without any motor signs [11, 12]. Our case proved that a combination of neurological vignettes (known non-cognitive, non-motor features of DLB, e.g., constipation and REM sleep behavior disorder, etc.) as well as neuroimaging can help to differentiate DLB from Alzheimer's disease in situ. In particular, the sensitivity and specificity of ioflupane DAT scan and MIBG myocardial scintigraphy are 85–90% [7] and approx. 90% [8, 9], respectively, adequate to noninvasively diagnose YOD-DLB. More recently, it has been reported that during a negative DAT scan period, a positive MIBG test result can be obtained in patients with premotor Lewy body disease [13]. Our case report has clear limitations, including the lack of analysis of cerebrospinal fluid for biological markers (tau, beta-amyloid, and alpha-synuclein) and no autopsy. Nevertheless, it is hoped that this case report will prompt and help facilitate a future prospective study to diagnose and follow YOD-DLB patients for their appropriate management and care.

In conclusion, we described the case of a 61-year-old man with YOD-DLB in situ. It is hoped that this case report will help facilitate a future prospective study to diagnose and follow YOD-DLB patients for appropriate management and care.

Statement of Ethics

The authors confirm that the approval of an institutional review board/patient consent was not required for this work.

Disclosure Statement

We have no conflict of interest.

Author Contributions

R. Sakakibara participated in the study concept and design, acquisition of patients and/or data, analysis and interpretation of data, and preparation of the manuscript. T. Ogata participated in the acquisition of patients and/or data. A. Imura participated in the acquisition of patients and/or data. F. Tateno participated in the acquisition, analysis, and interpretation of data. K. Terayama participated in the acquisition of patients and/or data. Y. Aiba participated in the acquisition of patients and/or data. S. Katsuragawa participated in the acquisition of patients and/or data. Y. Kato participated in the acquisition of patients and/or data. K. Suzuki participated in the acquisition of patients and/or data. H. Terada participated in the acquisition of patients and/or data. T. Inaoka participated in the acquisition of patients and/or data. T. Nakatsuka participated in the acquisition of patients and/or data.

References

- 1 Sampson EL, Warren JD, Rossor MN. Young onset dementia. *Postgrad Med J*. 2004 Mar;80(941):125–39.
- 2 Ikejima C, Yasuno F, Mizukami K, Sasaki M, Tanimukai S, Asada T. Prevalence and causes of early-onset dementia in Japan: a population-based study. *Stroke*. 2009 Aug;40(8):2709–14.
- 3 Snowden JS, Thompson JC, Stopford CL, Richardson AM, Gerhard A, Neary D, et al. The clinical diagnosis of early-onset dementias: diagnostic accuracy and clinicopathological relationships. *Brain*. 2011 Sep;134(Pt 9):2478–92.
- 4 Croisile B, Tedesco A, Bernard E, Gavant S, Minssieux-Catrix G, Mollion H. [Diagnostic profile of young-onset dementia before 65 years. Experience of a French Memory Referral Center]. *Rev Neurol (Paris)*. 2012 Feb;168(2):161–9.
- 5 McKeith IG, Boeve BF, Dickson DW, Halliday G, Taylor JP, Weintraub D, et al. Diagnosis and management of dementia with Lewy bodies: fourth consensus report of the DLB Consortium. *Neurology*. 2017 Jul;89(1):88–100.
- 6 Kamagata K, Nakatsuka T, Sakakibara R, Tsuyusaki Y, Takamura T, Sato K, et al. Diagnostic imaging of dementia with Lewy bodies by susceptibility-weighted imaging of nigrosomes versus striatal dopamine transporter single-photon emission computed tomography: a retrospective observational study. *Neuroradiology*. 2017 Jan;59(1):89–98.
- 7 Thomas AJ, Donaghy P, Roberts G, Colloby SJ, Barnett NA, Petrides G, et al. Diagnostic accuracy of dopaminergic imaging in prodromal dementia with Lewy bodies. *Psychol Med*. 2018 Apr;25:1–7.
- 8 Sakakibara R, Tateno F, Kishi M, Tsuyusaki Y, Terada H, Inaoka T. MIBG myocardial scintigraphy in pre-motor Parkinson's disease: a review. *Parkinsonism Relat Disord*. 2014 Mar;20(3):267–73.
- 9 Knudsen K, Fedorova TD, Hansen AK, Sommerauer M, Otto M, Svendsen KB, et al. In-vivo staging of pathology in REM sleep behaviour disorder: a multimodality imaging case-control study. *Lancet Neurol*. 2018 Jul;17(7):618–28.

