ATYPICAL PARKINSONISMS IN THE CLINICAL COURSE OF PROGRESSIVE MULTIPLE SCLEROSIS

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Introduction

Only few reports describe the association between multiple sclerosis (MS) and atypical parkinsonisms. We herein report on two patients with progressive forms of MS who developed **atypical parkinsonisms in the spectrum of progressive supranuclear palsy** (PSP).

Case no. 1

- 62 years old man with **primary progressive MS** (PPMS) diagnosed in 2012 after one year of progressive decline in cognitive performances associated with apathy, social withdrawal and gait instability.

- After a two years course of cyclophosphamide, the patient developed an **akinetic-rigid parkinsonism** with **limitation of vertical eye movements**

Case no. 2

- 66 years-old woman with a history of **secondary progressive MS** started with a typical relapsing form in 1986. In the early 2000s the patient started to show a **freezing of gait** during both straight walking and turning, along with memory disturbances. There were **no resting tremor and/or cogwheel rigidity**.

Methods

The two patients underwent brain and spinal cord MRI along with DaT-SCAN SPECT imaging in an outpatient setting at the University of Verona. L-Dopa was administered in both patients (300 mg thrice/daily).

Results

- MRI images of case no.1 are indicated in Figure 1 a-c. The final diagnosis was **probable PSP-Richardson syndrome associated with PPMS**.(1) DaT-SCAN SPECT was negative. Intravenous methylprednisolone was administered without any effect, while L-Dopa led to a slight amelioration of gait instability.

- MRI and DaT-SCAN SPECT of case no.2 are shown in Figure 2 a-d. The extrapyramidal syndrome seen in this patient resembled a probable **PSP-progressive gait freezing.** (1) Based on these findings, L-Dopa treatment was administered (Madopar 100/25 thrice/day) with a mild, subjective amelioration of gait disturbance. At the follow-up the patient remains stable, with no other clear extrapyramidal signs or symptoms except for gait freezing.

Conclusions

- Parkinsonism represents the rarest movement disorder in MS with 44 cases reported so far, and its appearance during the clinical course of MS may be either causal or coincidental. (2)

- Combined mechanisms of neurodegeneration and neuroinflammation have been implicated in the pathogenesis of several disorders such as MS and atypical parkinsonisms, with activated microglia being a common denominator. The chronic release of pro-inflammatory cytokines and reactive oxygen intermediates, as expected in MS, enhances the activation of CNS resident cells, thus leading to a consequent damage of neurons and synapses. (3) In this regard, it has been demonstrated that the activation of microglia presents a topographical distribution in PSP patients, with particular involvement of substantia nigra and subthalamic nucleus. (3)

- The coexistence of MS and atypical parkinsonisms is exceptional, being only reported in two cases of MS and concomitant Multiple System Atrophy. (4) To our knowledge, our cases represent the first reports of co-occurrence of progressive MS and atypical parkinsonisms in the PSP spectrum

