

# Aphasia, Prosopagnosia and Mania: A Case Diagnosed with Right Temporal Variant Semantic Dementia



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## SUMMARY

Neurologic disorders can produce “secondary” mania, and clinicians must distinguish secondary mania from bipolar disorders (BD). Patients with new and late onset mania require an evaluation that includes a thorough history, a neurologic examination, neuroimaging, and other selected tests. Neurologic causes of mania include strokes in the right basotemporal or inferofrontal region, strokes or tumors in the perihypothalamic region, Huntington’s disease and other movement disorders, multiple sclerosis and other white matter diseases, head trauma, infections such as neurosyphilis and Creutzfeldt-Jakob disease, and frontotemporal lobar degeneration. The term Frontotemporal Lobar Degeneration (FTLD) is suggested for neurodegenerative diseases characterized by focal degeneration such as Primer Progressive Aphasia (PPA), Frontal Lobe Dementia, PPA- Amyotrophic Lateral Sclerosis (ALS), and Corticobasal Degeneration. In this article, we report a frontotemporal dementia (FTD) case that referred with manic symptoms. The female patient was 46 years old, married, graduated from primary school, and had been admitted with complaints of hyperactivity, excessive talking, and decreased sleep for one week. She presented first with complaints that began three years ago that included the inability to remember names, recognize faces, use household appliances, and follow rules. She had also been repeating the same words and behaviors. Prosopagnosia, aphasia, and a positive family history of ALS were discussed with related index in our case.

**Keywords:** Aphasia, prosopagnosia, mania, ALS, FTD

## INTRODUCTION

Frontotemporal Dementia (FTD) is a clinical syndrome that leads to the atrophy of frontal and temporal lobes and is characterized by behavioral changes and progressive changes in language (Kertesz et al. 2007). In the 1990’s a study group on the subject recommended the term Frontotemporal Lobar Degeneration (FTLD) as a common name for all neurodegenerative diseases characterized by focal degenerations, including Primary Progressive Aphasia (PPA), Frontal Lobe Dementia PPA-Amyotrophic Lateral Sclerosis (ALS), and Cortico Basal Degeneration (Kertesz et al. 2003). In another classification attempt, through Neary criteria developed in 1998, FTLD was functionally separated into three types, which are Frontal Lobe Dementia, Semantic Dementia (Progressive fluent Aphasia), and Progressive non-fluent Aphasia (Perry and Hodges 2000), (table-1). In Semantic

Dementia, the frontotemporal region is affected. When the right temporal region is affected, face recognition difficulties and problems in the perception and expression of emotions are experienced.

Neurological disorders may produce secondary mania, and clinicians should be able to distinguish secondary mania from bipolar disorder (BPD). Early and late onset neurological disorders require a comprehensive evaluation including a detailed history, neurological examination, imaging, and other selected tests. Neurological symptoms are usually seen in elderly cases without a family history of BPD. Neurological causes of mania include strokes in the right basotemporal and lower frontal region, tumors around the hypothalamic region, Huntington’s disease or other movement disorders, multiple sclerosis and other white matter diseases, infections such as neurosyphilis and Creutzfeldt-Jakob disease, and frontotemporal lobar degeneration. It is important to note that manic

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symptoms appear due to the disappearance of inhibition on limbic structure as a consequence of the effect on frontotemporal pathways (Shulman 1997). Especially in disinhibition syndrome, which arises in cases involving the frontotemporal region (secondary mania), symptoms and signs were found to be consistent with the symptom cluster mentioned in DSM-IV-TR manic period diagnostic criteria (Gafoore and O'Keane 2003).

In this study, an FTD case presenting with mania is reported. Fluent aphasia, prosopagnosia, and a positive family history of ALS in our patient were discussed in view of the literature.

## **CASE**

### **History**

A 46 year old married woman who is a primary school graduate was referred to our outpatient clinic with the complaints of hyperactivity, increased speaking, and a decrease in sleep within the last week. Three years ago her initial complaints were being unable to remember names and recognize faces, repeating the same words and behaviors, not being able to use home appliances, and lack of organization and compliance with rules. Her relatives reported that her eating behavior had changed within the last year, that she fed herself irregularly with apple and other sweet juices, and her overall self-care was decreased and she was unable to take care of herself.

There was no response to antidepressant treatment three years ago, and one year ago she was told that she had Alzheimer's disease. Since then, she has been treated with a Rivastigmin transdermal patch 10 cm<sup>2</sup>/day and Quetiapin 100mg/day.

