Prodromal Alzheimer's disease presenting with early and prominent dyscalculia

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Background and Objectives

Alzheimer's disease (AD) is the most prevalent age-related degenerative dementia. In its prodromal stage, clinically presenting as Mild Cognitive Impairment (MCI), an amnestic syndrome of hippocampal type is the most frequent feature. However, other cognitive functions may result early impaired and even antedate memory deficits in AD variants with atypical presentation [1]. Dyscalculia is a common finding in mild to moderate AD patients: it results from impairment in several abilities such as number comprehension, number production, calculation, problem solving and numerical judgement [2].We report a case of prodromal AD in which dyscalculia was by far the earliest and most significant deficit.

Subject and Methods

Our patient was a 74-year-old woman without familial antecedents with a two-year history of progressive difficulties in finding words and doing even simple calculations, with relative preservation of daily life activities. She underwent neurological examination, neuropsychological assessment with particular detail on linguistic and mathematical skills, routine blood tests, EEG, brain MRI, FDG-PET, and amyloid tracer PET. Lumbar puncture couldn't be performed due to technical difficulties.

Results

Neurological examination only showed mild right pyramidal signs. MMSE score was 24/30. Her neuropsychological profile was characterized by deficits in short-term memory (with preservation of long-term memory), non-verbal abstract reasoning, attentional-executive functions, written language comprehension and severe dyscalculia (Table 1). MRI revealed diffuse, relatively symmetric cortical atrophy (Figure 2A), whereas FDG-PET disclosed reduction of glucose uptake in superior parietal and temporo-parietal cortices, prevailing on the left side, along with a less marked hypometabolism in superior frontal cortex, basal ganglia and thalami, prevailing on the right side (Figure 2B). Amyloid tracer PET evidenced diffuse burden of β-amyloid plaques, with the highest tracer retention in frontal areas. ApoE status was E3/E3. EEG showed diffusely dysregulated cerebral electric activity. The final diagnosis was multiple domain, non-amnestic MCI, probably due to AD pathology.

I – GENERAL NEUROPSYCHOLOGICAL EXAMINATION

NEUROPSYCOLOGICAL TEST	RAW SCORE	EQUIVALENT SCORE
Mini Mental State Examination (MMSE)	24/30	≥ 23,8*
ATTENTIONAL AND EXECUTIVE FUNCTIONS		
Frontal Assessment Battery (FAB)	**11/18**	**0**
Attentional Matrices	**25/60**	**0**
Phonological Verbal Fluency	30	2
Stroop Test: time	**126"**	**0**
Stroop Test: interfered Color Naming	**9.5**	**0**
SHORT-TERM MEMORY		
Digit Span Forward	**4**	**0**
Visuo-Spatial Span	**3**	**0**
LONG-TERM VERBAL MEMORY		
Story recall test: immediate recall	6.2/8	4
Story recall test: delayed recall	5.5/8	3
Rey's 15 word learning test: immediate recall	41/75	4
Rey's 15 word learning test: delayed recall	9/15	4
CONSTRUCTIONAL PRAXIS ABILITIES		
Clock Drawing Test (CDT: number correct)	6/10	≥ 6*
Copying simple geometrical drawings	10/14	1
LANGUAGE ABILITIES		
Semantic Verbal Fluency	**21**	**0**
Token Test	**27**	**0**
NON VERBAL REASONING ABILITIES		
Raven's Coloured Progressive Matrices	**18/36**	**0**
CLINICAL SCALE		
Frontal Behavioral Inventory (FBI)	5	≥ 23*
Instrumental Activities of Daily Living (IADL)	7/8	-

II - NEUROPSYCHOLOGICAL ASSESSMENT OF APHASIA

LINGUISTIC SKILLS	ITEMS	CORRECT SCORE	CUT-OFF
Repetition	Words	9.8	8,8
	Non-Words	4.5	2,0
	Phrases	3	3,0
Reading	Words	7.4	6,4
	Non-Words	5	4,0
	Phrases	1.9	1,3
Writing	Words	9.7	6,3
	Non-Words	3.4	1,4
	Phrases	1.6	0,6
Oral Naming	Words	10	8,2
	Verbs	7.6	6,1
	Colors	5	4,0
Written Naming	Words	4.1	2,7
	Verbs	5	3,0
Oral Comprehension	Words	20.6	18,4
	Phrases	14	11,6
Visual Comprehension	Words	18	17,0
	Phrases	9.8	11,3
Number	Repetition	9.2	8,8
	Reading	6.1	7,6
	Dictation	4.7	6,3
	Word→Digit	1.2	4,2
Calculation	Addition	0.8	2,2
	Subtraction	0.8	1,0
	Multiplication	0.4	1,4

