Frontotemporal Dementia

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Faculty Disclosure

Contributing faculty, Lauren E. Evans, MSW, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience

This introductory course is designed for psychologists who may intervene to support patients with frontotemporal dementia and their families.

Accreditations & Approvals

American Psychological Association

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Course Objective

The purpose of this course is to provide psychologists with current information on frontotemporal dementia (FTD). Understanding the epidemiology, pathology, clinical features, diagnostic process, genetics, symptom treatment/management, role of brain autopsy, and current research provides a foundation for the care of patients with FTD and support for their families.

Learning Objectives

Upon completion of this course, you should be able to:

1. Describe the epidemiology of frontotemporal dementia (FTD) in the United States.
2. Explain the brain changes of FTD and their general clinical manifestations.
3. Identify the three general presentations of FTD.
4. Review how a clinical diagnosis of FTD is made, including differentiation from Alzheimer disease.
5. Summarize the role of genetics in FTD.
6. Discuss strategies for managing symptoms of FTD and providing support to family caregivers.
7. Identify goals of current research on FTD.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Frontotemporal dementia (FTD) is a group of degenerative brain disorders characterized by behavior and language problems and also overlapping with some motor/movement diseases. FTD causes progressive deterioration in a person's ability to function as the result of damage to the frontal and temporal lobes of the brain. FTD is also referred to as frontotemporal degeneration, frontotemporal lobar degeneration, and Pick disease.

Dr. Arnold Pick, a Czech neurologist, psychiatrist, and neuropathologist, first described frontal and temporal lobe atrophy causing dementia and progressive aphasia in 1892 [1]. The clinical syndrome subsequently became known as "Pick disease." FTD is the third leading cause of dementia across all age groups, after Alzheimer disease (AD) and Lewy body dementia [2]. It is one of the most common causes of early-onset dementia, with onset typically between 45 and 64 years of age [2; 3].

The clinical presentation of FTD can be complex, and obtaining an accurate diagnosis can be challenging. The unique clinical symptoms of FTD, neuropsychologic assessment, and brain imaging can help distinguish it from AD and other dementias. There is presently no effective treatment for FTD, and symptom management can be challenging for healthcare providers and family caregivers. Research is in progress to better understand FTD, hopefully leading to effective treatment, cure, and prevention of this devastating disease.

EPIDEMIOLOGY OF FTD

It is estimated that FTD affects approximately 60,000 people in the United States [3]. As noted, the age of onset for FTD is typically 45 to 64 years, with a mean of 58.5 years and a reported range between 21 and 80 years of age [2; 3; 4; 5]. In the United States, the prevalence in people 45 to 64 years of age is estimated at 15 to 22 per 100,000 population; the incidence in this group is 2.7 to 4.1 per 100,000 [5]. It is estimated that 60% of those with FTD have onset between 45 and 64 years of age; 10% have onset before 45 years of age, and 30% have onset after 64 years of age [5]. FTD is now considered by some to be the most common form of pre-senile dementia in patients younger than age 60, even more common than AD in this group [6; 7; 8].

FTD affects both men and women. However, it is unclear if men and women are affected equally, or if some subtypes of FTD may be more common in one gender or the other [9]. Significant time (average: 3.6 years) often passes between symptom onset and actual clinical diagnosis [5].

The disease duration for FTD can range from 2 to 20 years from symptom onset to death, with a mean duration of 8 to 10 years [3; 5; 10]. Pneumonia is the most common cause of death [3].

PATHOGENESIS AND PATHOPHYSIOLOGY OF FTD

Patients with FTD experience a progressive loss of neurons in the frontal and anterior temporal lobes, resulting in atrophy in these areas of the brain. They may also develop gliosis in the frontal and temporal lobes where neurons have been lost or damaged.

In FTD, affected neurons have an abnormal accumulation of protein within the cell, called inclusions. Three types of intra-neuronal inclusions have been identified, based on the protein involved. In some cases, the inclusions are composed of an abnormal form of the protein tau. In other patients, the inclusions are composed of the transactive response DNA-binding protein 43 (TDP-43). In a smaller number of FTD cases, the inclusions are composed of fused in sarcoma (FUS) protein [11].

