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A Case of Logopenic Aphasia as a Variant of Alzheimer's Disease

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Abstract
Primary progressive aphasia (PPA) is a syndromic group of neurodegenerative diseases that have a particular tropism for the brain structures that implement language. By definition, the language impairment remains largely isolated for at least two years, before spreading, in most cases, to other cognitive functions such as executive processes, memory, praxis, or behavioral control. It was classified into three types: fluent (semantic), non-fluent, and logopenic. The logopenic variant is the least common one, characterized by slow word retrieval, impaired sentence repetition, and frequent word-finding pauses. On the other hand, motor speech, grammar, and single-word comprehension are often spared. Although logopenic PPA is diagnosed clinically, most cases share an underlying Alzheimer's disease (AD) pathology in comparison to the other two variants that are closely related to frontotemporal dementia (FTD). We report the case of a middle-aged man who presented to our center with progressive aphasia that was undiagnosed for two years. The patient's neuropsychological evaluation and predominant atrophy on MRI in the left perisylvian and posterior parietal regions were consistent with the diagnostic criteria for the logopenic variant of a primary progressive aphasia (lvPPA). The cerebrospinal fluid (CSF) analysis showed low amyloid $\beta_{1\text{-}42}$ (434 pg/ml), as well as a high Tau/Beta1-42 ratio (0.62) and low Innotest amyloid Tau index (IATI) (0,77), which is consistent with the AD profile.
Keywords: *Primary progressive aphasia, Logopenic variant of primary progressive aphasia, Alzheimer's disease*

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I. Introduction

Primary progressive aphasia (PPA) consists of three main syndromes [1]:progressive non-fluent aphasia, semantic dementia, and progressive logopenic aphasia.

-The non-fluent and an agrammatic variant of (APP-NF/G):This form of APP is characterized by the presence of agrammatism and/or apraxia of speech requiring an effort to avoid errors in the production of sounds (The motor aspect of language). Two of the following 3 criteria must also be present: difficulty in understanding syntactically complex sentences, comprehension of single words retained, and object knowledge retained.

- Semantic variant of PPA (PPA-S):This clinical form of PPA involves an impairment of semantic memory, difficulty in associating nouns and objects, and impaired understanding of isolated words. Three of the following four criteria must also be associated: loss of knowledge of objects, particularly those that are familiar and low-frequency objects, surface dyslexia or surface dysorthographia, preserved repetition, preserved speech production (motor and grammatical aspects of language preserved).

- The logopenic variant of primary progressive aphasia (lvPPA), also known as logopenic progressive aphasia, is characterized by anomia, word-finding difficulties in spontaneous speech and naming tests, impaired repetition of sentences and phrases with a length effect, speech (phonologic) errors in spontaneous speech and naming, spared single-word comprehension and object knowledge, spared motor speech, and lack of frank agrammatism. At least 3 of the following criteria must be present: phonological errors in spontaneous speech or in naming tests, retained comprehension of single words and objects, motor aspects of language retained, and absence of agrammatism. It is also characterized by atrophy shown in the left posterior temporal cortex and inferior parietal lobule [2, 3].

As with any neurodegenerative pathology, PPAs are also defined by the nature of the underlying neuropathological lesions, which help determine the etiological diagnosis. Logopenic PPAs are mostly underpinned by an Alzheimer's disease-type mechanism. This report describes a case of lvPPA as a variant of Alzheimer's Disease (AD).

