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# Frontotemporal dementia: From the clinic to the differential diagnosis

Daniel Antunes Pereira, Shara Aline Bueno Dantas, Marco Antônio Orsini Neves, Everton Gonçalves Pinto, Gilberto Canedo Martins Jr, Antonio Marcos da Silva Catharino

## ABSTRACT

**Introduction:** Frontotemporal dementia (FTD) is a disease that encompasses several syndromes that differ in their cognitive, behavioral, language signs, and motor phenomena. Only Alzheimer's disease causes more early-onset dementia cases than FTD. According to World Health Organization (WHO) projections, dementia rates will double every 20 years and reach 115.4 million people in 2050, ranging from 3% to 26%. The FTD spectrum encompasses three variant syndromes, namely the behavioral variant, the semantic variant, and the non-fluent/agrammatical variant. Frontotemporal lobar degeneration is neuropathologically related to the clinical phenotypes of FTD. Therefore, the frontal and temporal lobes suffer from gliosis and selective neuronal loss due to this neurodegenerative condition.

**Case Report:** A 62-year-old doctor with no comorbidities. According to the family, he reports delivering very slowly, which he doesn't and comes in the processing very efficiently. He claims that he already lost on the street but managed to restore his visuospatial function. He denies changes in his daily life to recent trauma. Neurological examination revealed impaired attention and behavioral changes, impaired short-term memory (mini-mental: 19/30 points), normal laboratory, regular liquor; skull magnetic resonance imaging (MRI) showed mild atrophy in the frontotemporal regions. Decreased activity in areas of the cortex was observed by cerebral perfusion scintigraphy.

**Conclusion:** Therefore, this report is relevant because it correlates a patient with neurological examination and tests with a good indication of FTD; however, the diagnosis can be confirmed with greater accuracy through brain perfusion scintigraphy. It is still possible to observe that although there has been a significant increase in the literature on FTD, its variants and its clinic still need further studies regarding their possible differential diagnoses, mainly related to psychiatric disorders and the behavioral variant of FTD.

**Keywords:** Behavior, Cognitive dysfunction, Frontotemporal dementia

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## INTRODUCTION

Frontotemporal dementia (FTD) is a disease that encompasses several syndromes that differ in their cognitive, behavioral, language signs, and motor phenomena. Only Alzheimer's disease causes more early-onset dementia cases than FTD [1].

The Czech neurologist and psychiatrist Arnold Pick first described a patient with FTD in 1892, later called Pick's disease. Frontotemporal dementia is a member of a group of neurodegenerative diseases known as tauopathies. According to the current neuropathological classification of FTD subtypes, specific deposits of intracellular proteins, including those of Tau, TDP-43, and FET proteins, are identified by immunohistochemical staining [2, 3].

The loss of appropriate interpersonal behavior brought on by a decline in social cognition skills is an early sign of FTD. Social cognition is a broad term used to describe cognitive processes related to perception and comprehension. It includes abilities like empathy, mentalization (or theory of mind), and emotion recognition [4].

Clinically, FTD usually manifests as a complex behavior disorder that primarily affects interpersonal behavior or communication (primary progressive aphasia, PPA), often in middle age. Primary progressive aphasia presents itself in FTD variants with a greater emphasis on communication [5].

According to WHO projections, dementia rates will double every 20 years and reach 115.4 million people in 2050, ranging from 3% to 26% [6].

The FTD spectrum encompasses three variant syndromes, namely the behavioral variant, the semantic variant, and the non-fluent/agrammatical variant [7].

The behavioral variant may initially be confused with a psychiatric illness, as it includes new behavioral symptoms such as compulsions, changes in diet, or symptoms such as apathy and lack of empathy [1].

The dysfunctions are in the medial frontal area, orbital frontal, anterior cingulate, and frontoinsular cortex. As the disease progresses, new symptoms that appear over time can localize the spread of neuropathological changes. Based on the regional spread in each patient, the behavioral variant has a wide range of clinical phenotypes [8].

As for the semantic variant, language-based symptoms with gradual loss of semantic memory are present when the left temporal lobe is affected. Behavioral symptoms are more common when the right temporal lobe is most affected. Of the significant clinical phenotypes in FTD, the semantic variant is the least likely to have an underlying genetic cause of the disease [1, 9].