FORMS OF FRONTOTEMPORAL DEGENERATION
Behavioral presentation • Behavioral variant FTD (bvFTD)
Language presentation, variants of primary progressive aphasia (PPA) • Nonfluent/agrammatic PPA (nfvPPA), previously called progressive non-fluent aphasia (PNFA) • Semantic variant PPA (svPPA), previously called semantic dementia (SD) • Logopenic variant PPA (lvPPA) (often found to have Alzheimer disease pathology at autopsy)
Associated movement disorders (not classified as FTD, but have shared symptoms) • Corticobasal syndrome (CBS) • Progressive supranuclear palsy (PSP) • Motor neuron disease, also called amyotrophic lateral sclerosis (FTD/MND or FTD/ALS)
Source: Compiled by Author — *Table 1*

The frontal and anterior temporal lobes of the brain control executive functions (e.g., planning, organizing, abstract thinking, judgment, decision making), personality, social behavior, and language. The changes associated with FTD causes impairments in executive function, personality, behavior, and/or language. The location of the neurodegeneration correlates fairly well with the clinical presentation [11]. Changes in other areas of the brain may cause overlapping movement problems. While the cause of most cases of FTD is not known, some cases are now known to be caused by genetic mutations.

CLINICAL PRESENTATION

FTD causes a gradual, progressive decline in behavior and/or language; movement disorders may also be involved. Behavior or language problems are typically the first and most prominent symptoms of FTD, whereas memory problems are the first symptoms of AD [5]. Subtypes of FTD have been identified based on clinical presentation (***Table 1***). Behavioral variant FTD (bvFTD) is the most common form and involves changes in behavior, personality, and emotions. Language presentations are referred to as primary progressive aphasia (PPA) and can take one of three forms: nonfluent/agrammatic variant PPA (nfvPPA), semantic variant PPA (svPPA), or logopenic variant PPA (lvPPA) [12]. Nonfluent/agrammatic PPA begins with problems in speech production, while svPPA involves impaired word comprehension and object recognition and lvPPA involves word-finding problems. A movement presentation may appear as progressive supranuclear palsy (PSP), corticobasal syndrome (CBS), or motor neuron disease (MND). Some patients may present with symptoms that overlap the different subtypes of FTD or may develop symptoms of other subtypes of FTD as the disease evolves. As more is learned about FTD, the terminology and classification of the subtypes may be revised.

BEHAVIORAL PRESENTATION

Behavioral Variant FTD

As noted, bvFTD is the most common type of FTD, estimated to account for more than half of all cases [13]. The prominent features include disinhibition, apathy/inertia, loss of empathy, compulsive behaviors, hyper-orality, and impaired executive function (***Table 2***) [14]. People with FTD may become socially withdrawn, inflexible, and impulsive. They may have a shortened attention span and a tendency to be easily distracted. Behavior may become socially inappropriate. People with bvFTD are usually unaware of the changes in their personality and behavior and the impact these changes have on others. Memory and visual-spatial functioning are initially relatively spared in bvFTD. Some individuals with bvFTD may develop symptoms similar to Parkinson disease, such as bradykinesia, rigidity, postural instability, and masked face.

BEHAVIORAL VARIANT FTD	
Major Clinical Features	**Examples**
Disinhibition	Making inappropriate comments, taking food off someone else's table at a restaurant, telling sexual jokes, shoplifting, hitting
Apathy	Less involved in old hobbies or activities, deterioration in personal hygiene
Loss of empathy	Indifferent when a family member is hurt
Compulsive behaviors	Repeating the same phrase, clapping hands in the same pattern repeatedly, checking the time repeatedly
Hyper-oral behaviors	Overeating, eating one certain type of food, eating excessive sweets
Impaired executive function	Poor performance at work, poor financial decisions, difficulty planning and preparing a meal

Source: Compiled by Author *Table 2*

LANGUAGE PRESENTATION

Nonfluent/Agrammatic Variant PPA

Nonfluent/agrammatic variant PPA, also referred to as progressive non-fluent aphasia (PNFA), accounts for about 25% of all FTD cases and involves problems with language expression [13]. People with nfvPPA have difficulty producing speech but retain the meaning of words and know what they want to say. As a result, speech may become hesitant, slow, and labored. Speech patterns may be "agrammatic" or "telegraphic," meaning that only the most important content words are used, without connecting words. For example, a patient might say "Tuesday... hospital...sister." Patients with nfvPPA have difficulty talking on the telephone and tend to talk progressively less. Eventually, some may become mute. While in the early stages, these patients continue to understand the speech of others, but this comprehension is eventually lost also. Reading and writing skills are better preserved than speech, although these abilities are also eventually lost. As the disease progresses, patients may develop behavioral symptoms. Some individuals with nfvPPA may develop extrapyramidal symptoms of rigidity and tremors, as seen in CBS and PSP.

Semantic Variant PPA

Semantic variant PPA, also referred to as semantic dementia, represents about 20% of FTD cases [13]. Semantic variant PPA involves the loss of understanding of the meaning of words and objects. Speech is still fluent and grammatically correct, but people with svPPA have a declining ability to comprehend the meaning of words (especially nouns) or to recognize familiar objects or faces. For example, a person with svPPA who is very familiar with vegetables might read a menu and ask: "What is broccoli?" If shown a picture of a carrot, the patient may not be able to name it and may not recognize the word when told. There are progressive word-finding problems, reading and spelling skills decline, and retrieving names becomes difficult. Later in the disease, people with svPPA may develop behavioral changes similar to those seen in patients with bvFTD.