II. Case description

A 58-year-old man, right-handed, married, and father of 3 living and healthy children, with an education level of NC6 according to the Barbizet scale with 13 years of study, working as an administrator at the University of International Trade, with no particular pathological history and no similar cases in the family, was referred to the neurology department of the hospital specialized in neurology and neurosurgery of ALI AIT IDIR of Algiers in April 2022. At the first visit, the patient was accompanied by his brother who provided us with all the information due to his communication difficulties. He presented progressively difficulty naming objects and finding words, giving the impression of having the word at the end of the tongue, and this about two years before presenting himself to our hospital with since 6 months a slight complaint of memory, like forgetting an appointment and misplacing objects, with the forgetting names of people. The brother reported that the problems were predominantly saying the names of everyday objects properly. The patient would refer to a "glass" or pen" as a "thing" because he was unable to recall the name of objects. At the same time, his language comprehension was relatively well- preserved. Firstly, language disorders were small and they did not affect daily activities. After, two years, the symptoms got stronger and became significant enough to limit the patient's verbal contact with others. Moreover, writing difficulties occurred. Recently he presented with phonemic paraphasias, affective and emotional disturbances with social withdrawal as well as difficulties in counting his money.

The patient was submitted to clinical, neurological, and neuropsychological assessment. The neurological exam was unremarkable.

The neuropsychological assessment was performed using the following tests:

- The Mini-Mental State Exam (MMSE) [4], for a Global Cognitive Assessment.
- The nine-image test (NIT-93) [5], for the evaluation of verbal episodic memory.
- The Forward digit span for the evaluation of short-term memory and the Reverse Digit Span, for an evaluation of working memory.
-The Frontal Assessment Battery (FAB) [6], for the Assessment of Executive Functions: Conceptual Elaboration, Mental Flexibility, Environmental Autonomy, Programming, Interference Sensitivity, and Inhibitory Control.
- The Frontal dysfunction scale "FDS" for the assessment of the severity of behavioral disorders.
-The instrumental activities of daily living (IADL) [1], for the impact of cognitive impairment on activities of daily living.
- The praxis battery for the evaluation of melokinetic, ideomotor, ideatory, and oral-facial praxis.
- The Categorical and Lexical Verbal Fluency Test, for an evaluation of semantic memory and/or executive functions.
- A language assessment including Oral Picture Naming Test " ON 80" and the Montreal-Toulouse Aphasia Language Testing Protocol (MT-86).

The neuropsychiatric evaluation, namely depression, and anxiety, was performed by the Hamilton Depression Scale and the Hamilton Anxiety Scale.

The patient's neuropsychological data are presented in Table 1.

The MMSE revealed mild cognitive impairment (MMSE: 20/30).

The language examination revealed disorders in retrieving single words in spontaneous speech and naming, partially improved by oral drafting, and disorders in repeating long words, sentences, and not short words. Comprehension of single words, simple, and complex sentences, and knowledge of objects are spared. Text comprehension, on the other hand, is impaired. Motor speech is spared and there is no agrammatism (see Table 1).

The evaluation of the numerical span shows an impairment of short-term memory and working memory. The forward numerical span was 3, while the back numerical span was 2. Neither apraxia of speech nor dysarthria was observed.

Assessment of executive functions revealed a dysexecutive syndrome with a FAB of 5/18. The disorder involved conceptualization, mental flexibility, programming, interference sensitivity, and inhibitory control.

Episodic memory was preserved.

The IADL reveals the mild impact of the cognitive deficit on activities of daily living.

The neuropsychiatric evaluation revealed mild depression and mild anxiety.

Table 1: Neuropsychological evaluation

Cognitive Scales	Score		
	Obtained	**Maximum theoretical**	**Threshold of normality**
MMSE	20 / 30	30/30	26
FAB Conceptualization disorder Mental flexibility disorder Environmental Autonomy Disorder Programming disorder Sensitivity to interference Loss of inhibitory control	5 /18 1 /3 0/3 3/3 1/3 0/3 0/3	18/18	**15**
Digit Span -The Forward digit span -The Reverse Digit Span.	 3 2		
NIT-93 -Immediate recall -Delayed callback Free deferred callback Delayed callback indexed Total score	 9/9 7/9 2/9 9/9		
Verbal fluency Categorical verbal fluency "Animals in 2 minutes" Lexical verbal fluency "Letter P in 2 minutes"	 4 2		
Oral Picture Naming Test " ON 80"	48/80		
MT-86			
Oral name	**17**	31	23
Word comprehension	9	9	39
Oral comprehension of sentences	38	38	
Copied writing	**8**	13	9
Reading aloud	33	33	
Text comprehension	**4**	6	
Reading comprehension of words	5	5	10
Writing comprehension of sentences	8	8	
Oral-facial praxis	6	6	3
Number reading	6	10	
IADL			1/4

