Atypical parkinsonism overlapping motor neuron disease
Presentation of a clinical case open

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Background

Interest in the possibility of a continuum between Frontotemporal Dementia (FTD) and Amyotrophic Lateral Sclerosis (ALS) was born from recent identification in anatomopathological studies of ubiquitinated cytoklasic inclusions and positive TDP-43 in almost all cases of ALS and in about half of the patients with FTD. In the ALS, the TDP43-correlated neuropathic framework can extend to extramotoneuronic anatomy structures and this discovery allows to explain the syndrome overlaps that can be observed in ALS patients.

Case study

A 73-year-old man, presented in 2014 with a 8-year history of progressive left leg weakness and balance disturbances. Initial intermittent motor instability and force deficit have become steady and progressive, with frequent falls, and the motor deficiency has extended to the left upper extremity. The neurological examination revealed left-side spastic hemiparesis to distal prevalence. Mild hypomyotrophy diffused, without fasciculations. Mild facial asymmetry. No sensory deficit was noted. No urinary disorders. From the age of 71, appearance of plastic hypertonia with left-sided dystonia and posture with laterodevision of the trunk and neck to the left and dysarthria with little verbal initiative. Global slowdown of conjugated movements of eye globes, especially in verticality. At present, the upper right limb shows an involuntary movement of the first three fingers.

Laboratory tests and analysis of spinal fluid showed no abnormalities. EMG showed evidence of slight signs of neurogenic damage, stabilized in the root area L4-L5-S1 on the left. MEPs disclosed no response from the lower left limb. Brain MRI did not showed recent ischemic lesions, thinning of the mesencephalic roof. The SPECT perfusion imaging and DAT SPECT have highlighted a bilateral temporo-parietal hypoperfusion and a reduction of the putamen striatal dopamine transporter (right>left) (Figure 1-2).

Mutations in TARDBP, C9ORF72, ATXN2, MAPT were negative. Heterozygous polymorphism rs9897526 of GRN gene was found. The patient underwent treatment with botulinum toxin with initial benefit and subsequent ineffectiveness; Levodopa-carbidopa therapy was initiated without significant improvements.

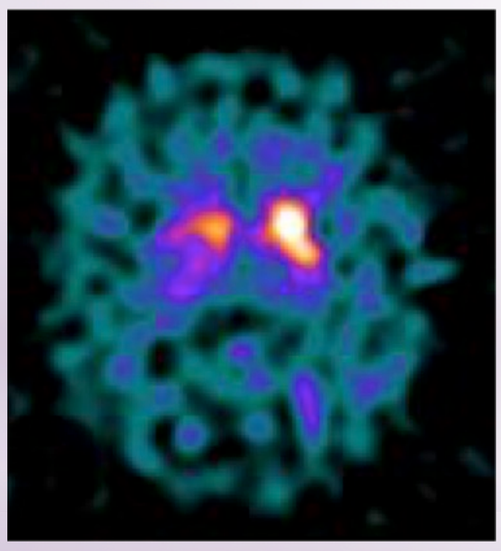

Figure 1. DaT SCAN: deficit of striatal dopamine transporter, particularly putamen, more markedly to the right.

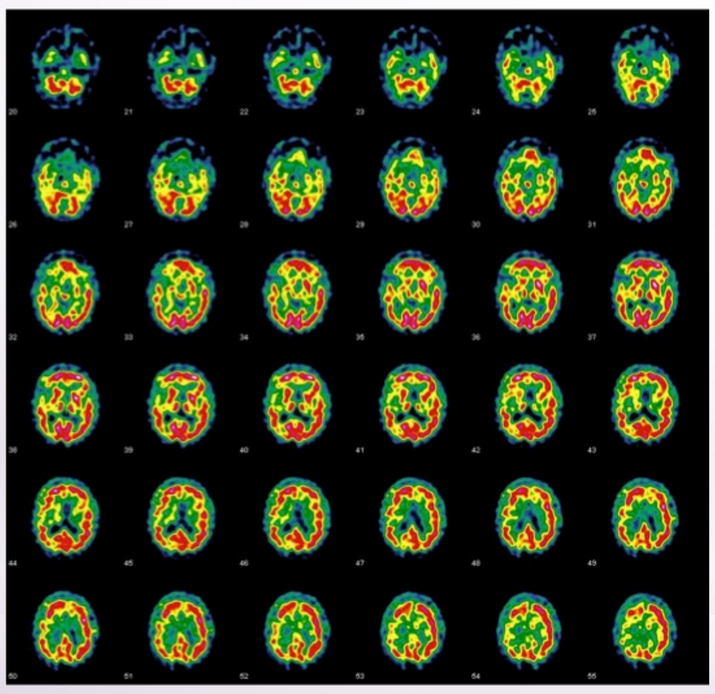

Figure 2. SPECT: non-homogeneous hypoperfusion on the temporal and parietal cortex of both sides.

Discussion and Conclusions

Our patient has a complex pyramid-extrapyramidal neurodegenerative syndrome, initiated with a slowly progressive ascending left spastic hemiparesis, which has targeted a Mills' hemiplegic variant of Primary Lateral Sclerosis (PLS).

Subsequently, the overlap of a left-sided plastic hypertony with dystonia, deposited for atypical parkinsonism, type Corticobasal syndrome (CBS). Our patient can be considered an overlap between Mills' syndrome, CBS and FTD. It is likely that such phenotypic variability will be influenced by other genetic factors such as the progranulin polymorphisms observed in our patient or other genes we have not yet detected, as well as environmental factors.

References

1. Mills CK. A case of unilateral progressive ascending paralysis, probably representing a new form of degenerative disease. J Nerv Ment Dis 1900; 27:195-200.
2. David R Williams, Andrew J Lees. Progressive supranuclear palsy: clinicopathological concepts and diagnostic challenges. Lancet Neurol 2009; 8:270-79.
3. Tim Van Langenhove, Julie Van der Zee & Christine van Broeckhoven. The molecular basis of the frontotemporal lobar degeneration – amyotrophic lateral sclerosis spectrum. Annals of Medicine, 2012; 44 817-828.
4. Tatsch K and Poepperl G. Nigrostriatal dopamine terminal imaging with dopamine transporter SPECT: an update. J Nucl Med. 2013; 54(8):1331-8.
5. Sleegers K, Brouwers N et al. Progranulin genetic variability contributes to amyotrophic lateral sclerosis. Neurology 2008; 71:253-259.

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