Frontotemporal Dementia: a Case Presentation

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ÖZET

Frontotemporal demans: Bir olgu sunumu

Fronto temporal demans (FTD), orta yaşlarda Alzheimer hastalığından sonra en sık görülen primer dejeneratif demans türüdür. Genellikle 45-65 yaşları arasında sinsi bir şekilde başlayan, her iki cinsiyette eşit sıklıkta görülen, kişilik, davranış ve duygulanım değişikliklerinin yanında içgörü kaybı, perseveratif ve stereotipik davranışlar ve yeme alışkanlıklarında değişikliklerin görülebildiği bir hastalıktır. Bu hastalarda nörolojik muayene, rutin elektroensefalogram (EEG) normaldir ve beyin görüntülemede, frontotemporal loblarda fokal anormallikler vardır. Yürütücü işlevlerde belirgin yetersizlikler vardır.

Bu yazıda, hastalığı ellili yaşlarda sinsice başlayan, kişilik değişikliği ve davranışta bozulmanın en çarpıcı belirtiler olduğu, içgörü kaybı, hiperoralite ve diyetle ilişkili değişiklikler, kompülsif ve stereotipik davranışlar, künt duygulanım, konuşma miktarında azalma ve dışa vuran davranışlarda yavaşlama, kişisel bakımda bozulma, altına idrar ve gaita kaçırmanın eşlik ettiği, demans için pozitif aile öyküsünün bulunduğu bir erkek FTD olgusu sunulmuştur. Hastada nörolojik muayene ve rutin EEG normaldi. Kraniyal Manyetik Rezonans Görüntüleme'de (MRG), sağ hemisferde belirgin olmak üzere, dorsolateral ve orbitofrontal bölgede asimetrik atrofi vardı. Hastaya yapılan Tc-99 HMPAO tek fotonlu emisyon tomografisinde (SPECT), sağ frontal ve paryetal lobları içine alan geniş bir alanda asimetrik hipoperfüzyon saptandı. Frontal yürütücü işlevlerde yetersizlik vardı. Hastada, ketiapin 300 mg/gün tedavisiyle davranışsal belirtilerde kısmen düzelme görüldü. Bu olgu, orta yaşlarda sinsi şekilde psikiyatrik belirtilerle başlayan olgularda mutlaka ayrıntılı öykü, fizik ve nörolojik muayene ve beyin görüntüleme dahil tıbbi inceleme yapılması gerektiğini göstermektedir.

Anahtar kelimeler: Frontotemporal demans, orta yaşlar, yürütücü işlevler, beyin görüntüleme

ABSTRACT

Frontotemporal dementia: a case presentation

Frontotemporal dementia (FTD) is, next to Alzheimer disease, the most frequently encountered form of primary degenerative dementia among middle-aged subjects. It generally begins insidiously between the ages of 45 and 65 years, and is seen in both genders with equal frequency. It is characterized by changes in personality, behavior, and affect, in addition to loss of insight, perseverative and stereotypical behaviours, and changes in eating habits. These patients appear normal upon neurological examination and routine electroencephalography (EEG), but brain imaging reveals focal abnormalities in the frontotemporal lobes. There is significant deficiency in executive functions.

This study describes a male patient with FTD that had began insidiously in his fifties, and in whom the changes in personality and impairment in behavior were the striking symptoms (loss of insight, hyperorality, and dietary changes; compulsive and stereotypical behaviours; blunted affect, decrease in the amount of speech and retardation in expressional behaviours; impairment in personal hygiene; urinary and fecal incontinence) along with a family history of dementia. The neurological examination and routine electroencephalogram (EEG) of the patient were normal. His cranial magnetic resonance imaging (MRI) revealed asymmetric atrophy, particularly in the right hemisphere at the dorsolateral and orbitofrontal regions. Tc-99 HMPAO single photon emission tomography (SPECT) detected asymmetric hypoperfusion within an extended region, including the right frontal and parietal lobes. There was deficiency in frontal executive functions. Partial improvement in behavioral symptoms was achieved by treating the patient with quetiapine 300 mg/day. The present case study showed that detailed history, as well as medical examination including physical and neurological examination and brain imaging, must be performed in the case of middle-aged patients with insidious onset of psychiatric symptoms.

