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Aphasia with left occipitotemporal hypometabolism: A novel presentation of posterior cortical atrophy?

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Abstract

Alzheimer's disease is a common neurodegenerative disease often characterized by initial episodic memory loss. Atypical focal cortical presentations have been described, including the logopenic variant of primary progressive aphasia (lvPPA) which presents with language impairment, and posterior cortical atrophy (PCA) which presents with prominent visuospatial deficits. Both lvPPA and PCA are characterized by specific patterns of hypometabolism: left temporoparietal in lvPPA and bilateral parietoccipital in PCA. However, not every patient fits neatly into these categories. We retrospectively identified two patients with progressive aphasia and visuospatial deficits from a speech and language based disorders study. The patients were further characterized by MRI, fluorodeoxyglucose F18 and Pittsburgh Compound B (PiB) positron emission tomography. Two women, ages 62 and 69, presented with a history of a few years of progressive aphasia characterized by fluent output with normal grammar and syntax, anomia without loss of word meaning, and relatively spared repetition. They demonstrated striking deficits in visuospatial

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Conflicts of Interest/Disclosures

Dr. Wicklund has nothing to disclose.

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function for which they were lacking insight. Prominent hypometabolism was noted in the left occipitotemporal region and diffuse retention of PiB was noted. Posterior cortical atrophy may present focally with left occipitotemporal metabolism characterized clinically with a progressive fluent aphasia and prominent ventral visuospatial deficits with loss of insight.

Keywords

Alzheimer dementia; Aphasia; Functional Neuroimaging; Neuropsychology; Visual agnosia

1. Introduction

Alzheimer's disease (AD) is a common neurodegenerative disease often characterized by initial episodic memory loss. Atypical focal cortical presentations have been described, including the logopenic variant of primary progressive aphasia (lvPPA) which presents with language impairment,¹ and posterior cortical atrophy (PCA) which presents with prominent visuospatial deficits.² Both lvPPA and PCA are characterized by specific patterns of hypometabolism: left temporoparietal in lvPPA³ and bilateral parietoccipital in PCA.⁴ However, not every patient fits neatly into these categories. We present here two patients with *in vivo* evidence of AD pathology presenting with a progressive aphasia syndrome as well as prominent visuospatial deficits with hypometabolism of the left occipitotemporal region that may provide a link between these two syndromes.

2. Methods

Patients with a progressive aphasia syndrome were recruited into a speech and language based disorders study. Each patient underwent a detailed speech and language analysis by a speech pathologist. A behavioral neurologist interviewed and examined each patient. A detailed neuropsychological battery was performed, as previously described.⁵ Two patients with an unusual pattern of visuospatial deficits on neuropsychological testing were retrospectively identified and provided consent for participation in this study. The study was approved by the Mayo Clinic institutional review board.

All subjects underwent 3T volumetric MRI, fluorodeoxyglucose 18-F (FDG) and Pittsburgh compound B (PiB) positron emission tomography (PET) imaging as previously described.⁵ All voxels in the FDG-PET images were normalized to the pons and z transformed compared to a normative database using CortexID software (GE Healthcare, Waukesha, Wisconsin, USA).⁶

3. Results

3.1 Case 1

A 62-year-old woman with 18 years of education presented with a 3-year history of progressive difficulty with word finding. Both she and family denied any difficulty with visuospatial processes. Neurological examination was normal beyond her language difficulties. Bedside cognitive testing was normal with scores of 28 on both the Mini-mental Status Examination (MMSE)⁷ and Montreal Cognitive Assessment (MoCA).⁸

Neuropsychological testing showed low average learning and memory on the Rey Auditory Verbal Learning Test. Immediate memory for paragraph length stories and visually presented designs was moderately impaired though there was some sparing of the minimal amount of information she learned. The Trail Making Test (TMT) was mildly impaired on parts A and B. Her drawing of the Rey-Osterrieth Complex Figure (Fig. 1a) was markedly impaired and she was able to complete only 3 of 10 cube analysis on the Visual Object and Space Perception test, which is profoundly impaired.⁹

Detailed language assessment demonstrated prosodically fluent speech output with normal grammar and syntax. Repetition was relatively spared. Her aphasia quotient on the Western Aphasia Battery¹⁰ was borderline at 95.8, with most prominent difficulties in naming and reading and writing irregular and non-words. Auditory comprehension was intact with 19/22 on Part V of the Token Test.¹¹ Despite normal naming abilities with 14/15 on the short form of the Boston Naming Test (BNT),¹² she score 46/52 with the picture version of the Pyramids and Palms Tree Test (PPTT),¹³ indicating greater impairment when deriving semantic meaning from visually presented stimuli.

3.2 Case 2

A 69-year-old woman with 14 years of education presented with a 2-year history of progressive difficulty with word finding and circumlocution. She had no other complaints. Neurological examination was normal. Bedside cognitive scores were 23 on the MMSE and 16 on the MoCA.

