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Efficacy of donepezil for the treatment of visual and multiple sensory hallucinations in dementia with Lewy bodies

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ABSTRACT

In this manuscript, we present a case report of a patient suffering from dementia with Lewy bodies who experienced not only visual but also four other sensory hallucinations, which were interdependent and may have influenced the patient's behavior. To the best of our knowledge, based on our search of the literature, this is the first such reported case of dementia with Lewy bodies. In this paper, we review the literature related to drug therapy for dementia with Lewy bodies, and propose, based on our clinical observations, that cholinesterase inhibitors, including donepezil, should be used as first-line drugs for the treatment and management of psychotic symptoms, including all five sensory hallucinations, in dementia with Lewy bodies.

Keywords: Behavioral and psychological symptoms of dementia (BPSD), cholinesterase inhibitors, complex multiple sensory hallucinations, dementia with Lewy bodies (DLB), donepezil

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INTRODUCTION

Antipsychotics have been used for more than 50 years for the treatment of psychotic symptoms, including hallucinations, and their efficacy for this use has been established. The efficacy of antipsychotics in delirium-related visual hallucinations in patients with dementia and Charles Bonnet syndrome is also well known [1-3].

Dementia with Lewy bodies (DLB) was initially described in the late 1970s by a Japanese researcher, K. Kosaka [4]. It is characterized by symptoms such as visual hallucinations, parkinsonism and rapid eye movement sleep behavior disorders [5]. No consensus has been reached regarding therapeutic approaches for DLB-related visual hallucinations. Second-generation antipsychotics, which are less likely to result in extrapyramidal side effects, can be effective for the treatment of DLB-related visual hallucinations [6]. The efficacy of cholinesterase inhibitors, including donepezil, for DLB-related psychotic symptoms has also been reported [3, 7-11]. However, donepezil-induced side effects, including the exacerbation of parkinsonism in patients with DLB, have also been reported [12].

In this manuscript, we report the case of a patient with probable DLB in whom donepezil administration led to the rapid disappearance of complex multiple sensory hallucinations. We also review the literature on the efficacy of drug treatments for DLB-related visual hallucinations.

CASE PRESENTATION

A 67-year-old male visited our outpatient clinic in March 200X. Disorientation, constructive apraxia,

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mild memory disorder, and mild cogwheel-like rigidity of the extremities were observed. The patient complained of visual hallucinations, saying things such as "people came to my home," "water was spilled on the floor," and "my desk was on fire." He also displayed bizarre behavior during the night: he would go outside wearing pajamas and be brought back home by the police, and he often woke up during the night to open the door to the bathroom or knock on his daughter's door.

Cranial magnetic resonance imaging (MRI) revealed no abnormalities. 123I-meta-iodobenzylguanidine (MIBG) uptake was disturbed in MIBG myocardial scintigraphy with a reduction in heart-to-mediastinum (H/M) ratio to 1.62 (<1.80) in the early image and 1.51 (<2.00) in the delayed image. Single photon emission computed tomography (SPECT) revealed a reduction in blood flow both in the parietal and occipital lobes, findings that are typical of DLB.

The patient received a probable diagnosis of DLB based on the consensus guidelines for DLB that were revised in 2005 [5]. After informed consent was obtained regarding off-label use, the administration of donepezil 5 mg resulted in the complete disappearance of visual hallucinations after 4 weeks of treatment. The detailed clinical course of this case was presented in a previous report [13].

Despite this treatment, a dramatic increase in his hallucinations was noted in March 200X+1. He experienced hallucinations, some of which he described as follows: "Big bones and rotten fish were in my food. It tasted awful"; "Salmon roe was in my rice, and when I chewed them, they burst open with a 'pu-tsu-pu-tsu' sound. It was delicious, with a fruity taste and smell"; "White, green, red, and blue balls were scattered on the floor. When I sneezed, these balls flew all over the place and made a lot of noise"; "When I touched my drugs, they suddenly changed color"; and "Colorful worms were falling on my face and body. It was extremely itchy." As described above, this patient presented with complex multiple sensory hallucinations, which were interdependent and may have influenced the patient's behavior.

Since these symptoms persisted for more than 4 weeks, the dose of donepezil was increased to 10 mg, and this resulted in the complete disappearance of the symptoms within 3 weeks. During this period, the patient's orientations were always perfect and abnormal behaviors were not observed. This indicated that the multiple sensory hallucinations were not due to delirium.

Subsequently, the patient has not experienced any hallucinations for more than 1 year, without any other concomitant treatments, and his cognitive functions have gradually improved. For example, his scores on the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS J-cog) were 15.3 in September 200X, 10.3 in June 200X+1, 7.3 in December 200X+1, and 5.0 in May 200X+2.

A second myocardial scintigraphy was performed in December 200X+1, and it showed a reduction of MIBG uptake in the H/M ratio to 1.37 in the early image and 1.15 in the delayed image, results that were worse than those in the first MIBG scintigraphy, despite the improvement in clinical symptoms.

DISCUSSION

Although several studies have demonstrated the efficacy of second-generation antipsychotics and cholinesterase inhibitors for DLB-related psychotic symptoms such as visual hallucinations [6-11], few reports have comprehensively reviewed drug therapies for DLB-related psychotic symptoms [5, 8].

It is well known that patients with DLB exhibit hypersensitivity to antipsychotics. The administration of second-generation antipsychotics exacerbates parkinsonism, making treatment impossible in some cases despite the presence of psychotic symptoms. On the other hand, there have been reports, although few, of patients with parkinsonism exacerbated by cholinesterase inhibitors [12]. Considering the probability of antipsychotic-induced adverse events, Kosaka recommended donepezil as a first-choice drug for DLB-related psychotic symptoms [14].

Although the exact pharmacological mechanism for the reduction of DLB-related hallucinations by donepezil remains to be clarified, we propose a general mechanism involving neurotransmitter imbalances. Specifically, in patients with DLB, the level of acetylcholine in the cerebral cortex is lower than that in Alzheimer's disease patients [15]. Therefore, there may be an appreciable neurotransmitter imbalance in the brain that results in psychotic symptoms, including visual hallucinations. Donepezil may rectify this imbalance, relieving the psychotic symptoms of DLB.

Our patient presented with complex, interdependent, multiple sensory hallucinations. To the best of our knowledge, this case is the first report in the literature of a patient presenting with complex and multiple sensory hallucinations involving all five senses. This patient may have an appreciable neurotransmitter imbalance in the brain not only in the visual area, but also in other sensory areas.

In order to use donepezil as a first-line therapy for DLB-related psychotic symptoms, it must be covered by health insurance. Clinicians in Japan are reluctant to select donepezil as the first-line treatment for DLB-related visual hallucinations even if they appreciate the potency of its effects because the use of donepezil for DLB is not covered by health insurance.

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CONFLICTS OF INTEREST

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