She had no history of psychiatric or physical disease, but her family history revealed that her father had amnesia in the last three years before he died at age 67. In addition, her brother was diagnosed with ALS at the age of 33 and has been confined to bed for the last two years.

### **Clinical evaluation and follow up**

In psychiatric and neurological examinations, the patient was found to have decreased self-care, looked older than her chronological age, and eye contact was difficult with her. Her psychomotor activity was increased, her need for sleep was decreased, and her mood was euphoric. Her speech was pressured, and had increased speed and spontaneity (logorrhea) in a perseverative manner. In a routine examination performed each morning, she acted as if she had just met her physician for the first time and repeated her sentences, which were successively memorized by the entire treatment team. In her relations with the other patients in the clinic, she also acted as if each meeting was their first contact, and she communicated through repeated monologues. Prosopagnosia was present,

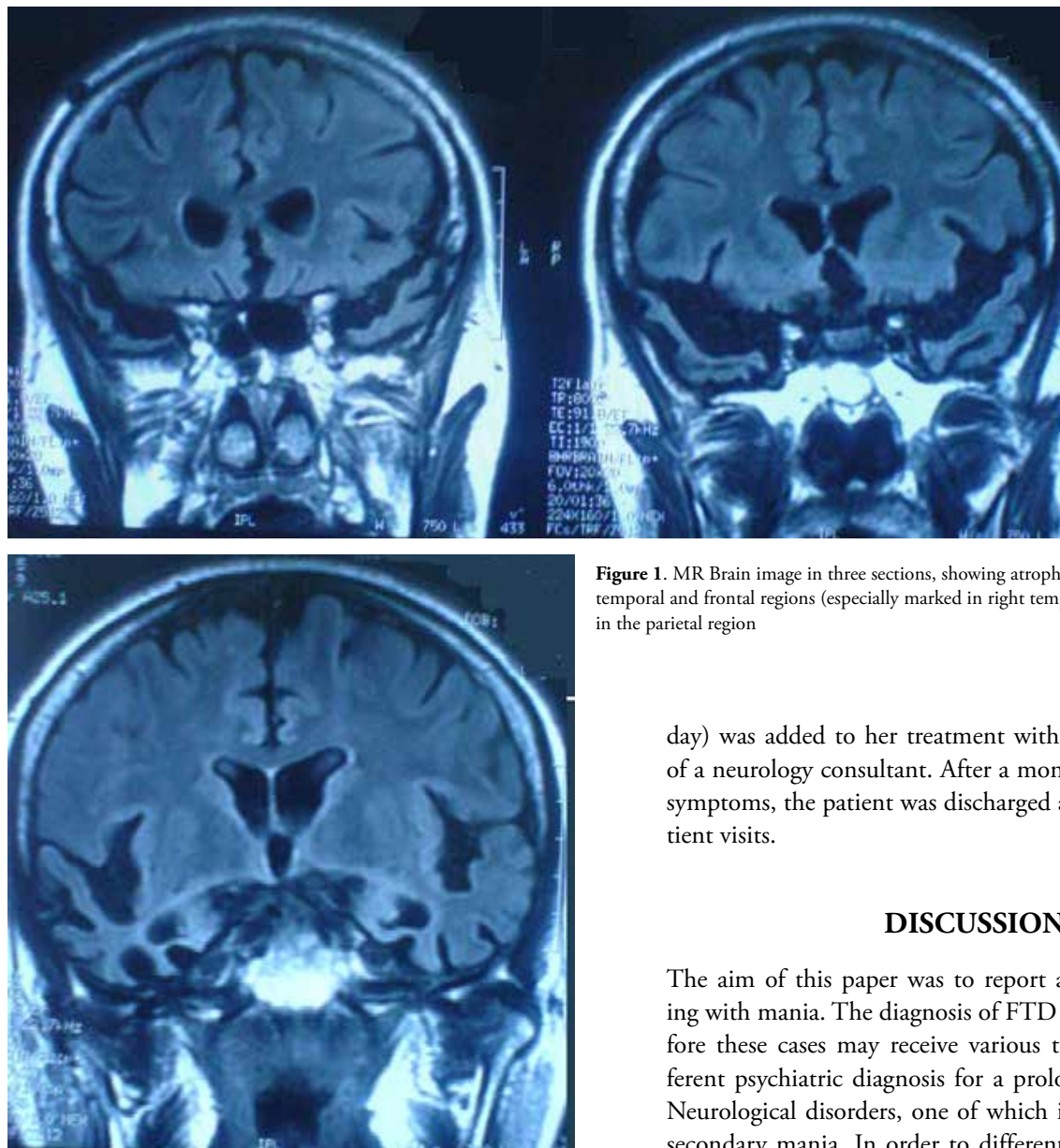
and recognition and naming of objects was partially protected. Person and time orientation was impaired, and while momentary memory was impaired, short term and long term memory was intact. Her attention span and her judgment on daily living activities were very weak, and she was unable to meet her basic needs.

