Primary Lateral Sclerosis Mimicking Corticobasal Syndrome At Onset: A Case Report

Vittoria Aprea[1], Sara Prioni[2], Giorgio Gelosa[1], Gemma Lombardi[1], Andrea Giordano[3], Giuseppe Di Fede[1], Nilo Riva[3], Paola Caroppo[1]

1. Neurology 8 – Dementias and degenerative diseases of CNS Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan,Italy
2. Clinical Neuropsychology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, 20133 Milano, Italy
3. Neurology 3 – Neuroalgology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

OBJECTIVES

Primary lateral sclerosis (PLS) is a rare clinical phenotype of motor neuron disease (MND), representing 2–3% of all MND cases. It **primarily involves upper motor neurons** and typically presents with symmetric motor impairment that predominantly affects the lower limbs at onset (1). Cognitive impairment can be an associated feature but rarely progresses to full-blown frontotemporal dementia (FTD).

Here we describe a case of a 56-year-old woman, presenting with asymmetric motor signs along with cognitive symptoms, initially mimicking a corticobasal syndrome (CBS).

MATERIALS

The patient presented a 3-year history of left lower limb weakness, gait disturbances and frequent falls. Symptoms progressed to left upper limb, with dystonic posturing and bradykinesia. She also developed a speech disorder (word-finding difficulties and semantic deficits), along with visuospatial deficits. The patient had already been diagnosed with corticobasal syndrome, although DaTSCAN resulted normal; genetic analysis of *C9orf72*, and NGS panel for FTD/ALS genes were negative. Three years after onset, she developed apathy, irritability and voracity.

METHODS

The patient underwent neurological and neuropsychological assessments and neurophysiological evaluation, including motor evoked potentials (MEPs) and Electromyography (EMG). Additionally, brain MRI and [18F]FDG-PET were performed.

COGNITIVE DOMAINS	TEST	CUT-OFF	TO
GLOBAL COGNITIVE IMPAIRMENT	Moca	18,58	16.15**
MEMORY			
Working memory	Digit span	< 4.26	3.17**
	Digit span backward	< 2.65	2.79
Verbal episodic memory	RAVLT - Immediate recall - Delayed recall	<28.53 <4.69	32.32 6.6
Visuo-spatial Memory Test	Rey-Osterrieth Complex Figure recall	<9.46	5**
VISUOSPATIAL ABILITIES	Rey-Osterrieth Complex Figure copy	< 28.87	25.85*
ATTENTION AND EXECUTIVE FUNCTIONS			
Executive abilities	FAB	≤ 13.4	8.37**
Set-shifting/Attention	MFTC		
	Execution time	135.73	158**
	Correct items		5/13**
	Fals Alarms	2.77	0**
	Accuracy	0.869	0.69**
	TMT-A	≥94	158**
	TMT-B	≥283	Interrupted
	TMT-B-A	≥186	Interrupted
LANGUAGE			
Fonemic-based word retrieval	Letter fluency task	< 23.58	11.2**

Fig.1. Neuropsychological evaluation (adjusted scores listed). *borderline, ** under cut-off. Interrupted:patient exceeded the allowable error threshold

RESULTS

- **Neurological examination** revealed mild recruitment deficits in the left finger and wrist extensors, interosseous, tibialis anterior, and peroneal muscles. Spastic hypertonia was more pronounced in the left limbs. Reflexes were notable for a positive jaw jerk, left-sided Hoffman and Babinski signs, and an extensor plantar response on the left. Gait was paraparetic-spastic, requiring bilateral support. No clinical signs of lower motor neuron involvement were observed.
- **Neuropsychological assessment** revealed a severe dysexecutive syndrome and language impairment associated with mild visuoconstructional deficits (Fig.1).
- **MEPs** showed central conduction abnormalities in both lower limbs (left > right) and in the left upper limb.
- **EMG** showed no evidence of lower motor neuron involvement.
- **MRI** showed asymmetric fronto-parietal atrophy (right > left) (Fig.2).
- **[18F]FDG-PE**T revealed severe, diffuse hypometabolism, especially in the frontal lobes, with relative sparing of the occipital cortex (Fig.3).

The patient was then diagnosed with PLS-FTD.

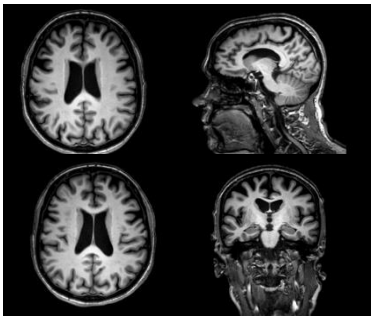

Fig.2. T1-weighted brain MRI demonstrating asymmetric fronto-parietal atrophy (right > left)

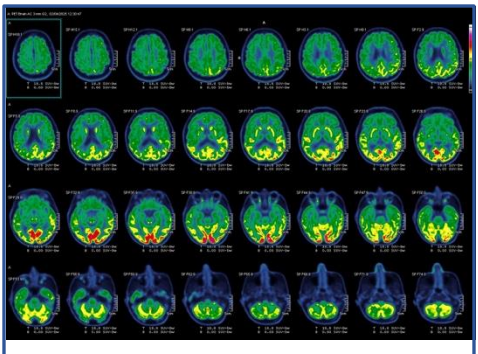

Fig.3 Severe, diffuse hypometabolism, especially in the frontal lobes, with relative sparing of the occipital cortex on [18F] FDG-PET.

DISCUSSION AND CONCLUSIONS

PLS may be misdiagnosed as parkinsonism, as previously reported (2). In this case, asymmetric spasticity, progressing from the leg to the ipsilateral arm, was interpreted as asymmetric rigidity, a hallmark of CBS (3).

✔ The combination of pyramidal and extrapyramidal-like signs may represent **a diagnostic challenge** in PLS diagnosis, especially in case of asymmetric onset.

References

1. Turner MR, Barohn RJ, Corcia P, et al. Primary lateral sclerosis: consensus diagnostic criteria. J Neurol Neurosurg Psychiatry. 2020;91(4):373-377. doi:10.1136/jnnp-2019-322541
2. (Norlinah IM, Bhatia KP, Ostergaard K, Howard R, Arabia G, Quinn NP. Primary lateral sclerosis mimicking atypical parkinsonism. Mov Disord. 2007 Oct 31;22(14):2057-62. doi: 10.1002/mds.21645. PMID: 17702034.
3. Murakami A, Koga S, Dickson DW. Asymmetrical Primary Lateral Sclerosis Presenting as Corticobasal Syndrome. J Neuropathol Exp Neurol. 2022 Jan 29;81(2):154-156. doi: 10.1093/jnen/nlab104. PMID: 35094073; PMCID: PMC8801232.