Revista Eletrônica
Acervo Saúde
Electronic Journal Collection Health ISSN 2178-2091

The progressive unfolding of aphasia: a diagnostic trajectory

O desdobramento progressivo da afasia: uma trajetória diagnóstica

El desarrollo progresivo de la afasia: una trayectoria diagnóstica

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ABSTRACT

Objective: To report a case of Frontotemporal Dementia Variant Primary Progressive Aphasia with agrammatism (FTD-PPA), a rare neurodegenerative disease that represents significant challenges in differential diagnosis, particularly with Alzheimer's Disease (AD). **Case detail:** A 62-year-old female initially presented with amnesia, anxiety, and speech difficulties, managed with fluoxetine, resulting in partial improvement. Over three years, she exhibited progressive cognitive and functional decline, including mental confusion, aphasia, motor difficulties, and significant weight loss. Mini-Mental State Examination scores deteriorated from 20/30 to 9/30. The diagnosis was established by prioritizing the decisive cerebrospinal fluid biomarker evidence, which excluded AD, and the dominant clinical phenotype of progressive aphasia over the atypical neuroimaging findings. Management included antidepressants, donepezil (later discontinued), and speech therapy, with limited cognitive improvement despite mood stabilization. **Final considerations:** This case highlights the complexities of diagnosing progressive cognitive impairment. Comprehensive clinical, neuropsychological, and biomarker evaluations were critical in differentiating FTD-PPA from AD. The predominance of linguistic deficits and biomarker results confirmed the diagnosis of the agrammatic variant of FTD-PPA. Multidisciplinary follow-up and individualized symptom management were essential in optimizing the patient's quality of life.

Keywords: Frontotemporal dementia, Primary progressive aphasia, Alzheimer's disease.

RESUMO

Objetivo: Relatar um caso de Afasia Progressiva Primária variante da Demência Frontotemporal com agramatismo (FTD-PPA), uma doença neurodegenerativa rara que apresenta desafios significativos no diagnóstico diferencial, particularmente com a Doença de Alzheimer (DA). **Detalhamento de caso:** Uma paciente de 62 anos inicialmente apresentou amnésia, ansiedade e dificuldades de fala, que foram gerenciadas com fluoxetina, resultando em melhora parcial. Ao longo de três anos, ela exibiu declínio cognitivo e funcional progressivo, incluindo confusão mental, afasia, dificuldades motoras e perda de peso significativa. As pontuações no Mini-Exame do Estado Mental (MMSE) deterioraram de 20/30 para 9/30. O diagnóstico foi estabelecido priorizando a evidência decisiva de biomarcadores no líquido cefalorraquidiano, que excluiu a DA, e o fenótipo clínico dominante de afasia progressiva em detrimento dos achados atípicos de neuroimagem. O tratamento incluiu antidepressivos, donepezil (posteriormente descontinuado) e fonoterapia, com melhora

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SUBMETIDO EM: 10/2025 | **ACEITO EM: 11/2025** | **PUBLICADO EM: 1/2026**

cognitiva limitada, apesar da estabilização do humor. **Considerações finais:** Este caso destaca as complexidades do diagnóstico de comprometimento cognitivo progressivo. Avaliações clínicas, neuropsicológicas e de biomarcadores abrangentes foram críticas na diferenciação da FTD-PPA da DA. A predominância de déficits linguísticos e os resultados dos biomarcadores confirmaram o diagnóstico da variante agramática da FTD-PPA. O acompanhamento multidisciplinar e o manejo individualizado dos sintomas foram essenciais para otimizar a qualidade de vida da paciente.

Palavras-chave: Demência frontotemporal, Afasia progressiva primária, Doença de Alzheimer.

