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Catatonia as the Initial Manifestation of Dementia with Lewy Bodies

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 92-year-old
Final Diagnosis: Dementia with Lewy bodies
Symptoms: Catatonia
Medication: —
Clinical Procedure: Biomarker
Specialty: Neurology • Psychiatry

Objective: Unusual clinical course

Background: Catatonia can occur in various neuropsychiatric disorders and is usually treated with benzodiazepines. So far, although 1 case of dementia with Lewy bodies (DLB) with catatonia has been reported, there have been no reports on patients with DLB whose initial symptom was a catatonia. Here, we present a patient who developed benzodiazepine-resistant catatonia and was subsequently diagnosed with DLB based on DLB biomarkers.

Case Report: The patient was a 92-year-old woman who had not been diagnosed with dementia before. At the age of 91, she experienced catatonia and was initially treated with lorazepam, which did not improve her condition. Later, she transferred to our hospital and was treated with amantadine. Amantadine improved her catatonic symptoms; however, a decline in her cognitive function was observed. We therefore explored the cause of cognitive impairment through imaging studies. We found that the patient did not have the core clinical features of DLB (ie, visual hallucinations, parkinsonism, cognitive fluctuations, and rapid eye movement sleep behavior disorder) but had 2 indicative biomarkers on ¹²³I-metaiodobenzylguanidine myocardial scintigraphy and dopamine transporter imaging. Possible DLB was diagnosed according to the diagnostic criteria.

Conclusions: Our case study suggests that catatonia can be an initial symptom of DLB. Moreover, considering the plausible pathophysiology of catatonia in DLB, amantadine treatment may be the most rational choice for the condition when benzodiazepine treatment is ineffective.

Keywords: Amantadine • Catatonia • Lewy Body Disease

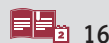
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Background

Dementia with Lewy bodies (DLB) is the second most common type of progressive neurodegenerative dementia following Alzheimer disease. It is characterized by 4 core clinical features: cognitive fluctuations, visual hallucinations, parkinsonism, and rapid eye movement (REM) sleep behavior disorder [1]. Recently, initial symptoms other than cognitive impairment, such as visual hallucinations, depression, and REM sleep behavior disorder, have been attracting attention in DLB [2]. In addition, indicative biomarkers of DLB on ^{123}I -metaiodobenzylguanidine (^{123}I -MIBG) myocardial scintigraphy and dopamine transporter imaging have been found to play important roles in the early diagnosis of DLB including during the prodromal stage [3-6].

Catatonia is a movement disorder characterized by immobility, mutism, inability or resistance to movement, and inappropriate response to external stimuli [7]. This condition can occur in various neuropsychiatric disorders, such as mood disorders, psychosis, drug intoxication, and neurodegenerative disorders [8], and is usually treated with benzodiazepines such as lorazepam and diazepam [7]. When benzodiazepine treatment is ineffective, alternative treatment such as antipsychotics, *N*-methyl-D-aspartate (NMDA) receptor antagonists (amantadine or memantine), nonbenzodiazepine hypnotic zolpidem, or electroconvulsive therapy are considered [7,9].

So far, although 1 case of catatonia in DLB has been reported, that case had core clinical features of DLB, including REM sleep behavior disorder and parkinsonism [8]. However, there are no reports of patients with DLB whose initial symptom was catatonia without the core clinical features of DLB (ie, visual hallucinations, parkinsonism, cognitive fluctuations, and REM sleep behavior disorder). Here, we report a patient who developed catatonia and was subsequently found to have DLB without core clinical features. The patient was successfully treated with amantadine for catatonia.

Case Report

The patient was a 92-year-old woman who had worked as a dietitian until the age of 80 years after graduating from a vocational school. She had no medical or family history of psychiatry or neurodegenerative diseases. At the age of 88 years, she was hospitalized for heat stroke; she subsequently started visiting a hospital for insomnia. At the age of 91 years, her Mini-Mental State Examination (MMSE) score was 21/30. A diagnosis of dementia was ruled out because she could perform basic self-care, shop, and take a walk by herself, and she received ramelteon as medication for insomnia. Three months later, she experienced stupor, waxy flexibility, mutism, negativism, and agitation. Catatonia was diagnosed according to the

diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition [10], and the patient was admitted to a psychiatric hospital. She was transferred to our hospital because lorazepam (up to 6 mg/d) treatment for 1 month did not improve her condition.