Memory may be impacted if the mesial temporal lobes are affected, but executive function and visuospatial abilities are typically unaffected.

The non-fluent variant is characterized by the production of slow, labored, interrupted speech, and the omission or inappropriate use of grammar. Even so, they can communicate effectively in writing. Broadman's area 44 and 45 (Broca's area) in the left inferior frontal gyrus and the anterior insula are neuroanatomical correlates for symptoms of this variant. The patient may eventually stop talking [1, 4].

Frontotemporal lobar degeneration is neuropathologically related to the clinical phenotypes of FTD. Therefore, the frontal and temporal lobes suffer from gliosis and selective neuronal loss due to this neurodegenerative condition [9, 10].

Neuroinflammation is considered a pathological hallmark of neurodegenerative diseases, a promising research avenue related to FTD. In addition, the autoimmunity associated with this disease remains lacking in studies, although a correlation between neurodegeneration and some autoimmune diseases has been observed [11, 12].

Regarding the neuroanatomical alterations of the three variants of FTD, all of them are present in the mesolimbic dopaminergic circuits related to reward and behavior. In a meta-analysis study, a strong relationship was observed between this alteration and the altered sensation of reward in patients affected by FTD [4].

## CASE REPORT

LCM, a 62-year-old male, physician, without comorbidities. He reported that he has been presenting much slow thinking and active processing, according to his family. He realizes that dyscalculia has begun to compromise him in his functional activities. He claims that he was once lost on the street but managed to re-establish his visuospatial function. He is apathetic and somewhat depressed but does not attribute depression to the current situation, as he has always had it. He denies changes in his daily life to recent trauma as triggering factors. Neurological examination reveals compromised attention and behavioral strategies (sometimes apathy and aggressiveness). Crying is part of the clinical picture; sometimes not explained. Compromised short-term memory (mini-mental: 19/30 points), with errors mainly in short-term memory, spatial dysfunction, and attention. He was using antidepressants and mood stabilizers without success. Family members cite abrupt changes in personality and behavior, difficulties in understanding and producing speech and writing add to the clinical picture, normal laboratory, normal liquor; skull magnetic resonance imaging (MRI) showed mild atrophy in frontotemporal regions and the hippocampus. This one is standard size and dimension. Electroencephalogram (EEG) was normal. Cerebral perfusion scintigraphy showed the left superior frontal cortex (yellow arrows—Figure 1), the anterior cingulate cortex (ACC) (blue arrow—Figure 2), and the right mesial temporal cortex (green arrows—Figure 3) with decreased activity.

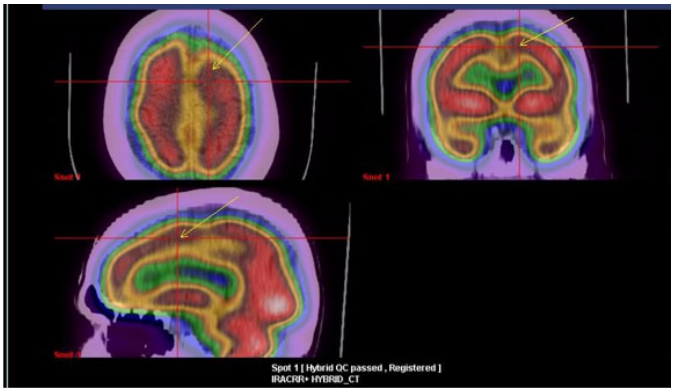


Figure 1: The left superior frontal cortex with decreased activity (yellow arrows).

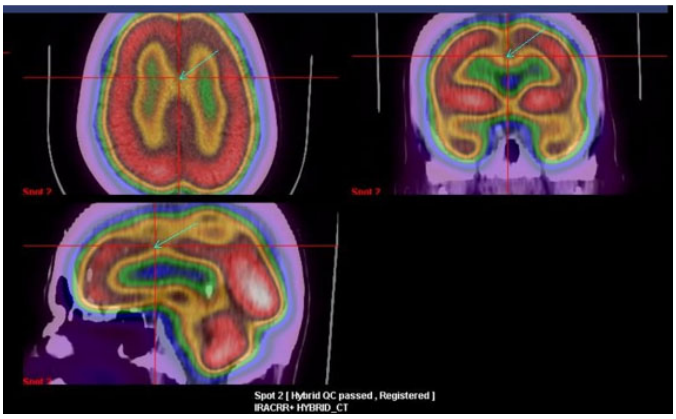


Figure 2: The anterior cingulate cortex with decreased activity (blue arrow).