Logopenic Variant PPA

Logopenic variant PPA is characterized by difficulty retrieving words, resulting in slow speech with frequent pauses. These patients may also have trouble repeating long phrases and understanding complex sentences. Eventually, people with lvPPA may become mute. Reading and writing skills are initially preserved, but these decline as the disease progresses. People with lvPPA have word-finding problems similar to people with AD and are often found to have AD pathology at autopsy [8].

For all patients with suspected language presentations of FTD, it is important to consider the role of culture and preferred language.

FTD OVERLAP WITH MOVEMENT DISORDERS

Progressive Supranuclear Palsy

PSP is a neurodegenerative condition characterized by problems with gait and balance, causing postural instability, falls, and difficulty with eye movement coordination. The pathophysiology of PSP shows a loss of cells in the basal ganglia, substantia nigra, subthalamus, and brainstem, and affected neurons have inclusions composed of abnormal tau protein. There are similarities between PSP and Parkinson disease, including bradykinesia, rigidity, masked face, dysarthria, dysphagia, apathy, and depression. Some people with PSP develop behavioral problems, but these are often milder than those seen in other types of FTD. Some people with PSP may develop progressive memory and language problems, and there may be a decline in executive function.

Corticobasal Syndrome

CBS is a neurodegenerative condition that may initially present with movement problems, dementia, or both. In CBS, there is atrophy in multiple areas of the brain, including the frontoparietal regions, basal ganglia, and cerebral peduncles. Neuronal inclusions are usually composed of abnormal tau protein. Signs of CBS typically begin with decreased movement on one side of the body, muscle rigidity, and tremor. A hand, arm, or leg on the affected side may demonstrate apraxia (i.e., inability to make the limb follow commands). Patients may describe the affected limb as not feeling like a part of their body, a sensation referred to as "alien limb syndrome." Symptoms may become bilateral as the disease progresses. People with CBS may also experience personality changes, executive dysfunction, and language problems as the disease progresses.

FTD with Motor Neuron Disease

Approximately 30% of people with FTD also develop problems with motor neurons that control voluntary movement [3]. This is referred to as FTD with motor neuron disease (FTD/MND) or FTD with amyotrophic lateral sclerosis (FTD/ALS). Pathologically, in addition to frontal and temporal lobe atrophy, there is also atrophy in the motor regions of the cortex and loss of motor neurons in the brain stem and spinal cord. In FTD/MND, damaged neurons usually have abnormal inclusions composed of the protein TDP-43. Patients may present with behavior or language problems, but then additionally develop muscle problems, including weakness, stiffness, twitches, cramps, and/or atrophy. Muscle problems can affect arms, legs, face, mouth, and tongue, causing patients to experience clumsiness, dysphagia, dysarthria, and hyper-reflexia. An estimated 50% of patients with MND or ALS go on to develop behavioral and executive dysfunction symptoms of FTD as their disease progresses [3].

CLINICAL DIAGNOSIS OF FTD

The diagnosis of FTD can be challenging because of the wide range of symptoms, the relatively early age of onset, and the slow progression. There is no single test to diagnose FTD, and it may be initially misdiagnosed as a psychiatric disorder (e.g., depression, schizophrenia), AD, Parkinson disease, or vascular dementia. Accurate diagnosis of FTD is important because some of the medications used to treat these other diseases may be detrimental to patients with FTD. Patients with suspected FTD are often referred to neurologists or neuropsychologists with special expertise in FTD and related neurodegenerative disorders for a comprehensive evaluation.

The clinical diagnosis of FTD is based on the clinical history, family history, neurologic examination, neuropsychologic evaluation, and neuroimaging. Other tests may also be performed for differential diagnosis. The diagnostic process may take time, and the diagnosis may change as more tests are done or as new symptoms appear.

The clinical history is obtained from the patient and his/her family or friends. It is important that family or friends provide information regarding symptoms, as patients are often unaware of their behavior changes.

The family history should focus on whether any other relatives have had a neurodegenerative disease. Any cases of dementia, language problems, or movement disorders should be noted, along with specific information about symptoms, diagnosis, age of onset, course of disease, age at death, and autopsy findings. Such background information may be valuable for both diagnosis and understanding genetic risk.

The neurologic examination typically includes assessment of the patient's general appearance and speech, mental status, cranial nerves, motor system, sensation, reflexes, and cerebellar function (coordination and balance). Consulting a neurologist who has knowledge and experience in FTD can be valuable when reaching a definitive diagnosis.

