Autoimmune Frontotemporal Dementia: a new nosological entity?

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BCACKGROUND

Frontotemporal dementia (FTD) is a heterogeneous group of neurodegenerative disorders characterized by progressive deterioration of social behavior and personality, deficits of executive functions and language impairment. An autosomal dominant inherited trait is reported in almost 40% of patients. However, for the majority of sporadic FTD patients the determination of susceptibility or causative factors remains largely unknown. Some authors hypothesised that an immune response may have triggered the neurodegenerative process [1]. In this report, we provided the description of a case that met the criteria for FTD, which resulted positive for antibodies for autoimmune encephalitis.

CASE REPORT

A 41-year-old male has developed progressive language disturbances, binge eating, personal neglect and irritability over the past six months. In the past two years, he has complained of social withdrawal, apathy and emotional flatness, which were attributed to job problems. No family history of neurodegenerative disorders was reported. Neurological examination was unremarkable, but frontal release signs were appreciated. The patient underwent an extensive neuropsychological assessment (**Table 1**). Brain MRI revealed marked frontotemporal cortical and subcortical atrophy, slightly prevalent on the left side, and increased T2-FLAIR signal in white matter in frontal and temporal lobes, sparing U-fibers and partially involving the corpus callosum (**Figure 1, panel A and B**). PET-FDG demonstrated severe hypometabolism in the left frontal lobe and in the temporal-occipital cortex (**Figure 1, panel C**). No mutations within GRN, C9ORF72, MAPT or CSF1 were identified. An analysis of CSF ruled out atypical Alzheimer's disease. Screening for autoantibodies associated with autoimmune encephalitis was carried out. The patient was found to be positive for anti-AMPA receptor glutamate receptor subunit 3 (GluR3) antibodies in serum and cerebrospinal fluid. Paraneoplastic disease and other autoimmune disorders were ruled out.

