THE UNIVERSITY OF ARIZONA
COLLEGE OF MEDICINE TUCSON
Center on Aging
www.aging.arizona.edu

January 2023

ELDER CARE

A Resource for Interprofessional Providers

Frontotemporal Dementia

Steven Z Rapcsak, M.D., University of Arizona College of Medicine

Dementia is a common problem for older adults; roughly 2/3 of cases are diagnosed as Alzheimer's disease (AD). One third of patients, therefore, have other types of dementia, most commonly vascular dementia, Lewy body dementia, and frontotemporal dementia (FTD). This issue of Elder Care will review frontotemporal dementia, which is sometimes misdiagnosed as AD.

Frontotemporal dementia is the current term for a dementia syndrome that used to be known by several different names, including Pick's Disease, progressive aphasia, semantic dementia, and frontal dementia of the non-Alzheimer's type. The common pathophysiological finding in these syndromes is brain atrophy that is most marked in the frontal and temporal lobes – hence the name frontotemporal dementia.

About 40% of patients with FTD have family histories of a similar dementia syndrome; many of them have a mutation of the tau protein gene on chromosome 17. Other mutations also occur, involving the progranulin and C9ORF72 genes. The remaining 60% of cases are sporadic.

Prevalence and Age of Onset

The true prevalence of FTD is unclear, as not all clinicians consider FTD in the differential diagnosis of dementia. As a result, FTD is often confused with, and mislabeled as, AD. One important clue to the diagnosis of FTD, however, is its earlier onset than AD, with most cases appearing before age 65. Among people with dementia in their early 60s, the relative prevalence of FTD and AD is about the same. With increasing age, AD becomes more common. Overall, FTD is thought to account for about 2-5% of all cases of dementia, though some estimates go as high as 10-15%.

Recognizing Frontotemporal Dementia

As well as an earlier age of onset, FTD has other characteristics that distinguish it from AD. These are shown in Table 1. Three major clinical phenotypes of FTD are currently recognized: the behavioral variant, and the non-fluent variant and semantic variants of primary progressive aphasia.

Table 1. Frontotemporal Dementia vs Alzheimer's Disease

Characteristic	*Frontotemporal Dementia*	*Alzheimer's Disease*
Age of Onset	Usually < 65 yrs	Usually > 65 yrs
Memory Deficits	Late	Early
Executive Function Deficits	Early	Late
Behavioral Disturbance	Early	Late
Language Impairment	Early	Typically develops after memory loss
Brain Imaging	Focal frontal/temporal atrophy	Hippocampal and posterior temporo-parietal atrophy
Response to cholinesterase inhibitors	None	Some

Behavioral variant FTD (bvFTD) is characterized by personality changes (Table 2), especially in the initial stages. Executive function (e.g., planning, organizing, and task completion) is also impaired early on in the course of the illness. Only later does memory impairment develop.

Personality and behavioral changes fall into one of three initial patterns. Over time, these patterns blend and patients frequently demonstrate aspects of all three.

The most common pattern is disinhibition, in which patients lose learned social behaviors. They may steal or use foul language. They may lose a sense of safety (people with FTD have been known to try to exit moving automobiles). They may demonstrate bizarre behavior, poor financial judgment, and compulsive buying, leading to an incorrect diagnosis of bipolar disorder or schizophrenia.

Another pattern of personality change is withdrawal, in which patients become apathetic and don't participate in daily activities. They may need prompting even for basic activities like personal hygiene. Patients typically lose their capacity for empathy and sympathy, exhibiting diminished responsiveness to the feelings and needs of others. The loss of personal warmth that characterizes this syndrome can be highly disturbing and stressful to caregivers.

TIPS for Diagnosis Frontotemporal Dementia (FTD)

- Consider FTD when dementia occurs in individuals younger than age 65, or in older individuals with dementia when there is a family history of early-onset dementia.
- Consider FTD when behavior disturbances, such as disinhibition or withdrawal, outweigh memory impairment.
- Consider FTD when impairments of executive function predominate over memory impairment.
- Consider FTD in patients who present with progressive language impairment.
- When FTD is suspected, order brain imaging to detect atrophy of the frontal and/or temporal lobes.

Continued from front page

The third pattern is repetitive/compulsive behaviors. An individual might wash repeatedly, read the same book over and over, or eat excessively.

