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PARKINSON'S DISEASE and AMYOTROPHIC LATERAL SCLEROSIS COMPLEX:

a case report of sporadic Brait-Fahn-Schwarz disease

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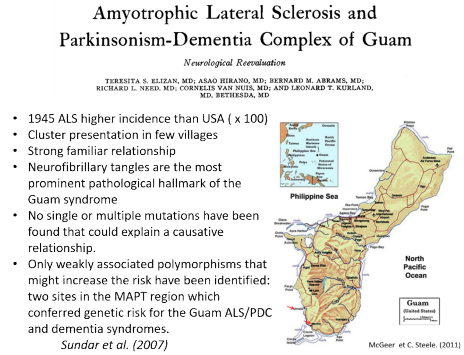
OBJECTIVE

We describe a case of sporadic Brait-Fahn-Schwarz disease, a rare neurodegenerative complex with no clear genetic definition, clinically defined by a levodopa-responsive parkinsonism followed by amyotrophic lateral sclerosis (ALS).

INTRODUCTION



The association of sporadic Parkinson's disease (PD) with ALS represents a neuro-degenerative complex that has been largely considered confined in the Guam island and Kii peninsula as a variant of the Parkinson-dementia complex.

Outside the specific geographical regions, the combination of PD with ALS is a rare condition described in less than 100 cases published in the literature, first described by Brait et al. in 1973. The cases reported so far show quite a high variability of clinical presentations and do not share a common genetic substrate.

One possible pathophysiological mechanism involved is mitophagy. Mitochondrial function is essential for the survival of cells and the correlation between mitochondrial turnover and neurodegenerative disorders is well established. Recycling of damaged mitochondria is mediated by the products of genes involved both in PD and ALS, namely PINK1, Parkin, Optineurin, DJ1 and others. On the other hand C9orf72 expansion has also been associated to extra-pyramidal signs.

CASE REPORT

We present the case of a 71-year-old male patient without family history of neurodegenerative disorders, who at 67 developed progressive bradykinesia at the right arm followed by cramps at the lower limbs. He came to our attention 2 years after the onset of symptoms and presented with predominantly right rigidity, hypophonia and resting tremor on the right hand, gait impairment, frequent falls caused by a mixed increase of tone in the lower limbs, signs of first and second motor neurons involvement at the lower limbs. The MDS-UPRDS score was 27.

- The SPECT with DATSCAN showed a mild reduction dopaminergic uptake at the left putamen.
- The brain MRI scan described iron accumulation in the substantia nigra (confirmed and stable two years later) without neuromelanin reduction.
- The MRI scan of the cervical spine displayed an osteoarthritis stenosis of the spinal canal at C3-C4 level without evidence of compression.
- The neurophysiological investigation confirmed an axonal motor neuropathy with EMG descriptions of neurogenic potentials in 3 districts: upper and lower limbs and thorax.
- Neuropsychological assessment for dementia or frontal lobe degeneration did not detect any pathological findings.

EMG Summary Table

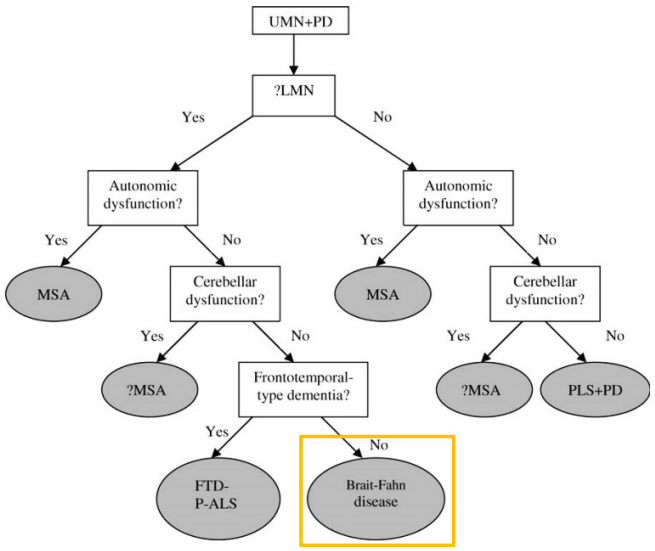
	Spontaneous					MUAP			Recruitment
	IA	Fib	PSW	Fasc	H.F.	Amp	Dur.	PPP	Pattern
S. TIB ANTERIOR	N	2+	2+	None	None	1+	2+	2+	1-
S. TIB POSTERIOR	N	None	None	None	None	1+	2+	2+	Reduced
S. VAST LATERALIS	N	None	None	2+ (slow)	None	N	2+	2+	N
D. FIRST D INTEROSS	N	None	None	None	None	N	N	N	N
D. EXT POLL BREVIS	N	None	None	2+ (slow)	None	N	2+	2+	Reduced
D. THOR PSP (M)	N	None	None	2+ (slow)	None	N	1+	2+	N
S. THOR PSP (M)	N	None	None	2+ (slow)	None	N	1+	2+	N
S. TIROARITENOIDEO	N	None	None	None	None	N	N	N	N

Genetic evaluation was performed but no genes was found mutated or expanded:

MND	PK
C9orf 72	
SOD1 - TARDBP - FUS - OPTN - SQSTM1 - VCP	SNCA - LRRK2 - VPS35 - PRKN - PINK1 - PARK7 (DJ1)

A diagnosis of Parkinson disease (**clinical probable PD** according to MDS criteria) was made together with a suspected diagnosis of motor neuron disorder (**Probable, laboratory-supported ALS** according to EL Escorial revised criteria; ALSFRS-r 38/48).

A prescription/removal levodopa test confirmed a partial motor response to the drug, which was therefore prescribed. The patient was also prescribed riluzole.



After 6 months the ALSFRS-R total score was 34/48. The MDS-UPDRS total score was 34/132 under levodopa therapy. A mixed type of rigidity, with both plastic and spastic components, was observed in the four limbs.

During the one year of follow-up, the patient presented a mild worsening of the underlying parkinsonism, with marked bradykinesia and rest tremor of the right upper limb. There was also a progression of the motor neuron involvement, with bilateral fasciculations of the upper limb muscles and quadriceps femoris and bilateral ankle clonus.

CONCLUSIONS

- It has long been recognized that signs of motor neuron disease may accompany clinical evidence of parkinsonism.
- With this case report we want to emphasize the possible extrapyramidal contribution in ALS as part of the improving evidence of extensive extra motor involvement of this disease. Mutation in C9orf72, DJ1 and MAPT genes have been inconstantly reported to be the possible causes of this neurodegenerative complex.
- Further studies are required to better determine the incidence of this comorbidity as well as the pathological condition underlying it

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