



January 2023

# ELDER CARE

## A Resource for Interprofessional Providers

### Not All Dementia is Alzheimer's Disease

Richard Caselli, MD, Department of Neurology, Mayo Clinic Scottsdale

Alzheimer's disease is the most common cause of dementia, but it is important not to overlook other causes of dementia, especially the 10-15% of these cases that may be reversible. Examples of dementia-like illnesses that may be confused with Alzheimer's disease are shown in Table 1.

Four features of dementia-like illnesses should raise concern about causes other than Alzheimer's disease. They include (1) speed of onset, (2) age of onset, (3) the patient's clinical profile, and (4) a medical history that might indicate a non-Alzheimer's cause.

#### Speed of Onset and Progression

The more rapid the onset, the less likely a dementia-like condition is Alzheimer's disease. Examples of conditions confused with Alzheimer's but which have a more rapid-onset or progression range from delirium to mercury toxicity (Table 1).

#### Age at Onset

The younger the age at onset, the greater the chance of a non-Alzheimer's dementia. This is particularly true if there

is no family history of early-onset Alzheimer's.

#### Clinical Profile

Alzheimer's disease is a slowly progressive disorder that begins by affecting memory and gradually affects other domains including executive skills and naming.

Anosognosia (lack of awareness of one's disability) may also develop, as may personality changes. But, gait and non-neurological functions are usually spared. Patterns different than this should raise the possibility of a non-Alzheimer's dementia.

#### Medical History

A patient's medical history and medications should be considered. Many medical conditions, ranging from cerebrovascular disease to drug side effects, can cause a dementia-like illness that is confused with Alzheimer's.

#### Reversible Imitators of Alzheimer's Disease

Although reversible causes account for only 10-15% of cases of dementia-like illnesses, it is essential not to overlook them. The following case illustrates a real-life

Table 1. Examples of Dementia-Like Illnesses that Can Be Confused with Alzheimer's Disease			
Speed of Onset			
Underlying Cause	Acute	Subacute	Chronic
Degenerative	Delirium	ALS-dementia with hypoventilation	See Table 2
Infectious	Viral encephalitis	Fungal meningitis	Neurosyphilis
Inflammation	Disseminated Encephalomyelitis	Paraneoplastic syndrome	Autoimmune encephalopathy
Neoplastic	Obstructive hydrocephalus	Glioblastoma	Orbitofrontal meningioma
Nutritional	Wernicke-Korsakoff		Vitamin B12 deficiency
Psychiatric	Acute psychosis	Inadequately controlled psychosis	Severe depression
Toxic	Drug or alcohol intoxication	Mercury toxicity	Polypharmacy
Traumatic	Acute head injury	Subdural hematoma	Chronic traumatic encephalopathy
Vascular	Acute stroke	Disseminated intravascular coagulation	Vascular dementia

#### TIPS FOR RECOGNIZING NON-ALZHEIMER'S DEMENTIA SYNDROMES

- When patients are being evaluated because of cognitive impairment, consider causes other than Alzheimer's disease when the impairment develops at a young age, when it develops over a short period of time, or when a movement disorder, including gait disorder, is a predominant symptom.
- Always consider potentially reversible causes of cognitive impairment, like drug side effects, infection, depression, nutritional deficiencies, and delirium.

# ELDER CARE

Continued from front page

patient who was initially labeled as having Alzheimer's dementia, but who subsequently turned out to have a reversible medical condition.

**Case- Drug Toxicity:** A 72-year-old man with a history of bipolar disorder had a 7-month history of memory loss and two years of impaired gait. He scored 18/30 on a Mini-Mental State Exam (MMSE). He was on a stable dose of lithium for years but blood work showed an elevated level. After 3 days off lithium his cognition and gait returned to normal.

## Non-Reversible Causes of Dementia

Although Alzheimer's disease is the most common and well-known form of dementia, accounting for about 70% of cases, several other degenerative neurological disorders can cause irreversible dementia and are often confused with Alzheimer's disease.

The most common of these disorders is vascular dementia (now called vascular cognitive impairment), which accounts for about 15-20% of dementia cases and is often mixed with Alzheimer's. Other common syndromes include Lewy body dementia and fronto-temporal dementia, each accounting for about 10% of cases. Key characteristics of these syndromes are shown in Table 2. Although not reversible, recognizing these conditions allows for more accurate prognosis and more effective use of symptom-modifying medications. As we age, there is increasing overlap between these entities which is not always evident clinically but has been shown in brain autopsy studies.