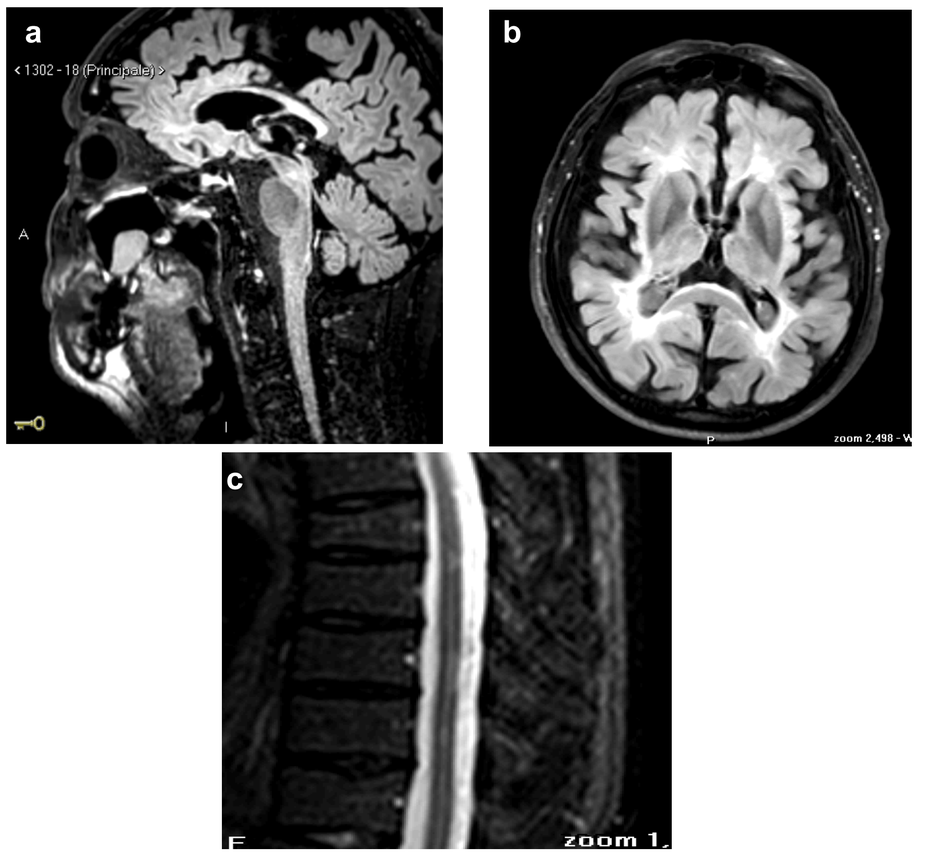

Figure 1 a-c. Leukoencephalopathy along with several inactive spinal cord demyelinating lesions. Diffuse brain atrophy, with marked involvement of midbrain and superior cerebellar peduncles, can be noted (midbrain to pons ratio = 0,57)

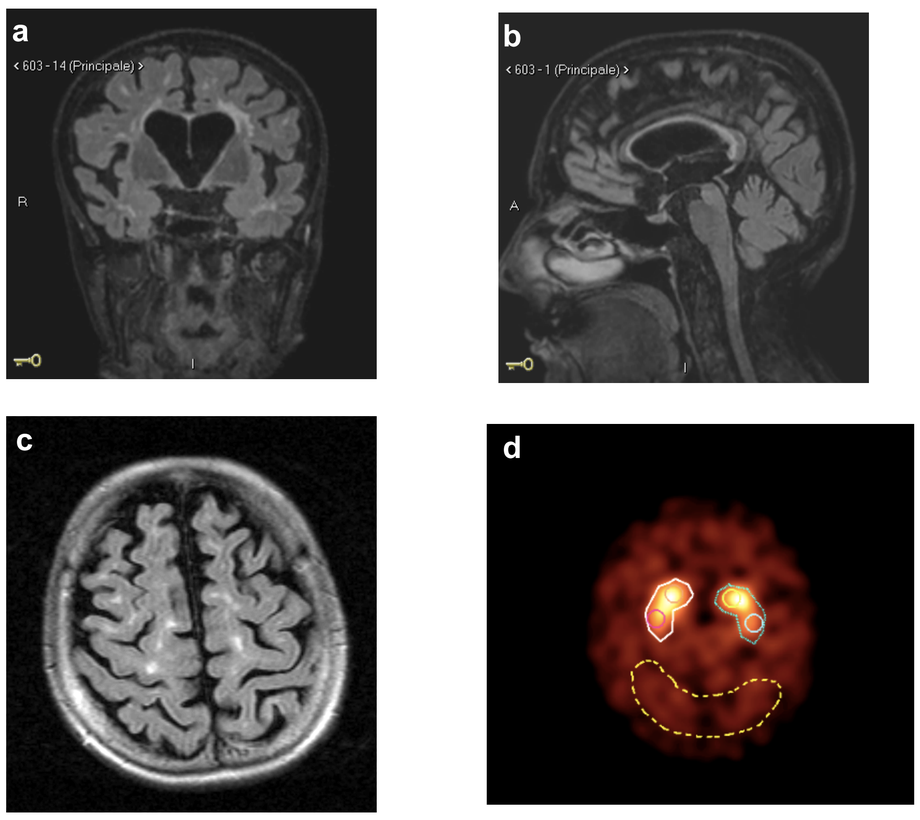

Figure 2 a-c. In case 2 several cortical and subcortical demyelinating lesions, besides of cerebral atrophy also involving the midbrain ("Hummingbird sign"; midbrain to pons ratio = 0,64), can be observed.
Figure 2 d. DaT-SCAN SPECT showing a lower tracer uptake in the left putamen.

Bibliography

1 Hoglinger G et al. Clinical diagnosis of progressive supranuclear palsy: The Movement Disorder Society criteria. *Mov Disord* 2017

2 Bougea A et al. Multiple sclerosis and Parkinson's disease: the two faces of neurodegeneration. Report of the first Greek case and review of the literature. *Neurol Sci* 2015

3 Fernández-Botrán R et al. Cytokine expression and microglial activation in progressive supranuclear palsy. *Parkinsonism Rel Dis* 2011

4 Jellinger et al. Overlaps Between Multiple System Atrophy and Multiple Sclerosis: A Novel Perspective. *Mov Disord* 2016