Non-fluent and semantic variants of primary progressive aphasia (nfPPA and svPPA) have language changes as the predominant symptom. Initially, these may constitute the only abnormality. nfPPA is characterized by slow, effortful speech with unclear articulation such as dysarthria or apraxia. Patients may demonstrate agrammatism or telegraphic speech, manifested by simplified grammatical structure and the tendency to produce short phrases or isolated words rather than full sentences. With progression of the disease, patients may become mute. By contrast, comprehension of speech in nfPPA is relatively preserved and may be intact at the single-word level.

In svPPA, speech output is fluent and does not show evidence of agrammatism or motor speech abnormalities. Despite fluent speech production, patients have severe naming impairment (anomia), as well as deficits in single-word comprehension. Failure to recognize common objects and familiar people are also common clinical findings indicating a pervasive loss of semantic knowledge that extends beyond language production and comprehension.

Diagnosis

FTD is suggested by the clinical presentation. When evaluated by neuropsychological tests, patients may perform more poorly on tests of executive function or language and better on measures related to memory.

Imaging with CT or MRI often shows the typical focal atrophy of the frontal and/or temporal lobes. In nfPPA the atrophy may primarily involve left frontal cortex whereas in svPPA the atrophy is most severe in left anterior temporal lobe structures.

It is important to note that the full clinical spectrum of FTD overlaps with disorders such as corticobasal degeneration, progressive supranuclear palsy, and amyotrophic lateral sclerosis (ALS). Due to these overlaps, it is important to examine patients suspected of FTD for motor signs and symptoms that are characteristic of those related disorders.

Thus, referral to neurology is suggested.

Treatment

There is no cure for FTD. Drug treatment is aimed at controlling behavioral symptoms. Selective serotonin reuptake inhibitors may help with withdrawal or compulsive behaviors. The newer "atypical" antipsychotics may help with aggressive behaviors or disorganized thinking, but there has been limited study of their use. Prescription of the older, "typical" antipsychotics is not recommended.

Cholinesterase inhibitors, which are widely used for AD disease, have no benefit in FTD and have caused worsening symptoms in some patients. The role of memantine is being studied.

Overall, none of these medications has a major influence on the course or outcomes of FTD. The Food and Drug Administration has not approved any medications for treating FTD.

Prognosis

FTD is a fatal illness. Life expectancy from time of diagnosis ranges from 2-17 years (mean 8 years).

Table 2. Various Symptoms of Frontotemporal Dementia (adapted from Vossel Reference)

Behavioral-Variant FTD	***Non-Fluent Primary Progressive Aphasia***
• Disinhibited and inappropriate social behaviors that are uncharacteristic, such as stealing, using foul language in public, or inappropriate sexual behaviors	• Effortful, slow speech, with unclear articulation
• Lack of awareness of behavior changes	• Agrammatism
• Loss of concern about appearance and hygiene	• Motor speech errors sometimes progressing to mutism
• Apathy, social withdrawal, loss or drive or empathy	***Semantic-Variant Primary Progressive Aphasia***
• Compulsive/repetitive behaviors (e.g., pacing, handwashing)	• Fluent speech without agrammatism or motor speech problems
	• Severe anomia and impaired single word comprehension
	• Defective recognition of objects and people.

References and Resources

Frontotemporal Dementia. Memory and Aging Center: University of California, San Francisco. 2008. http://memory.ucsf.edu/ftd/

Frontotemporal Dementia Connections Reprint. National Institute on Aging: Alzheimer's Disease Education & Referral Center. www.alz.org/dementia/fronto-temporal-dementia-ftd-symptoms.asp

Gorno-Tempini ML, et al. Classification of primary progressive aphasia and its variants. Neurology, 2011, 76:1006-1014.

Rackovsky K, et al. Sensitivity of revised diagnostic criteria for the behavioral variant of frontotemporal dementia. Brain, 2011, 134:2456-2477

Types of Dementia: Frontotemporal Dementia. Dementia Guide, Halifax, Nova Scotia, 2007. https://www.dementiaguide.com/aboutdementia/typesofdementia/?pageContent=frontotemporal

Vossel KA, Miller BL. New approaches to the treatment of frontotemporal lobar degeneration. Curr Opin Neurol. 2008; 21(6): 708-16.

.

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; Teri Kennedy, PhD, MSW, LCSW, ACSW; Jeannie Lee, PharmD, BCPS; Marisa Menchola, PhD; Francisco Moreno, MD; Lisa O'Neill, 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.