RESUMEN

Objetivo: Informar un caso de Afasia Progresiva Primaria variante de Demencia Frontotemporal con agramatismo (FTD-PPA), una enfermedad neurodegenerativa rara que presenta desafíos significativos en el diagnóstico diferencial, particularmente con la Enfermedad de Alzheimer (AD). **Detalle del caso:** Una paciente de 62 años se presentó inicialmente con amnesia, ansiedad y dificultades del lenguaje, que se manejaron con fluoxetina, lo que resultó en una mejora parcial. A lo largo de tres años, mostró un deterioro cognitivo y funcional progresivo, incluyendo confusión mental, afasia, dificultades motoras y una pérdida de peso significativa. Las puntuaciones en el Examen de Estado Mental Mini-Mental (MMSE) se deterioraron de 20/30 a 9/30. El diagnóstico se estableció priorizando la evidencia decisiva de biomarcadores en el líquido cefalorraquídeo, que excluyó la DA, y el fenotipo clínico dominante de la afasia progresiva sobre los hallazgos atípicos de neuroimagen. El manejo incluyó antidepresivos, donepezil (que se suspendió más tarde) y terapia del habla, con una mejora cognitiva limitada a pesar de la estabilización del estado de ánimo. **Consideraciones finales:** Este caso destaca las complejidades del diagnóstico del deterioro cognitivo progresivo. Las evaluaciones clínicas, neuropsicológicas y de biomarcadores integrales fueron críticas para diferenciar la FTD-PPA de la AD. La predominancia de los déficits lingüísticos y los resultados de los biomarcadores confirmaron el diagnóstico de la variante agramática de FTD-PPA. El seguimiento multidisciplinario y el manejo individualizado de los síntomas fueron esenciales para optimizar la calidad de vida de la paciente.

Palabras clave: Demencia frontotemporal, Afasia progresiva primaria, Enfermedad de Alzheimer.

INTRODUCTION

Primary Progressive Aphasia (PPA) is a form of frontotemporal dementia that manifests as a gradual and irreversible impairment of linguistic abilities, initially preserving the integrity of other cognitive functions. PPA has a low prevalence, approximately 3 in 100,000 individuals, representing a considerable diagnostic challenge, especially in its early stages (BELDER CRS, et al., 2024; MAGNIN E, et al., 2016; COYLE-GILCHRIST IT, et al., 2016). This condition has a heterogeneous pathophysiology, characterized by atrophy in brain regions related to language processing skills (MARSHALL CR, 2018).

There are three main subtypes of PPA, which are defined according to the dominant clinical characteristics and patterns of brain atrophy observed: nonfluent/agrammatic, semantic, and logopenic. The core features of nonfluent/agrammatic PPA are agrammatism and/or phonetic distortions, leading to a laborious and hesitant speech pattern. Semantic PPA is characterized by a decline in the ability to name objects and understand word meanings, while fluency and word articulation are preserved. Logopenic PPA is clinically defined by impairments in both single-word retrieval, evident during spontaneous speech and naming tasks, and the repetition of sentences and phrases (BELDER CRS, et al., 2024, GORNO-TEMPINI ML, et al., 2011). Although the clinical presentation of logopenic aphasia involves language deficits, its cerebrospinal fluid profile is like that of Alzheimer's disease, and its treatment also involves cholinesterase inhibitors (MARSHALL CR, et al., 2018).

As a primary disease of communication, PPA presents significant challenges for neurobiological characterization, diagnosis, and management, making it susceptible to misinterpretation and delayed recognition (BELDER CRS, et al., 2024; HARDY CJ, et al., 2023; MAGNIN E, et al., 2013). Typically, the first

clinical signs of PPA are related to language and may remain the only cognitive manifestations or signs for about 10 to 14 years. Other symptoms emerge as the disease progresses, but language dysfunctions continue to be the primary alterations. Thus, the diagnosis is facilitated when the patient is evaluated in the initial stages. The initial manifestations of the disease can appear between the ages of 40 and 80 (MESULAM M, 2013).

Due to the diagnostic complexity of PPA, this article aims to clarify the approach to this syndrome through a case study, exemplifying how the suspicion of PPA should prevail over that of Alzheimer's disease (AD) through detailed clinical evaluation, radiological exams, and cerebrospinal fluid (CSF) analysis. This is a case study assessed and approved by the Research Ethics Committee (CEP) (Opinion 7.775.179 and CAAE 85971924.8.0000.5149).

CASE DETAIL

A 62-year-old female patient presented to a primary care service with a history of amnesia, anxiety, and speech difficulties, for which she had been on fluoxetine 20 mg daily for one year. Initial follow-up three months later revealed partial improvement in her anxiety and amnesia. However, her condition progressively worsened over the next year, with the persistence of amnesia and speech difficulties and the emergence of new symptoms, including mental confusion and impaired concentration. These cognitive deficits significantly impacted her professional life, leading to her dismissal from a five-year job due to memory lapses. While she retained the ability to accurately describe her health status and medication regimen, she consistently demonstrated difficulty in retaining new information presented during consultations.

