Alzheimer Disease: A Commonsense Approach to Evaluation and Management

December 31, 2006
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An 84-year-old woman presents with a 3-year history of slowly progressive memory impairment accompanied by functional decline. The patient lives alone but has been receiving an increasing amount of support from her 2 daughters, who accompany her to the appointment. The daughters first noticed that their mother was having trouble driving. About a year ago, she started forgetting family recipes. She also left food cooking on the stove unattended and burned several pans. Currently, the daughters are providing meals and transportation, assisting with housework, and doing their mother's laundry. They have become increasingly alarmed because she takes her medications only sporadically, despite the fact that they fill her pillboxes and call her regularly with reminders. Their chief concern is whether it is safe for their mother to continue to live alone.

THE CASE:
An 84-year-old woman presents with a 3-year history of slowly progressive memory impairment accompanied by functional decline. The patient lives alone but has been receiving an increasing amount of support from her 2 daughters, who accompany her to the appointment. The daughters first noticed that their mother was having trouble driving. About a year ago, she started forgetting family recipes. She also left food cooking on the stove unattended and burned several pans. Currently, the daughters are providing meals and transportation, assisting with housework, and doing their mother's laundry. They have become increasingly alarmed because she takes her medications only sporadically, despite the fact that they fill her pillboxes and call her regularly with reminders. Their chief concern is whether it is safe for their mother to continue to live alone. The patient feels that her memory problems are normal for her age. Other complaints include insomnia, chronic urge incontinence, and long-standing depression, for which she takes acetaminophen/diphenhydramine, tolterodine, and paroxetine, respectively. Examination reveals a mildly anxious but pleasant patient. There is no evidence of weight loss. Neurologic examination results are normal. Folstein Mini-Mental State Examination score is 18/30. The patient is unable to organize a clock drawing. 

What further steps are needed to identify the cause of this patient's memory impairment? Dementia is an increasingly common disorder seen in primary care practice. Approximately 4 million Americans are thought to have dementia; of these, approximately two thirds have Alzheimer disease (AD). The main risk factor for dementia is advancing age. The prevalence at 65 years is about 6%; at 85 years, it is nearly 30%. The criteria for dementia include a loss of memory and 1 or more other cognitive abilities (such as language, calculations, orientation, and judgment) and substantial impairment in social or occupational functioning (Table 1). In patients with probable AD, symptoms have an insidious onset and progress gradually. History. It may be difficult to obtain a comprehensive history from a patient with suspected dementia; hence, a family informant plays a crucial role. The informant must be interviewed separately from the patient, because family members generally downplay the seriousness of the symptoms in the patient's presence. Informants may also be in denial of the patient's condition or misrepresent his or her motives ("Of course Mom has stopped cooking; she's tired after 50 years."). An informant who is the patient's spouse may be cognitively impaired as well. Because many elderly persons are no longer active in the occupational or social realm, questions must be geared toward identifying the patient's degree of impaired function. For example, has the patient stopped going to bridge club because she can no longer understand the bidding, or stopped crocheting because she can no longer remember how to do the stitches? Once a determination of dementia has been made, it is essential that the diagnosis be as specific as possible. AD is no longer considered a diagnosis of exclusion. Although a definitive diagnosis is possible only at the time of autopsy, clinical history, characteristic decline, and absence of reversible factors allow a diagnosis of probable AD to be made with nearly 90% specificity. Diagnostic tests. Specific domains of memory, language, orientation, and visual-spatial disturbance are most frequently tested with the 30-item Folstein Mini-Mental State Examination. Although interpretation can vary according to educational background, a score below 24 in a typical high school graduate suggests cognitive
dysfunction. Abstract thought is particularly vulnerable to AD. For this reason, it is useful to ask an open-ended question, such as "How do you spend your day?" A vague but socially appropriate answer, such as "Oh, I keep busy," is characteristic of AD. Similarly, this patient's comment that her memory problems are normal for her age is a socially appropriate statement that does not imply insight. Patients who express insight into their memory problem are less likely to have dementia and more likely to be depressed.

