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CASE REPORT

Recurrent Episodes of Transient Global Amnesia: A Rare Clinical Entity

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Abstract

Transient global amnesia (TGA) is a syndrome characterized by anterograde amnesia with otherwise intact cognitive function, resolving within 24 h of onset, occurring in the absence of neurological changes. Recurrent episodes remain rare. We report an interesting case of recurrent episodes of TGA in a 63-year-old woman presenting with altered mental status. She had no memory of antecedent events and demonstrated repetitive questioning but retained awareness of self. Physical examination and laboratory diagnostics were unremarkable. Brain magnetic resonance imaging revealed scattered foci of increased FLAIR signal within the bilateral periventricular and subcortical white matter. She was notably diagnosed with TGA a few months prior when she had presented with similar symptoms. During the current hospitalization, she remained alert and fully oriented, with resolution of perseveration. This case emphasizes the recognition of TGA as an important neurological diagnosis, uniquely describes not only the recurrence, but the short interval between recurrent episodes.

Keywords: Transient global amnesia, Anterograde amnesia, Memory disturbance, Recurrent amnesia, Perseveration

1. Introduction

Transient Global Amnesia (TGA) is a clinical syndrome characterized by acute onset anterograde amnesia with otherwise intact cognitive function. An episode of TGA resolves within 24 h, occurs in the absence of other neurological changes, and results in an overall recovery of memory function excluding memories related to the episode.[1] Primarily occurring in older adults, the mean age of onset is between 60 and 65 years of age, without reported major gender differences.[2] The annual incidence of TGA in the general population is estimated to be rare at 3.4–10.4 per 100,000 individuals.[1,3] Despite several hypotheses, there is no clear consensus on the underlying etiology. Recurrence of TGA is a somewhat rare phenomenon, with an estimated annual recurrence rate of less than 5.8%.[2] We present an interesting case of recurrent TGA in a 63-year-old woman with acute onset anterograde amnesia lasting several hours.

2. Case description

A 63-year-old female flight attendant presented to the emergency room with altered mental status and a witnessed episode of confusion lasting 4 h. She was found to be wandering outside of her home with no memory of antecedent events. On presentation, she was asking repetitive questions about her current location, yet had retained awareness of self (name/profession), and complained of a mild, diffuse headache. She remembered putting on make-up and dressing herself earlier that day. She appeared to be doing some yard work, in the afternoon, and was subsequently found wandering around in the yard, confused, by her roommate.

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Given this alteration in her mental status, emergency services were called, and she was brought to the hospital.

Over time, her confusional state resolved, but she continued to have amnesia with no memory of antecedent events. She denied any focal numbness, weakness, changes in speech or visual disturbances, fevers, chills, lightheadedness, or dizziness. Her medical history was remarkable for diabetes mellitus and depression. She denied tobacco, alcohol, or recreational drug use. She was notably diagnosed with TGA a few months prior at a hospital in her home state when she had presented with similar symptoms. At that time, laboratory workup including ethanol and toxicology screening, erythrocyte sedimentation rate and C-reactive protein were within normal limits. She had a non-contrast computed tomography (CT) scan of the head and non-contrast magnetic resonance imaging (MRI) of the brain, which did not reveal any acute intracranial abnormality. The episode had lasted about 7 h. She was evaluated by neurology, diagnosed with TGA and discharged home the following day. Prior to this current event she had returned to her baseline and experienced no further issues in the interim.

On initial physical examination, she was alert and oriented to person, place, time, and situation. She had persistence of repetitive questioning. She had no focal neurological deficits and an intact cranial nerve exam. Strength was 5/5 in all extremities and sensation to light touch was normal. Deep tendon reflexes were 2+ throughout and Babinski reflex was down-going bilaterally. Initial laboratory diagnostics were largely unremarkable except for a mild elevation in aspartate aminotransferase (56 units/L; reference range: 0–33 units/L). Urine toxicology and ethanol level were unremarkable. Urinalysis did not reveal evidence of infection. Initial diagnostic imaging included a non-contrast head Computed Tomography (CT) which showed no acute intracranial abnormality and a CT angiogram of the head and neck which revealed no perfusion defect, no large vessel occlusion, and no hemodynamically significant stenosis or aneurysm intracranially or within the neck arterial circulation. She was admitted to the hospital for further evaluation and management.

While hospitalized, the patient's mental status remained the same including her anterograde amnesia. She remained alert and oriented to person, place, time, and situation, with a stable neurological exam, and resolution of perseveration. Further diagnostic workup revealed unremarkable Vitamin B12 level, thyroid stimulating hormone/free T4, and syphilis screening. A subsequent non-contrast Magnetic Resonance Imaging (MRI) of the brain revealed no acute infarct or hemorrhage but noted scattered foci of signal abnormality within the bilateral periventricular and subcortical white matter, likely due to chronic microvascular ischemia (Fig. 1). Given the negative diagnostic workup and unclear etiology of symptoms, Neurology was consulted for further evaluation. Given her past medical history, acute onset of anterograde amnesia, unremarkable laboratory studies and negative imaging, she was diagnosed with a recurrent episode of TGA. She was discharged from the hospital in stable condition, with planned outpatient follow-up with her primary care provider and neurologist.

