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Clinical Subtypes of Frontotemporal Dementia

Sayantani Ghosh, MBBS[1], and Carol F. Lippa, MD[1]

Abstract

Frontotemporal dementia (FTD) was one of the lesser known dementias until the recent advancements revealing its genetic and pathological foundation. This common neurodegenerative disorder has three clinical subtypes- behavioral, semantic and progressive non fluent aphasia. The behavioral variant mostly exhibits personality changes, while the other two encompass various language deficits. This review discusses the basic pathology, genetics, clinical and histological presentation and the diagnosis of the 3 subtypes. It also deliberates the different therapeutic modalities currently available for frontotemporal dementia and the challenges faced by the caregivers. Lastly it explores the scope of further research into the diagnosis and management of FTD.

Keywords

frontotemporal dementia, behavioral variant, semantic dementia, progressive non-fluent aphasia, genetics, pathology, management

Introduction

Frontotemporal dementia (FTD) describes a spectrum of heterogeneous neurodegenerative disorders characterized by a range of behavioral and language deficits. It is often associated with asymmetrical, focal atrophy of the frontal and/or temporal lobes of the brain.[1] The FTD is considered to be the third leading cause of dementia across all age groups, following Alzheimer's disease (AD) and dementia with Lewy bodies.[2] It accounts for approximately 5% to 10% of all cases of pathologically confirmed dementia.[3]

In 1892, Arnold Pick described[4] the first case of FTD; and hence for many years, the clinical syndrome was known as Pick's disease. Although it was identified long back, the underlying biology and genetics were poorly understood until the 1990s.[1,5,6] However, recent research suggests loss of structural and functional plasticity in the synapse plays a role in the early symptomatology of FTD as it plays in the case of another prevalent dementia, the AD.[7]

Clinically, FTD can be categorized into 3 broad subtypes—the behavioral variant of FTD (bvFTD), semantic dementia (SD), and progressive nonfluent aphasia (PNFA). Additionally, there is significant clinical, genetic, and pathological overlap between FTD and certain other neurological syndromes such as corticobasal syndrome (CBS), progressive supranuclear palsy (PSP), motor neuron disease (MND), amyotrophic lateral sclerosis (ALS), and atypical parkinsonian syndromes. In this article, we have described the 3 clinical subtypes of FTD, their epidemiology, genetic and histopathogical basis, diagnosis, treatment, and the challenges faced with their management and future scope of research.

Epidemiology

The estimated point prevalence and incidence of FTD in the general population of United States is about 15 to 22 of 100 000 and 2.7 to 4.1 of 100 000, respectively.[8] The age of onset for FTD is generally younger than that of most dementias, with a mean age of onset between 55 and 60 years[9,10]; however, onset of symptoms may range from the fourth to the eighth decade of life.[3,8,11] Also, a study of patients with an autosomal dominant FTD syndrome suggested that subtle cognitive or behavioral abnormalities may arise in childhood or adolescence in some of the family members.[12] There is no significant difference between the various clinical variants of FTD in the mean age of symptom onset; however, bvFTD and FTD associated with motor neuron disease (FTD-MND) patients are typically younger at the time of diagnosis than patients with PNFA.[13] In patients younger than 60 years of age, FTD is often the commonest form of dementia, even more prevalent than AD.[14-17]

The FTD is a more rapidly progressing disorder than other forms of dementias. From the time of symptom onset, the mean survival in all FTD is estimated to range from 6 to 10 years.[8,18,19] Although SD[18,20] and PNFA[18] have longer survival time from symptom onset about 11 to 12 years and 9 years, respectively,

[1] Department of Neurology, Drexel University College of Medicine, Philadelphia, PA, USA

Corresponding Author:
Sayantani Ghosh, MBBS, Department of Neurology, Drexel University College of Medicine, 245 N 15th St. Mailstop 428, Philadelphia, PA 19102, USA.
Email: 87sayantani@gmail.com

bvFTD has a survival time of about 6 years.[13] Language impairment, including word-finding difficulty and semantic deficits, was identified as negative prognostic indicators in patients with bvFTD.[21] The FTD-MND has an even shorter course and has the median survival from symptom onset to death of around 3 years.[13] The mean survival from time of clinical diagnosis of all FTD cases is estimated to range between 3 and 4 years.[13] These figures indicate that there is a significant delay from symptom onset to diagnosis.[8] The average delay between symptom onset and diagnosis in FTD has been estimated at 3.6 years compared to 2.7 years in patients with AD.[11] Hence, early diagnosis of FTDs can raise the survival by 3 years.