The neuropsychologic examination assesses brain function and may identify areas of the brain that have been damaged. It typically involves an interview and the administration of written tests. These tests may focus on attention and concentration, memory, orientation, language, visual-spatial abilities, and/or executive functions (e.g., reasoning, planning, organizing, problem solving). Patients with FTD may show deterioration in the areas of attention and concentration, language, and executive function, but may do relatively well on memory and visual-spatial tests.

The Neuropsychiatric Inventory (NPI) may be administered to caregivers of patients with suspected FTD. This survey helps assess behavior and psychopathology by inquiring about the patient's delusions, hallucinations, agitation/aggression, dysphoria, anxiety, euphoria, apathy, disinhibition, irritability, unusual motor activity, nighttime behavioral problems, and eating abnormalities.

Brain scans are important tools in the diagnosis of FTD. Computed tomography (CT) may be done to determine if there is a tumor, hemorrhage, or other brain injury that could account for the symptoms. Magnetic resonance imaging (MRI) provides better visualization of the brain than CT and is often done to evaluate brain atrophy when FTD is suspected. Patients with FTD have progressive frontal and anterior temporal atrophy apparent on MRI. Typically, in bvFTD, there is atrophy of the frontal lobe (involved in personality, judgment, and executive function) and the anterior temporal lobe. In nfvPPA, there is left frontal lobe atrophy (involved in speech production). In svPPA, the atrophy is focused in the anterior temporal lobe (involved in language and face recognition). In specialty or research centers, positron emission tomography (PET), single photon emission computed tomography (SPECT), or functional MRI (fMRI) brain scans may be done to further evaluate brain functioning.

While there is no laboratory test that can diagnose FTD, some tests may be ordered to rule out other diseases with symptoms similar to those of FTD. Blood work may be ordered to identify dehydration, thyroid disease, vitamin B12 deficiency, or infections affecting the brain. An electroencephalogram (EEG) may be done if there is concern that seizures might be causing the patient's symptoms. In the early stages of FTD, EEG findings are usually normal or have non-specific findings. Lumbar puncture may be done to evaluate cerebral spinal fluid and rule out rare brain infections or cancer. Electromyography may be used to identify muscle weakness or myoclonus if MND (or ALS) is being considered as a possible diagnosis. In addition, language evaluation by a speech pathologist can be an important tool in diagnosing patients with nonfluent/agrammatic, semantic, or logopenic variant PPA.

EARLY SIGNS AND SYMPTOMS OF FTD VERSUS ALZHEIMER DISEASE		
Clinical Features	**FTD**	**Alzheimer Disease**
Hallmark	Decline in behavior, language, and/or movement; memory is retained initially	Decline in memory; socially appropriate behavior is retained initially
Initial language problems	May involve speech production, understanding words and recognizing familiar objects, or retrieving words	Word-finding or name recall
Age at onset	Usually 45 to 64 years of age	Usually 65 years of age or older
Movement problems	May have early movement disorder, with gait and balance problems, rigidity, apraxia, or muscle weakness	Usually no movement problems early in disease

Source: [3; 8; 15] *Table 3*

It may be challenging to clinically differentiate FTD from early AD (***Table 3***). The only way to establish an unquestionable diagnosis of FTD is through a brain autopsy after a patient has died. Examination of the brain tissue will show the precise location and severity of the brain atrophy, and microscopic studies can determine the protein composition of the inclusions in affected neurons.

For families, brain autopsy can confirm the diagnosis (or identify a different cause of the dementia) and bring a measure of closure. Accurate diagnosis may be especially important if there is concern about genetic risk to other family members.

Discussion about brain autopsy should be handled delicately and with compassion at a time that is appropriate for the family; the subject may be emotionally difficult for some families. Introducing the topic ahead of time allows families to consider their feelings about brain autopsy aside from the emotional crisis of the death of a loved one and the immediate time pressure of funeral arrangements. Families may then discuss the topic among themselves and come to a consensus.

Should a family wish to have a brain autopsy done when the patient dies, the physician can help identify a pathology service experienced in neurologic disorders and preliminary logistical planning can be done ahead of time. Arrangements may be coordinated with a research center that specializes in brain autopsy for FTD. The autopsy is done as soon as possible after death, often within 6 to 24 hours. The procedure is not disfiguring, so open-casket funerals may be planned if the family so chooses.

In addition to answering families' questions regarding diagnosis, brain autopsy can also aid researchers in better understanding the correlation between the clinical signs of FTD and the pathologic changes in the brain. This may benefit future generations by improving diagnosis and advancing research on therapies for FTD.