No pathological finding was observed upon physical examination. Her laboratory analyses and electroencephalography (EEG) were normal. No hormonal impairment was established in the Hypothalamo pituitary thyroid, hypothalamo pituitary adrenal, or hypothalamo pituitary gonadal axis. The results of autoimmunological analyses were also normal. In chromosomal analysis, no structural or numerical abnormality was found.

For neuro psychological evaluation, our patient underwent the Digit Span Test, Wechsler Memory Scale, cube and hour drawing test, Stroop Test, Wisconsin Chart Matching Test, verbal fluency test, Bender Test, and Benton face recognition test. After these neuropsychological tests, it was determined that her time and space orientation and personal and actual information were weak, and that her judgment and interpretation, arithmetical skills, logical memory, and conceptualization were inadequate. The patient's momentary memory was very weak, and transferring information to short term memory, recording, storing, retrieval and recognition processes and learning skills were markedly weakened. Her attention span was shortened and she was unable to attain verbal fluency, her semantic production was weak, she was not able to maintain interclass installation, and perseverations were present. In the Bender test, there was organizational disorder and marked rotations in drawings, which suggested organic disorder. In the Benton face recognition test, advanced impairment was seen in visual memory, visual perception, and recognition

In MR brain imaging, marked folia in the cerebellar hemispheres and vermis were seen (figure-1). In the bilateral temporal lobe, substantial temporal atrophy was present and her lateral ventricles were slightly enlarged. Hemispheric cortical sulcus was marked, the cortex was thinner, and the volume of cortical white matter was decreased. In addition, the subarachnoid space was enlarged. In both lateral ventricle temporal horns, asymmetrical dilation and bilateral hippocampal atrophy was observed.

When her history, examination, and investigational findings were evaluated together, it was thought that she was in the process of dementia, and when onset of age and symptom clusters were taken into account, this process was considered to be compatible with frontotemporal dementia. Fluent aphasia and a positive family history of ALS suggested the concurrence of PPA-ALS. When evaluated together with prosopagnosia, our patient was diagnosed with FTLT, semantic dementia, right temporal variant. In addition, her present



**Figure 1.** MR Brain image in three sections, showing atrophy in both the temporal and frontal regions (especially marked in right temporal) and partially in the parietal region

day) was added to her treatment with the recommendation of a neurology consultant. After a month without any mood symptoms, the patient was discharged and invited for outpatient visits.

## DISCUSSION

The aim of this paper was to report an FTD case presenting with mania. The diagnosis of FTD takes time, and therefore these cases may receive various treatments with a different psychiatric diagnosis for a prolonged period of time. Neurological disorders, one of which is FTD, may produce secondary mania. In order to differentiate secondary mania from bipolar (BPD), new and late onset mania cases should undergo a comprehensive evaluation including a detailed history, neurological examination, brain imaging, and other selected tests. Aphasia, prosopagnosia, and a positive family history of ALS in our patient suggest the diagnosis of FTD, including its subtype.

In semantic dementia classified under the FTLT category according to Neary criteria developed in 1998, the fronto temporal region is influenced (Perry and Hodges 2000). In cases with right temporal involvement, severe impairment of naming and conceptual knowledge, difficulty in face recognition, and problems in perception and expression of emotions are experienced, while in cases where the left fronto temporal region is involved, language problems (in fluent aphasia type) are experienced (Neary et al. 2005, Mizuno and Takeda 2009, George and Jose 2009). The progressive fluent aphasia present in our patient is consistent with semantic dementia.

mood and psychomotor activity symptoms corresponded to symptom cluster mentioned in manic period diagnostic criteria. In view of the age of onset and the lack of family history of mood disorders, this was linked to a general medical condition.

