Primary Progressive Aphasia and Transient Global Amnesia

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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.

Arch Neurol. 2012;69(3):401-404

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. When 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...
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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<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Education, y</td>
<td>12</td>
<td>&gt;20</td>
<td>12</td>
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<tr>
<td>Age at onset of PPA symptoms, y</td>
<td>74</td>
<td>61</td>
<td>73</td>
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<tr>
<td>Time from onset to initial presentation, y</td>
<td>&lt;1</td>
<td>5</td>
<td>2</td>
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<tr>
<td>Time from TGA to onset of PPA symptoms, y</td>
<td>-3</td>
<td>9</td>
<td>1</td>
</tr>
<tr>
<td>Pattern of cortical dysfunction</td>
<td>Left anterior medial temporal lobe</td>
<td>Perisylvian atrophy</td>
<td>Lateral temporal and inferior parietal lobes</td>
</tr>
<tr>
<td>PPA subclassificationb</td>
<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.
atrophy on magnetic resonance imaging and focal left tem-
peral hypoperfusion on single-photon emission com-
puted 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 oc-
curring shortly afterward. His family reported that he had
occasional word choice errors and difficulty in pronounc-
ing and spelling words. His spouse reported that he would
say “a word he didn’t mean” but that often “sounded some-
what 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 flu-
ency 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 sim-
plification of grammar with agrammatic structure, nor-
mal naming, and occasional vowel and consonant dis-
tortions, consistent with apraxia of speech. Magnetic
resonance images of the head (Figure) revealed left
perisylvian atrophy. Fludeoxyglucose F 18–positron
emission tomography demonstrated mild hypometabo-
lism in the left more than the right posterofrontal re-
gion. Given his speech and language characteristics
had aggramatism, intact naming and repetition, and
imaging findings, the patient was diagnosed as having
the agrammatic 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 approxi-
mately 24 hours. She had another episode of TGA 3 years
before presentation. Her chief complaint at the time of pre-
sentation 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.9
Formal speech and language evaluation revealed that she
was linguistically fluent, with impaired repetition and con-
frontation naming. On the Boston Naming Test, she scored
24 out of 40 on the first 40 items but benefited from pho-
netic cueing. There was evidence of loss of word meaning;
e.g., 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 dys-
function. Magnetic resonance imaging revealed mild to
moderate bilateral hippocampal atrophy and moderate leu-
koearia. Fludeoxyglucose F 18–positron emission to-
omography of the brain revealed asymmetrically, abnor-
mal fludeoxyglucose F 18 uptake predominantly
within the left lateral and medial and lateral pa-
rietal lobes (Figure). Although the patient’s speech and lan-
guage characteristics had features of logopenic and seman-
tic 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.

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 associ-
tion 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 relation-
ship between TGA and Alzheimer disease would appear
more intuitive. It is possible that this association is oc-
curring 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 develop-
ment of PPA or whether patients who are destined to de-
velop PPA aphasia 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 fami-
lies have a significantly higher incidence of learning dis-
abilities, including dyslexia, suggesting a familial pro-
penity to developmental and degenerative disorders of
the language network.10 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 symp-
toms of PPA before TGA. Furthermore, all 3 of our pa-
tients had recurrent episodes of TGA, which occurs only
in 10% of patients with TGA, suggesting that these pa-
tients may have been more susceptible.11 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 hemispheric abnormalities
and a decreased size of the left frontal and temporal lobes,
suggesting that an environmental insult might predis-
pose to PPA.12 Perhaps patients who have multiple epis-
odes 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 re-
relationship, which might have important implications in
recognizing PPA early in the diagnosis.

 Accepted for Publication: June 17, 2011.

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 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.

Financial Disclosure: None reported.

Funding/Support: Dr Josephs is funded by R01-DC010367 (principle investigator [PI]), R01-AG037491 (PI), and R21-AG38736 (coinvestigator) from the National Institutes of Health and by the Dana Foundation (PI).

REFERENCES