At a follow-up visit, the patient's first Mini-Mental State Examination (MMSE) was conducted, revealing a score of 20/30. Her performance was marked by deficits in several domains, including a prominent inability to perform calculations, read, or write. She also showed difficulties with language tasks, such as repeating a sentence and following a three-stage command. Noteworthy strengths included intact spatial orientation and good drawing ability. In addition to her cognitive decline, she had noticeable difficulty recalling recent memories and had lost 5.5 kg, with her BMI recorded at 27.9 kg/m².

Due to initial reports of mood improvement, fluoxetine was discontinued. This decision, however, was proved premature, as her mood worsened within one month, leading to a formal diagnosis of Major Depressive Disorder (MDD) according to DSM-5 criteria and the subsequent initiation of sertraline. The dosage was increased from 50 mg to 100 mg daily to achieve a more robust therapeutic effect. Despite this, the patient's condition progressed, evidenced by increasing difficulty with instrumental activities of daily living (IADLs), such as forgetting a pot on the stove and experiencing motor difficulties. These new symptoms, coupled with a decline in her MMSE score to 15/30, shifted the diagnostic focus toward a neurodegenerative process, with Alzheimer's Disease (AD) emerging as the primary hypothesis at that time.

Six months later, at 65 years of age, the patient's condition showed significant progression, marked by worsening sleep disturbances that required daytime naps for compensation. She also experienced her first fall, which resulted in a head trauma requiring simple sutures, though radiographic studies were unremarkable. Clinically, there was greater impairment of recent memory, while long-term memory remained intact. Her persistent speech difficulties evolved to include impaired object naming and sentence completion, consistent with aphasia.

These clinical changes were reflected in her cognitive and functional assessments: her MMSE score deteriorated to 9/30, and her Pfeffer Functional Activities Questionnaire (PFAQ) score was 11. The predominance of language impairment over other cognitive deficits led clinicians to reconsider the initial diagnosis of AD, raising the possibility of a progressive dementia with a more pronounced language component.

As a result, she was referred to a speech therapist specializing in neurolinguistics, and a therapeutic trial with donepezil 5 mg daily was initiated, while sertraline was continued. At her one-month follow-up, despite good medication adherence, she showed no improvement in her dementia-related symptoms and her sleep quality continued to worsen. Consequently, the donepezil dose was increased to 10 mg daily.

Five months later, the patient exhibited a slight improvement in recent memory and object naming. A lumbar puncture was then performed, and the results for cerebrospinal fluid (CSF) analysis were presented in **Table 1** and **Table 2**. The Innotest Amyloid Tau Index (IATI) was calculated during the consultation, yielding a result of 0.987. Concurrent assessments showed a PFAQ score of 9, and the patient's cumulative weight loss reached 11.9 kg, resulting in a BMI of 25.31 kg/m².

To address both mood and weight loss, sertraline was replaced with mirtazapine, starting at 15 mg and adjusted to 30 mg after 15 days. After one month on the new medication, the patient demonstrated good adaptation with improved mood. However, her amnesia persisted, notably with a profound loss of semantic knowledge. Donepezil was ultimately discontinued based on the stronger clinical suspicion of Frontotemporal Dementia, Progressive Primary Aphasia variant with agrammatism, supported by the results of the CSF analysis.

Table 1 - Alzheimer's disease biomarkers. Method: enzyme-linked immunosorbent assay.

Alzheimer's Disease Biomarkers	Results
Total Tau Protein	789 pg/mL
Phosphorylated Tau Protein	107 pg/mL
Beta-Amyloid Peptide (1-42)	1156 pg/mL
Beta-Amyloid Peptide (1-40)	10584 pg/mL
Beta-Amyloid Ratio (1-42/1-40)	0,11 pg/mL