Her Young Mania Rating Scale (YMRS) score was 35, and she was prescribed a treatment of lithium carbonate (1600 mg/day) and quetiapine XR (800 mg/day). After the fourth week of treatment, her psychomotor activity improved, and her sleeplessness and pressured speech disappeared. Symptoms of mania subsided (YMRS score 8) and the quetiapine was gradually withdrawn. Her blood lithium level was adequate for maintenance treatment, and in order to prevent impulsive and repetitive symptoms related to the impairment of frontal inhibition (Freedman 2007, Mendez 2009), sertraline (50 mg/

The presence of prosopagnosia, associative agnosia, pressured speech, dyslexia, and dysgraphia is consistent with the diagnosis of the right temporal variant. However, fluent speech without content suggests that in this case, left fronto temporal regions are also associated with the degenerative process. In addition to these findings, the presence of euphoria, increase in psychomotor activity, decrease in the need for sleep, and pressured speech fulfill the criteria of mania. However, it is important to note that manic symptoms arise with the disappearance of inhibition on limbic structures as a consequence of the involvement of frontotemporal pathways (Shulman 1997, Woolley et al. 2007). In the literature, it is reported that dysinhibition syndrome (secondary mania) emerging in cases with the involvement of right frontotemporal region symptoms and signs meet mania criteria (Gafoor and O'Keane 2003, Chan et al. 2009). Given this information, mania added to the clinical picture in our patient may be interpreted as the consequence of frontotemporal region involvement influenced by the degenerative process.

In the brain imaging of our patient atrophy was observed in both the temporal and frontal regions, especially in the right temporal and partly in the parietal region (figure-1). As for the parietal region, in addition to frontal and temporal dysfunction in FTLT, parietal involvement also accounts for disturbances in somatosensorial area (Tsermantseli et al. 2011). As seen frequently in the diagnosis of FTLT (Hu et al. 2011), EEG was found to be normal in our patient. In FTLT, impairment in tests evaluating the maintenance of attention, reasoning, and abstraction is expected (Flaherty-Craig et al. 2011). Momentary memory was very weak as was her ability to transfer information to short term memory, while weakening of her recording, storing, retrieval and recognition processes and learning skills was observed. Our patient had a shortened attention span and was unable to keep track of the trail of conversation. As to verbal fluency, semantic production was weak and she was unable to maintain interclass installation, while perseveration was present. In the evaluation of semantic dementia, right temporal variant, a face recognition test and prosody differentiation tests were used (Flaherty-Craig et al. 2011). In the Benton face recognition test, a marked impairment was seen in her visual memory, visual perception, and recognition.

FTLT occurs at the rate of 12-15% among dementias and 50% among those with early onset dementia (Kertesz et al. 2010). It frequently starts between the age range of 45-65 and both sexes are influenced equally. Mean survival after the onset of symptoms is reported to be 6-8 years. It has been reported that survival is longer in familial cases. In FTLT, an initial severe impairment in cognitive functions is not seen, and in mild or moderate FTLT, impairment in visuo spatial skills is rare. In view of this information, it can be said that our patient is at an advanced stage. From her medical history, our

patient's cognitive impairment started three years ago. Age of onset, which was calculated to be 43 in our patient, may be defined as an early onset for FTLT cases. It should be stressed here that low educational level is a risk factor and predictor of unfavorable prognosis in all dementia cases (Kertesz et al. 2010). In fact, the highest level of schooling our patient completed was primary school.

In some FTLT cases, concurrence of PPA and ALS was defined (Kertesz et al 2003, Kim et al. 2009). Coexistence of these two clinical pictures is significant for the genetics of neurodegenerative disorders. In 40% of FTLT cases, there is a positive family history. The genetic abnormality first demonstrated in FTLT is a mutation in the gene of tau protein (MAPT) and is linked to q21-22 region of chromosome 17 (Kryndushkin and Shewmaker 2007). In 17q21 locus, inclusions produced secondary to another mutation defined as tau (-), ubiquitin (+) and progranuline (+) and which has ubiquitin immunoreactivity were determined to be TDP-43, which is coded in chromosome 1 under normal conditions and is a nuclear protein (Kryndushkin and Shewmaker 2007). TDP-43 gene mutations have been reported to be associated with familial ALS (Kumar-Singh 2011). In addition to this, a few FTD and FTD-ALS families have been described with some gene mutations in chromosomes 3, 9 and 16. As another genetic abnormality, FTD and ALS were reported to develop together in rats that had a damaged FUS gene (Huang et al. 2011).