Genetics

It is now well recognized that FTD has an impressive genetic component, up to 40% of FTD is familial,[22] and 10% to 30% of patients with a family history have a mutation in the microtubule-associated protein tau (*MAPT*) gene located on chromosome 17.[23] In 2005, a study[24] indicated that about 18% of all patients with FTD observe an autosomal dominant inheritance pattern. The bvFTD is the most prominent subtype with family history, especially when concomitant symptoms of MND are present (60%), while SD appeared to be the least hereditary FTD subtype (<20%).[24]

After *MAPT* mutations, *C9ORF72*, a recently identified hexa-nucleotide repeat expansion on chromosome 9, has been identified as the genetic abnormality underlying the majority of cases of both familial FTD and familial ALS.[25,26] However, in another recent study, the mutation was observed among 6% of caucasians diagnosed with sporadic FTD and almost 67% Asians with familial FTD.[27] Progranulin mutations (*PGRN*), on chromosome 17, are also found in about 5% to 10% of total patients with FTD.[28,29] Mutations in *PGRN*, *MAPT*, and *C9ORF72*, taken together, account for at least 17% of total patients with FTD.[27] Both charged multivesicular body protein (*CHMP2B*) mutations on chromosome 3 and mutations of the valosin-containing protein (*VCP*) gene on chromosome 9 are detected in <1% of the patients with familial FTD.[30] Some rare mutations in common ALS genes, TAR-DNA-binding protein (*TARDBP*), and fused in sarcoma (*FUS)* are also present clinically with FTD.[31,32]

Histopathology

Pathologically, FTD can be divided based on its intraneuronal (cytoplasmic) inclusions. Tau-positive inclusions[23,24,33,34] are commonly found in Pick's disease, FTD with MAPT mutations, PSP, CBS, argyrophilic grain disease, neurofibrillary tangle dementia, and sporadic multiple system tauopathy with dementia.[34] Pick's disease is a bvFTD subtype and is characterized by the presence of Pick bodies, inclusions composed primarily of 3R (repeated) tau.[35] There are also tau-negative but ubiquitin-positive inclusion proteins like TDP-43[36-40] that are found in sporadic and familial cases of FTD involving *PGRN* and *VCP* gene mutations, FTD with or without MND with *C9ORF72* hexanucleotide repeat, and familial and sporadic cases of ALS.[24,34,41-43] The third major histological variety is tau-negative, TDP-43 negative, ubiquitin-positive, and FUS[40,44,45] proteins that are identified in the behavioral variant.

Other inclusion bodies such as intermediate filament immunoreactive inclusions, basophilic inclusions, and P62-positive inclusions are also found in some patients.[33,34,41] Patients with ALS exhibiting FTD symptoms or the ALS-FTD has ubiquitin-positive, α-synuclein, and tau-negative inclusion bodies in the frontal cortex and hippocampus, and spongiform change in the first 2 layers of frontal cortex, along with degeneration of motor neurons in the brainstem and anterior horn of the spinal cord.[46] Dementia lacking distinctive histology[36] is a comprehensive term used to represent the remaining patients with FTD that cannot be positively diagnosed as any of the above.

Clinical Subtypes

Among the 3 clinical subtypes discussed earlier—the commonest clinical presentation of FTD is the frontal or the behavioral variant,[47,48] represented by a change in social, interpersonal, and emotional behavior. The SD is also referred to as the temporal variant of FTD[6] and is characterized by a gradual loss of knowledge and word comprehension associated with progressive speech disturbance but intact fluency; there are associated socioemotional dysfunctions as well which intensify with the disease duration.[49] The PNFA is another variant of FTD exhibiting speech disorder with loss of fluency, anomia, agrammatism, and loss of comprehension of complex sentences, while behavioral abnormalities and executive dysfunction develop later in the disease course.[49-51] Callossal gliosis is common in all patients with FTD and worsens anomia and other cognitive symptoms.[52] In reality, many individuals have overlapping features or may evolve to include additional FTD signs.

