PROBABLE FRONTOTEMPORAL DEMENTIA IN TWO SIBLINGS FROM A CONSANGUINEOUS FAMILY: A SINGLE CLINICAL CASE WITH CONCORDANT DIAGNOSTIC FINDINGS

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OBJECTIVES

To describe a single clinical case involving two sisters diagnosed with probable behavioral variant frontotemporal dementia (bvFTD), born to consanguineous parents and with maternal history of dementia, highlighting clinical, instrumental and biomarker features suggestive of a genetic etiology.

MATERIALS AND METHODS

Two female siblings (aged 75 and 69) were evaluated at our center. Both presented with a clinical picture consistent with the behavioral variant of FTD (bvFTD). Anamnestic, neuropsychological, neuroimaging (brain MRI, FDG-PET), EEG, CSF biomarker data, and blood samples for genetic analysis were collected.

Diagnosis was established according to Rascovsky et al. (2011) criteria for bvFTD. A comparative evaluation between the two patients was performed, focusing on overlapping clinical and instrumental findings. CSF biomarkers (total Tau, phospho-Tau, beta-amyloid) and family history were assessed to explore potential hereditary transmission.

RESULTS

Both patients presented with early behavioral onset (disinhibition, apathy, loss of empathy),executive dysfunction, and progressive functional decline. Instrumental findings were concordant and consistent with a diagnosis of frontotemporal dementia: FDG-PET showed bilateral frontotemporal hypometabolism, predominantly on the left, extending to the parietal cortex in both patients. Brain MRI revealed frontal and temporal lobe atrophy, enlargement of periventricular CSF spaces, and gliotic changes. CSF biomarkers demonstrated a neurodegenerative profile: both patients had elevated total Tau and phospho-Tau, with reduced beta-amyloid 1-42 levels and a low Aβ42/p-Tau ratio. EEG showed diffuse theta slowing with symmetric background rhythm. Neuropsychological profiles confirmed executive and memory impairment, with mixed behavioral symptoms. Their mother had early-onset dementia, and parental consanguinity was reported. Genetic testing was initiated for known mutations and potential recessive variants.

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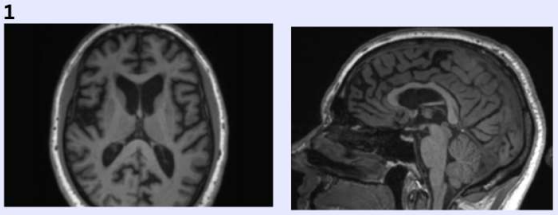

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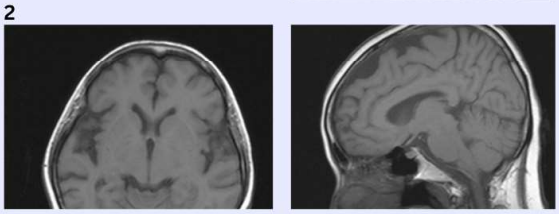

Figure 1: Comparative Table: Clinical and Instrumental Findings in Two Siblings with bvFTD

Feature	Patient 1 (75 y.o.)	Patient 2 (69 y.o.)
Clinical Onset	Apathy, disinhibition	Apathy, disinhibition
Brain MRI	Bilateral frontotemporal atrophy	Bilateral frontotemporal atrophy
FDG-PET	Frontal hypometabolism, left > right	Frontal hypometabolism, left > right
CSF Analysis	↑ Total Tau, ↓ Aβ42	↑ Total Tau, ↓ Aβ42
EEG	Diffuse theta slowing	Diffuse theta slowing
Neuropsychological Profile	Executive dysfunction and memory impairment	Executive dysfunction and memory impairment

DISCUSSION

This single familial case underscores the importance of a structured diagnostic workup in bvFTD. The convergence of clinical, neuroimaging, and CSF biomarker findings across both sisters supports a diagnosis of probable bvFTD. The high degree of phenotypic similarity, relatively early onset, positive family history, and consanguinity suggest an underlying genetic form, possibly recessive. The occurrenceof similar cases in siblings strengthens the hypothesis of hereditary transmission, potentially due tohomozygous mutations not typically observed in non-consanguineous populations.

CONCLUSIONS

This case underscore the importance of considering a genetic etiology in familial FTD, especially in thecontext of consanguinity. Ongoing genetic investigations may contribute to a broader understanding of inherited forms of FTD, including underrecognized recessive mutations

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