Note: Laboratory Reference values: Total Tau Protein: greather than 614pg/mL (positive); between 466 and 614pg/mL (indeterminate); less than 466pg/mL (negative). Phosphorylated Tau Protein: greater than 61 pg/mL (positive); less than or equal to 61pg/mL (negative). Beta-amyloid Peptide (1-42): less than 550 pg/mL (positive); between 550 and 651 pg/mL (indeterminate); greater than 651 pg/mL (negative). Beta-Amyloid Peptide (1-40) not applicable. Beta-Amyloid Ration 1-42/1-40: less than or equal to 0.10 (positive); greater than 0.10 (negative). Laboratory Notes: 1. A positive result for beta-amyloid peptide (1-42), beta-amyloid 1-42/1-40 ratio, total Tau, or phosphorylated Tau does not establish a diagnosis of Alzheimer's disease (AD) or another cognitive disorder. The results of AD biomarkers in cerebrospinal fluid (CSF) should be interpreted in conjunction with clinical history data and other complementary examinations, such as imaging studies. 2. The diagnosis of AD is a clinico-biological one, requiring the presence of a specific AD clinical phenotype and evidence of biomarkers consistent with the disease's pathology (amyloid-positive and Tau-positive). 3. Decreased concentrations of beta-amyloid peptide (1-42) or, preferably, a reduced beta-amyloid 1-42/1-40 ratio are indicative of amyloid pathology. 4. The beta-amyloid 1-42/1-40 ratio is the preferred marker of amyloid pathology. By normalizing the influence of pre-analytical and biological variables (such as high or low producers) on beta-amyloid peptide (1-42) concentrations, the ratio is considered a more sensitive and specific marker for AD. 5. Elevated concentrations of phosphorylated Tau are indicative of Tau pathology, as it is more specific for AD than total Tau protein. 6. An isolated reduction in beta-amyloid peptide (1-42) concentration or, more rarely, in the beta-amyloid 1-42/1-40 ratio, without correspondence to AD clinical phenotypes, should be interpreted with caution. Several pre-analytical interferences can affect the sample, resulting in falsely reduced results, including improper collection, blood contamination, storage temperature, transfer between tubes, repeated freeze/thaw cycles, inappropriate collection/transport tubes, and low sample volume relative to the tube's internal surface area. To avoid such issues, strict adherence to the collection and transport instructions for CSF samples is recommended.
Source: Thomaz MS, et al., 2026.

Table 2 - Routine cerebrospinal fluid analysis.

Routine Cerebrospinal Fluid Analysis	Results
Appearance	Clear
Color	Colorless
Clot	Absent
Nucleated Cells	0/mm^3
Red Blood Cells	0/mm3
Neutrophils	0%
Lymphocytes	0%
Monocytes	0%
Eosinophils	0%
Basophils	0%
Macrophages	0%

Source: Thomaz MS, et al., 2026.

Table 3 - Biochemical tests.

Biochemical Tests	Results
Glucose	52 mg/dL
Total Protein	29 mg/dL
Chloride	129 meq/L
VDRL	Non-reactive

Source: Thomaz MS, et al., 2026.

Magnetic Resonance Imaging (MRI) of the brain revealed moderate global brain volume loss, characterized by prominent high convexity cortical sulci and enlarged ventricles (**Figure 1**). The imaging also showed significant bilateral hippocampal atrophy (MTA scale 2). Additionally, scattered T2/FLAIR hyperintense foci were noted in the supratentorial white matter, consistent with a mild, nonspecific white matter disease (Fazekas 1) likely caused by chronic microvascular ischemia or gliosis. No evidence of acute ischemia, mass effect, or intra/extra-axial collections was found, and the brainstem and cerebellum appeared normal. It is important to note that the quality of the examination was technically limited by motion artifacts.

Figure 1 - Cranial Magnetic Resonance Imaging (MRI) revealed isolated signal alterations in the supratentorial white matter bilaterally, which are nonspecific to the method and may correspond to gliosis, myelin rarefaction, and/or chronic ischemic processes (Fazekas 1). Signs of moderate volumetric brain reduction were also observed (MTA 2). The examination was technically compromised due to movement artifacts.



Source: Thomaz MS, et al., 2026.

Two months after the MRI and following a 20-day discontinuation of donepezil, the patient's condition showed new behavioral and sleep-related symptoms. She experienced an episode of inexplicably cutting an earphone and two episodes of vivid dreams. Three months later, at 66 years of age, her sleep became interrupted, accompanied by nocturnal agitation and worsening mood. Her aphasia and motor difficulties in performing tasks, such as putting on shoes, also persisted. At this point, her cumulative weight loss had reached 19.4 kg, with a BMI of 22.2. To address these new issues quetiapine 25 mg daily was added to manage the nocturnal agitation. This therapy led to a subsequent improvement in her sleep quality.