Neuropsychological testing showed significant impairment in memory and learning, though visual memory was more severely affected than verbal memory, as measured by the Wechsler Memory Scale-III.¹⁴ TMT part A was moderately impaired, but she refused to complete Part B. Her Rey-Osterreith Complex Figure (Fig. 1b) was markedly impaired and she was also only able to complete only 3 of 10 cube analysis.

Results of her language assessment were similar to case 1, though she was more severely affected. She had prosodically fluent speech with relative sparing of repetition. Her aphasia quotient was mildly impaired at 92.5. Auditory comprehension was impaired with 8/22 on the Token Test. She scored 3/15 on a short form of the BNT. Her PPTT was disproportionately severe at 8/52.

3.3 Imaging findings

FDG-PET in each patient showed asymmetric, marked hypometabolism of left occipitotemporal regions, with milder involvement of parietal and frontal lobes and relative sparing of the primary visual cortex (Fig. 2a). MRI obtained in case 1 showed mild atrophy focused in the left occipital and posterior temporal regions (Fig. 2b, **Case 1**). MRI in case 2 showed mild parietal and occipital atrophy, worse in the left hemisphere, and involvement of the left posterior inferior temporal lobe (Fig. 2b, **Case 2**). Visual assessment of PiB-PET demonstrated significant retention in both patients (Fig. 2c).¹⁵

4. Discussion

We have documented two cases of progressive aphasia with prominent visuospatial deficits characterized by asymmetric left occipitotemporal hypometabolism. The insidiously progressive disturbance in language suggests a primary progressive aphasia (PPA).¹ However, these patients do not fulfill criteria for PPA as the most prominent clinical feature is not clearly a language disturbance.¹ In addition, they do not clearly delineate into any of the three recognized subtypes (non-fluent, semantic or logopenic).

While the impaired single word retrieval resembles lvPPA, the impaired object recognition in these patients, as demonstrated by the PPTT, argues for additional categorization as it is likely a reflection of visuoperceptual difficulties rather than semantic deficits in these patients. In addition, the occipitotemporal hypometabolism described here is not consistent with the usual left temporoparietal hypometabolism described in lvPPA.³

The neuropsychological profiles of these patients demonstrated multi-domain impairment with prominent and unexpected impairment in visuospatial functioning, suggesting these patients may have a variant of PCA. The hallmark feature of PCA is neuropsychological deficits in higher order visual processing.¹⁶ However, those deficits are often in the dorsal visual stream, as measured by neuropsychological profiles¹⁷ and metabolic patterns.^{4,18}

Though early case reports have argued for separate dorsal, ventral and primary visual variants of PCA^{16,19,20} current criteria for PCA rely on the presence of dorsal visual features such as Balint syndrome and preserved insight, neither of which these patients had.¹⁶ However, these patients had atrophy of posterior cortical regions, suggesting that criteria for PCA need refinement and should allow for the fact that not all patients complain of spatial and perceptual deficits, and may have more ventral stream features and atrophy.

Furthermore, the language impairment of the patients here is similar to that described in patients with PCA, who often present with alexia and agraphia,¹⁷ which may then be followed by difficulties in spoken language with phonological errors, impaired comprehension, and relative sparing of repetition.^{21,22}

Neither patient in our study underwent pathological analysis, but the diffuse retention of PiB suggests underlying beta-amyloid pathology, and hence AD pathology.¹⁵ Patients with PCA likewise show diffuse PiB retention.^{23,24} As with other focal variants of AD, areas of hypometabolism correlate strongly with the focal symptoms,^{3,4,18,24} as neurofibrillary tangles may have a strong contribution to the clinical features.²³ In fact, most AD patients presenting with aphasia have an asymmetrical increase in left hemispheric neurofibrillary tangle density as compared to typical AD patients.²⁵

This study is limited by the retrospective nature of review of just two cases. However, it does widen the phenotypical spectrum of neurodegenerative disease, particularly among PPA, PCA and focal AD variants, confirming that these disorders are not readily neatly subdivided at the present time. By appreciating the wide variability, we realize the importance of detailed clinical and neuropsychological evaluations for patients presenting

with language signs and symptoms not only to guide future studies in these disorders but also offer appropriate counseling and treatment.

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Fig. 1.
The Rey-Osterrieth Complex Figure Drawing showing marked impairment for (a) case 1,
and (b) case 2.

Fig. 2.

(a) Statistical stereotactic surface projection maps showing hypometabolism predominantly affecting left greater than right occipitotemporal lobes, with milder involvement of frontal and parietal lobes. (b) Coronal MRI showing occipital atrophy. (c) Axial Pittsburgh Compound B positron emission tomography showing amyloid retention.