Behavioral Variant

The bvFTD is associated with focal atrophy of the orbital and mesial frontal lobes and anterior temporal lobes.[53,54] Its hallmark is change in the personality that is manifested by apathy with social withdrawal, loss of empathy, loss of spontaneity, abulia, disinhibited outbursts, emotional bluntness, and change in eating patterns,[55] inability to adhere to routines, inflexibility, and loss of attention span.[36] A subscale analysis to identify the eating patterns of patients with FTD via Food-Related Problems Questionnaire to the caregivers indicated impairment in observed satiety, improper eating pattern, and inappropriate responses when food was not available.[55] These patients remain partially aware of their deficits. Socially aberrant behaviors have been identified with greater involvement of the right hemisphere.[56,57]

As the disease progresses, the dorsolateral prefrontal systems are also affected, and neurocognitive deficits, such as impairment of executive functions, problem solving, judgment, organization, and planning, emerge.[58,59] However, in dysexecutive variant of FTD, patients may present at early stages with problem in planning, organization, and complex thinking with

relative preservation of memory, overall behavior, and language function.[60] Altered speech pattern, with stereotypy, echolalia, lack of spontaneity, and in later stages mutism, although not very common in patients with FTD, is also seldom observed.[6] Frontal release signs like snout, grasp and sucking reflexes, and incontinence may also be seen at an earlier disease stage in FTD than in AD.[59]

Histologically, at postmortem of patients with bvFTD, bilateral frontotemporal atrophy with neuronal loss, microvacuolation, and a variable degree of gliosis is observed.[61] The progression of this atrophy has been examined by mapping the pattern in patients with different disease durations.[62] Initially, mesial and orbital frontal regions are affected, followed by the temporal lobe, hippocampal formation, dorsolateral frontal cortex, and the basal ganglia with prominent sparing of the posterior cortical regions and visuospatial function.[63] The pattern of progression of atrophy has also been shown to relate to the volume of cortical and subcortical regions and to the underlying neuron loss.[64,65] Immunohistochemistry of neurons of patients with bvFTD reveal almost equal proportion of tau- and TDP-43-positive cases[48,66] and a small proportion of FUS-positive[67] ones.

In coronal magnetic resonance imaging (MRI) sections, atrophy of the mesial frontal, orbitofrontal, and anterior insular cortices can be reliably observed.[68] A combination of frontal and anterior temporal and basal ganglia atrophy might also be seen at presentation in some patients.[69] However, an apparently normal MRI on visual inspection does not completely exclude the diagnosis, because the changes can be subtle in the early stages. Symmetrical frontal lobe atrophy in patients with bvFTD is associated with *C9ORF72* and *MAPT* gene mutations, whereas the asymmetrical pattern is associated with *PGRN* gene mutations.[70] Patients with ALS who exhibit an FTD syndrome clinically (ALS-FTD) show atrophy in the frontal and temporal regions.[46]

In resting state functional MRI, abnormalities occur in bvFTD, involving not only the salience network but also the default mode and frontoparietal network associated with attention and working memory modulation.[71] Frontal hypoperfusion is present on single-photon emission computed tomography (SPECT) or fluorodeoxyglucose-positron emission tomography (FDG-PET) in bvFTD, and it differs from the pattern of hypoperfusion observed in AD, which is predominant in the temporoparietal and posterior cingulate cortices. These changes are detected before any changes are visible on structural MRI, making FDG-PET the most sensitive diagnostic tool currently available.

Semantic Dementia

The SD presents in 20% to 25% of the patients with FTD.[9] It involves degeneration of the temporal lobe. This syndrome presents predominantly with language symptoms. However, in contrast to patients with PNFA, patients withSD have a fluent speech and impaired word comprehension.[36] In addition to lexical difficulty in retrieving the word, patients also have problems retrieving information based on nonverbal modalities. Behavioral abnormalities, such as disinhibition and dietary changes, are frequent.[49] Obsessions and compulsions are particularly common.[72] Patients with SD lack complete awareness of their deficits; they acknowledge their word-finding difficulty but not their impaired comprehension.

Right temporal deficits may have less obvious language deficits and would have symptoms that include prosopagnosia,[73] phonagnosia,[74,75] and poor insight. In patients with SD, there are deficits in semantic memory,[76] which is the aspect of long-term memory that contains knowledge of objects, facts, concepts, words, and vocabulary; but episodic memory is relatively preserved.[77] On verbal fluency tests, patients with SD have more difficulty with semantic fluency rather than letter fluency, while patients with PNFA and bvFTD have equal impairments in both the tests.[78]

In structural MRI, SD is characterized by temporal lobe atrophy, which is more pronounced anteriorly, involving polar, anterior parahippocampal, and fusiform regions including the perirhinal cortex. The atrophy is bilateral, but typically asymmetric and often more severe on the left side[79;] in contrast, patients with AD have more symmetric bilateral temporal lobe affection without any anteroposterior gradient.[80] Diffusion tensor imaging (DTI) is a new age imaging modality, commonly used for dementia studies, which involves measurement of the restricted diffusion of water in tissue in order to produce neural tract image. A recent DTI study in patients with SD[81] has revealed significantly higher mean diffusivity, parallel and transverse, and significantly lower fractional anisotropy, in the inferior longitudinal fasciculus, arcuate fasciculus, and uncinate fasciculus. The frontoparietal superior longitudinal fasciculi also illustrated significant difference observed for transverse diffusivity and fractional anisotropy. Also, the genu of the corpus callosum demonstrated lower fractional anisotropy.