GENETICS AND FTD

Understanding of the role of genetics in FTD is still evolving. Presently, it appears that most cases of FTD (approximately 60%) are sporadic, meaning one person in a family has the disease, there is no family history of any relative with the disease, and the disease does not appear to be inherited.

However, approximately 40% of those with FTD report a family history of one or more relatives with a neurodegenerative disease [6; 9; 11]. This is referred to as familial FTD. In some cases of familial FTD, no specific genetic mutation can be identified as the cause. The risk to family members of a person with familial FTD without an identified genetic mutation is increased over the general population, but the specific increased risk is unclear.

An estimated 10% to 20% of all FTD cases are caused by an inherited genetic mutation [6; 8]. Patients with a strong family history of multiple relatives with FTD and/or MND are more likely to have an inherited form of FTD caused by a genetic mutation. Genetic mutations causing FTD are inherited in an autosomal dominant inheritance pattern, meaning each child of an affected parent is born with a 50% chance of inheriting the genetic mutation.

Several specific genetic mutations have been identified as being implicated in inherited FTD. In 1998, the first gene associated with hereditary FTD—the microtubule-associated protein tau (MAPT) gene on chromosome 17—was discovered [16; 17]. Mutations in this gene cause an abnormal accumulation of tau protein in affected neurons. MAPT mutations are thought to account for 5% to 20% of familial FTD cases [18]. These mutations most commonly cause bvFTD but may also cause svPPA, PSP, and/or CBS. FTD symptoms may vary widely, even within families.

In 2006, mutations in the progranulin (GRN) gene on chromosome 17 were discovered to cause FTD [20; 21]. Mutations in the GRN gene cause abnormal accumulations of TDP-43 protein in affected neurons. GRN mutations are thought to represent about 5% to 10% of all inherited FTD cases [19]. They most commonly cause bvFTD, but are also associated with nfvPPA and CBS. GRN mutations appear to have decreased penetrance, meaning that, for unknown reasons, some people with the mutation may not develop symptoms of the disease.

In 2011, the genetic mutation *C9orf72* was discovered on chromosome 9 [22; 23]. Mutations in *C9orf72* cause an abnormal accumulation of TDP-43 in affected neurons. To date, *C9orf72* mutations are the most common genetic cause of FTD, found in about 25% of familial FTD and 6% of sporadic cases [24]. *C9orf72* mutations appear to cause FTD (usually bvFTD or language presentation), MND, and a combination of FTD and MND.

Other very rare genetic mutations have also been associated with FTD. Mutations in the gene valosin-containing protein (VCP) on chromosome 9, charged multivesicular body protein 2B (CHMP2B) on chromosome 3, TAR DNA-binding protein (TARDBP), FUS, TBK1, EXT2, and SQSTM1 have been associated with FTD [31].

Clinical genetic testing is available for the *MAPT*, *GRN*, and *C9orf72* genetic mutations causing hereditary FTD, as well as some of the other very rare genetic mutations. Genetic testing may be ordered after informed consent and clear discussion of the implications with the patient and his/her family. For patients with FTD, identification of a genetic mutation confirms the diagnosis of FTD and provides information about risk to other family members. Each of the patient's siblings and each of the patient's children would be at 50/50 risk for having inherited the genetic mutation causing FTD. If a genetic mutation causing FTD is identified, other at-risk family members may be tested.

If a genetic mutation causing FTD is identified in a patient with FTD, unaffected at-risk family members could choose to have pre-symptomatic (predictive) genetic testing done to determine if they have inherited the genetic mutation that would someday cause FTD. Individuals considering pre-symptomatic genetic testing are referred for formal professional genetic counseling to help them make the best decision regarding whether or not to learn their FTD genetic status.

MANAGEMENT OF FTD

There is presently no treatment to slow the progression of or cure FTD. No medication has been approved by the U.S. Food and Drug Administration (FDA) for the treatment of FTD; however, medications used to treat other disorders may be prescribed off-label for the management of FTD symptoms. Their use may be limited by the potential adverse effects. Antidepressants, particularly selective serotonin reuptake inhibitors (SSRIs), may be prescribed for behavioral symptoms of FTD, and low-dose trazodone has been used for agitation and aggression [9].

