CASE STUDY

Diagnosing Alzheimer's Disease

by Richard R. Delisle, MD and Steven Fishman, MD

History

Mr. Fortuno, a 68-year-old retired Italian accountant, comes to your office because he is worried about memory problems. His medical history is uncomplicated. He has been suffering from hypertension, well controlled with a diuretic, for the last five years. He has had surgery for benign prostatic hypertrophy. His deceased uncle had Alzheimer's disease (AD). While Mr. Fortuno has always enjoyed an excellent memory, particularly for numbers, he now has difficulty remembering telephone numbers. When his wife sends him to run errands, he needs a list in order to remember everything. When he meets an old friend, he does not immediately recall his name. He also has trouble remembering where he has put things in the house. This is particularly distressing to him because he has always prided himself on his memory.

He has a score of 28/30 on the Mini-Mental State Examination (MMSE). His two errors are calling a pen a pencil and repeating "no ifs, and or but" instead of "no ifs, ands or buts." He draws a clock perfectly on his clock-drawing test, but when asked to draw 11:10 pm, he draws a straight line from the 10 to the two. His physical examination is normal, including his prostate. The neurologic examination is normal as well.

Question

- **People frequently complain of memory problems as they age. Normal aging is often accompanied by decreased memory performance. Similarly, AD often begins with memory problems. How can we differentiate between the two?**

Comment

Benign memory problems associated with aging include forgetting where objects were left and forgetting the names of less-familiar acquaintances. These forgotten details are frequently remembered later as if the deficit were affecting information access (memory retrieval). The forgotten details are more likely to be accessed by cueing. Pathologic memory problems involve forgetting more significant facts, such as holidays and current events. These events are forgotten as they occur, reflecting impairment of more fundamental mechanisms of memory storage.

In Mr. Fortuno's case, language difficulties influenced his results on the MMSE. It is not uncommon for patients with a mother tongue other than English to lose a point in the naming exercise. His sentence repetition mistake can also be attributed to his less than perfect mastery of the English language. All his other memory symptoms are consistent with a normal age-associated decline in memory efficiency.

The inaccurate placement of the hands on the clock, however, suggests that Mr. Fortuno's cognitive difficulties may not be benign. It is usually not possible to establish the etiology of such an error in the absence of any other deficits. Mr. Fortuno should be reassessed after a few months to confirm or refute a pathologic cognitive decline. If Mr. Fortuno cannot be reassured and/or will not wait a few months, he should be referred to a specialist. Given his high pre-morbid level of intellectual functioning, a decline in cognitive functioning may not manifest at this early stage on his MMSE. Common reasons for referral include:

- Atypical clinical presentation, cognitive assessment or positive family history
- Onset earlier than 60 years of age
- Clinical concern about a potentially complicating comorbid condition
- A patient or family request

At this point, a routine laboratory work-up is advised. It should include:

- Complete blood count
- Thyroid function tests
- Serum electrolytes, calcium
- Serum glucose

Progress

Fifteen months later, Mr. Fortuno comes to your office again, and this time, he is accompanied by his wife. He did not come earlier because he had forgotten his appointment. His wife is worried because the memory problems have worsened. She also reports that he is showing significant word-finding problems, to the point that he is increasingly substituting English words with Italian. When questioned, he sometimes hesitates, seems perplexed and turns to his wife to answer for him. He appears more anxious. His son now takes care of the finances. Mr. Fortuno still dresses himself, but he has trouble choosing the appropriate clothes. He scores 22/30 on the MMSE. In the clock-drawing questions he now places a little number 10 beside the number 11. His physical and neurologic examinations are still normal.