TABLE 1

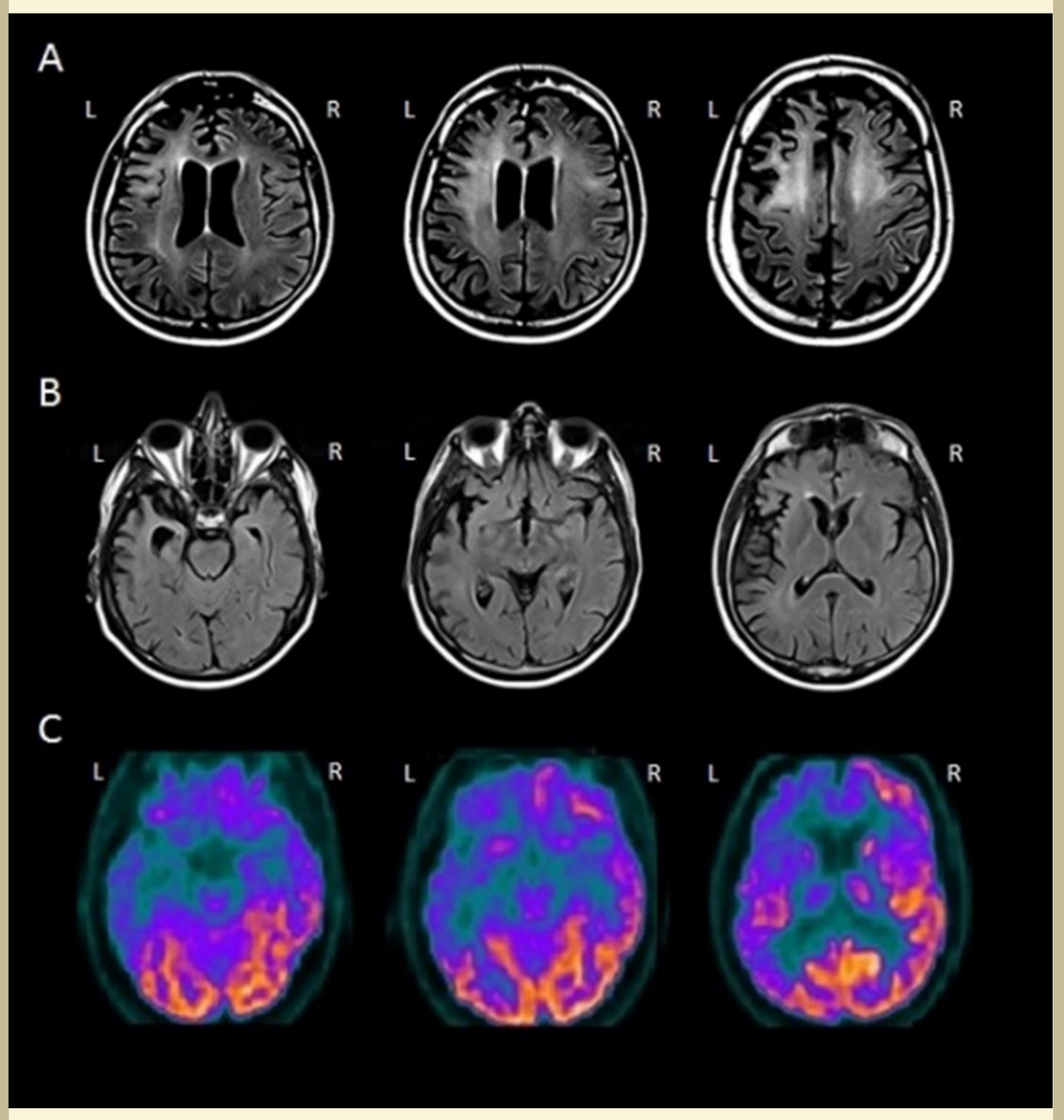
	Raw score	Corrected score	Cut-off
General intelligence			
Mini-Mental State Examination (max = 30)	25	23.21	≥ 23.8
Memory			
Short memory test (max = 28)	2.5	1	> 7.5
Rey-Osterrieth Complex Figure, Recall (max = 36)	0	0	> 9.46
Digit span forward	4	3.47	> 4.25
Spatial span forward	4	3.43	> 3.45
Executive functions			
Trail Making Test A	39	49	< 94
Trail Making Test B	500	539	< 283
Digit span backward	0	0	> 2.64
Praxis			
Ideomotor praxis, right (max = 72)	61	-	> 52
Ideomotor praxis, left (max = 72)	67	-	> 52
Visuospatial Functions			
Rey-Osterrieth Complex Figure, Copy (max = 36)	26.5	24.25	> 28.88
Language			
Phonological verbal fluency	4	0	> 16
Semantic verbal fluency	13	6	> 24
Aachener Aphasie Test			
Token Test	34	-	< 8
Repetition	128	-	> 141
Reading	29	-	> 27
Handwriting	18	-	> 26
Naming	83	-	> 103
Comprehension	83	-	> 107
Functional and behavioural assessment			
Basic Activities of Daily Living, lost (max = 6)	0	-	
Instrumental Activities of Daily Living, lost (max = 5)	3	-	
Neuropsychiatric Inventory	18	-	
Frontal Behavioural Inventory	24	-	

Patient's neuropsychological assessment
The table shows deficits in language tasks, executive functions , working memory, visuospatial planning, selective attention and shifting abilities. Scores below the cut-off according to Italian normative data are in bold.

DISCUSSION

Autoimmune dementia is a condition in which altered cognition is the principal clinical presentation and autoimmunity is the underlying pathogenic mechanism [3]. In FTD, the link between autoimmunity and the neurodegenerative process has been explored in very few studies [1, 2]. Although the presence of an autoimmune response has been hypothesized, to the best of our knowledge, no FTD cases that fulfill current clinical criteria have been reported that have been found to be positive for an autoimmune antibody. This case report argues for a novel pathogenetic mechanism in patients with FTD diagnosis, which is potentially treatable and triggered by autoantibodies involved in glutamatergic neurotransmission.

FIGURE 1



Brain Magnetic Resonance Imaging (MRI) and brain Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET)
Panel A. Axial T2-FLAIR MRI scan, showing frontotemporal atrophy, prevalent on the left side
Panel B. Axial T1-weighted MRI scan, showing frontotemporal atrophy, prevalent on the left side
Panel C. FDG-PET scan showing hypometabolism in frontotemporal cortical regions, prevalent on the left L=left; R=right

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