Lewy Body Dementia: Case Report and Discussion

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Background: Lewy body dementia is a common but frequently underdiagnosed cause of dementia often mistaken for the more familiar entity of Alzheimer disease. Clinically the distinction is important, because it can have profound implications for management.

Methods: The medical literature was searched using the keywords "Lewy bodies," "Lewy body dementia," "Alzheimer dementia," and "parkinsonian disorders." A case of Lewy body dementia is described.

Results: An elderly man had long-standing diagnoses of Alzheimer disease and Parkinson disease. After he was evaluated thoroughly, the diagnosis was revised to Lewy body dementia, leading to changes in treatment that were associated with dramatic improvement in the patient's mental status. Evidence from the literature suggests that Lewy body dementia can be diagnosed in primary care settings based on clinical criteria. The physician should be alert to this diagnosis, and special attention should be paid to dementia patients who exhibit parkinsonism, hallucinations, fluctuating cognition, or prominent visuosperceptual deficits.

Conclusions: The diagnosis of Lewy body dementia has important implications. It is associated with a high incidence of neuroleptic sensitivity, necessitating great caution in the use of these common anti-psychotic agents. Early studies indicate cholinesterase inhibitors can be beneficial for treating the hallucinations and behavior disturbances that afflict these patients and might also improve cognition.(J Am Board Fam Pract 2002;15:50–4.)

Lewy body dementia is a common cause of dementia in the elderly, accounting for perhaps 15% to 25% of dementia cases.^{1,2} Evidence suggests that Lewy body dementia might be underdiagnosed, often being mistaken for the more familiar Alzheimer disease. Clinically the distinction is important, as it can have profound implications for management and prognosis. An alternative diagnosis of Lewy body dementia can lead to a trial of treatment that can be associated with dramatic improvement in the patient's symptoms.

Methods

The medical literature was searched using the keywords "Lewy bodies," "Lewy body dementia," "Alzheimer's dementia," and "parkinsonian disorders." An illustrative case report describes a case of Lewy body dementia initially diagnosed as Alzheimer dementia in which a change of diagnosis and treatment led to striking improvements in the patient's symptoms.

Case Report

A 79-year-old man was brought to the emergency department of a county hospital in November 2000 after having been found by the police wandering on the street. The patient reported no complaints with the exception of visual hallucinations, which were of a nonthreatening nature (eg, the patient had seen objects in the room, such as flowers and bread on the table). At this point the patient was confused and unable to provide a detailed history; therefore, the admitting physician relied on the patient's wife and daughter for most of the information.

Eight years earlier, the patient had Parkinson disease diagnosed. He was examined by a neurologist and was started on a combination carbidopalevodopa medication. The dosage was titrated up to 50 mg of carbidopa and 200 mg of levodopa four times a day. Although the prescribing physician noted no improvement in his parkinsonian symptoms, the medication was continued. Less than a

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year later, the patient developed memory problems, and Alzheimer disease was diagnosed. During the next 5 years, the patient's condition remained stable, and he continued to work as an attorney.

Two years before the November 2000 emergency department visit, the patient began experiencing frequent visual hallucinations, thought by the neurologist to be related to the antiparkinsonian medication. The neurologist prescribed quetiapine (125 mg in the morning and 100 mg in the evening) in an attempt to control these hallucinations. Despite this treatment, these symptoms continued to occur intermittently. At the time the patient was seen in the emergency department, he was still taking carbidopa-levodopa and quetiapine at the above dosages. He was taking no other medications.

The patient's medical history, in addition to the above, included a left hip replacement, glaucoma, and a left arm fracture. The patient had worked as an attorney in his family's law firm for several decades and had retired only 2 years previously. He was a respected and prominent member of his community. He had no history of smoking, alcohol, or drug abuse. There was no reason to suspect exposure to the human immunodeficiency virus.

