Vascular Ischemia as a Cause of Transient Global Amnesia: A Patient Series

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ABSTRACT

Introduction: Epileptic, migrainous, and vascular pathologies may cause transient global amnesia (TGA); however, the mechanism of causation remains unclear. We investigated possible vascular causes of TGA.

Methods: We retrospectively evaluated the clinical and radiologic studies of 13 patients with TGA. On admission, patients underwent diffusion-weighted imaging (DWI) and intra- and extracranial magnetic resonance angiography (MRA); vascular risk factor profiles for diabetes, hypertension, and hyperlipidemia; electroencephalography; and neuropsychological tests. Seven patients underwent control DWIs 24 h after symptom onset.

Results: One patient had two punctiform acute infarcts in the left hippocampus, and one had a left pontine paramedian acute infarct. In the second patient, control DWI showed additional left hippocampal and right frontal acute infarcts. None of the patients had electroencephalographic evidence of epileptic activity. All patients except for one had at least one vascular risk factor. The second patient was shown to have paroxysmal atrial fibrillation during follow-up.

Conclusion: Minor posterior circulation ischemic stroke appears to cause TGA in some patients. Evaluations such as DWI and vascular risk factor assessment may be helpful in making the diagnosis.

Keywords: Transient global amnesia, diffusion MR, ischemia

INTRODUCTION

Transient global amnesia (TGA) is a temporary amnestic condition lasting 1-24h. It is characterized by anterograde and recent retrograde memory disorders, with loss of place and time orientation but without a disturbance in consciousness (1). The exact cause of TGA is still unknown. Epileptic transient amnesia may be seen in complex partial seizures and mimic TGA but should not be confused with it (2,3). Migraine, physical exercise, emotional stress, sexual intercourse, psychologic disorders, cerebral hypextension, vertebral angiography, and jugular vein incompetency are among the triggering factors/responsible mechanisms (4,5). In addition, recent diffusion-weighted magnetic resonance imaging (DWI MRI) studies suggest that delayed detected hippocampal ischemia contributes to the cause of TGA; however, its mechanism remain obscure (6).

In animal studies, migraine has been reported to cause glutamate-mediated transient neuronal and glial depolarization through cortical spreading depression, which in turn affects CA1 neurons in the hippocampus, thereby disrupting cortical integrity and resulting in TGA (7). However, the presence of cortical spreading depression in the hippocampus has not been confirmed in human studies (8).

Because of its high sensitivity and specificity in detecting ischemia in small areas, DWI MRI has been increasingly used to investigate vascular causes of TGA. Studies often report that the foci of signal increases in the mesial temporal areas, which is consistent with punctuate and focal ischemia (4,9). Serial MR studies showing the time dynamics of DWI lesions suggest that the underlying mechanism is delayed ischemia rather than acute focal cerebral ischemia (5,6).

In this study, we looked for evidence of vascular ischemia in patients diagnosed as having TGA by evaluating their early and late cranial MRI and clinical characteristics.

METHODS

The study was approved by the Institutional Review Board. The data from all patients who presented to the neurology emergency service between January 2006 and January 2011 and in whom TGA was diagnosed were retrospectively analyzed.
All patients underwent cranial MRI, including DWI and intra- and extracranial magnetic resonance angiography (MRA), at presentation. In some of them, a control DWI examination was performed 24 h after admission. The possibility of an associated epileptic amnesia was assessed with electroencephalography (EEG). The amnestic process was evaluated with neuropsychological tests in some patients. The presence of precipitating factors such as emotional stress, physical activity, vascular risk factors (diabetes, hypertension, and hyperlipidemia), history of migraine, somatic symptoms during TGA throughout the duration of the episode, and history of similar episodes were determined from the medical records.

### RESULTS

We evaluated 13 patients (eight women) between ages 51 and 78 years [mean (SD) age 65 years (11)]. Mean (median−interquartile ranges) duration of symptoms was 8 (8−3.5/11) h (Table 1). Mean interval between the onset of symptoms and MRI examination was 11 h.

Infarcts were detected in the early phase in 2 of the 13 patients, whereas 1 of the 7 patients who underwent control DWI imaging had a new lesion in addition to the ischemic lesions detected in the initial DWI. The control DWI study of patient (11) showed no additional findings, whereas patient 13 had additional ischemic infarcts in the left hippocampal and right frontal areas (Table 1). In patient 4, right posterior cerebral artery P2 stenosis was causing a hippocampal perfusion defect despite the absence of an acute ischemic lesion in the same territory. Interestingly, there was a chronic infarction in the right posterior cerebral artery (PCA) territory (Table 1).