DISCUSSION

This case illustrates the complexities of diagnosing and managing patients with progressive cognitive impairment. The patient's initial presentation, including anxiety, amnesia, and aphasia, was managed with fluoxetine. However, discontinuation of this medication resulted in worsening anxiety, leading to a diagnosis of major depressive disorder and suggesting an evolution of her clinical condition. Subsequently, the patient developed further symptoms indicative of dementia, such as recent memory impairment, difficulties with daily living activities, and behavioral changes, including nocturnal agitation.

The differential diagnosis between Frontotemporal Dementia (FTD) variant Primary Progressive Aphasia and Alzheimer's Disease is challenging because both share initial symptoms like memory loss. However, PPA is typically characterized by more prominent and rapid linguistic and behavioral symptoms, such as agrammatism and telegraphic speech.

The absence of clear evidence for AD shifts the diagnostic focus toward other neurodegenerative pathologies, making the concept of Suspected Non-Alzheimer Disease Pathophysiology (SNAP) highly relevant. This concept applies to individuals with cognitive impairment who have negative biomarkers for amyloid pathology but show other signs of neurodegeneration. (RIZZI L, et al., 2021; JACK CR, et al., 2016; JACK CR, et al., 2016) In this case, the combination of linguistic and behavioral symptoms supported the SNAP hypothesis, pointing to a specific Frontotemporal Dementia variant. This diagnostic approach highlights the importance of a comprehensive clinical evaluation beyond AD when classifying and managing dementias. (VOS SJB, et al., 2024)

The patient was ultimately diagnosed with the agrammatic variant of PPA, based on specific clinical criteria: agrammatic language production, preserved single-word comprehension and object knowledge, as well as phonological errors in spontaneous speech. While some features of the logopenic variant were present, the primary findings were more consistent with the agrammatic subtype. The diagnosis was established on robust clinical criteria, as imaging, histopathology, and genetic evidence were not available to confirm it. (ELDER CRS, et al., 2024; GORNO-TEMPINI ML, et al., 2011; GORNO-TEMPINI ML, et al., 2004)

A diagnosis of Primary Progressive Aphasia requires several criteria to be met: the most prominent clinical feature is language difficulty; language deficits are the main cause of limitation in daily activities; and aphasia is the most prominent deficit at the onset of symptoms and in the initial stages of the disease. Additionally, four criteria must be negatively answered: the pattern of deficits is not better explained by other non-neurodegenerative nervous system disorders or medical conditions; cognitive disturbance is not better explained by a psychiatric diagnosis; there are no prominent initial impairments in episodic memory, visual memory, and visuospatial abilities; and there are no prominent initial behavioral disturbances (GORNO-TEMPINI ML, et al., 2011).

Once the underlying diagnosis is established, the classification of primary progressive aphasias into specific variants involves evaluating the presence or absence of salient speech and language features, including speech production, repetition, comprehension, naming, semantic knowledge, and reading/writing. The detailed clinical criteria allow for accurate patient classification, requiring either a quick 20-minute evaluation or a more detailed analysis by a speech-language pathologist. Classification can occur at three levels: clinical, supported by imaging, or definitive pathological diagnosis. Clinical diagnosis involves detecting characteristics in the patient's clinical history along with a detailed neuropsychological evaluation, identifying speech and language features typical of a variant. Imaging diagnosis requires matching identified symptoms with the visualization of neuroanatomical changes characteristic of each variant. Definitive pathological diagnosis involves detecting biomarkers, confirming the presence of pathological or genetic mutations associated with specific etiologies. Biological markers, such as Positron Emission Tomography with Pittsburgh Compound B and Cerebrospinal Fluid (CSF) may also be considered in the classification (GORNO-TEMPINI ML, et al., 2011).