Progressive Nonfluent Aphasia

The PNFA is the second most prevalent presentation of FTD, after bvFTD, accounting for about 25% of total the patients with FTD.[9] Here, anomia is the first deficit to appear.[82] The speech of the patients with PNFA is slow and nonfluent, sometimes telegraphic, with agrammatism and phonemic paraphasic errors.[36,83] There is difficulty with comprehension of sentences that are syntactically complex, and ultimately the patients may become mute.[82] Deficits may be restricted to expressive language function, from few to several years before a more global dementia supervenes.[50,51] Patients with PNFA may develop behavioral dysfunctions or symptoms of MND or corticobasal degeneration.[49-51]

The SD and PNFA are sometimes referred together under a broader spectrum language disorder syndrome known as primary progressive aphasia (PPA). International group of PPA investigators have published 3 clinical variants of PPA[84] based on the specific speech and language features characteristic to that specific subgroup. First such variant was termed as nonfluent or agrammatic or PNFA, and it has the features of agrammatism, speech apraxia, and impaired comprehension of complex sentences. Semantic variant or SD is characterized by impaired confrontation naming, impaired word comprehension, impaired object knowledge, and surface dyslexia or dysgraphia, whereas the logopenic variant exhibits impaired

single-word retrieval and naming and impaired repetition with spared single-word comprehension and object knowledge. These clinical variants can then be further specified as imaging supported if the expected pattern of atrophy is found or with definite pathology and if the pathologic data are available.[84]

Patients with PNFA show left frontal and perisylvian atrophy on structural MRI, with hypoperfusion and hypometabolism demonstrated in the same regions on functional imaging.[83] In those who have become mute, a pattern of atrophy affecting the left perisylvian region and extending into the left basal ganglia has been demonstrated.[85] In 2003, another case series on FDG-PET analyses of patients with PNFA revealed notable hypometabolism in the left anterior insular or frontal opercular region.[86]

Associated Disorders

Corticobasal Syndrome. The CBS is more likely to develop in patients who initially present with PNFA.[87] This syndrome is characterized by apraxia, cortical sensory loss, myoclonic jerks, bradykinesia, rigidity, tremor, and dystonia.[88] Rarely, patients may develop an alien limb phenomenon, in which there are involuntary movements and personification of the limb. Patients who have CBS can develop personality changes, and executive dysfunction similar to those observed in bvFTD.[87] The MRI shows asymmetric atrophy involving frontoparietal regions, basal ganglia, and cerebral peduncles.[88]

Progressive Supranuclear Palsy. The PSP is characterized by early falls, bradykinesia, axial rigidity, vertical gaze palsy, anisocoria, mild-to-moderate dementia, personality changes, nonfluent aphasia, and dysphagia.[89] Neuropsychological testing demonstrates some mild-to-moderate frontal lobe deficiencies. The MRI shows symmetric atrophy of superior cerebellar peduncle and midbrain.[89]

Motor Neuron Disease. The MND is defined as any evidence of pyramidal tract degeneration or anterior horn cell disease. The MND frequently coexists with bvFTD and is infrequently reported with SD and PNFA. Typically in these cases, there are findings of lower MND or mixed upper and lower MND.[90] The MRI may show variable bifrontal atrophy.[90]

Approach to the Patient and Management

Clinical Diagnostic Criteria. In 1998, a consensus on clinical criteria specific to the 3 clinical subtypes of FTD was published.[6] But these criteria exhibited substantial limitations, especially for the bvFTD[91] that subsequently led to the revision of the criterion for bvFTD by the Frontotemporal Dementia Consortium in 2011.[92] The revised criteria categorized potential patients with bvFTD into "possible," "probable," and "definite frontotemporal degeneration." "Possible" bvFTD required 3 of the 6 clinically discriminating features—disinhibition, apathy/inertia, loss of sympathy/empathy, perseverative/compulsive behaviors, hyperorality, and dysexecutive neuropsychological profile, "probable" bvFTD also requires functional disability and characteristic neuroimaging in addition to these, and "definite" bvFTD requires an added histopathological confirmation or a pathogenic mutation.