Question

- **What is your diagnosis?**

Comment

There is no doubt the clinical picture has worsened. The patient presents with a history and findings of recent memory impairment. Anomia is difficult to evaluate in this case because English is not his mother tongue. There are clear signs of concrete thinking and constructional apraxia (clock drawing test). Notice the "turning of the head" behavior. His difficulty in choosing clothes and managing finances suggest impairment of executive functioning. The Diagnostic and Statistical Manual of Mental Disorders (DSM) IV's diagnostic criteria for dementia of the Alzheimer's type is the development of multiple cognitive deficits manifested by the following:

- Memory impairment
- One or more of: aphasia (problems with language; comprehension, naming), apraxia (the loss of ability to carry out familiar, purposeful movements in the absence of paralysis or other motor/sensory impairment), agnosia (the failure of recognition; especially people) or disturbance in executive functioning

According to the DSM-IV, Mr. Fortuno's presentation fulfills the diagnostic criteria for dementia of the Alzheimer's type. According to common convention, a score of less than 24/30 on the MMSE suggests a mild Alzheimer's dementia.

Progress

A year later, Mr. Fortuno is no longer driving his car. He does not join in the conversation except when prompted. His remarks are often confused. He shows disorientation to time (*i.e.*, month and season). His family says he remains well oriented in familiar environments, but he is unable to come to the clinic on his own. He recognizes his wife and two children, yet he has forgotten whole pieces of his own history. He appears more irritable. During the interview, he states that he believes strangers are trying to steal from him. He requires almost constant care for dressing and hygiene. He scores 17/30 on his MMSE. The neurologic examination remains normal.

Question

- **What stage of AD has the patient reached?**

Comment

According to his MMSE score, the patient now has moderate dementia. He is more dependent on his family and requires almost constant care. Concrete judgment is considerably affected. Behavioral problems and delirium frequently appear at this stage.

Progress

Twenty-one months later, Mr. Fortuno is totally dependent for eating, hygiene and dressing. He is incontinent and he shows complete disorientation to time and space. He cannot walk by himself because of poor balance. His speech is considerably altered, superficial and disjointed. He no longer recognizes his children and occasionally does not recognize his wife, whom he mistakes for an imposter. He talks about his own deceased parents as if they were still alive. His wife is exhausted and is considering placement in an institution. His score on the MMSE is 8/30. His neurologic examination reveals an apraxia for walking and the presence of primitive reflexes.

Question

- **What is this presentation suggestive of?**

Comment

Mr. Fortuno's presentation is that of severe dementia. It is common at this stage to place the patient in an institution. Primitive reflexes are not specific to a particular type of dementia, but they appear at later stages in advanced dementia. In general, balance problems and incontinence appear late in AD. Their early occurrence would suggest another diagnosis, such as normal pressure hydrocephalus or vascular dementia.

Learning Points

- Differentiating between benign and pathologic changes in memory is critical to the early recognition of dementia.
- The MMSE is not sufficiently sensitive to early stages of dementia to be used exclusively to make a finding of cognitive decline indicative of dementia.
- To rule out other medical causes, a routine blood work-up is advised when dementia of the Alzheimer's type is suspected.
- Transitions from mild to moderate to severe dementia are marked by a number of cognitive and behavioral developments.

Suggested Readings:

1. Morris JC, McKeel DW, et al: Very mild Alzheimer's disease: informant-based clinical, psychometric and pathologic distribution from normal aging. Neurology 1991; 41:469-78.
2. Corey-Bloom J, Thal L, et al: Diagnosis and evaluation of dementia. Neurology 1995; 45:216-8.
3. Jacobs DM, Sano M, et al: Neuropsychological detection and characterization of preclinical Alzheimer's disease. Neurology 1995; 45:957-62.
4. Geldmacher DS, Whitehouse PJ: Evaluation of dementia. N Engl J Med 1996; 335:330-6.
5. Geldmacher DS, Whitehouse PJ: Differential diagnosis of Alzheimer's disease. Neurology 1997; 48(Suppl 6):S2-S9.
6. Orgogozo JM, Auriacombe S: Syndrome démential. Encycl. Méd. Chir. Neurologie. Paris, 1995, 17-023-A, p.5.