On admission, she scored 37/69 on the Bush-Francis Catatonia Rating Scale (BFCRS) [7]. Electroencephalography and laboratory blood test results showed no significant findings. Brain magnetic resonance imaging showed diffuse mild cerebral atrophy and leukoaraiosis (Figure 1A). The effectiveness of amantadine for catatonia was previously reported [9]. Therefore, to treat the muscle rigidity associated with catatonia, amantadine 100 mg/d was given through a nasogastric tube from day 2. On day 9, partial response was noticed as reflected by a BFCRS score of 25/69. Therefore, the dose of amantadine was increased gradually up to 200 mg/d from day 9. On day 15, the patient's catatonia almost disappeared (4/69 on the BFCRS). Subsequently, she showed amnesia, impaired visuospatial function, and disorientation, and her MMSE score was 13/30.

To identify the cause of cognitive impairment, imaging studies for DLB biomarkers were performed. The heart-to-mediastinum ratios of ^{123}I -MIBG myocardial scintigraphy were decreased (early: 1.31, delayed: 1.00, cutoff: 2.20) (Figure 1B). Iodine 123-*N*-omega-fluoropropyl-2-beta-carbomethoxy-3-beta-(4-iodophenyl) nortropane (^{123}I -FP-CIT) single-photon emission computed tomography (SPECT) showed reduced bilateral dopamine transporter availability in the striatum (Figure 1C). Carbon 11-Pittsburgh compound B-positron emission tomography revealed amyloid negativity. Although the patient had no core clinical features of DLB, she had 2 indicative biomarkers on ^{123}I -MIBG myocardial scintigraphy and ^{123}I -FP-CIT SPECT, and possible DLB was diagnosed according to the diagnostic criteria [1]. On day 29, the patient was referred to the previous psychiatric hospital for rehabilitation. About 6 months after discharge, she developed visual hallucinations and symptoms of parkinsonism, such as bradykinesia and dysphagia, which are core clinical features of DLB and confirmed the diagnosis of probable DLB [1].

Discussion

The case we report here had no core clinical features of DLB prior to the onset of catatonia, and DLB was finally diagnosed using ^{123}I -MIBG myocardial scintigraphy and ^{123}I -FP-CIT SPECT. This report is the first to show catatonia as an initial symptom of DLB. The dopaminergic system is assumed to be involved in the pathophysiology of catatonia [11]. Furthermore, a previous report on catatonia in Parkinson disease, the same Lewy body disease as DLB, pointed out that dysregulation of the dopaminergic system could play a role in the development of

