Primary Progressive Aphasia and Transient Global Amnesia

Jonathan Graff-Radford, MD; Keith A. Josephs, MD, MST, MSc

Objective: To describe 3 patients with a history of transient global amnesia (TGA) who developed primary progressive aphasia (PPA).

Design: Case series.

Setting: Tertiary care center.

Patients: The study included 3 patients who presented to the neurology clinic with language complaints.

Main Outcome Measure: Presence of recurrent TGA and PPA.

Results: Three patients with a history of TGA were subsequently diagnosed as having PPA. All patients had recurrent attacks of TGA. The diagnoses of PPA were supported by speech pathology evaluations, neuropsychometric testing results, and imaging findings. Positron emission tomography revealed left posterior frontal hypometabolism in 1 patient and predominantly left temporal parietal hypometabolism in 1 patient, while single-photon emission computed tomography demonstrated decreased perfusion in the anterior left temporal and frontal lobes in the third patient.

Conclusion: There may be a relationship between recurrent TGA and the development of PPA.

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REPORT OF CASES

CASE 1

A 66-year-old right-handed man presented with cognitive impairment. His cognitive decline began 5 years before presentation. Initially, he would misuse words that apparently were similar to words within the same category. He subsequently had trouble naming people and poor comprehension, which affected him at work. One year before presentation, he had 12 hours of amnesia, consistent with TGA, and 6 months before presentation, he had another episode of amnesia, which lasted 6 hours. The findings of outside head imaging and lumbar puncture did not reveal any cause for his amnesia. When he was first examined, he had a severe aphasia that precluded formal bedside cognitive testing. He was asked to give the year or the month, he was unable to do so. However, when he was asked to point to the date on the calendar, he easily pointed to the correct date. He scored 0 on a verbal letter fluency test (letter F) and was able to come up only with 3 animals in 60 seconds on an animal fluency test, although he had 12 years of formal education. He had significant trouble naming and difficulty with the meaning of words; eg, he was only able to name 3 out of 10 of the

Author Affiliations: Department of Neurology (Behavioral Neurology and Movement Disorders), Mayo Clinic, Rochester, Minnesota.
first 20 items on the Boston Naming Test. He did not know what a lobster or a key was. When asked “What color is grass,” he said white. He recalled 2 out of 4 items that were given to him. He had considerable insight into his deficits and was frustrated by limitations in his self-expression and comprehension. His motor examination was notable only for mild ataxia. Formal neuropsychometric testing revealed aphasia with a marked deficit in auditory comprehension, word finding impairment, and semantic paraphasias. His visual-constructional ability was preserved. Magnetic resonance imaging showed focal left anterior medial temporal lobe atrophy (Figure). Single-photon emission computed tomography revealed severe decreased perfusion in the left temporal neocortex, with a 30% to 40% reduction compared with the right temporal lobe, as well as mild (10%-20%) decreased middle and lower left frontal lobe perfusion (Figure). Given his poor naming ability and loss of word meaning, semantic paraphasias, and poor comprehension, in association with focal left anterior medial temporal lobe

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
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<tr>
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<tr>
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<td>Perisylvian atrophy</td>
<td>Lateral temporal and inferior parietal lobes</td>
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<td>PPA-semantic</td>
<td>PPA-agrammatic</td>
<td>PPA-logopenic</td>
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</tbody>
</table>

*a All patients were right-handed.

*b Based on recent consensus recommendations.

**Figure.** Imaging findings. A, T2-weighted fluid-attenuated inversion recovery (FLAIR) axial magnetic resonance image (MRI) demonstrating predominantly left (L) anterior medial temporal lobe atrophy (patient 1). R indicates right. B, Technetium Tc99m bicisate (Neurolite; Du Pont Merck Pharmaceutical Co) axial and coronal single-photon emission computed tomographic images demonstrating decreased perfusion in the L temporal lobe compared with the R temporal lobe (patient 1). C, T1-weighted coronal MRI shows L perisylvian atrophy (patient 2). D, Fludeoxyglucose F 18–positron emission tomographic (FDG-PET) images demonstrate mild hypometabolism in the L more than the R posterior frontal region (patient 2). E, T2-weighted FLAIR MRI reveals predominantly L temporal parietal atrophy (patient 3). F, FDG-PET images reveal asymmetrical, abnormally decreased FDG uptake predominantly within the L lateral temporal and medial and lateral parietal lobes (patient 3).
atrophy on magnetic resonance imaging and focal left temporal hypoperfusion on single-photon emission computed tomography, his presentation was believed to be most consistent with a semantic variant of PPA.