Key words: Frontotemporal dementia, middle ages, executive functions, brain imaging

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INTRODUCTION

Frontotemporal dementia (FTD) is the most prevalent type of primary degenerative dementia after Alzheimer's disease in middle ages and makes up 20% of cases with presenile dementia (1). FTD, represents with behavioral changes and these symptoms dominate during the course of the disease (2). Clinical manifestations of FTD is heterogeneous (1) and there may be disinhibition, overactivity, blunt affection (2),

apathy (3), lack of insight (4), difficulty in will and changing mental set and perseverative tendencies (1). Among other symptoms and signs, there are repetitive compulsive and stereotypical behaviors (5), changes in eating habits (6) and reduced speech (5). Onset of FTD is between 45-65 years and is seen equally at each gender (2). In a study, prevalence of FTD between 50-59 years of age was found 0.036% (7). Mean disease duration from onset of symptoms till death is 6-8 years (2). Known risk factors of FTD are positive family history of FTD and head trauma and thyroid disease (3).

FTD is pathologically heterogeneous as well (8). In postmortem pathological examinations, bilateral atrophy in frontal and temporal lobes and striatal degeneration was observed (1). Executive functions are impaired in patients with FTD; however, unlike Alzheimer's disease, memory and spatial functions are preserved (2). Focal anomalies in frontotemporal lobes in brain imaging and non-existence of neurological signs at the early period, support the clinical diagnosis (5). Diagnostic criteria were developed for clinical diagnosis of FTD. These are Lund and Manchester group (9), Neary et al. (10) and McKhann et al. (11) consecutively.

In this study, a male case with frontotemporal dementia whom onset was insidious in middle age, psychiatric symptoms such as changes in behavior, personality and affect predominated and a had positive family history of dementia.

CASE PRESENTATION

First symptoms of the male patient who was 55 years old, married and high school graduate, started 4-5 years ago. His premorbid personality was extrovert, pleasant, hard-working and social but became introvert and withdrew himself from others. His speech gradually decreased. He was not working for 4 years. He goes out and walks for hours and return back without getting lost. He was not interested in his house anymore (for

Table 1: Clinical Diagnosis Consensus Criteria for Frontoemporal Dementia (9)

Clinical Profile: Foremost symptoms and signs at the onset and course of the disease are impairment in social behavior and change in personality.

Main Diagnostic Criteria
Insidious onset and graded progression
Early impairment in social and interpersonal behavior
Early inadequacy in regulating personal behavior
Early emotional bluntness
Early loss of insight

Supporting Diagnostic Characteristics
Impairment in personal hygiene and self-care
Mental rigidity and inflexibility
Attention deficit and low attention span
Hyperorality and changes in diet
Perseverative and stereotypical behavior

Speech and language
Reduction of speech, loss of spontaneity and restricted speech
Stereotypical speech
Echolalia
Perseveration
Mutism

Physical Characteristics
Primitive reflexes
Incontinence
Akinesia, rigidity and tremor
Low and labile blood pressure

Laboratory Tests
Neuropsychology: Severe amnesia, aphasia or significant impairment in frontal lobe tests without impaired visual-spatial functions
Electroencephalography (EEG): Normal conventional EEG despite clinical signs of dementia
Brain Imaging (Structural and Functional): Predominantly frontal or anterior temporal anomalies