Genetic Testing. Genetic testing is available for all of the identified mutations associated with FTD. Apart from diagnosing FTD, sometimes the genetic testing also provides a greater insight about the clinical variant of FTD present, the expected imaging results, and the ultimate outcome. The *PGRN* mutations are associated with an asymmetrical fronto–parietotemporal pattern of atrophy, whereas *MAPT* mutations are associated with more significant symmetrical anteromedial temporal and orbitofrontal atrophy.[70,93-95] The *C9ORF72* mutation has frontal involvement more than temporal.[95] The *PGRN* mutations have been most commonly associated with bvFTD and PNFA[96-98] and rarely MND.[99,100] The *MAPT* mutations are found in bvFTD, SD, and the atypical parkinsonian syndromes: PSP and CBS.[96,98] The *C9ORF72* mutations are most often associated with bvFTD with or without MND, while the mutation does not appear with PNFA phenotypes.[101] In patients with *CHMP2B* mutations, dysexecutive functions precede the clinical diagnosis of FTD by several years,[102] while in *VCP* mutations, an autosomal dominant inclusion body myopathy coexists with Paget's disease and FTD.[103]

As genetic testing can be expensive and complicated, there is a well-accepted algorithm for the testing in patients with FTD in accordance with their clinical and neuroimaging phenotypes and also the family history and autopsy information.[104] Genetic testing should be preceded by proper genetic counseling.[105] However, as all possible mutations in familial FTD are yet to be discovered, a negative test does not rule out FTD.

Imaging. Structural MRI may be normal in the early course of the disease, and the atrophic patterns for the various subtypes (see above) may intensify with the disease duration.[62,82] Hence, functional neuroimaging techniques such as SPECT, perfusion MRI, or FDG-PET are more sensitive in diagnosing an early disease.[50,56,77,88] The DTI shows abnormal diffusivity of gray matter in the affected regions.[81,106] Incorporating routine PET scans in complex, atypical, or unclear patients can have a significant effect on the early management of FTD.[107]

Cerebrospinal Fluid Biomarkers. The cerebrospinal fluid (CSF) profile in FTD is variable; changes in CSF tau levels are less consistent than in AD.[36] One study differentiated patients with FTD and AD by looking at the combination of CSF tau and Abeta-42 levels and concluded that patients with FTD have a rise in tau and a fall in Abeta-42 levels.[108] But yet there is paucity of evidence to include CSF results for the diagnosis of a patient with FTD.

Neuropsychological Testing. Role of neuropsychological tests in diagnosis of FTD is limited, as the tests may be normal at early disease.[61] Test administrators also need to be aware of the fact that deficits in one area may mislead to the perception of deficit in another area. However, when compared to patients with AD, patients with FTD may show worse performance in frontal

executive function and social cognition while better performance on tests of memory and visual spatial function.[61,77]

The Neuropsychiatric Inventory (NPI) scoring is a vital part of neuropsychological evaluation in FTD. The scale was initially developed by Cummings et al in 1994[109] to assess dementia-related behavioral symptoms that other measures did not sufficiently address; he further expanded the scale in 1997.[109] It currently examines 12 subdomains of behavioral functioning, delusions, hallucinations, agitation/aggression, dysphoria, anxiety, euphoria, apathy, disinhibition, irritability, aberrant motor activity, nighttime behavioral disturbances, and appetite and eating abnormalities, and is administrated to caregivers of patients with dementia.[109,110] The Frontal Behavioral Inventory is another scale mostly used to assess frontal lobe dementias.[111] It is a 24-item questionnaire that measures behaviors such as apathy, indifference, disorganization, inattention, personal neglect, aspontaneity, inflexibility, concreteness, loss of insight, logopenia, verbal apraxia, and alien hand.