While the anticholinesterase inhibitors donepezil, galantamine, and rivastigmine are beneficial for some patients with AD, they generally have not been helpful for patients with FTD [9]. The glutamate NMDA receptor antagonist memantine, used for moderate-to-severe AD, has been used for patients with FTD as well, but a 2013 study showed that it provided no benefit to patients with FTD and that it may be harmful to cognition [25]. Antipsychotics are occasionally used to treat significant agitation and behavioral symptoms, but only with caution, as antipsychotics can have serious adverse effects such as extrapyramidal adverse effects (parkinsonism), depression, sedation, falls, incontinence, and disinhibition, and patients with FTD may have an increased susceptibility to these effects [9]. Elderly patients with dementia who take antipsychotics have a 1.6- to 1.7-fold increase in mortality secondary to cardiac problems or infection, prompting the FDA to issue a warning about their use in older patients with behavioral disturbances [9]. L-DOPA has shown a minimal response for parkinsonism in patients with PSP and CBD [30]. Research is being done to further evaluate the use of available medications for the management of FTD and to find new, more effective treatments.

According to the Royal Australian and New Zealand College of Psychiatrists, general principles of dementia care apply for the management of frontotemporal dementia, but specific issues relate to the early onset of the illness in middle life and that affected persons may lack insight into their deficits leading to occupational and social problems.

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Strength of Recommendation/Level of Evidence: Expert Opinion/Consensus Statement

Management of FTD includes providing care to patients with FTD and support to their families. Caring for a person with FTD involves managing the symptoms, keeping the patient safe, and providing help in activities of daily living.

Apathy is a common symptom in patients with bvFTD, often resulting in neglect of their personal hygiene and grooming. Supervision, encouragement, and help with bathing, dressing, and grooming may be needed. For behavioral problems, simple interventions like distraction (e.g., introducing a new activity) may help interrupt the troublesome behavior. For some patients, modification of the environment or behavior may help minimize the potential for harm. For example, if the patient is pacing, creating a safe route for him or her to walk can be helpful. Physical therapists may be able to help develop an exercise program to maintain mobility. Exercise has also been shown to improve mood and cognition and may improve behavior management in patients with dementia [26]. If behaviors such as agitation or aggression become severe, a medication may be prescribed off-label to control difficult or dangerous behaviors. Supervision may be necessary to ensure patients take medications as prescribed.

Some individuals with FTD have eating problems, such as overeating, eating just one type of food, or craving sweets. For these patients, it may be necessary to monitor weight and provide help with meal preparation to provide a balanced, nutritious diet. Access to additional foods, drinks, or sweets should be limited.

Speech pathologists or therapists may be helpful in diagnosing the specific language problems exhibited by patients with FTD, including nonfluent/agrammatic, semantic, or logopenic variant PPA. Speech therapy may also help patients to find new communication strategies, such as sign language, carrying cards with specific messages, or using a computer with pre-programmed words or phrases [27]. Such techniques may help those with language problems communicate with family and friends. Speech therapists may also be able to evaluate and address swallowing problems, if these arise.

Caring for a patient with FTD includes maintaining a safe environment for the patient and for those around him/her. A structured environment and keeping the daily routine the same is often helpful.

In addition, persons with FTD should no longer drive, and safety measures should be taken at home, especially in the kitchen and bathroom. If a patient with FTD shows aggression, disinhibition, or poor judgment, close supervision is necessary when he/she is around others, especially children or the frail elderly, to prevent them from being inadvertently harmed.

It also may be necessary to monitor the patient's behavior in public places. If an individual displays inappropriate behavior, tense situations may be diffused by explaining that he or she has FTD and cannot control his/her behavior. Simple cards with this brief explanation can be made, carried, and shared with people who might be disturbed by a patient's inappropriate behavior.

If a patient with FTD has gait and balance problems, measures should be taken to prevent falls. This may include keeping the home environment free of obstacles and loose rugs and installing shower bars and a raised toilet seat. Mobility aids may be helpful. Occupational therapists should provide intervention to help patients with FTD complete activities of daily living as the disease progresses.

CAREGIVER SUPPORT

FTD places enormous burdens on the family. Most dementia care is provided at home by family caregivers, often spouses. Caregivers for those with FTD face physical, emotional, and financial challenges. FTD caregiver burden, stress, and depression are greater even than that seen with AD [28; 29].

The first challenge that families of those with FTD may face is obtaining an accurate diagnosis. The process can involve years of uncertainty and stress before the correct clinical diagnosis of FTD is made. Even during the diagnosis process, support for families begins with information and education about FTD. Accurate information can lead to understanding and a greater sense of control over the stressful situation. It is important for families and caregivers to understand that the behavior changes they observe are the result of the disease. Their loved one may display behaviors that are embarrassing, offensive, self-centered, uncaring, and aggressive, with complete lack of insight about how the behavior affects others. The caregiver may feel like he/she is suddenly living with a stranger.

The aggression, disinhibition, and poor judgment associated with FTD can put family members at risk of harm. Because FTD affects people at a relatively young age, there may still be children in the home. Families should recognize the risk to others in the home and seek help creating strategies to keep themselves and other family members safe.

