Disentangling among clinical and pathogenic aspects of Posterior Cortical Atrophy: two case reports

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Introduction

Posterior Cortical Atrophy (PCA) is a neurodegenerative syndrome characterized predominantly by higher-order visual field dysfunctions, even though phenotype can vary widely among different patients. Likewise, pathogenesis is also variable, spanning from the most common Alzheimer disease pathology, to Lewy body disease and corticobasal degeneration. [1]

We aimed at describing clinical, cognitive and neuroanatomical features of two cases with posterior cortical atrophy [A.R. and D.N.], that were likely to harbor Alzheimer's disease (AD) and corticobasal degeneration (CBD) pathology, respectively. [1]

Methods

Table 1. Main patients demographic and clinical data

Patient	A. R.	D. N.
Age	63	61
History	No familiarity for neurological diseases	Mother with PD and cognitive decline Genetic data: no mutation in APP, PS1, PS2 genes; APoE e3/e3 genotype
Clinical findings (besides cognitive data)	No extrapyramidal signs	• Bradikinesia • Axial and limb (right >left) rigidity • Upward gaze limitation • Alien limb phenomenon (right)
CSF analysis	Aβ42: 247	Aβ42: 559
	t-Tau: 170	t-Tau: 577
	p-Tau: 40	p-Tau: 68
	p-Tau/Aβ42: **0.16**	p-Tau/Aβ42: **0.12**

Table 2. Neuropsychological Evaluation

Patient	A. R.	D. N.
MMSE (c.o 24)	15.2/30*	9/30*
Dorsal Visual system		
Optic ataxia	Pathologic (R>L)	Pathologic (R>L)
Oculomotor apraxia	1/4*	1/4*
Simultagnosia	Pathologic (R>L)	Pathologic (R>L)
Neglect (Geren battery)	Mild right deficit	Pathologic (R>L)
Right-left distinction		
Own body	Normal	Pathologic
Other's body	Pathologic	Pathologic
Digital Agnosia		
Own hand	Normal	Pathologic
Other's hand	Pathologic	Pathologic

Table 3. Neuropsychological Evaluation cont'd

Patient	A. R.	D. N.
Acalculia	6/12*	2/12*
Agraphia	1/3*	0/3*
Apraxia	Pathologic (R>L)	Pathologic
Order (R; L)	9/12; 2/12*	4/12*; 2/12*
Constructive apraxia (CDT; Odgen scene)	Pathologic	Pathologic
Ventral Visual System		
Visual pattern matching	0/7*	0/7*
CaGi (denomination)	40/48 (a.s. 39.76)*	30/48 (a.s. 29.76)*
Memory		
Spatial span, inverse	2/7*	0/7*
Verbal span, inverse	3/8*	3/8*

Legend:
- p-Tau/Aβ42 cut-off taken for discrimination of AD pathology is **0.12**. [Taken from *de Jong D, et al., J. Gerontol. A. Biol. Sci. Med. Sci. 61, 755–758*].
- Red colour and * identifies items in which performances resulted pathologic.

Abbreviations: *a.s.*, adjusted score; *c.o.*, cut-off; *CDT*, Clock Drawing Test; *MMSE*, Mini-mental State Exam.

Neuroimaging studies:
- **3.0T multiparametric MRI**
- **^{18}F-FDG-PET**
- **Electroencephalography (EEG)**