Eleven patients had at least one of the following vascular risk factors: diabetes mellitus (n=2), hypertension (n=7), or hyperlipidemia (n=11). Three patients had a history of migraine. All patients underwent EEG; patient 11 underwent EEG during the episode and all the other patients underwent EEG after the episode. No patients had an epileptic activity. Three patients had disorganization in the anterior aspects of the hemispheres, and one had rapid rhythms in the anterior aspects of the hemispheres. Neuropsychological evaluations after the attacks showed that eight patients had no amnestic deficits. Symptoms began after an emotional stress in four patients and while driving in two patients. One patient also had paresthesias in the legs during the attack. We would provide detailed information about selected patients with TGA who also had an evidence of vascular ischemia in our series.

Case 1

A 56-year-old woman (patient 11) had a history of hyperlipidemia and migraine. Neurologic examination was normal. A DWI MRI taken 7 h after the onset of symptoms showed two hippocampal focal diffusion restriction areas in the medial aspect of the temporal lobe. The re-

### Table 1. Clinical and radiological findings in patients with a diagnosis of transient global amnesia

<table>
<thead>
<tr>
<th>Patient number, sex, and age, y</th>
<th>Findings from initial diffusion-weighted imaging</th>
<th>Findings from control diffusion-weighted imaging</th>
<th>Magnetic resonance angiography</th>
<th>Vascular risk factors</th>
<th>EEG</th>
<th>TGA duration, h</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 F 78</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>HT, HL</td>
<td>N</td>
<td>10</td>
</tr>
<tr>
<td>2 F 60</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>HL</td>
<td>N</td>
<td>4</td>
</tr>
<tr>
<td>3 M 71</td>
<td>-</td>
<td>-</td>
<td>Left ICA mid cervical segment moderate stenosis</td>
<td>-</td>
<td>N</td>
<td>2</td>
</tr>
<tr>
<td>4 F 73</td>
<td>-</td>
<td>-</td>
<td>Lack of flow in right PCA, stenosis of left PCA in P2 and left MCA at M2. Extracranial MRA showed 80% and 40% narrowing in left and right ICA.</td>
<td>HT, HL, DM</td>
<td>Disorganization in the anterior of the hemispheres</td>
<td>1</td>
</tr>
<tr>
<td>5 F 64</td>
<td>-</td>
<td>-</td>
<td>R VA V4 stenosis</td>
<td>HL</td>
<td>N</td>
<td>6 a</td>
</tr>
<tr>
<td>6 M 51</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>HL, MG</td>
<td>N</td>
<td>24</td>
</tr>
<tr>
<td>7 M 66</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>HT, HL</td>
<td>N</td>
<td>7.5</td>
</tr>
<tr>
<td>8 F 70</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>HT, HL</td>
<td>N</td>
<td>3.5 a</td>
</tr>
<tr>
<td>9 F 60</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>N</td>
<td>12</td>
</tr>
<tr>
<td>10 M 75</td>
<td>-</td>
<td>7x6 mm bilobulated left PCOMA aneurysm</td>
<td>HT, HL</td>
<td>N</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>11 F 56</td>
<td>Two punctuate acute infarcts in the left hippocampus.</td>
<td>-</td>
<td>-</td>
<td>HL, MG</td>
<td>Disorganization in the anterior of the hemispheres</td>
<td>12</td>
</tr>
<tr>
<td>12 M 57</td>
<td>-</td>
<td>-</td>
<td>Left frontotemporal disorganization</td>
<td>HT, HL, DM</td>
<td>Left frontotemporal disorganization</td>
<td>3</td>
</tr>
<tr>
<td>13 F 62</td>
<td>Left pontine paramedian acute infarct</td>
<td>Punctuate ischemic infarcts in the left hippocampus and right frontal areas</td>
<td>-</td>
<td>HL, MG</td>
<td>Rapid rhythms in the anterior of the hemispheres</td>
<td>10</td>
</tr>
</tbody>
</table>

* A history of TGA  
  N: normal; MG: migraine; ICA: internal carotid artery; PCA: posterior cerebral artery; MCA: medial cerebral artery; VA: vertebral artery; PCOMA: posterior communicating artery; HT: hypertension; HL: hyperlipidemia; DM: diabetes mellitus
sults of intra- and extracranial MRA studies were normal (Figure 1). Her symptoms improved after 8 h, although the same lesions were visible in her control DWI MRI taken after 17 h. Except for mild disorganization in the anterior of the hemispheres, EEG results were normal. Electrocardiography showed a sinus rhythm, and transesophageal echocardiography and Holter monitoring results were normal. Antiplatelet and antihyperlipidemic treatments were initiated. She had no symptoms during the 1-year follow-up.