Language may be impaired in people with FTD, making communication difficult. This can interfere not only with communication between the patient and the caregiver, but it can also limit participation in larger social activities. Speech therapy can provide new approaches to communication, helping not only the patient but also the caregiver.

Because FTD usually begins at a relatively young age, it can cause a significant financial burden for families. There may be loss of income, and retirement benefits may be affected because the patient is unable to continue working. Financial and legal issues that should be addressed include insurance, social security disability, financial planning for the future (when additional care will be needed), power-of-attorney arrangements, and a living will. Social workers, financial advisors, and attorneys are resources available to families to help address these issues.

The demands on caregivers increase as FTD progresses. Caregivers will be required to provide more supervision and increasing assistance for activities of daily living. While providing care for an individual with FTD, the caregiver may also be grieving the loss of his or her previously healthy loved one. Family caregivers can become physically and emotionally exhausted, and they may feel isolated in their role as caregiver. Interventions to help reduce caregiver stress include an individualized patient management plan, environmental changes to promote safety and facilitate care, and strengthening caregiver coping

strategies and skills. Family caregivers should be encouraged to ask for and accept help in caring for their loved one with FTD, allowing them to take time for themselves and address their own health needs. Connection with community resources may also be helpful. Community resources for FTD caregivers include national organizations such as the Association for Frontotemporal Degeneration, attorneys and financial planners, social service programs, adult day care programs, respite care, support groups, and individual or family counseling.

Family caregivers should look ahead and consider how they wish care to be provided to their loved one as FTD progresses. Patients with FTD will become more dependent and more difficult to safely manage at home by a family caregiver as the disease progresses. Social workers can be a good resource to caregivers as they consider options such as extra in-home nursing care, care communities, and long-term care facilities. Locating an appropriate care facility that accepts patients with FTD can be challenging. These patients are often younger, stronger, and more active than the typical residents of care facilities. Facility staff may need education and support to understand the unique features of FTD and to learn how to provide care to these patients while maintaining a safe environment for all residents in the facility.

Nurses play an important role in caring for those with FTD and providing support to their families. Nurses interact with patients with FTD and their families in the outpatient clinic setting, in-home care setting, and long-term care facility and may be involved in monitoring symptoms, developing and implementing individualized patient care plans, and providing direct patient care. It is important for all healthcare providers to coordinate care for the patient with FTD. All members of the interdisciplinary healthcare team can support families by listening to them, providing ongoing information and education about FTD, offering guidance to improve caregiving skills, and helping families connect to appropriate resources.

PROGRESSION OF FTD

The prognosis for people with FTD is poor. FTD worsens progressively, usually over several years, and patients require increasing behavioral supervision and personal care. Eventually, people with advanced FTD become mute and bedbound and require full care at home or in a care facility. As patients with FTD become more debilitated, they are vulnerable to complications such as infections and falls. The most common cause of death in people with FTD is infection (e.g., pneumonia) [3; 8]. The average duration of the disease is 6 to 13 years, but it can range from 2 to 20 years [3; 5].

RESEARCH RELATED TO FTD

The goals for research on FTD include gaining a better understanding of the pathology; identifying causes and risk factors (genetic and environmental); improving the diagnosis of FTD through enhanced neuroimaging, biomarkers, and characterization of clinical features; developing therapies to treat, cure, or prevent FTD; and exploring new ways to support family caregivers. However, research on FTD is challenging. It is an uncommon disease, so awareness is low, there are fewer potential subjects available for research studies, and there is a relatively small market for medications. FTD is a complicated disease with a wide variety of presentations (behavior, language, and movement problems) and underlying causes (sporadic and genetic). Pathologically, microscopic brain inclusions may consist of different abnormal proteins (e.g., tau, TDP-43, FUS), and up until recently, there were no good biomarkers to diagnose FTD or to monitor the progression of the disease. However, ongoing studies have begun to show promise in this area. Biomarkers such as the neurofilament light-chain protein have been shown to rise before the onset of FTD symptoms, which may help in early identification and diagnosis of asymptomatic carriers of FTD [10]. Drug development still faces the challenge of creating a medication to treat FTD that can cross the blood/brain barrier.

Despite these challenges, the pace of research on FTD has accelerated rapidly. There are an increasing number of studies and a better awareness of the varied symptoms of FTD. In the past few decades, there have been discoveries of the genetic mutations underlying some causes of FTD and a growing understanding of the changes that occur in the brain of those with FTD. Presently, there are clinical trials underway for potential medications to treat FTD. Information on clinical research studies, including participation in studies, can be found at the National Institutes of Health website https://clinicaltrials.gov.

CASE STUDY

Patient A was a high school homecoming queen who completed two years of college, worked in an office, then married and had three children. She was an energetic homemaker and an active community volunteer, serving as school parent-teacher association president for several years, and was fastidious about her appearance.