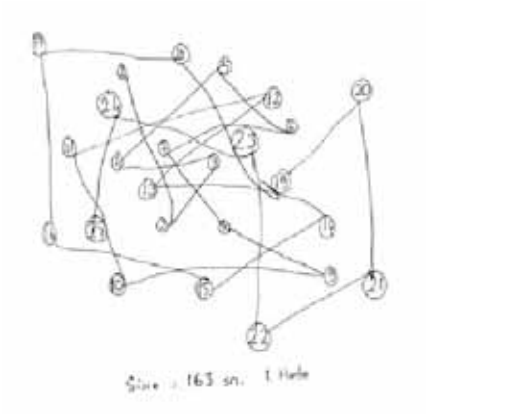


Figure 1: Trail-making Test Part A

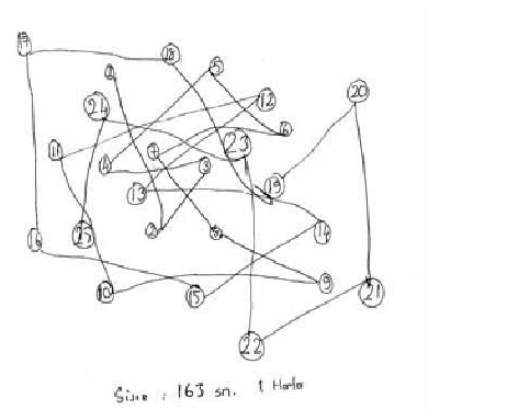


Figure 2: Trail-making Test Part B

Figure 3: Patients drawing in Luria alternating series test

example, he did not care about the absence of electricity at home due to unpaid bills). Although he was in a bad economic status he used to say he was a very rich man. He said he was the bodyguard of some important people. He had paranoid persecutive ideas about people coming to his house. He sometimes walked by crossing his feet. He had abnormal behaviors such as frequent finger counting, counting his steps and not stepping on the fissures of pavements, reading car license plates and murmuring with swear. He interpreted about women whom he does not know that they were dishonest. He used to be a clean and tidy man before the disease but started to soil and wet his clothes and bed in recent months. He did not change her clothes unless his wife gave him clean clothes. His appetite was enormously increased. He especially preferred fatty and sweet foods.

He has no history of head trauma, alcohol or substance abuse, exposure to toxins or any psychiatric or medical disease. In his family history, a similar clinical condition is described in his two uncles with onset in sixth decade; both of them died.

In his mental status examination; he was alert, fully-oriented and cooperated. Speech pace and quantity was decreased. His spontaneous attention was impaired. His affect was blunt. His memory, including instant memory and other cognitive functions were normal. His associations were slow and thought content was poor. There were compulsive and stereotypical behaviors. He had no insight of his condition.

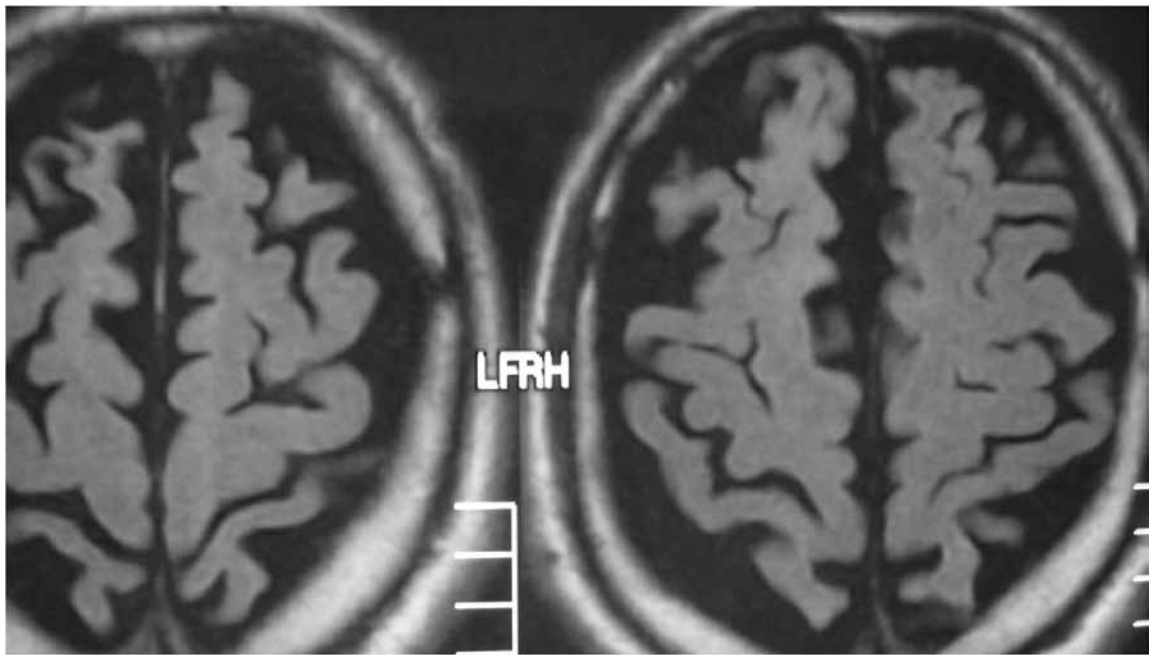
No pathological finding was observed in his physical and neurological examination. There was no agnosia or acalculia. Mini Mental Examination score was 29/30 in neuropsychological examination.

He completed part A of trail-making test in 163 seconds with one error and part B in 955 seconds with 9 errors. These scores were highly above normal threshold values (Figure 1 and 2).