Table 1. *Neuropsychological evaluation.* ***Note****: an equivalent score* ***0*** *means below the normal range, 1 means within normal limits, 2 to 4 mean normal range. * For these tests, equivalent scores are not provided, but only cut-off scores for normal range.*

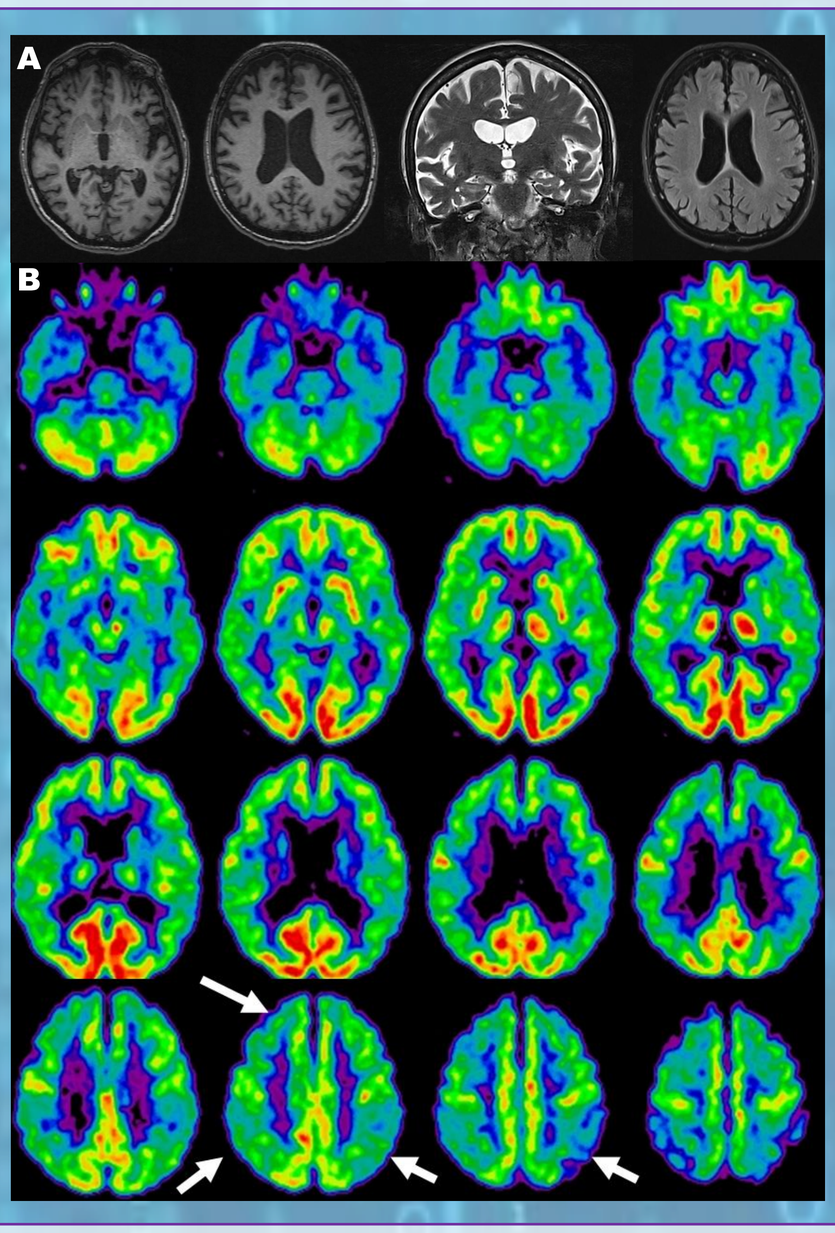

Figure 2. *A: T1-weighted axial, T2-weighted coronal and FLAIR axial MRI scans showing a moderate, diffuse cortical atrophy, with very slight left hemispheric prevalence and without remarkable hippocampal involvement. B: [18]FDG-PET disclosing hypometabolism mainly in superior parietal and temporo-parietal cortices, more marked on the left side, along with less evident hypometabolism in superior frontal cortex, prevailing on the right side (arrows). A slight reduction in glucose uptake is also evident in basal ganglia and thalami, especially on the right side.*

Discussion and Conclusions

Calculation deficits are associated with left parietal lobe dysfunction, whereas other related abilities, such as knowledge of arithmetic and problem solving skills, rely upon temporal and frontal activation respectively [3]. Our patient performed poorly on tests exploring calculation, number production and comprehension skills, displaying also partial impairment in frontal cognitive functions and language. The peculiar neuropsychological findings of our case may be explained by an early disruption of the network involving temporo-parietal cortex, frontal cortex and subcortical structures. The present case paradigmatically highlights that AD since its prodromal stage may present without memory impairment but with several "focal" cognitive syndromes, reflecting considerable variability in the progression of neurodegeneration.

References

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