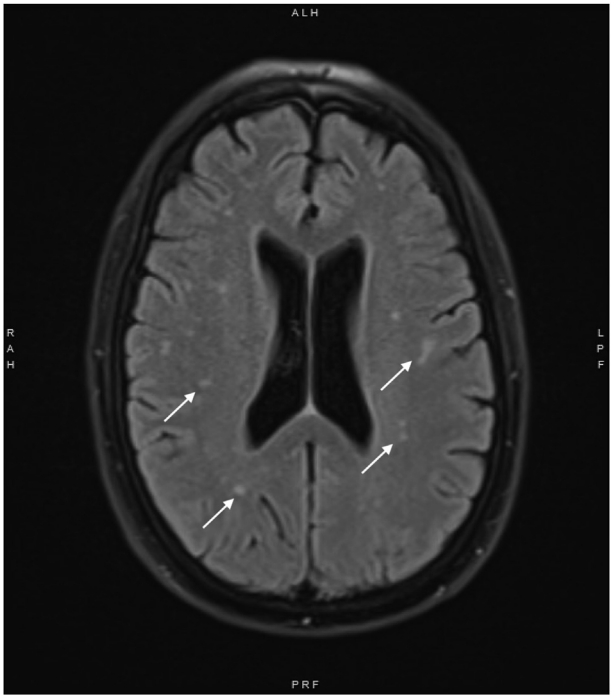

Fig. 1. MRI brain without contrast showing no acute infarct or hemorrhage, but scattered foci of increased FLAIR signal (white arrows) within the bilateral periventricular and subcortical white matter.

3. Discussion

TGA is a rare clinical syndrome characterized by the acute onset of anterograde amnesia, characterized by the inability to form new memories, that can last up to 24 h.[1] It is seen most often in the middle aged and elderly, with an annual incidence of 23.5 per 100,000 in adults over 50 years old (annual incidence of 3.4–10.4 per 100,000 people in the general population).[1] Patients typically present with acute confusion, amnesia, and repetitive questioning (specifically regarding location or environment), often without any focal neurologic deficits or

epileptic features and with intact cognition.[1,4] Episodes of TGA are often preceded by a stressful event, any activity associated with the Valsalva maneuver, sexual intercourse, or pain.[1] A patient with TGA may appear restless on examination but alert and able to communicate.[1,4] Although the patient remains unaware of their situation, their personal identity, procedural memory (learned memory, such as the ability to drive), ability to recognize family members, speech, motor, and sensory functions are all preserved.[1,4] There have been no specific risk factors identified, but TGA may occur more often in patients who experience migraines.[1] Notably, our patient did not have a history of migraines but was noted to have a headache associated with her event.

The differential diagnosis for TGA includes transient ischemic attack (TIA), stroke, seizure (specifically transient epileptic amnesia), dissociative fugue, or other psychogenic causes.[1] TIA or stroke typically present with more neurologic deficits rather than amnesia alone, and should be considered in patients with vascular risk factors.[1] Episodes of transient epileptic amnesia are often much shorter in duration than TGA (<1 h as opposed to 4–6 h on average for TGA), recurrent, and typically present with retrograde amnesia rather than anterograde amnesia.[1,2,5] Psychogenic amnesia or dissociative amnesia often presents with loss of autobiographical memories such as personal identity, which is not present in TGA.[5]

While the pathophysiology of TGA remains poorly understood, multiple theories have been proposed focusing on vascular, epileptic, and migraine-related origins. The vascular mechanisms described for TGA are either from arterial ischemia or impaired venous flow. The more prominent vascular theory suggests that venous congestion caused by retrograde flow during Valsalva in a patient with incompetent venous valves, results in congestion in the mesial temporal lobes which houses the hippocampus and CA1 neurons. Hippocampal CA1 neurons are exquisitely sensitive to metabolic and ischemic insults, and given their unique role in new memory formation, stress in this area may result in transient anterograde amnesia.[1]

Multiple studies have shown that of those who experience an episode of TGA, women with a history of migraines are at an increased risk.[6] Cortical spreading depression, a widespread neuronal depolarization that can affect the excitability of the CA1 neurons in the hippocampus, is a common feature of migraine headaches and may predispose to aberrations in anterograde memory.[1,7] Although temporal lobe epilepsy with subsequent post-ictal confusion, known as transient epileptic amnesia, can resemble an episode of TGA, transient epileptic amnesia is usually much shorter and recurrent.[1] Electroencephalogram (EEG) findings during an episode of TGA are normal and the use of EEG during an episode of TGA is not recommended.[1]

Neuroimaging is often performed in these patients who present with acute onset amnesia and the findings are often normal on CT. On MRI, in contrast, punctate hyperintensities in the hippocampus on diffusion-weighted imaging (DWI) have been reported.[1,2,8] Correspondingly, multiple studies have discussed whether arterial ischemia is the underlying mechanism for TGA,[2,8] however, these findings are inconsistent and they do not persist over time.[1,8] Furthermore, although DWI is sensitive for ischemia, it is non-specific, and punctate hyperintensities have been seen in other disorders such as seizure, metabolic disturbances, and cortical spreading depression.[1,2,8] A prior study investigating the diagnostic utility of functional MRI during and after recovery from TGA reported scene-encoding deficits in a temporolimbic circuit, recovering over time, as well as recruitment of frontoparietal areas during the amnestic state.[9]

Treatment for TGA remains supportive, given its self-limiting nature, with symptoms generally resolving within 24 h. Initial workup generally includes evaluation of multiple etiologies of altered mentation with imaging including an DWI sequence MRI for evaluation of ischemia.[10] Recurrent episodes of TGA remain somewhat rare. One retrospective cohort study found a recurrence rate of 13.7% and furthermore highlighted that migraines were more associated with recurrence.[11] In this study, the mean time interval between the initial TGA episode and the recurrence was 4.1 years,[11] which appears to be congruent with other studies published in smaller cohorts.[12] Our case is unique not only in the context of the TGA recurrence, but the short interval delay between the recurrent episodes.

Data availability statement

Patient information was accessed through medical records at MedStar Health and is unavailable for release due to patient confidentiality.

Notes on patient consent

Consent for publication has been obtained and the individual who is being reported on is aware of the possible consequences of that reporting.

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Conflict of interest

None of the authors have any conflicts of interest.

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