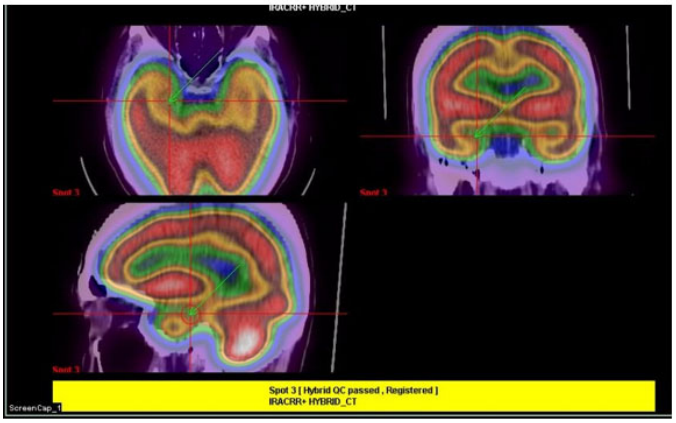


Figure 3: The right mesial temporal cortex with decreased activity (green arrows).

## DISCUSSION

The clinical criterion for the diagnosis of FTD is indisputable from the report and the neuroimaging corroborating it. According to international consensus criteria, it is possible to infer a possible behavioral variant in the report [10, 13].

The case demonstrated progressive cognitive decline (mini-mental: 19/30), mainly in short-term memory and behavioral change. In addition to impairment in social behaviors and speech and writing difficulties. These symptoms markedly affected his daily function.

Analyzing the MRI, mild atrophy was observed in frontotemporal regions, but in the scintigraphy, it can be more specific in analyzing the images.

The ACC is a subregion of the ventromedial frontal cortex that is anatomically distinct. It is formed by the cingulate sulcus and gyrus, located ventrally to the superior frontal gyrus and dorsally to the corpus callosum, respectively. It includes Broadmann Area 24 and surroundings. In short, there is consensus that this area is related to focused attention [14].

The authors had to assess whether the primary differential diagnoses, potentially reversible, of different etiologies, such as metabolic alterations, intoxications, infections, and nutritional deficiencies, were compatible with the patient. However, as reported, the careful clinical evaluation and physical and neurological examinations associated with neuroimaging may allow greater accuracy in the case [5, 13].

The analysis of the literature, as mentioned above, shows that patients affected by FTD, mainly the behavioral variant, manifest violations of rules or moral norms at the beginning of their illness. Several studies correlate this dementia with antisocial behavior, aggression, and difficulty in impulse control [15, 16].

Given the report, it is also possible to evaluate the differential diagnosis of psychiatric disorders, such as schizophrenic/psychotic spectrum, depressive, bipolar, and obsessive-compulsive disorders. It is difficult to differentiate the boundary between these diseases and FTD in many patients due to their behavioral aspects [16].

## CONCLUSION

Therefore, this report is relevant because it correlates a patient with neurological examination and tests with a good indication of FTD; however, the diagnosis can be confirmed with greater accuracy through brain perfusion scintigraphy. It is still possible to observe that although there has been a significant increase in the literature on FTD, its variants and its clinic still need further studies regarding their possible differential diagnoses, mainly related to psychiatric disorders and the behavioral variant of FTD. Therefore, more research is needed to define these behavioral occurrences of FTD better.

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## Author Contributions

Daniel Antunes Pereira – Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Shara Aline Bueno Dantas – Conception of the work, Design of the work, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Marco Antônio Orsini Neves – Conception of the work, Design of the work, Acquisition of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Written informed consent was obtained from the patient for publication of this article.

## Conflict of Interest

Authors declare no conflict of interest.

## Data Availability

All relevant data are within the paper and its Supporting Information files.