Patient A's mother, three maternal uncles, a maternal grandfather, and great-grandmother died with dementia; her brother and maternal aunt are living with the disease. The mean age of onset of dementia in the family is 51 years, and the mean age at death is 67 years.

When Patient A is 52 years of age, her husband notices changes in her behavior. She often appears distracted, and her impeccable grooming declines. She is less affectionate toward him and she stops participating in community activities. She has difficulty making arrangements for a planned vacation. Her previously gourmet meals become simple, functional meals. She becomes obsessed with repeatedly raking the lawn, eventually killing all the grass in the yard. When her grandchildren visit, Patient A alternates between ignoring them and playing too rough. Patient A begins to impulsively leave the house for fast-paced walks, but she always returns home and never gets lost. She frequently visits a local shopping mall, getting down on her hands and knees looking for dropped change near the cash registers. She is once stopped by mall security for shoplifting. When shopping with her husband, she approaches strangers, stands inappropriately close to them, and announces "We don't know you."

Patient A's husband brings her to a dementia clinic for evaluation. A neurologic examination and neuropsychologic testing are completed. Memory and visual-spatial performance are in the normal range, but personality, judgment, and executive function show significant decline. A brain MRI shows frontal and anterior temporal lobe atrophy, and the diagnosis of familial bvFTD is made. Clinical genetic testing identifies a mutation in the MAPT gene on chromosome 17, the believed cause of the dementia.

Patient A's husband stops working in order to care for her at home. As her disease progresses, Patient A requires increasing care and supervision. She spends much of her day watching television, writing numbers in a notebook, and pacing. She develops a craving for sweets and often rummages through kitchen cabinets looking for candy. At mealtime, Patient A stuffs her mouth with food before chewing and swallowing properly, precipitating episodes of choking. She also develops a pattern of hand-clapping that she repeats every few minutes, along with the phrase "We haven't had any phone calls lately."

Patient A's husband is encouraged to accept help from others (such as their adult children), consider local adult day care programs, and utilize respite care at a nearby nursing home. He is in monthly phone contact with nursing staff to review symptoms and develop strategies for managing symptoms. At different times during her illness, Patient A is prescribed an antidepressant and an antipsychotic medication (off label) to treat difficult behavioral symptoms, but both were eventually discontinued. The family faces financial difficulties as a result of the husband's loss of income, diminished retirement benefits, and the later cost of nursing home care. Social work support helps the family address issues such as insurance, social security benefits, adult day care programs, and selecting a nursing facility for eventual long-term care.

When Patient A is 60 years of age, her husband is no longer able to care for her at home and she is admitted to a skilled nursing facility. She is incontinent and requires full care for all activities of daily living. Her husband visits twice daily, and she always appears to recognize him. That same year, Patient A dies unexpectedly of a myocardial infarction. A brain autopsy is done and confirms the diagnosis of FTD.

Patient A's husband shares the results of her genetic testing and autopsy with their three adult children. Each of Patient A's three children is at a 50% risk for having inherited the MAPT genetic mutation. Two of the children request pre-symptomatic genetic testing. The two children who request pre-symptomatic genetic testing are referred to professional genetic counselors. After genetic counseling, they both choose to have pre-symptomatic genetic testing done. One defers getting the results for two years, underscoring the very difficult personal decision it can be to choose pre-symptomatic genetic testing.

Patient A demonstrated the typical symptoms of bvFTD and her evaluation was done at a dementia center by specialists with expertise in FTD, so her initial diagnosis was strong. The neurologic evaluation, blood tests, neuropsychologic testing, and neuroimaging together led to the clinical diagnosis of bvFTD. Patient A's family history showed a pattern of autosomal dominant inheritance. The genetic cause of her FTD was confirmed by clinical genetic testing, which documented a mutation in the MAPT gene.

CONCLUSION

FTD is now recognized as one of the most common causes of dementia in persons younger than 65 years of age. This course has provided an overview of FTD epidemiology, pathophysiology, clinical presentation, diagnosis, management, prognosis, and current research. Understanding FTD can help healthcare professionals provide better care to patients with FTD and support to their families.

RESOURCES

Association for Frontotemporal Degeneration
2700 Horizon Drive, Suite 120
King of Prussia, PA 19406
(866) 507-7222
https://www.theaftd.org

National Institute on Aging
Building 31, Room 5C27
31 Center Drive, MSC 2292
Bethesda, MD 20892-2292
(800) 222-2225
https://www.nia.nih.gov

National Institute of Neurological Disorders and Stroke
P.O. Box 5801
Bethesda, MD 20824
(800) 352-9424
https://www.ninds.nih.gov

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