C9ORF72 INTERMEDIATE REPEAT EXPANSION IN A PATIENT WITH PSYCHIATRIC DISORDERS AND ISOLATED CEREBELLAR ATAXIA

R. Farris, M.Meloni, D.Ciaccio, G. Orofino, P.Solla,
M.M.Mascia, A.Cannas, F.Marrosu

Movement Disorders Center, Department of Neurology,
University of Cagliari

INTRODUCTION

C9ORF72 hexanucleotide repeat expansions are the most common causes of familial frontotemporal dementia (FTD) and amyotrophic lateral sclerosis (ALS). The pathogenic role of intermediate C9ORF72 repeat expansions ranging between 20 and 29 repeats in typical Parkinson's disease with psychosis and atypical parkinsonisms with or without dementia has been recently investigated. Psychotic symptoms have been described as a phenotypic manifestation in patients carrying intermediate C9ORF72 repeat expansions. Recently, a case of pure cerebellar ataxia linked to large C9ORF72 repeat expansion, has been described . However, no cases of progressive late-onset cerebellar ataxia and psychiatric disorders in patient carrying intermediate C9ORF72 repeat expansions has been reported so far.

OBJECTIVE

To describe a case of a patient with psychiatric disorders who developed a cerebellar syndrome and who was found to have C9ORF72 intermediate repeat expansion.

MATERIALS AND METHODS

A 71-year-old woman was affected by mixed anxiety-depressive disorder associated to somatization and histrionic personality disorders (cluster B personality disorder), REM sleep behavior disorder (RBD) and bilateral sensorineural deafness. At the age of 64, she developed progressive ataxic gait, dysphagia, dysarthria , and pyramidal signs. No family history for neurodegenerative diseases.

PARAMETERS	RESULTS
Time of onset	64
Years of disease	7
Cerebellar symptoms	+++
Dysautonomia	-
Extrapyramidal signs	-
Cognitive impairment	+
Mood disorder	+
SARA scale	26
RBD	+
DAT SCAN	+
TA	-

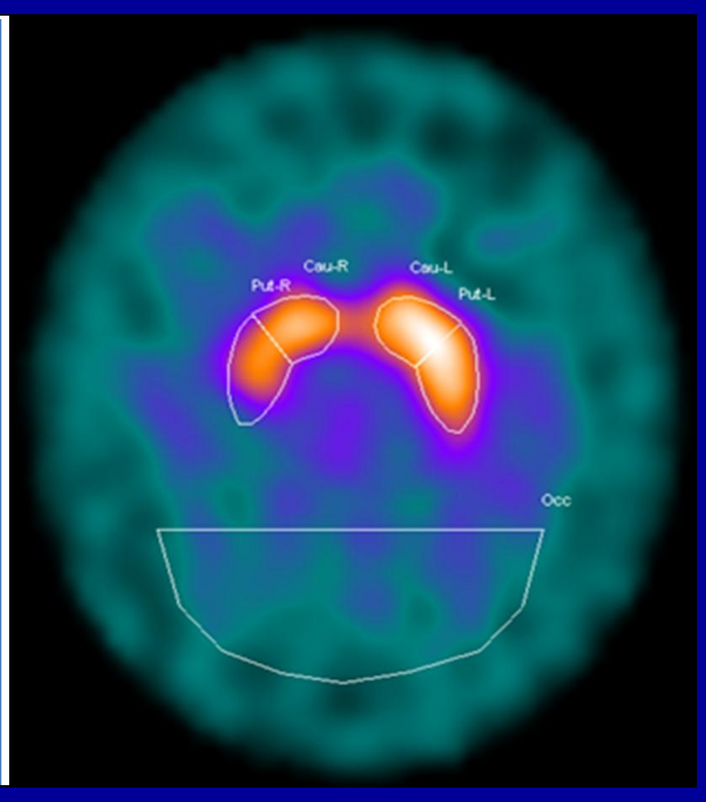

Table: cerebellar symptoms (ataxia,dysarthria,dysphagia); SARA scale (scale for the assesment and rating of ataxia); TA (Topography of atrophy: involvement of brainstem or cerebellum)

RESULTS

Haematological and biochemical studies showed only a modest anemy (Hb 9.6); Muscle biopsy (negative); Motor and somatosensory evoked potentials (abnormal lower limbs central motor conduction time and abnormal upper and lower limbs central sensory conduction time); Brain MRI (moderate diffuse atrophy without brainstem and cerebellar involvement); DATSCAN (reduced dopaminergic innervation in the right putamen); neuropsychological assessment (mild cognitive impairment) ; Mutations screening for SCA 1,2,3,6,7, 17 and TARDBP (negative). The mutational analysis of GGGGCC hexanucleotide in the gene C9ORF72 showed 21 repeats .

DISCUSSION AND CONCLUSIONS

The clinical framework of this patient could initially depose for MSA-C (cerebellar symptoms and RBD) or for SCA 17 (positive DATSCAN , mood disorder and cognitive impairment). We ruled out the MSA-C diagnosis because of the absence of dysautonomic and extrapyramidals signs as well as the long disease duration. The exact clinical diagnosis of our patient remains an open question. It seemed interesting to us the genetic data of intermediate C9ORF72 repeat expansion, even if a certain correlation with cerebellar ataxia remains unproved. We speculated that the intermediate C9ORF72 repeat expansion may have a pathogenic role in the co-occurrence of cerebellar ataxia, psychiatric disorders (histrionic personality and somatization disorders) and mild cognitive impairment.

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