LETTER TO THE EDITOR

To The Editor

Retrosplenial Stroke Mimicking Transient Global Amnesia

Keywords: Retrosplenial infarct, Retrosplenial stroke, Transient global amnesia, Ischemic amnesia

An 89-year-old, right-hand-dominant female was brought to hospital by her family for acute confusion. The patient was fully independent at home, without cognitive impairment, and had a history of essential tremor, glaucoma, and hypertension. Her medications were irbesartan and amlodipine. She reported sudden-onset dizziness, headache, nausea, and a feeling that her "brain was not working as it should be" during volunteer work. She was aware that her memory was not at baseline; she could not recall in detail any events leading up to or during the episode. Roughly 1 hour later, she experienced some improvement and attempted to return home. She reported feeling disoriented, taking multiple detours and wrong turns on her way home. She was brought to hospital a few hours later by her sons. They reported that the patient repeatedly asked the same questions and did not remember events from earlier in the day.

On examination, her vital signs were normal. Mini-Mental State Examination (MMSE) score was 26/30 with deficits in orientation to time, spontaneous recall, and inability to draw intersecting pentagons. The remainder of her neurological exam was entirely normal. Non-contrast computed tomography and computed tomography angiography of the head and neck showed chronic white matter microvascular ischemic changes and multiple areas of intracranial and extracranial stenosis with no acute abnormalities (not shown). She was kept in hospital overnight with a working diagnosis of transient global amnesia (TGA).

Electroencephalogram performed the following day found mild intermittent left temporal slowing without any epileptiform discharges. Brain magnetic resonance imaging (MRI) did not show any hippocampal abnormality but instead revealed acute left retrosplenial ischemia (Figure 1). Her headache, dizziness, and nausea had completely resolved. Repeat examination revealed an MMSE score of 30/30 with no neurological deficits. She was discharged with outpatient follow-up, including a 24-hour Holter monitor which revealed sinus rhythm and occasional premature atrial complexes but no atrial fibrillation. She had an echocardiogram 6 months prior which showed mild left ventricular hypertrophy, left atrial dilation, and trace mitral regurgitation. Although no clear etiology for her stroke was established, the mechanism was thought to be atheroembolic given her imaging findings. She was maintained on aspirin and lipid-lowering therapy for secondary stroke prevention.

This case presents an example of a left-sided retrosplenial stroke mimicking TGA. TGA is a benign syndrome characterized by an acute episode of anterograde amnesia that resolves within 24 hours. This classically presents as a patient repeatedly asking the same questions and being unable to orient to their current situation. Patients may also experience retrograde amnesia, though this is typically less pronounced than the anterograde amnesia. Awareness and domains of cognition other than memory characteristically remain intact.[1] Associated nonfocal symptoms may include headache, dizziness, and nausea,[1] which were seen in our case.

Memory deficits caused by acute stroke often present with accompanying focal deficits that can be used to clinically exclude TGA.[1] Stroke in the hippocampus, thalamus, caudate, and fornix (isolated or in combination) have been shown to present with a primary amnestic deficit, which makes these lesions difficult to distinguish from TGA.[1] MRI diffusion-weighted imaging (DWI) is the best study to differentiate between stroke and TGA.[1] Hippocampal punctate enhancement may be seen in TGA, which is distinct from typical cerebrovascular-associated lesions.[1]

The retrosplenial region is composed of the retrosplenial cortex and cingulate bundle. Both structures play a significant role in learning and memory: the cingulate bundle is a component of the Papez circuit, and the retrosplenial cortex shares connections with the anterior thalamus and hippocampus.[2] Anterograde amnesia caused by a lesion in the retrosplenial region was coined "retrosplenial amnesia" by Valenstein et al.,[3] who reported the first case of this phenomenon caused by a ruptured arterio-venous malformation in 1987. Since then, several other cases caused by hemorrhagic stroke have been reported.[4,5] In contrast, there have been very few cases of retrosplenial amnesia caused by ischemic stroke. Lesions to the retrosplenial cortex have also been shown to cause deficits in spatial memory in both animal and human models.[6]

We conducted a systematic literature review of all cases of anterograde amnesia caused by unilateral ischemia of the