Results

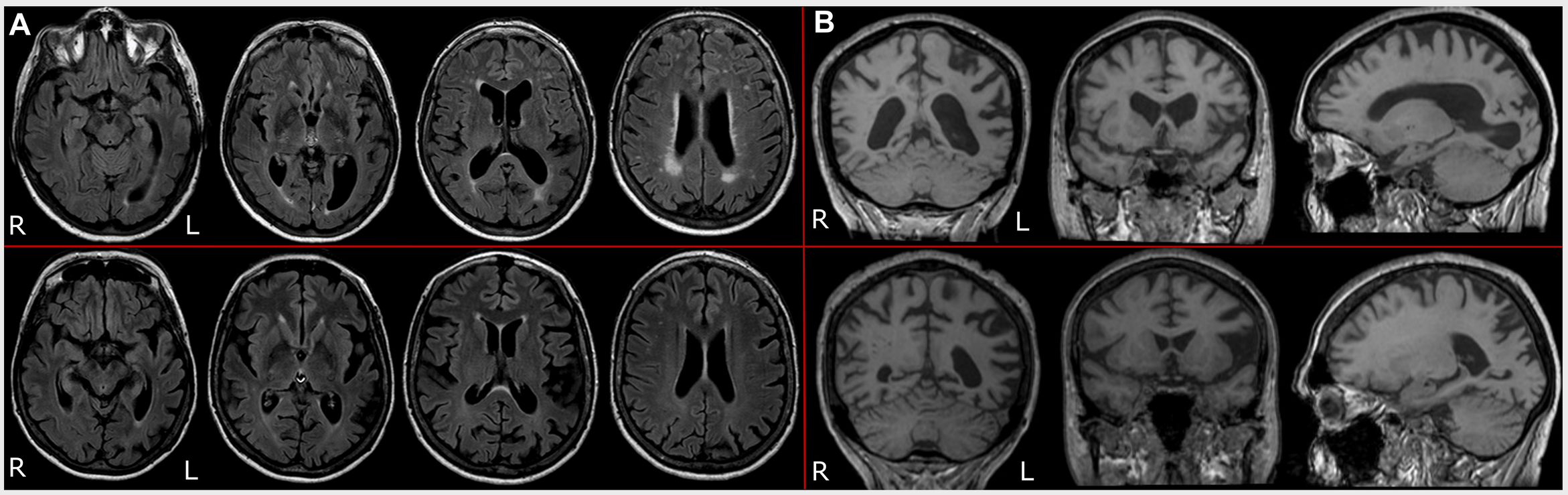

Figure legend: (A) *T2w* FLAIR MR images of A.R. (above) and D.N. (below). (B) Structural T1w images in coronal and sagittal projections of A.R. (above) and D.N. (below); sagittal projections images refer to left hemisphere of both patients.

EEG

- ***A.R.***: Modest alteration of organization symmetrical on both hemispheres. Focal slow waves found in left temporal region.
- ***D.N.***: Modest alteration of organization symmetrical on both hemispheres. Focal slow waves seen synchronously and asynchronously in the posterior areas of both hemispheres.

^{18}F-FDG-PET

- ***A.R.***: Hypometabolism in **temporal-parietal-occipital regions** bilaterally, more severe in the left hemisphere compared to the right one.
- ***D.N.***: Prominent areas of hypometabolism in the **temporal, parietal and occipital regions bilaterally** associated to **hypometabolism in the cerebellar hemispheres bilaterally** and to milder degrees of hypometabolism in the **left frontal region, at peri-opercolar level, and in the homolateral insular cortex**.

Conclusions

A.R. had **memory impairment** besides visual deficits and brain damage mainly in posterior regions, **consistent with her AD-like pathology**. On the other hand, in ***N.D.*** the presence of **extrapyramidal signs**, **attentive-executive deficits** and **non-AD CSF profile** were suggestive for an **underlying CBD pathology**.

Despite PCA being classically defined as an atypical AD variant [1], some cases with an underlying CBD pathology have been reported. [2, 3] For these reasons, a **multimodal approach** is needed in the diagnostic challenge and for **in-vivo pathology prediction** that might allow correct patients' enrollment for future protein-specific clinical trials.

Bibliography

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[3] Peng et al., *Posterior cortical atrophy as a primary clinical phenotype of corticobasal syndrome with a progranulin gene rs5848 TT genotype*, Orphanet Journal of Rare Diseases (2016) 11:13