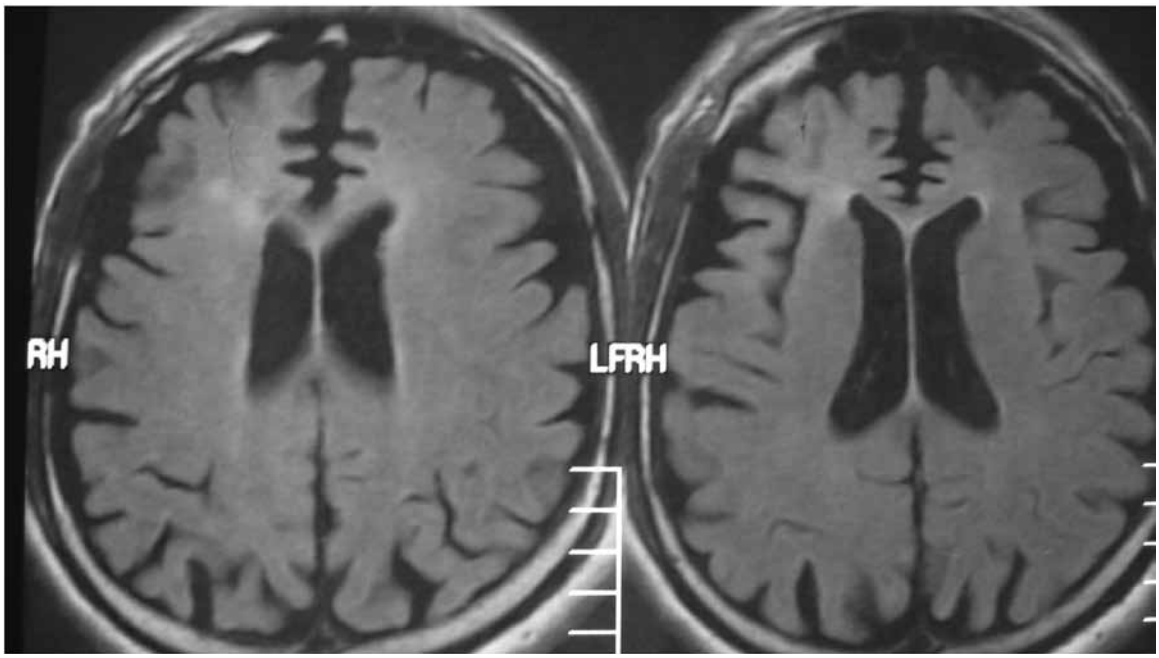
In Luria alternating series, perseveration deficit was found (Figure 3). In his verbal fluency test, animal names he was able to count was 9 in one minute (normal >18) and had one perseveration.

In Stroop test, he read first card in 13.9 seconds and fifth card in 46 seconds. While reading the first card, he did not any mistake. While reading the fifth card he made 7 mistakes and corrected them 5 times. Reading duration ratios between the first and fifth cards and his mistakes and corrections in the fifth card were considered significant for FTD.

In laboratory tests, thyroid function tests, vitamin B12 and folic acid levels, routine biochemical and hematological tests, urinalysis, chest X-ray and



Picture 1: In MRI, dorsolateral part of right frontal region was detected more atrophic than left.



Picture 2: In MRI, no difference was detected between the ventromedial parts of the frontal regions of both hemispheres.

electrocardiogram (ECG) were within normal limits. Hepatitis markers (HBsAg and Anti-HCV negative, Anti-Hbs positive), Anti-HIV and serological tests (VDRL/RPR) were negative. Routine EEG was normal. In computed tomography (CT) scan, there was significant atrophy in right frontotemporal areas and a lacunar infarct in right temporal region. In MRI, there was asymmetric atrophy in dorsolateral and orbitofrontal areas predominantly in right hemisphere (Picture 1). No atrophy was found in ventromedial area (Picture 2). In

Picture 3: In SPECT, lower blood flow was detected in right frontal region compared to left.

Tc-99 HMPAO SPECT, asymmetric hypoperfusion was detected in a wide area containing right frontal and parietal lobes (Picture 3). In Apoplipoprotein E (ApoE) (E2, E3, E4) mutation test, normal allele E3/E3 was detected.

During the clinical course patient continued finger counting movements, sometimes cried without a cause and murmured. He preferred to be alone in the ward, his communication with other patients was limited and his behaviors were slow.