When examined, the patient was a well-nourished, well-hydrated elderly white man in no apparent distress. He had no fever; his pulse was 68 beats per minute, blood pressure was 150/70 mm Hg, and respirations were 16/min. The patient was alert and oriented to person but not to place or time. He had an obvious tremor in both hands and feet. The tremor was coarse, symmetrical, and perceptible at rest and on intentional movement. His gait was unsteady. There were no other neurological findings. His score on Folstein's Mini-Mental State Examination (MMSE)³ was 20/30. We performed a standard workup, ruling out reversible causes of dementia (depression, hypothyroidism, vitamin B₁₂ and folate deficiency, neurosyphilis, subdural hematoma, brain tumor, and normal pressure hydrocephalus) and causes of delirium (including infection, electrolyte abnormalities, uremia, toxic ingestion, hypoxia, stroke, and myocardial infarction). All laboratory test results were unremarkable. A computed tomogram of the head showed only age-related cerebral atrophy.

The provisional diagnosis of Lewy body dementia was made, and the patient was given donepezil (Aricept) 5 mg at bedtime. The carbidopa-levodopa

and quetiapine were both discontinued. Interestingly, there was no change in the parkinsonian symptoms as a result. By the end of the second week of treatment with donepezil, the patient became increasingly alert and cooperative with caretakers. His interactions with family and staff improved considerably. His MMSE score at the end of the fourth week of treatment had risen to 27/30. He was still unable to reproduce the intersecting pentagons, his recall was 2/3 after 5 minutes, and he made one mistake when following a 3-step command. Because the patient's parkinsonism and hallucinations persisted, the levodopa-carbidopa and quetiapine were both subsequently restarted at lower doses. The patient was discharged from the hospital and is currently being cared for by his neurologist and his primary care physician.

Discussion

Lewy body dementia is named after the German physician Fritz Heinrich Lewy, who at the beginning of the 20th century first described distinctive extranuclear inclusions on microscopic brain tissue examination. These inclusions became known as Lewy bodies. It was not until the latter part of the 20th century that the importance of these lesions began to be recognized. Initially, a subgroup of Alzheimer disease patients was determined to have characteristic pathologic findings of cortical or brainstem Lewy bodies at autopsy.^{1,2} Later it became clear that these patients with Lewy bodies constituted a distinct neuropathologic and clinical entity, which became known as dementia with Lewy bodies or Lewy body dementia.⁴ Various subtypes have been described based on pathologic findings, details of which can be found in the literature.4,5

The disease is more common in men than women with a ratio of 2:1. The mean age at onset of symptoms is 68 years. The average time from onset to death is 6.4 years, with the most frequent cause of death being aspiration pneumonia. The cause of Lewy body dementia remains unknown. Some speculate that genetics plays a role, and studies are underway to investigate this possibility. It remains to be seen whether genetic testing will ever be sufficiently sensitive and specific to help in the clinical diagnosis of Lewy body dementia.

Diagnosis

Currently, definitive diagnosis of Lewy body dementia can be made only at autopsy. Clinically, as illustrated by this case, there is considerable overlap between Lewy body dementia and both Alzheimer disease and Parkinson disease. To improve the sensitivity and specificity of the clinical diagnosis, a set of clinical criteria for Lewy body dementia was drafted in 1996 by the Consortium on Dementia with Lewy Bodies.⁴ To diagnose Lewy body dementia using these criteria, there must be progressive cognitive decline that interferes with normal social or occupational functioning. Memory and visuospatial deficits are often, but not necessarily, prominent. In addition, two of the following three features must also be present: recurrent visual hallucinations⁶ (which are typically well detailed), fluctuating cognition, and spontaneous motor features of parkinsonism. Supportive of the diagnosis are repeated falls, syncope, transient loss of consciousness, systematized delusions, neuroleptic sensitivity, and hallucinations in other sensory modalities. The absence of stroke, focal neurological signs, and delirium makes the diagnosis of Lewy body dementia more likely.

These clinical criteria, when compared with the reference standard of autopsy, have been found to be highly specific (specificity 79%-100%) but to lack sensitivity (sensitivity 22%-75%.),⁷ implying that these criteria are useful for confirming the diagnosis but cannot be relied on for screening. This limitation of the clinical criteria is due at least to the following two factors. First, there is considerable overlap between the features of Lewy body dementia and those of other dementias. Second, the characteristic or diagnostic features of Lewy body dementia frequently do not become manifest until a late stage in the disease. Given the high prevalence of Lewy body dementia and its unique implications for management, the prudent primary care physician must be particularly alert for this diagnosis. As for any dementia, a thorough history (including interviews with family members and caregivers) and physical, neurological, and cognitive examinations are essential.