Evaluation of speech production/articulation, syntax and single-word comprehension, repetition, confrontation, naming, semantic knowledge, reading, and writing is necessary for the classification of patients with SD and PNFA. The language evaluation can be performed with a 20-minute bedside assessment or by a speech pathologist to yield higher diagnostic accuracy.[84] A third clinical linguistic variant termed as logopenic aphasia (LPA) has been described[84,112] but based on the current clinic–pathological understanding, it is not considered a FTD variant. The hallmark of LPA is left parietotemporal atrophy,[112-114] and its clinical features include slow rate of speech output with frequent pauses, impaired repetition, and impaired syntactic comprehension and naming with relatively intact single-word comprehension.[113,114]

Pharmacological Therapy. There is no Food and Drug Administration (FDA)-approved medications yet for the management of FTD; so, all the current management recommendations are off label.[115] Serotonergic medications are popular prescriptions for FTD, as abnormal serotonin activity has been demonstrated in autopsy, neuroimaging, and CSF studies in such patients.[116] Serotonin selective reuptake inhibitors such as sertraline, fluvoxamine, and paroxetine have improved multiple behavioral symptoms in patients with FTD.[117-119] Low doses of trazodone have been effective in treating agitation and aggression.[116] Atypical antipsychotics like olanzapine, quetiapine, and aripiprazole also help with agitation and other behavioral symptoms while having minimal extrapyramidal side effects.[118,120,121]

Cholinesterase inhibitors such as donepezil, galantamine, and rivastigmine and the N-methyl-D-aspartate receptor antagonist, memantine, are used for memory and intellectual enhancement in patients with AD, but none of these drugs were found to be helpful in clinical trials on patients with FTD.[122-125] Anxiolytics and mood stabilizers however help in the cognitive symptoms in FTD.[126] Various research studies are actively pursuing for innovative therapeutic options for patients with FTD like modulation of CNS oxytocin and vasopressin circuits to ease some of the core emotional and social behavioral deficits.[127] Symptomatic treatment is approached while combating the subsidiary associations of FTD such as MND, Parkinsonism, urinary retention, and so on,[115] and this approach of pharmacological tools to target the symptomatology in FTD is actually helping in improving quality of life of such patients.[128]

Nonpharmacological Support. Many novel unconventional therapies are increasingly being tried for patients with FTD—recently a study with lavender aroma therapy for 8 weeks led to significantly improved NPI scores and decreased requirement of antipsychotic medications.[129] Some patients may benefit from speech therapy,[130] which can aid in their ability to communicate with family and friends. Regular cardiovascular exercises are proved to benefit the mood and cognition of the patients,[131] while antioxidants and vitamins in diet or as food supplements help in preventing or delaying the disease progression.[132] Physical therapy can also help with balance and assist in maintaining mobility.[133] The patients with FTD often have reversed sleep–wake cycles, so for such patients, environment control interventions at home may help.[134]

Safety is a big concern for patients with dementia, and someone living alone with dementia is at a very high risk and requires nursing home placements. Physical aids at home such as raised toilet seats or removal of unsecured rugs can also reduce potential injuries at home.[135] Drivers with dementia can be dangerous on roads; hence, per the guidelines of Quality Standards Subcommittee of the American Academy of Neurology (AAN),[136] patients with Clinical Dementia Rating[137] of 1.0 or above are advised not to drive.

Caregiver Burden

The FTD strikes at a relatively young age so that the disease often causes dramatic financial burden that can be stressful for the entire family. Patients with dementia require assistance with activities of daily living, behavioral supervision, assistance with medication use, and essentially assistance with every aspect of daily life; hence, caring for a patient with dementia is a taxing job and can commonly lead to caregiver burnout and depression[138] The most burdensome symptoms of FTD are not only offensive, egocentric, and quarrelsome behaviors but also apathy, indifference, lack of insight, and aphasic symptoms leading to misinterpretations.

Caregivers require comprehensive information about the disease to enhance their understanding of the patients and to avoid unnecessary feelings of self-blame. The long-term social support,[138] educational, and supportive services available through organizations, such as the Association for Frontotemporal Degeneration,[139] and the development of strategies to maintain emotional and physical safety[139] have been shown to have a significant and sustained reduction in depressive symptoms in caregivers.[138,139]

Conclusion

Recent progresses in our knowledge regarding the genetics, pathogenesis, and varied clinical subtypes of FTD have been highly encouraging. Although pathology remains the gold standard for definitive diagnosis, clinical presentation and imaging

modalities are helpful in differentiating FTD from other causes of dementia. Although there are no FDA-approved medications currently available for the treatment of patients with FTD, advances in understanding the biology of FTD have suggested possibilities for new treatment options designed specifically to interfere with FTD-associated brain pathology. For proper management of FTD, apart from early diagnosis and pharmacological remedy, ensuring the safety of the patients and the sanity of the caregivers are equally vital. To conclude multidisciplinary research efforts and mass awareness and support initiatives both go hand in hand in our crusade toward FTD.

Declaration of Conflicting Interests

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