A 63-Year-Old Man with Lewy Body Dementia and Multiple Symptoms

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The patient is a 63-year-old man with Lewy body dementia that was diagnosed 7 years prior, who was taking dopamine agonists for severe parkinsonism. His presenting symptoms included obsessive-compulsive behaviors of excessive cleaning, rearranging, and punding (for example, purposely rearranging an organized room of boxes several times). Cognitive deficits became noticeable concomitantly. He exhibited confusion about the nature of his work and his schedule, experienced onset of sleep-wake cycle reversal, and started interacting with visual hallucinations of a little girl. He was forced to retire from his job of several decades as a telecommunications technologist (in 2008, at age 57 years), and became convinced that it was a plot by coworkers to push him out of the company. The onset of tremor in his right hand occurred within 1 year of these cognitive and behavioral changes, and it progressed to a dopamine-responsive diffuse tremor with axial rigidity and freezing episodes.

In addition to continuing treatment with a dopamine agonist for motor symptoms, the patient was started on the cholinesterase inhibitor donepezil in 2011 (at age 60 years). This occurred prior to relocation to another state and required transfer of care to physicians who had not previously interacted with the patient. A subsequent increase in his visual hallucinations, paranoia, and agitation was thought to be secondary to the recent move and change in routine. His new neurologist attempted to decrease his carbidopa/levodopa due to persistent psychotic symptoms, resulting in worsened motor symptoms, emotional lability, and vociferous suicidal ideation. His visual hallucinations persisted, and his delusions intensified due to his belief that his uncontrolled motor symptoms were due to being poisoned. The patient ultimately required acute psychiatric hospitalization and was given clonazepam at night for rapid eye movement (REM) behavioral disorder symptoms, with noted improvement in nighttime sleep consolidation.

However, early every morning and every afternoon, he screamed in response to visual hallucinations of “people sneaking around,” requiring lorazepam on an as-needed basis for severe agitation. During periods of lucidity, he expressed some insight into his condition and apologized for “bad behavior” that he did not remember but was told about by family. His diurnal patterns of inconsolable paranoid delusional outbursts and irregular sleep cycle were suggestive of a more complicated sleep-wake cycle disturbance.
Donepezil was stopped based on the hypothesis that it may be contributing to these symptoms, due to acetylcholine’s involvement in initiation of REM sleep.1,2

When the donepezil was discontinued, the patient’s visual hallucinations, agitation, persecutory beliefs, tremor, and urinary urgency promptly diminished and he no longer required unscheduled psychotropic medications for behavioral agitation. One week after cessation of donepezil, the patient was administered rivastigmine. However, it was stopped after 7 days due to notable increase in the same diurnal pattern of paranoia and agitation the patient exhibited when he was taking donepezil. Additionally, tremor, urinary urgency, and need for unscheduled medications for behavioral agitation recurred on this second acetylcholinesterase inhibitor. Once stopped, the same pattern of symptom improvement was noted once again. Furthermore, the patient’s dopamine agonist was switched to a controlled-release form and titrated to better address his tremor, without an increase in psychotic symptoms. At the 6-month follow-up, he remained psychiatrically stable.

**DISCUSSION**

Dementia with Lewy bodies (DLB) is a neurodegenerative disorder characterized by cognitive fluctuations, visual hallucinations, parkinsonism, dysautonomia, sleep disorders, and neuroleptic sensitivity.3,4 Treatment of DLB is challenging. Because dopamine agonists used to treat motor symptoms may precipitate or worsen psychotic symptoms associated with DLB, tapering or discontinuing these agents is a common first consideration. Neuroleptic drugs used to treat psychotic symptoms are often ineffective and worsen motor symptoms.4 Visual hallucinations in patients with DLB are associated with cholinergic deficits,2 and cholinesterase inhibitors are considered first-line therapy in treating hallucinations and behavioral disturbances in DLB.3,5

Dopaminergic agents are frequently implicated in manifesting psychotic symptoms.6 This case illustrates that acetylcholinesterase inhibitors may contribute to visual hallucinations and delusions in susceptible patients, possibly depending on the location and severity of brain lesions from neurodegeneration. There is a large body of literature detailing the role of acetylcholine in regulating the sleep-wake cycle, the mechanisms of which corroborate the possibility of this hypothesis, but that are beyond the scope of this case report.1,2 In brief, acetylcholine-enhancing medications, such as donepezil, may indiscriminately activate both the pons and basal forebrain, which have competing roles in sleep-wake physiology.1,2 This could contribute to wakefulness and insomnia in the evening, and REM intrusion into wakefulness during the day.

This wakeful dreaming could be mistaken for vivid visual hallucinations and delusions; activation of the visual component of REM sleep without the typical concomitant muscle atonia would allow the patient to appear awake and alert despite being aslepp.

In this patient, stopping dopamine agonists increased his behavioral disturbance, whereas stopping treatment with acetylcholinesterase inhibitors diminished his behavioral disturbance and psychosis. Although there is no known way for prescribers to identify situations in which acetylcholinesterase inhibitors might provoke REM intrusion into wakefulness, those caring for DLB patients with prominent behavioral and psychotic symptoms may wish to consider the possibility that cholinergic medications may exacerbate those symptoms and adversely affect a patient’s quality of life.

**REFERENCES**