- 10 Génier Marchand D, Postuma RB, Escudier F, De Roy J, Pelletier A, Montplaisir J, et al. How does dementia with Lewy bodies start? prodromal cognitive changes in REM sleep behavior disorder. *Ann Neurol*. 2018 May;83(5):1016–26.
- 11 Sakakibara R, Ogata T, Haruta M, Kishi M, Tsuyusaki Y, Tateno A, et al. Amnestic mild cognitive impairment with low myocardial metaiodobenzylguanidine uptake. *Am J Neurodegener Dis*. 2012;1(2):146–51.
- 12 Fujishiro H, Kawakami I, Oshima K, Niizato K, Iritani S. Delirium prior to dementia as a clinical phenotype of Lewy body disease: an autopsied case report. *Int Psychogeriatr*. 2017 Apr;29(4):687–9.
- 13 Tateno H, Sakakibara R, Tateno F, Tuyusaki Y, Aiba Y, Kishi M, et al. Metaiodobenzylguanidine myocardial scintigraphy identifies premotor Parkinson's disease during a negative dopamine transporter scan. *J Am Geriatr Soc*. 2015 Nov;63(11):2428–30.

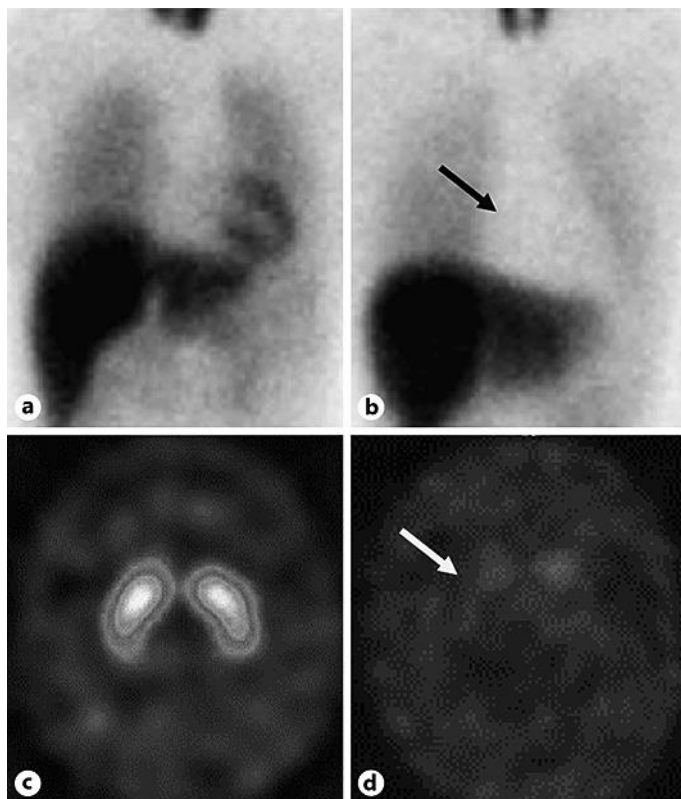


Fig. 1. ^{123}I -metaiodobenzylguanidine (MIBG) myocardial scintigraphy and ioflupane dopamine transporter (DAT) scan imaging. **a, c** Control. **b, d** Patient. **b** Heart-to-mediastinum ratio of delayed imaging 1.24 (normal >2.0). **d** Specific binding ratio in the striatum on the right side (-0.16) and left side (-0.79 , normal >3.0).

Table 1. Cognitive test of the patient

	MMSE (0–30, normal >24)	FAB (0–18, normal >16)	ADAS-cog (0–70, normal <10)
2012	22	11	11
2013	21	12	12
2014	23	10	12
2015	14	9	16
2016	11	6	26
2017	10	7	36
2018	5–0	na	na

MMSE, Mini-Mental State Examination; FAB, Frontal Assessment Battery; ADAS-cog, Alzheimer’s Disease Assessment Scale-Cognitive Behavior Section.