Frontotemporal dementia with *C9orf72* mutation presenting with bizarre psychosis and right flail leg syndrome

A. Mazzonetto[1], G. Pigato[2], C. Bussè[1], D. Cecchin[3], S. Mozzetta[1], M. Corbetta[1], A. Cagnin[1]

1. Department of Neuroscience (DNS), University of Padova, Padova, Italy.
2. Psychiatry Ward, Padova University Hospital, Italy.
3. Department of Medicine, Unit of Nuclear Medicine, University Hospital of Padova, Padova, Italy.

Background

Expansion in the C9orf72 gene is recognized as the most frequent genetic cause of amyotrophic lateral sclerosis (ALS), and in most cases ALS is associated with frontotemporal dementia (FTD). In this report we present a case of atypical presentation of C9 positive bvFTD with late-onset psychosis with bizarre content and focal asymmetric lower motor deficit.

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Case report

A 64-year-old man was seen at the multidisciplinary neuropsychiatric outpatient clinic of Padua Hospital for a tendency to isolation and reported fear of interacting individuals of the opposite sex.
At the neurological examination we found slight nonfluent speech, reduced tendon reflexes in all limbs. Three months later he developed right foot drop with muscle strength deficit in the dorsiflexion of the big toe and foot.

Investigations

Brain FDG-PET showed moderate diffuse hypometabolism of the fronto-mesial and fronto-parietal cortex bilaterally with involvement of subcortical regions and right cerebellar hemisphere.
Electromyography revealed neurophysiological findings compatible with neurogenic suffering with multi-metamorphic distribution, involving 3 of 4 sectors, excluding the bulbar.
Motor evoked potentials from magnetic stimulation of the 4 limbs were compatible with functional suffering of the central motor pathways pertaining to the 4 limbs.
Genetic testing revealed a mutation of the repeated exonucleotide sequence in the C9ORF72 gene.
Given the clinical and radiological findings, a diagnosis of frontotemporal dementia and degenerative pathology of the first and second motor neurons was made.

Fig. 1. Photo of right foot causing a foot drop.

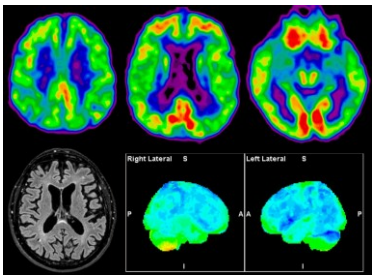

Fig. 2.
(A) Top row: [18F] FDG-PET transaxial images showing diffuse hypometabolism of the fronto-parietal cortex bilaterally, fronto-mesial cortex bilaterally and lateral temporal especially on the left with modest involvement of the polar region. (B) Bottom row: Left: brain MRI FLAIR sequence showing moderate cerebral atrophy (Global Cortical Atrophy scale =1) and frontal mesial atrophy. Right: [18F] FDG-PET images shown as three-dimensional stereotactic surface projection (3D-SSP) obtained with Neurostat (blue color indicates a significant decreased metabolism of the subject compared to a group of normal controls; green color denotes normal metabolism)

Discussion and conclusions

We report a case of late-onset psychosis and flail-leg syndrome as an atypical presentation of bvFTD plus ALS. A late-onset psychosis is very often the first manifestation of neurodegenerative diseases (up to 90% of cases), and FTD is the predominant form among them, in which genetic forms have atypical hypometabolic patterns.
Our report underlines the importance of broad genetic assay in the diagnostic work-up of frontal lobe syndrome. In cases with rapidly progressive behavioral disturbances and in the absence of MRI alterations, FDG-PET can add important information although expanding the pattern of hypometabolism beyond the frontal and temporal cortical regions.

Presenter and contacts: Dr. Alice Mazzonetto, E-mail: mazzonetto.alice@gmail.com

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