Although there is considerable interest in the role of functional imaging techniques designed to distinguish Lewy body dementia form Alzheimer disease, these techniques are not available for routine use. Essentially, radioisotope scans reflect either regional blood flow,⁸ regional glucose metab-

olism,⁹ or dopaminergic neuronal degeneration.¹⁰ It is hoped that these types of imaging studies will eventually become widely available for definitive antemortem diagnosis.

Therapeutic Implications

Perhaps the most clinically important feature of Lewy body dementia is the tendency for neuroleptic sensitivity. Studies suggest that about 50% of patients develop severe extrapyramidal symptoms, such as rigidity, altered consciousness, pyrexia, and collapse when exposed to neuroleptic agents. That these reactions can be irreversible and sometimes fatal^{11,12} has important implications for the management of psychotic symptoms in these patients. Other strategies for managing these symptoms should be exhausted before resorting to medications; when neuroleptics are necessary, it might be wise to consider admission to the hospital for dose titration. There is some debate in the literature^{13,14} about whether atypical neuroleptics, such as risperidone and quetiapine, might provide useful antipsychotic effects in Lewy body dementia without causing substantial extrapyramidal side effects, but this possibility has not been thoroughly investigated.

Despite the parkinsonian features, many patients with Lewy body dementia exhibit limited clinical response to L-dopa. Further, it should be noted that L-dopa can cause or exacerbate visual hallucinations, which tend to occur in these patients. For patients with Lewy body dementia, therefore, the risks of treatment with L-dopa will frequently outweigh the benefits. A possible explanation for the limited response to L-dopa lies in the finding that, compared with patients with Parkinson disease, those with Lewy body dementia have a lower density of dopamine D₂ receptors in the corpus striatum.¹⁵ This finding might also explain the increased sensitivity to neuroleptics, which are dopamine antagonists.

A few studies have examined the effects of cholinesterase inhibitors (including donepezil and rivastigmine) in patients with Lewy body dementia. The main outcomes studied were hallucinations, behavior, and cognition. In two case series^{16,17} where donepezil was used for 8 to 24 weeks at doses of 5 to 10 mg, there was a decrease in the frequency and duration of hallucinations. One of these series¹⁷ also found an improvement in cognition (mean increase in MMSE score of 4.4 in 7 of 9 patients). The response to donepezil observed in our patient was thus consistent with previously reported findings but was rather more dramatic than would typically be expected. Studies of rivastigmine include an open trial¹⁸ and a randomized doubleblind placebo-controlled study.¹⁹ Doses ranged from 3–12 mg/d. Findings after 12 to 20 weeks of treatment included decreased hallucinations and delusions, improved behavior, and in the latter study¹⁹ a trend (not statistically significant) toward improved cognition. Although further studies are needed, the current evidence suggests that the cholinesterase inhibitors might have an important role to play in the management of Lewy body dementia.

Summary and Conclusions

We have described the case of a 79-year-old patient who had visual hallucinations and long-standing diagnoses of Alzheimer dementia and Parkinson disease (for which he was treated with carbidopa/ levodopa without improvement). The patient's condition was thoroughly evaluated and, taking into consideration all the symptoms and findings, a diagnosis of Lewy body dementia was made.

This change in diagnosis led to a change in the patient's therapeutic regimen, first, by adding donepezil, and second, by reducing the doses of antiparkinsonian medications and neuroleptics. The patient responded extremely well to the treatment, and by the end of the fourth week, he was surprising both medical staff and his own family by appearing alert, responsive, and inquisitive. The dramatic improvement was perhaps best summed up by his wife's remark, "I haven't heard him ask questions like this for at least a couple of years."

This case illustrates some important lessons regarding the diagnosis and management of dementia. The diagnosis of Lewy body dementia should be considered whenever hallucinations, fluctuating cognition, parkinsonian symptoms, or visuospatial deficits are prominent. A thorough history, physical examination, and cognitive assessment are required to make the diagnosis, which in turn has important implications for management and prognosis. It is clear that neuroleptics should be either avoided in these patients or used with great caution. This case illustrates that cholinesterase inhibitors can have beneficial, sometimes dramatic, effects.

We found the management of this patient's condition to be an extremely rewarding experience. By sharing it with other primary care physicians, we hope that we can help them to be more cognizant of Lewy body dementia as an important clinical entity.

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