## Treating Alzheimer's Disease.

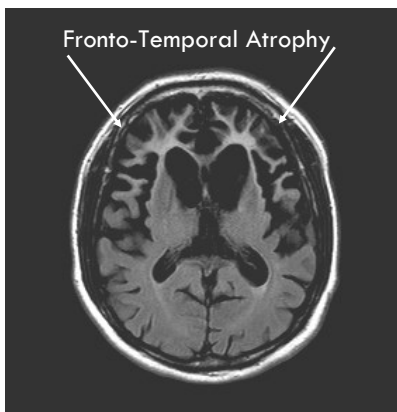
Until very recently all therapies have been largely symptomatic, meaning that they help with symptoms but do not interfere with the disease itself, which therefore continues to progress despite such treatment. Such symptomatic medications have included donepezil, rivastigmine, galantamine, and memantine. Recently a new treatment received FDA approval contingent upon further demonstration of clinical benefit. This form of treatment is called a "monoclonal antibody" and it

essentially mimics the effects of the immune system in attacking amyloid in the brain. In doing so, it activates an inflammatory reaction that clears amyloid from the brain. It is highly controversial not only because of potentially serious side effects and high cost, but

**Table 2. Non-Reversible Dementia Syndromes That May Be Misdiagnosed as Alzheimer's Disease**

Syndrome	Key Features
Vascular Dementia	<ul style="list-style-type: none"><li>- Risk factors for cerebrovascular disease</li><li>- Cerebrovascular disease on brain imaging</li><li>- Psychomotor retardation w/slowed gait</li></ul>
Lewy Body Dementia	<ul style="list-style-type: none"><li>- New onset of hallucinations</li><li>- Dream-enactment behaviors (e.g., yelling, kicking, spitting, flailing during REM sleep)</li><li>- Parkinson-like movement disorder</li></ul>
Fronto-Temporal Dementia	<ul style="list-style-type: none"><li>- Frontotemporal atrophy on imaging (see Figure)</li><li>- Behavioral variant: apathy, social withdrawal, disinhibition (lack of social tact)</li><li>- Semantic variant (trouble finding words)</li></ul>

because the actual clinical benefit has been relatively minor and inconsistent. Nonetheless this could be



use are far from agreed upon.

considered disease modifying therapy, akin to chemotherapy for cancer, and there are further treatments on the horizon that act in a similar fashion. These should be considered very carefully in consultation with a dementia specialist as their indications and proper

## References and Resources

- Caselli RJ, Tariot PN. Alzheimer's Disease and Its Variants. New York, NY: Oxford University Press; 2010.
- Graus F, Titulaer MJ, Balu R, et al. A clinical approach to diagnosis of autoimmune encephalitis. *Lancet Neurol.* 2016;15(4):391-404.
- Kawas CH, Kim RC, Sonnen JA, Bullain SS, Trieu T, Corrada MM. Multiple pathologies are common and related to dementia in the oldest-old: the 90+ study. *Neurology.* 2015; 85(6): 535-542.
- Porter VR, Avidan AY. Clinical overview of REM sleep behavior disorder. *Semin Neurol.* 2017; 37(4):461-470.

## Interprofessional care improves the outcomes of older adults with complex health problems.

Editors: Mindy Fain, MD; Jane Mohler, NP-c, MPH, PhD; and Barry D. Weiss, MD

Interprofessional Associate Editors: Tracy Carroll, PT, CHT, MPH; David Coon, PhD; Marilyn Gilbert, MS, CHES;

Jeannie Lee, PharmD, BCPS; Linnea Nagel, PA-C, MPAS, Marisa Menchola, PhD; Francisco Moreno, MD; Lisa O'Neill, DBH, MPH; Floribella Redondo; Laura Vitkus, BA  
The University of Arizona, PO Box 245069, Tucson, AZ 85724-5069 | (520) 626-5800 | <http://aging.arizona.edu>

Supported by: Donald W. Reynolds Foundation, Arizona Geriatrics Workforce Enhancement Program and the University of Arizona Center on Aging

This project was supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number U1QHP28721, Arizona Geriatrics Workforce Enhancement Program. This information or content and conclusions are those of the author and should not be construed as the official position or policy of, nor should any endorsements be inferred by HRSA, HHS or the U.S. Government.