Our patient's brother suffered from ALS. During the process of clinical follow up, another degenerative process not present at the onset, such as progressive nuclear palsy, corticobasal degeneration, or ALS may be superimposed (Strong and Yang 2011). In this respect, careful follow up both in our patient and her brother is significant with respect to the probability of the development of other neurodegenerative disease. In FTLT, other motor abnormalities may be seen apart from ALS. In a clinical study of 60 cases with FTLT, involvement of 27 cases (45%) was reported (Seilhean et al. 2011). In a recent case presentation, the coexistence of FTLT and Spinal Progressive Muscular Atrophy was mentioned (Mitsuyama 2011).

Taupathies such as FTD and Alzheimer's disease are characterized by the aggregation of microtubules in the nerve cell together with tau protein. This condition impairing axonal transport is phosphorylation dependent. It has been suggested that in this period preceding neuronal death, GSK (glycogen synthetase kinase) 3 beta inhibition may reverse pathological changes and improve axonal transport (Mudher et al. 2004, De Carvalho and Swash 2011). Lithium is one of the inhibitors of GSK 3 beta and has been recommended to be used in taupathies (Freedman 2007). Its use was planned in the present patient with secondary mania after the relief of manic symptoms and was used beyond that for maintenance treatment.

**Table 1.** FTLT classification according to adapted Neary criteria**Frontal Lobe Dementia**

- 1-Main clinical findings
  - a. insidious onset and slow progression
  - b. impairment in interpersonal social relations in the early period
  - c. Impairment in the regulation of personal behavior in the early period
  - d. emotional dullness in the early period
  - e. loss of insight in the early period
- 2- Supportive Diagnostic Characteristics
  - a. behavioral disorder
  - b. speech and language disorder
    - 1- alterations in speech output
    - 2- stereotypical speech
    - 3- echolalia
    - 4- perseveration
    - 5- mutism
- 3-Brain Imaging (structural and / or functional):  
Nondominant frontal and /or anterior temporal lobe abnormality.

**Progressive non-fluent Aphasia**

- 1-Main clinical findings
  - a. insidious onset, slow progression
  - b. non-fluent spontaneous speech and at least one of the following:  
Agramatism, phonemic paraphasias, anomia
- 2-Supportive diagnostic characteristics
  - a. Speech and language
    - 1- stuttering or oral apraxia
    - 2- rumination disorder
    - 3- alexia, agraphia
    - 4- protection of the meaning of words in the early period
    - 5- mutism in the late period
  - b. Behavior

- 1- protection of social skills in the early period
- 2- Behavioral changes similar to FTD in the late period
- 3- Brain Imaging (structural and /or functional): Asymmetrical abnormality influencing especially dominant (left) hemisphere.

**Progressive fluent aphasia / Semantic Dementia**

- 1-Main clinical findings
  - a. insidious onset and slow progression
  - b. language disorder characterised with the following:
    - 1- progressive, fluent, spontaneous speech without content
    - 2- loss of the meaning of the word manifested by naming and understanding disorder
    - 3- semantic paraphasias
- 2- Supportive Diagnostic Characteristics
  - a. pressured speech
  - b. idiosyncratic vocabulary
  - c. surface dyslexia and dysgraphia
- 3-Brain Imaging (structural and /or functional): Asymmetrical abnormality influencing especially dominant (left) anterior temporal lobe.

**Prosopagnosia (Right Temporal Variant Semantic Dementia)**

- 1.Main clinical findings
  - a. insidious onset and slow progression
  - b. perception disorder characterised by the following :
    - 1- Prosopagnosia: impairment in the recognition of familiar faces and/or
    - 2- Associative agnosia: Impairment in object recognition
- 2-Supportive Diagnostic Characteristics
  - a. pressured speech
  - b. idiosyncratic vocabulary
  - c. surface dyslexia and dysgraphia
- 3-Brain Imaging (structural and / or functional): Asymmetrical abnormality influencing especially non-dominant (right) anterior temporal lobe

In conclusion, an FTD case referring with mania is presented. Fluent aphasia and a positive family history of ALS points to the coexistence of PPA-ALS. Prosopagnosia and mania exemplifies FTLT according to Neary criteria, semantic dementia, right temporal variant.

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