The biological tests were within the normal range, in particular, the results of the complete blood count, the complete metabolic workup, in particular that of the dosage of vitamin B12, folic acid, homocysteine, the thyroid workup with the dosage of anti-thyreoglobulin antibodies, the syphilitic and HIV (Acquired Immune Deficiency Virus) serologies as well as the autoimmunity workup.

Magnetic resonance imaging (MRI) of the brain revealed perisylvian and left posterior parietal atrophy and bilateral hippocampal atrophy. (Cf. Figure 1 and 2).

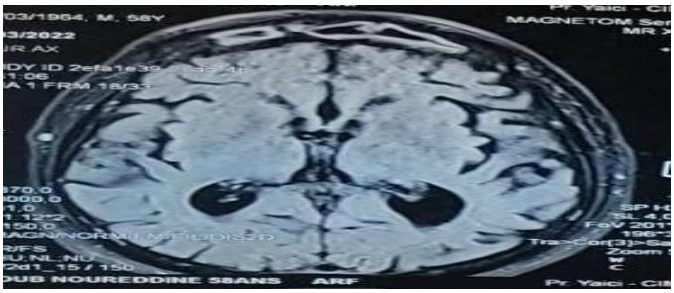

Figure1: Brain MRI (Axial FLAIR image): Mild focal atrophy in the left posterior superior temporal and left inferior parietal junction regions.

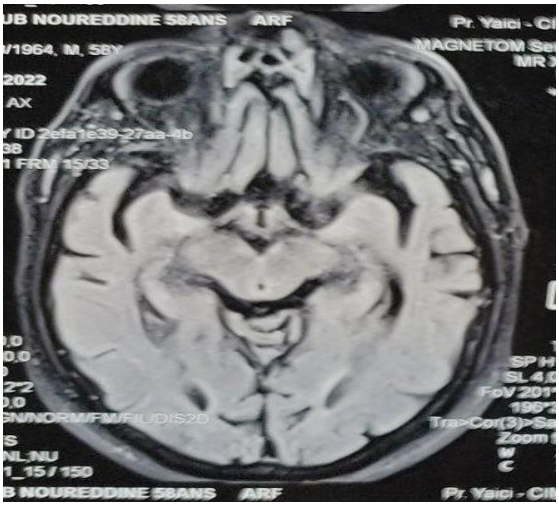

Figure1: Brain MRI (Axial FLAIR image): Bilateral medial temporal atrophy

Lumbar puncture with the determination of biomarkers of Alzheimer's disease in cerebrospinal fluid: Amyloid Beta1-42 peptide (AB 1-42), total Tau protein (T-Tau), phosphorylated Tau protein (P-Tau), as well as the calculation of the Tau/ABeta1-42 ratio and the Innotest Amyloid Tau Index (IAT), defined as the ratio Aβ42/(240 +1.18 x tau) (IAIT), was carried out. A biological profile in favor of Alzheimer's disease was observed with an assay of Amyloid Beta1-42 (AB 1-42) peptide decreased to 434 pg/ml for a standard of 725-1717 pg/ml, as well as a Tau/Beta1-42 ratio higher than 0.5 (0.62) and IATI lower than 0,8(Cf. Table 2).