The physical examination in a patient with AD is often unrevealing. The neurologic examination results are usually normal; focal or motor deficits point to another cause. Laboratory studies--such as a metabolic profile and tests of thyroid function and vitamin B₁₂ level--may be ordered to rule out medical causes of cognitive impairment. Other laboratory tests can be ordered as indicated--for example, a hepatic function test in a patient with a history of alcohol abuse. Controversy exists about whether imaging studies of the head are warranted; a noncontrast CT scan or MRI is a reasonable test to rule out cerebrovascular disease. Other imaging modalities, such as single photon emission computed tomography and positron emission tomography, are used as research tools only. Apolipoprotein E genotyping and other genetic studies are not clinically useful. Other disorders, such as depression or delirium, must be ruled out and/or treated before a definitive diagnosis is made. If possible, discontinue medications that have potential anticholinergic side effects, to see whether the sensorium clears. **Benefits of pinpointing the diagnosis.** There are at least 3 important reasons to make a specific diagnosis of AD as early as possible. First, early recognition allows time to treat patients before marked deterioration begins. Acetylcholinesterase inhibitors, which enhance cholinergic neurotransmission, moderately improve cognitive function and global performance and should be offered to every patient with suspected mild to moderate AD if the workup for reversible causes has been unrevealing (Table 2). These agents prolong the time the patient spends in the early stages of the disease and ultimately slow the decline. Estimates of improvement vary widely; in 1 report, 15% to 26% of patients showed improvement and up to 80% were stable at 6 months.⁴ All acetylcholinesterase inhibitors act by increasing the availability of acetylcholine and therefore have similar efficacy and toxicity. Data suggest that when these agents are discontinued, a precipitous drop in function occurs. Therefore, it is unclear when to discontinue therapy. Many practitioners feel that patients experience a greater degree or rate of decline if therapy is stopped and choose to continue the medication unless there is a clear reason not to do so--such as nausea, weight loss, noncompliance, or cost concerns. Memantine--a newly approved N-methyl-D-aspartate receptor antagonist--is indicated for patients with moderate to severe AD. A recent study of 322 patients with moderate to severe AD found that the combination of memantine and stable doses of donepezil resulted in significantly better outcomes than placebo on measures of cognition, activities of daily living, global outcome, and behavior.⁵ The second reason to make this diagnosis as early as possible is that it allows the caregiver additional time to deal with all of the ramifications. Educate the patient's family about expected disease progression and provide support; agencies such as the Alzheimer's Association (www.alzheimers.org or 800-272-3900) are good resources. Discuss with the caregiver behavior problems, such as wandering and agitation; ways of managing potentially unsafe behaviors, such as cooking and driving; and financial management. Finally, and perhaps most important, an early diagnosis allows the patient to participate in planning for the future. Although discussions regarding end-of-life issues are never easy, preparing a living will and establishing durable power of attorney for health care and finances can avert difficult and perhaps costly decisions in the future. **OUTCOME OF THIS CASE**

The patient's laboratory evaluation and CT scan were unremarkable. The acetaminophen/diphenhydramine was discontinued, because diphenhydramine can exacerbate confusion. The antidepressant was changed to sertraline, because paroxetine is somewhat more sedating and has more severe anticholinergic side effects than other selective serotonin reuptake inhibitors.⁶ (Although tolterodine is an anticholinergic, it was providing significant benefit to the patient. It could be discontinued if necessary.) Treatment was initiated with donepezil, 5 mg/d for 4 weeks; the dosage was then increased to 10 mg/d. The patient's daughters were instructed to supervise her medications more closely. Referral was made to the Alzheimer's Association for education and information about support groups. The patient began 2 days per week of adult day care. Advance directive documents were drawn up. After 8 weeks, the patient and her daughters all felt that the patient's thinking was clearer and that she was "more like herself."

**References:**

1. Geldmacher, David S. *Contemporary Diagnosis and Management of Alzheimer's Disease.*


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