A DOUBLE MUTATION IN PROGRANULIN GENE IN BEHAVIOURAL VARIANT FRONTOTEMPORAL DEMENTIA. A CASE REPORT.

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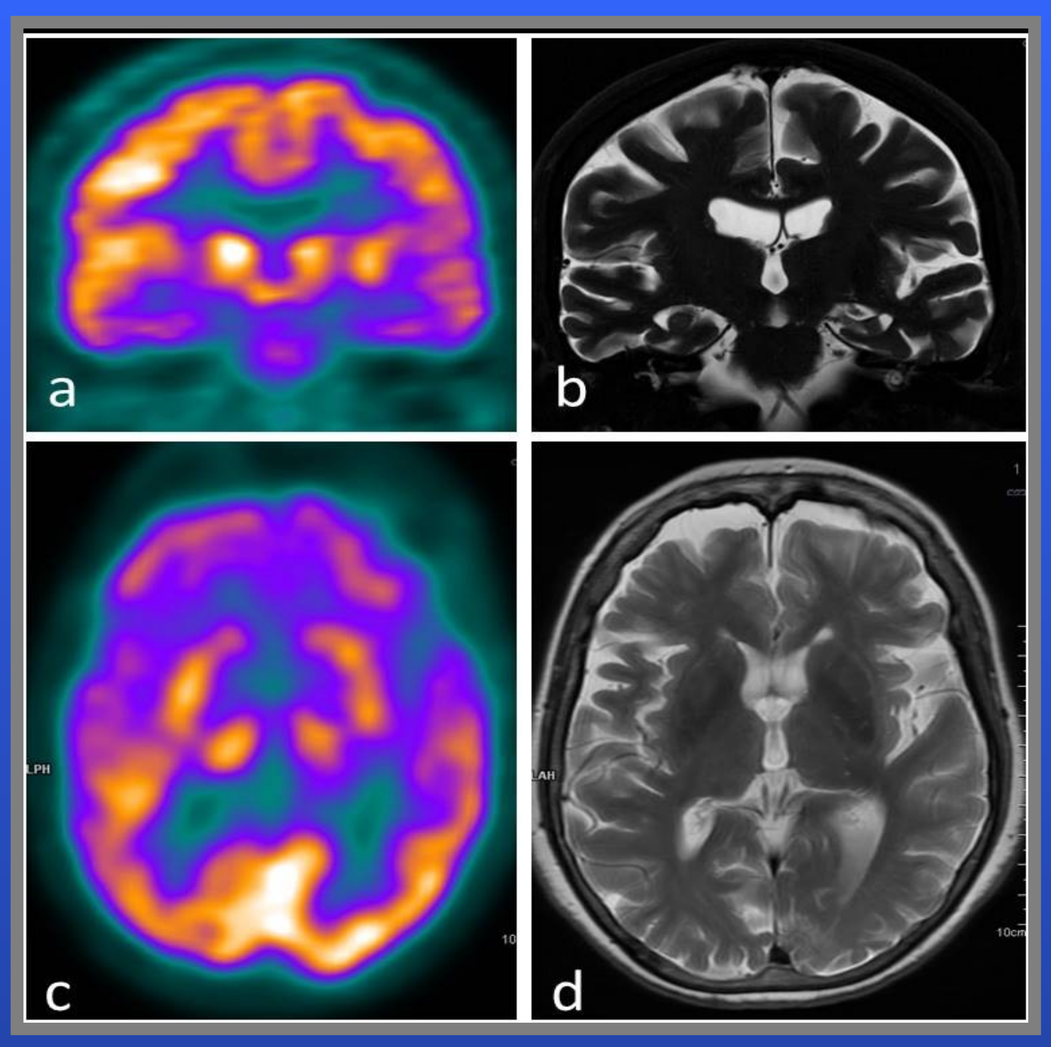
INTRODUCTION

Frontotemporal dementia (FTD) is genetically and pathologically heterogeneous neurodegenerative disorder.[1] Two phenotypes are recognized: behavioural-variant FTD (bvFTD) and primary progressive aphasia (PPA) that includes progressive non-fluent aphasia, semantic dementia and the logopenic/phonologic variant of PPA. FTD is commonly familial with autosomal dominant inherited. Most common mutations affecting microtubule-associated protein tau (*MAPT)* and progranulin (*GRN)* genes.[2]

CASE REPORT

Here, we describe a 72-year-old woman with autosomal dominant familial history of behavioural disorders, presented with a ten-year clinical history of progressive behavioural symptoms such as anxiety, apathy, mood depression, hyperorality, hyperreligiosity. After seven years from disease onset hand tremor, generalized slowness of movements and visual religious hallucinations appeared. Neurological examination showed bilateral postural hand tremor; bradykinesia-rigidity with brisk deep tendon reflexes in all limbs; bilaterally grasp reflex and Epstein sign. The neuropsychological evaluation demonstrated a mild cognitive impairment more evident for executive functions. Laboratory serologic tests were normal as well as EEG and EMG examinations. 3 Tesla brain MRI examination demonstrated bilateral temporal and frontal atrophy more evident in left hemisphere. A (18)F-fluorodeoxyglucose-PET showed bilateral hypometabolism predominant in left fronto-temporal lobes. Dopamine transporter (DAT-SPECT) showed normal striatal binding. The patient underwent genetic test that showed a double variation in *GRN* gene: missense variation p.Cys139Arg, absent in 100 healthy subjects, and the common variant c.*78C>T at 3'UTR[3].



Axial and coronal PET views (a, c) show hypometabolism in left cortical, subcortical, frontal (especially inferior gyrus) and temporal regions. MRI coronal T2-Propeller and axial T2-weighted (b,d) images show, on the left side, enlarged sylvian fissure, temporal horn and frontal subarachnoid spaces, indicating left temporal and frontal lobes volume loss.

CONCLUSIONS

Our case report shows a double mutation (p.Cys139Arg and c.*78C>T) in GRN gene in the same patient with a peculiar bvFTD phenotype. These results confirm that a screening in GRN gene is recommended in bvFTD patients with hyperreligiosity and religious visual hallucinations.

REFERENCES

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XLVI CONGRESSO SOCIETA' ITALIANA DI NEUROLOGIA
GENOVA, 10-13 OTTOBRE 2015