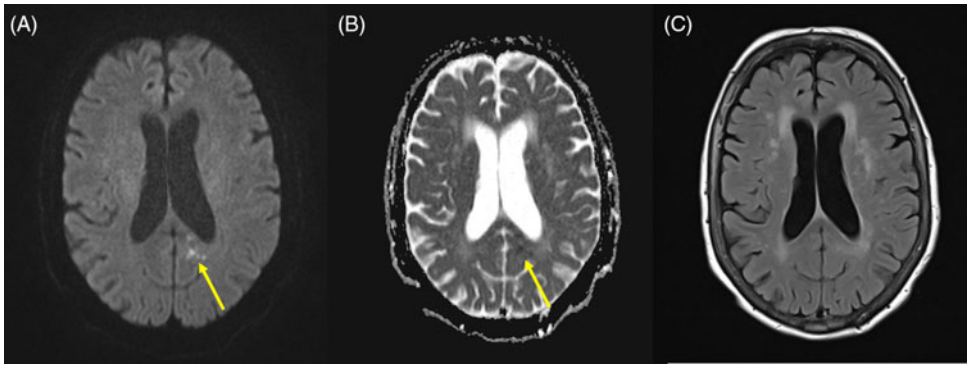

Figure 1: *Axial MRI, DWI (A) and corresponding ADC (B) demonstrate restricted diffusion in the left splenium and retrosplenium (arrow) consistent with acute infarction. T2 FLAIR (C) hyperintensities in diffuse periventricular and subcortical white matter consistent with chronic ischemic changes. DWI = diffusion weighted imaging, ADC = apparent diffusion coefficient, FLAIR = fluid attenuated inversion recovery.*

https://doi.org/10.1017/cjn.2021.6 Published online by Cambridge University Press

Table 1: Cases of transient amnesia caused by unilateral retrosplenial ischemic lesions

Case report	Patient age, gender, handedness	Areas of infarction	Clinical features
Yasuda et al. 1997[2]	39, male, right	Right splenium Right retrosplenial region	Anterograde amnesia, left-hand weakness, left hemiparesis, dizziness, gait disturbance, dysarthria
Saito et al., 2003[7]	58, male, right	Left retrosplenium	Anterograde amnesia, recent retrograde amnesia
Kim et al., 2007[8]	57, male, right	Left retrosplenium Left splenium	Anterograde amnesia, retrograde amnesia, alexia without agraphia

retrosplenial region. PubMed was searched on August 10, 2020 with the search terms (retrosplenial OR retrosplenium OR retrospleni*) AND (stroke OR infarct OR infarct* OR ischemia OR amnesia). Inclusion criteria were: (1) anterograde amnesia was reported as a clinical feature; (2) the lesion was caused by ischemia; (3) the study reported imaging confirmed damage to the retrosplenial region; and (4) the complete manuscript was available in English. Exclusion criteria were: (1) primary subjects were not human; and (2) bilateral lesions. Duplicate studies were removed using the Rayyan systematic reviews web application (https://rayyan.qcri.org).

In total, three case reports were included (Table 1): two left-sided cases and one right-sided case.[2,7,8] Two cases featured focal neurologic-deficits weakness,[2] dysarthria,[2] and disconnection syndromes[8] as red flags suggesting an alternative diagnosis to TGA. Only one case reported ischemic retrosplenial amnesia that presented as a true TGA mimic: Saito et al.[7] described a 58-year-old, right-handed man who presented with severe anterograde amnesia with recent retrograde amnesia. MRI DWI revealed acute ischemic stroke in the left retrosplenium, with mechanism thought to be paradoxical embolism via patent foramen ovale.

Along with our reported case, these cases highlight that retrosplenial infarcts may present with transient, isolated amnesia mimicking TGA. Clinical features suggestive of a TGA mimic in our case included topographic disorientation and awareness of the memory deficit. Topographic disorientation in particular is noteworthy as this finding is typical for lesions to the retrosplenial cortex[6] and is not commonly seen in TGA. Seizure, hypoxia, and psychogenic amnesia are other causes of acute amnesia that can mimic TGA and should be kept in mind when making the diagnosis.[1] Clinicians should have a low threshold for imaging in patients with any atypical features of classic TGA.

Acknowledgments

The authors report no disclosures or conflicts of interest. No financial support was received in writing this article.

Disclosures

The authors have no conflicts of interest to declare.

Statement of Authorship

DM – drafting the original manuscript and performing literature review, MA – drafting the original manuscript and revising the manuscript for intellectual content, JR – revising the manuscript for intellectual content, and TC – conceptualization of the manuscript and revising the manuscript for intellectual content.

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https://doi.org/10.1017/cjn.2021.6 Published online by Cambridge University Press