The diagnostic evaluation utilized a comprehensive approach, incorporating a clinical history provided by a close family member, neuropsychological testing via the Mini-Mental State Examination and the Pfeffer Functional Activities Questionnaire, and ancillary investigations, including a lumbar puncture and cranial MRI. Given the diagnostic complexity, the CSF biomarkers were analyzed within the A/T/N classification framework. The results revealed a profile negative for amyloid pathology (A-), as the β-amyloid 1-42/1-40 ratio was 0.11, a value above the laboratory's cutoff for positivity (**Table 1**). Conversely, the profile was positive for tau pathology (T+), with an elevated phosphorylated Tau level of 107 pg/mL, and positive for neurodegeneration (N+), confirmed by an elevated total Tau level of 789 pg/mL and cerebral atrophy on magnetic resonance imaging (**Figure 1**). Crucially, while 'A' and 'T' markers are specific for Alzheimer's pathology, the 'N' category is a less specific marker of neuronal injury that can be found in a variety of other conditions. This combination yielded a biological profile of A-/T+/N+, which is inconsistent with a typical AD diagnosis and is formally categorized as SNAP (JACK CR, et al., 2016; MOLINUEVO JL, et al., 2014). Although a supplementary calculation of the IATI yielded a borderline result of 0.987, where values < 1.0 can suggest AD, this finding was interpreted with caution due to the index's lower sensitivity. (SOUZA LC, et al., 2014) Therefore, the diagnostic conclusion was primarily based on integrating the A-/T+/N+ biological profile with the overarching clinical picture — dominated by linguistic deficits — and the patient's lack of response to donepezil, which collectively argued against AD.

To complement the clinical findings and biomarker analysis, and to visualize structural brain changes, neuroimaging was employed as a core investigative tool in the evaluation of this neurodegenerative disorder (PEET BT, et al., 2021; WHITWELL J AND JOSEPHS K, 2012). The cranial MRI (**Figure 1**) revealed "significant bilateral hippocampal atrophy (MTA scale 2)." This finding is atypical, as the agrammatic variant of PPA is most commonly characterized by atrophy in the left inferior frontal gyrus and anterior insula. While studies have demonstrated that hippocampal volume loss can be present in FTD, it is typically less severe than that observed in Alzheimer's Disease. (LAAKSO MP, et al., 2000) The presence of atrophy rated as "significant" in this case may be understood within the context of FTD's clinical and pathological heterogeneity. The topographic distribution of neurodegeneration in FTD can vary, and it is plausible that in certain cases, the underlying proteinopathy extends beyond the classic frontotemporal networks causing significant atrophy in a wide network of brain regions, including the hippocampi (RABINOVICI GD AND MILLER BL, 2010; GORNO-TEMPINI ML, 2004).

This atypical presentation underscores the concept that FTD represents a spectrum of neurodegenerative processes. Furthermore, the impact of technical limitations cannot be dismissed, as the report explicitly states that the examination was "technically limited by motion artifacts," which can lead to systematic underestimation of gray matter volume and potentially exaggerate the perceived degree of atrophy (REUTER M, et al., 2015). Therefore, the observed hippocampal atrophy, while seemingly contradictory, can be interpreted as a feature of this patient's specific FTD phenotype, compounded by technical imaging factors.

The diagnosis of PPA was established through a complex integration of clinical, biomarker, and imaging data, where the different modalities presented conflicting evidence. The CSF analysis played the decisive role by revealing a biomarker profile (A-/T+/N+) that strongly argued against AD. This finding was crucial because the neuroimaging was not supportive of FTD; in fact, the MRI showed significant hippocampal atrophy, a pattern more characteristic of AD, creating a clinicoradiological dissociation. Therefore, the diagnosis was ultimately guided by prioritizing the specific biomarker evidence that excluded AD and the dominant clinical syndrome of progressive aphasia over the atypical imaging findings. This approach highlights the necessity of a multimodal evaluation to navigate the diagnostic complexities of neurodegenerative disorders.

As there are currently no approved disease-modifying treatments for FTD, the therapeutic management is fundamentally supportive, focusing on maximizing the patient's quality of life (OLNEY NT, et al., 2017). This strategy includes the targeted pharmacological control of symptoms, such as using antipsychotics like quetiapine for behavioral disturbances (GUIMET NM, et al., 2022; CHOW TW AND MENDEZ MF, 2002). Crucially, this approach must be embedded within a multidisciplinary follow-up that provides emotional support, guidance to caregivers, and continuous monitoring of the disease's progression.

This case demonstrates the diagnostic complexity of progressive neurodegenerative disorders. The predominance of linguistic deficits and biomarker results that excluded AD pathology were decisive in diagnosing the agrammatic variant of PPA. Despite an atypical finding on magnetic resonance imaging that is more commonly associated with AD, the diagnostic conclusion prioritized the dominant clinical picture and biomarker evidence. As there are no treatments to alter the disease course, therapeutic management focused on symptom control, caregiver support, and multidisciplinary follow-up.

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