Table 2: Biomarkers of AD in CSF

CSF Biomarkers	Rate	Norms
Amyloid Beta peptide 1-42	**434 pg/ml**	725-1777 pg/ml
Total Tau Protein (T-Tau)	271 pg/ml	146-410 pg/ml
Phosphorylated tau protein (P-tau 181)	50,1 pg/ml	21,5- 59 pg/ml
Ratio LMP Tau/ A Beta 1-42	0,62	< 0,5
IATI	0,77	>0,8

III. Discussion

Language disorders are often the first symptoms of dementias with a neurodegenerative basis, including primary progressive aphasia (PPA), which corresponds to a syndromic group of neurodegenerative diseases that have a particular tropism for the cerebral structures implementing language. Language disorders remain largely isolated for at least two years before spreading, in most cases, to other cognitive functions such as executive processes, memory, praxis, or behavioral control.

PPAs affect relatively young patients, often before the age of 65, thus having a considerable socio-professional impact because they affect a fundamental capacity of our cognition, including aspects such as syntax and lexicon structure, which are unique to the human species. Language disorders do not have a major impact on the ability to generate reasoning, but they do alter the ability to express and/or receive it.

The pathophysiological approach makes it possible to consider PPAs more as syndromes than as diseases. The clinical entities are well-defined, they are underpinned by heterogeneous pathological processes within the same syndrome.

The neuropathology is most often that of an FTD (Frontotemporal Dementia) in the agrammatic and semantic forms. APP-NF/G is thought to be linked to FTD-tau in 50% of cases, amyloidopathy in 31% of cases, and FTD-ubiquitin+ involving the TDP-43 protein in 19% of cases. Concerning APP-S, FTD-TDP-43 was found in 68% of cases, amyloidopathy in 16% of cases, and FTD-tau in 16% of cases. In the logopenic situation, amyloidopathy is most often observed (77% of cases), followed by FTD-TDP (14%), and finally FTD-tau (9%) [7-10].

The case presented is singular in the progressive aspect of the symptoms, the predominant complaint related to language for at least 2 years, deficits in cognitive screening tests of MMSE, direct and indirect digit span, executive functions, MTL (automatic language - content, repetition) and verbal fluency (phonemic and categorical) concomitant with relative sparing of IADL and oral comprehension.

In the informal assessment, the key aspects that emerged were the absence of agrammatism and apraxia, as well as the sparing of motor language. The presence of perisylvian and left posterior parietal atrophy on brain MRI was an argument in favor.

Although the patient met the diagnostic criteria for lvPPA, the diagnosis was not convincingly supported by neuroimaging criteria as the patient had not only perisylvian and left posterior parietal atrophy, but also hippocampal atrophy, which could suggest typical AD. Hippocampal atrophy is the best-established imaging biomarker for AD. In contrast, lvPPA is associated with greater atrophy in the left temporal lobe, mainly affecting the perisylvian and posterior temporoparietal regions (angular gyrus, posterior middle temporal gyrus, superior temporal gyrus, and superior temporal sulcus) [11].

The clinical diagnosis of the reported case was shared between lvPPA and AD at certain stages of the disease. Based on the initial symptoms reported by the family member, language was the first area affected, which argues for a diagnosis of PPA.

However, the patient evolved with the presentation of not only language symptoms, but also non-verbal domains, while also presenting with neuroimaging findings suggestive of the clinical diagnoses of lvPPA, and AD. The lumbar puncture with biomarker assays: AB1-42, T-Tau, and P-Tau and calculation of IATI as well as the Tau/A Beta 1-42 ratio, confirmed the diagnosis of AD. Diagnosed with Alzheimer's disease, he has been prescribed donepezil and is under regular follow-up.

Our case is in line with the literature suggesting that APLV may be an initial symptom of AD. This case suggests that logopenic PPA and dementia caused by AD can be part of a temporal spectrum of the same pathophysiological process.

The density of Neuro Fibrillary Degeneracies is greater in the left lateral temporal and parietal regions in patients with logopenic PPA compared to those with typical Alzheimer's disease, in the absence of a significative difference in the hippocampi [12], although some authors report relative preservation of the hippocampi in language-related Alzheimer's disease [13].

IV. Conclusion

Patients presenting with language symptoms consistent with logopenic PPA should undergo evaluations for AD pathology, to better define the course, diagnosis, and treatment options.

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