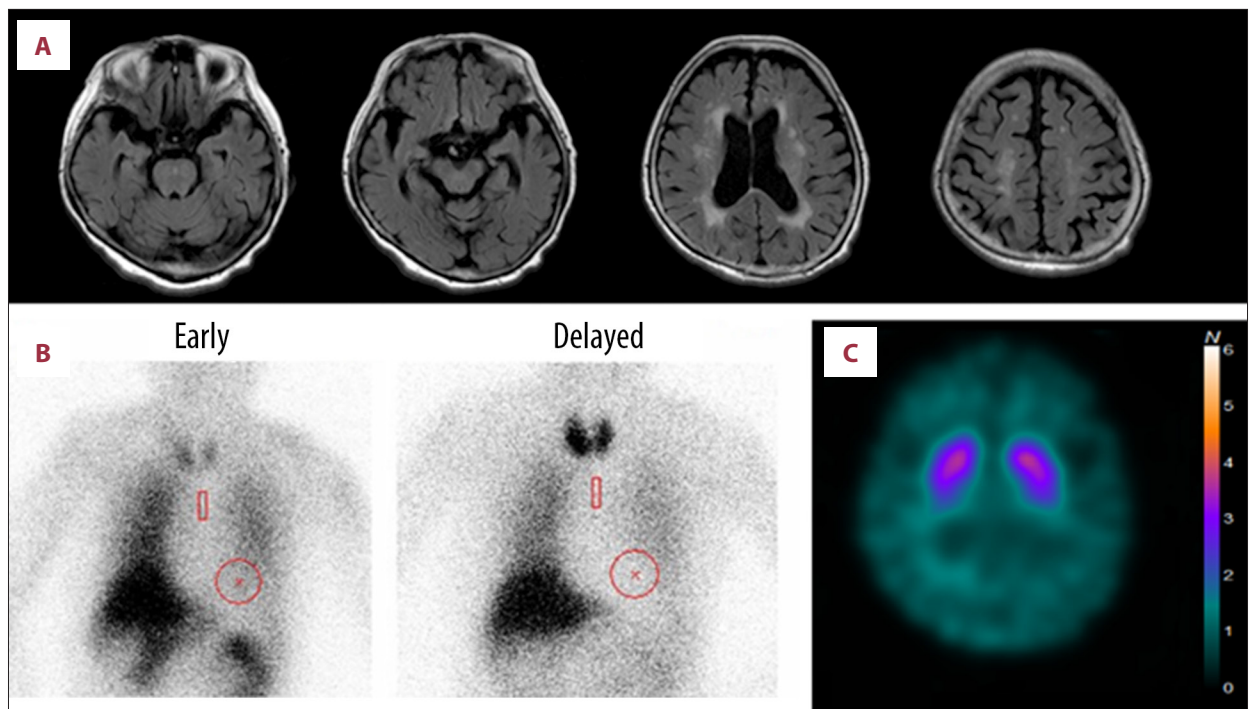


Figure 1. Neuroradiological findings. (A) Magnetic resonance fluid-attenuated inversion recovery image shows diffuse mild atrophy and mild leukoaraiosis. (B) Iodine 123-metiodobenzylguanidine myocardial scintigraphy showing no decrease according to the heart-to-mediastinum ratios. (C) Iodine 123-N-omega-fluoropropyl-2-beta-carbomethoxy-3-beta (4-iodophenyl) nortropane single-photon emission computed tomography showing reduced dopamine transporter availability in the bilateral striatum. The average specific binding ratio (SBR) for the whole striatum using DaTView software (AZE Corp., Tokyo, Japan) was 2.77 (right striatal SBR=3.05; left striatal SBR=2.48).

catatonia [12]. Thus, the catatonia in the present case may have been caused by the dopaminergic system related to DLB [1]. However, according to this hypothesis, most DLB must be followed by catatonia since dysfunction of the dopaminergic system is the fundamental pathophysiology underlying DLB [1]; however, there have been very few reports of catatonia in DLB [8]. There are 2 possible explanations for this phenomenon.

First, recent studies have reported that catatonia can be easily overlooked by neurologists [13]. Since DLB usually presents with extrapyramidal signs, catatonia may be confused with the latter [13]. The very few reports regarding catatonia in DLB may be attributed to the underdiagnosis of catatonia in DLB. A second explanation for the phenomenon is that, in addition to dysfunction of the dopaminergic systems, other mechanisms may increase the risk of developing catatonia in DLB. It is postulated that hyperactivity of the NMDA receptor coexisting with dysfunction of the dopaminergic system in the striato-cortical or the cortico-cortical pathways is involved in the pathophysiology of catatonia [14]. In the present case, amantadine, which has NMDA receptor antagonistic and dopamine receptor agonistic properties [14], was effective for catatonia occurring in DLB. Therefore, 2 mechanisms (ie, dopaminergic and glutamatergic systems) may have been

involved in the development of catatonia in the present case. Furthermore, the rarity of catatonia in DLB may be explained by it emerging under the situation of NMDA hyperactivity together with dopaminergic hypofunction.

Recommended therapies for catatonia, other than benzodiazepines, include atypical antipsychotics, electroconvulsive therapy, and amantadine [7,9]. DLB is associated with loss of dopaminergic neurons in the substantia nigra and is characterized by cognitive impairment, visual hallucinations, parkinsonism, and a marked sensitivity to antipsychotics, precluding extensive use of antipsychotics in its treatment [1]. In fact, we recently reported that quetiapine, an atypical antipsychotic drug, induced neuroleptic malignant syndrome in a DLB patient [15]. Electroconvulsive therapy has the risk of cognitive impairment, and consequently, it is not recommended for very elderly patients [16]. Therefore, considering the plausible pathophysiology of catatonia in DLB and the adverse effects of alternative treatments, amantadine treatment may be the most rational choice for the condition when benzodiazepine treatment is ineffective. In addition, as with amantadine, it is also important to investigate whether memantine and nonbenzodiazepine hypnotic zolpidem are effective for benzodiazepine-resistant catatonia in DLB.

Conclusions

Patients with DLB who do not exhibit the core clinical features of DLB may not receive an accurate diagnosis without the biomarkers. Therefore, the development of catatonia should be considered an initial symptom of DLB. Moreover, given the plausible pathophysiology of benzodiazepine-resistant catatonia in DLB and the adverse effects of alternative treatments, amantadine treatment may be the most rational choice for the condition.

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Conflict of Interest

None.

Ethics Approval

This study was approved by the Ethics Committee of Yamagata University School of Medicine.

Declaration of Figures Authenticity

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