Case 2
A 62-year-old woman (patient 13) had an amnestic episode 1 year ago that lasted for approximately an hour. She also had hyperlipidemia and a history of migraine. Results of a neurologic examination were normal. Her symptoms improved within 10 h; however, she had a migraine attack 15 h later, which resolved with symptomatic treatment. A DWI MRI taken 7 h after the onset of symptoms showed a paramedian acute ischemic area in the superior aspects of the left pons. The results of cervical and intracranial MRA and perfusion MR studies were normal (Figure 2). Electrocardiography showed normal sinus rhythm. Transesophageal echocardiography, performed to determine the possibility of ischemic stroke with cardioembolic origin, showed the ejection fraction to be 65% and the left atrial diameter to be 3.8 cm, with mild mitral and aortic insufficiency and no evidence of intracardiac thrombus. The control cranial MRI taken 36 h after the onset of symptoms showed additional acute infarct areas in the left hippocampal and right frontal areas, a millimeter-sized diffusion restriction not visible in the initial MRI (Figure 2). Neuropsychological tests revealed only a mild disturbance in long-term spontaneous recall. The anterior aspects of the hemispheres showed rapid rhythm in EEG. Holter monitoring showed paroxysmal atrial fibrillation, and the patient was started on warfarin 3 months after presentation. Her symptoms did not recur during the 1-year follow-up.

Case 3
A 73-year-old woman (patient 4) with a history of hypertension, hyperlipidemia, diabetes mellitus, and ischemic stroke at presentation had TGA. These symptoms improved one hour after onset. Neurologic examination revealed only a left homonymous hemianopsia sequela. No acute ischemic lesions were visible on the DWI taken 3.5 h after symptom onset; however, there were chronic ischemic infarcts in the right cerebellum and right PCA perfusion area (Figure 3). Perfusion MRI showed perfusion defects in the left PCA and left middle cerebral artery (MCA) inferior perfusion areas. Intracranial MR angiography showed occlusion of the right PCA and stenosis of the left PCA in P2 and the left MCA at M2. Extracranial MRA showed 80% and 40% narrowing in the left internal carotid artery (ICA) and right ICA, respectively. Disseminated intra- and extracranial atherosclerosis was suspected. EEG showed disorganization in the anterior aspects of both hemispheres. A control DWI MR obtained 24 h after the onset of symptoms showed no new lesions. Because the patient had a history of hypertension, hyperlipidemia, and diabetes, treatment of vascular risk factors was reviewed and anticoagulation treatment was continued.

DISCUSSION
The prevalence of patients with TGA having lesions detectable by DWI ranges from 52% to 84% (5,6,10). These high rates have been linked to serial MRIs in these studies, which observed that ischemic lesions were mostly detected between 12 and 72 h after symptom onset (10). Enzinger et al. found 14 punctuate lesions in 10 of 86 patients with TGA undergoing DWI, mostly in the mesial temporal areas, hippocampus, dentate gyrus, cornu ammonis, and the parahippocampal gyrus (4). In our group, 2 out of 13 patients (15%) had an ischemic lesion, and 1 out of 7 patients (13%) had a delayed additional ischemic lesion on control MRI.

Functional anatomic analysis of these lesions revealed a selective distribution into the CA1 area of the hippocampal cornu ammonis. It is hypothesized that the selective sensitivity of CA1 neurons to metabolic stress may be the key link in the pathological cascade of TGA. The augmented metabolic stress in these neurons increases the glutamate-mediated intracellular Ca\(^{2+}\) influx; thus, anaerobic glycolysis and the production of lactate are increased. This condition decreases cellular diffusion and causes the transient lesions...
Ischemic lesions in the left mesial temporal lobe (16) and bilateral mesial temporal lobe infarcts have been reported in a patient who experienced TGA after cerebral angiography (17). The presence of ischemic foci in locations other than in the expected hippocampus locations (18,19,20), including in the posterior or even the anterior circulation and in regions which may not result in memory disturbance, may indicate multiple ischemic foci arising from cardioembolism. This finding correlates with the pontine and frontal infarcts that are thought to be unrelated to TGA in patient 13. Ischemia in the posterior circulation other than hippocampus, particularly the vertebrobasilar system, is also linked to TGA (21,22,23). The TGA in patient 4 occurred in the presence of an old temporoparietal infarct associated with bilateral perfusion deficit in the PCA territory due to widespread intracranial atherosclerosis. The presence of mesial temporal hypoperfusion, including the hippocampus, may have facilitated the development of TGA in the neuronal network of this area.

Although there is no agreement on the contribution of ischemic injury to the occurrence of TGA, ischemic vascular processes appear to contribute to the cause in a subset of TGA patients. Our results also strongly support vascular ischemia as a cause in some patients. Neuroimaging studies and vascular risk factor assessments are important components of diagnosis.

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REFERENCES