Quetiapine was started to the patient to control behavioral symptoms and dose was gradually increased to 300 mg/day. By this treatment his self-care and communication with others partially increased and cried less. However, after his discharge and during follow-up his stereotypical and compulsive behaviors such as murmuring, license plate reading, counting steps and finger counting were continuing.

DISCUSSION

In patients with FTD, while language and memory were relatively preserved in the beginning, there were deep changes in social and personal behaviors, repetitive compulsive and stereotypical behaviors and reduced speech with language preserved (5). Neurological findings generally do not exist in the early period of FTD or limited to primitive reflexes and routine EEG is always normal (1). In MRI, frontotemporal atrophy is seen and is evident in both frontal lobes in frontal type FTD patients but in medial temporal lobes in Alzheimer's disease (3). Frontal and temporal lobe atrophy may be asymmetrical in MRI in FTD and abnormalities are detected in anterior cerebral hemisphere in SPECT (2). In patients having pathological changes predominantly in the right hemisphere, social behavior is impaired greater (1).

In our case, disease onset was at 50 years of age. Character changes and impairment in social behavior were predominant manifestations at the onset and during the course of the disease. There were loss of insight, hyperorality and changes in diet, blunted affect, reduced speech, impairment in self-care, compulsive and stereotypical behaviors, grandiosity, persecutive and reference ideas, slowing outward behaviors and soiling and wetting from onset. Neurological examination and routine EEG were normal. Frontal executive functions were impaired. Clinical manifestations of our case cover the criteria of Lund and Manchester group (9), Neary et al. (10) and McKhann et al. (11) for the diagnosis of FTD to a great degree. Thus, we diagnosed our case as FTD .

There are three major sub-groups of FTD: frontal type, semantic dementia and progressive non-fluent aphasia (8,12). Frontal type starts insidiously (3) and behavioral impairment is predominant (12). Stereotypical behaviors are mainly in anterior temporal lobes (2) and striatum (1) which atrophy is predominant (1). Semantic dementia typically starts with a lingual abnormality which meaning of words and word memory is lost and is seen with bilateral atrophy in middle and anterior

temporal neocortex (3). Progressive non-fluent aphasia is a linguistic disorder with severe problems in word recall from current vocabulary and is seen with asymmetric atrophy in left hemisphere (2). Clinical manifestations and brain imaging findings in our case is harmonious with frontal type of FTD. In approximately half of patients with FTD, there is a positive family history of dementia (1). In two uncles of our patient, there is a history of a disease with similar symptoms.

Executive dysfunction which characterizes FTD consists of impairment in planning, judgment, problem solving, organization, attention, abstract thinking and mental flexibility; however, primary instrumental lingual functions, elementary visual perception, spatial functions and memory is well preserved but performance in frontal executive function tests are impaired (2). MMSE is not reliable to detect and follow patients with FTD (3). In our case, although clinical signs lead to dementia, MMSE score was 29/30.

In a previous study, it was stated that hyperorality, loss of social awareness, stereotypical and perseverative behaviors and progressive loss of speech are important in differential diagnosis of FTD and Alzheimer's disease (13). Changes in affect and lack of insight were also reported to be key tools to differentiate FTD from Alzheimer's disease and vascular dementia (1, 2). In our case, all features were present except perseverative behaviors and progressive speech loss.

In patients with FTD, it was proposed that there is no abnormality in the cholinergic system in FTD so pharmacological agents developed for Alzheimer's disease will not be efficacious in this population (1). It was reported that there are abnormalities in serotonin metabolism in FTD (2) and selective serotonin reuptake inhibitors (SSRIs) are effective on behavioral but not on cognitive symptoms (3). Behavioral symptoms such as dysinhibition, excessive eating and compulsions may particularly benefit from treatment with SSRIs (1). Deficient serotonin metabolism in FTD may cause hyperorality and SSRIs may be beneficial to treat this symptom (14). Patients with FTD are particularly sensitive to extrapyramidal side effects of neuroleptics (3). We used 300 mg/day quetiapine to treat behavioral symptoms in our case. Behavioral symptoms of our case were partially remitted by this treatment. However, stereotypical behaviors and compulsions persisted.

In conclusion, our case indicates that FTD should be considered in middle-aged patients with insidious personality, behavioral and psychiatric changes accompanied by hyperorality and changes in diet, compulsions, stereotypical behaviors and lack of insight. In such cases, a detailed history, physical and neurological examination, neuropsychological evaluation and brain imaging should be performed.

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