CASE 2

A 74-year-old right-handed man presented with an approximately 1-year history of word-finding difficulties. He had previously been diagnosed twice as having TGA. The first episode started while he was using a chain saw 9 years before presentation, with a second episode occurring shortly afterward. His family reported that he had occasional word choice errors and difficulty in pronouncing and spelling words. His spouse reported that he would say “a word he didn’t mean” but that often “sounded somewhat similar in nature.” He denied memory difficulties. His Mini-Mental Status Examination score was 22 out of 30. He had trouble with attention and could not spell world backward. He recalled 2 of 3 items. His letter fluency was reduced to 10 (total) for 3 letters (F, A, and S) in 60 seconds; his animal fluency was 9. He had more than 20 years of formal education. He had mild apraxia of speech. His confrontation naming was normal. He scored 15 out of 15 on a short version of the Boston Naming Test. Formal speech evaluation revealed simplification of grammar with agrammatic structure, normal naming, and occasional vowel and consonant distortions, consistent with apraxia of speech. Magnetic resonance images of the head (Figure) revealed left perisylvian atrophy. Fludeoxyglucose F 18–positron emission tomography demonstrated mild hypometabolism in the left more than the right posterofrontal region. Given his speech and language characteristics had features of logopenic and semantic dementia, the finding of poor repetition and poor naming, which benefited from phonetic cueing in the presence of lateral temporal parietal hypometabolism, her classification was most consistent with the logopenic variant of PPA.

CASE 3

A 75-year-old right-handed woman presented with a 2-year history of worsening language abilities. Ten years before presentation, she had an episode of amnestic confusion and was diagnosed as having TGA. The episode lasted approximately 24 hours. She had another episode of TGA 3 years before presentation. Her chief complaint at the time of presentation was the misuse of words. For example, she would call a heating blanket a “light.” The patient and her family denied that she had difficulty with memory. She scored 28 out of 38 on the Kokmen Short Test of Mental Status. Formal speech and language evaluation revealed that she was linguistically fluent, with impaired repetition and confrontation naming. On the Boston Naming Test, she scored 24 out of 40 on the first 40 items but benefited from phonetic cueing. There was evidence of loss of word meaning; eg, she did not know what an octopus was. During reading, she made many phonological errors and had trouble reading orthographically irregular as well as nonreal words. Neuropsychometric testing also identified executive dysfunction. Magnetic resonance imaging revealed mild to moderate bilateral hippocampal atrophy and moderate leukoaraiosis. Fludeoxyglucose F 18–positron emission tomography of the brain revealed asymmetrically, abnormally decreased fludeoxyglucose F 18 uptake predominantly within the left lateral temporal and medial and lateral parietal lobes (Figure). Although the patient’s speech and language characteristics had features of logopenic and semantic dementia, the finding of poor repetition and poor naming, which benefited from phonetic cueing in the presence of lateral temporal parietal hypometabolism, her classification was most consistent with the logopenic variant of PPA.

COMMENT

We describe 3 patients with PPA who had TGA before presentation. All 3 patients had recurrent episodes of TGA, which is extremely rare, suggesting a possible association between TGA and PPA. The pathogenesis of TGA remains unclear, and its possible relationship with PPA is even more uncertain. Given the neuroimaging data of medial temporal lobe involvement in TGA, a relationship between TGA and Alzheimer disease would appear more intuitive. It is possible that this association is occurring by chance; however, because of the rarity of both disorders, we cannot ignore the possibility of a bona fide association. This reasoning then raises the question of whether having TGA may predispose to the development of PPA or whether patients who are destined to develop PPA aphasias are more susceptible to TGA.

Although PPA is a neurodegenerative disease of the elderly, there is recent evidence that some patients with PPA may be born with a susceptibility to degeneration of the language network. Patients with PPA and their families have a significantly higher incidence of learning disabilities, including dyslexia, suggesting a familial propensity to developmental and degenerative disorders of the language network. One possibility is that patients who are susceptible to a degenerative process involving the left hemisphere may also be more susceptible to TGA, which may explain why patient 1 had the onset of symptoms of PPA before TGA. Furthermore, all 3 of our patients had recurrent episodes of TGA le, which occurs only in 10% of patients with TGA, suggesting that these patients may have been more susceptible. Alternatively, TGA may increase the likelihood that PPA will develop.

In one study, 2 patients developed PPA and were found on brain imaging to have left hemicraniosynostosis and a decreased size of the left frontal and temporal lobes, suggesting that an environmental insult might predispose to PPA. Perhaps patients who have multiple episodes of TGA are more likely to develop PPA.

To the best of our knowledge, this is the first report describing a possible relationship between TGA and PPA. Further research needs to be done to elucidate this relationship, which might have important implications in recognizing PPA early in the diagnosis.

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Correspondence: Keith A. Josephs, MD, MST, MSc, Department of Neurology, Mayo Clinic, 200 1st St SW, Rochester, MN 55905 (Josephs.keith@mayo.edu).
Author Contributions: Dr Josephs had full access to all of the data in the study and takes responsibility for the
integrity of the data and the accuracy of the data analysis. Study concept and design: Graff-Radford and Josephs. Acquisition of data: Graff-Radford and Josephs. Analysis and interpretation of data: Graff-Radford and Josephs. Drafting of the manuscript: Graff-Radford. Critical revision of the manuscript for important intellectual content: Graff-Radford and Josephs. Statistical analysis: Graff-Radford. Administrative, technical, and material support: Graff-Radford. Study supervision: Josephs.

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REFERENCES


