ONLINE EXCLUSIVE

Sudden onset of amnesia in a healthy woman

Our patient's prolonged inability to recall events of the day was not associated with any other neurologic deficits.

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CASE ▸ A 63-year-old woman came to our emergency department with her fiancé following an abrupt onset of confusion that began 1 hour earlier. The patient had been working outside in the yard when she approached her fiancé, repeatedly asking where she was and what she was doing. She remained conscious of her identity, however, and exhibited no other neurologic symptoms, such as muscle weakness, gait imbalance, sensory loss, vision changes, slurred speech, or facial droop. The fiancé did not witness any loss of consciousness, head trauma, or seizure-like activity.

Before the event, the patient was feeling well, without any fever, headache, emesis, or vertigo. She denied using tobacco, alcohol, or illicit drugs. Her medical history was unremarkable, including an absence of diabetes, hypertension, and hyperlipidemia. The only significant finding in her family history was a stroke her mother experienced at an advanced age. During our interview, the patient remained confused about where she was and what was happening. She was aware of her confusion and distressed by it.

On examination, the patient was alert and oriented to self and year. She appeared appropriately anxious about her situation. She was afebrile and slightly hypertensive. Her other vital signs were normal. She could not recall events immediately preceding her arrival at the emergency department, but could recall events of the day before and earlier. There was no evidence of trauma. Head, neck, cardiovascular, lung, and abdominal exams were within normal limits.

Her neurologic exam revealed intact cranial nerves, symmetric face, 5/5 muscle strength in all extremities, intact sensation, and normal gait. Grossly, visual fields were intact. There was no Babinski sign, clonus, or pronator drift. She had 3/3 immediate recall of named objects, but 0/3 recall at 5 minutes. Results for complete blood count, basic metabolic panel, and urinalysis were within normal limits, including a blood glucose level of 77 mg/dL and a low-density lipoprotein level of 161 mg/dL. The result for cardiac enzymes was negative. Noncontrast computed tomography of the head revealed a remote pontine lacunar infarct.

WHAT IS THE MOST LIKELY EXPLANATION FOR HER CONDITION?

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Transient global amnesia

We admitted the patient for further evaluation with a presumptive diagnosis of transient global amnesia (TGA).

With a chief complaint of amnesia, the differential diagnosis is broad (**TABLE 1**).[1-3] In this case, a stroke was unlikely given the absence of neurologic deficits, specifically the lack of visual field defects. The elapsed time of her symptoms was too long for a transient ischemic attack or seizure. There was no supporting evidence for encephalitis, intracranial bleed, or hypoglycemia. While delirium could be considered, its characteristic features of inattention and a waxing and waning course were not present, nor was there any obvious underlying cause, such as infection or polypharmacy. The patient had no loss of self-identity that would suggest a psychogenic cause. The time course and the patient's symptoms were congruent with the clinical criteria for TGA, and we confidently based our diagnosis on this.

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Type of memory loss as a clue to cause

Amnesia occurs when memory and learning in an alert person are impaired to a degree out of proportion to the person's overall neurologic status. It may affect the formation of new memories (anterograde amnesia) or the recall of past memories (retrograde amnesia).

How memory works. Memory can be broken down into categories (**TABLE 2**).[1] Explicit memory requires a conscious effort to recall. An example is episodic memory, in which memories are framed within a context, such as recalling what was served for dinner the night before. Its function is critical to creating new memories. Other forms of explicit memory are semantic memory—memorized facts that are independent of a context—and working memory, in which focused attention is used to manipulate information. Implicit memory operates subconsciously. The prime example is procedural memory, involving the ability to learn new skills and perform them without total concentration.

Memory function affected in TGA. In TGA, episodic memory—critical in the laying down of new memories—is most affected. Episodic memory relies heavily on the hippocampus to function correctly. When it dysfunctions, a person cannot consolidate and retain new information, thus resulting in anterograde amnesia.[1]

Retrograde amnesia generally requires dysfunction of the frontal lobe in addition to the temporal lobe.[3] However, it may be present concurrently with anterograde amnesia when a lesion is isolated to the hippocampus; it is usually limited to more recent memories.

TABLE 1

Rule out these disorders with acute anterograde amnesia[1-3]

Transient ischemic attack
Delirium
Intoxication or alcohol/drug withdrawal
Concussion
Intracranial bleed
Complex partial seizures
Postictal state
Hypoglycemia
Encephalitis
Transient global amnesia
Psychogenic amnesia
Wernicke's encephalopathy

TABLE 2

Categories of memory function[1]

Explicit memory: requiring conscious effort to recall information.
Episodic memory: memory is framed within a context, such as recalling a meal from the night before.
Semantic memory: hard facts—eg, the capital of your home state.
Working memory: a higher functioning requiring attention to allow for information to be manipulated.
Implicit memory: recall is done subconsciously.
Procedural memory: contains skills, such as driving.

That recent memories tend to be the more vulnerable is known as Ribot's law. If retrograde amnesia is present, it usually resolves before anterograde amnesia.[4]

In TGA, procedural memory is unaffected. Thus, activities of daily living and instrumental activities of daily living remain intact—eg, the patient retains the necessary skills to drive a car.

Most often the prognosis is good

TGA is an unusual manifestation of anterograde amnesia that is self-limited and tends not to recur.[5] An episode typically lasts 1 to 8 hours.[6] Although the disorder was first described in 1956, a set of clinical criteria (**TABLE 3**) was not defined until 1990.[7] The highlights of these criteria are that self-identity is preserved and no evidence exists for neurologic deficit or seizure activity.[6] The incidence of TGA is 3 to 10 in 100,000.[5] TGA usually affects patients in their early 60s,[2] and men and women are affected equally.

Interestingly, more than half of patients with TGA report a precipitating event, usually involving physical activity or a Valsalva maneuver.[6] Classically, the patient repeatedly asks the same questions. The most common associated symptoms are headache, dizziness, and nausea.[2,6]

Generally, the patient's prognosis is good, without long-term sequelae. Importantly, reassure patients and their families that there will be no memories of the event itself, as their memory-making ability was impaired.[2]

If episodes do recur

A small subset of people may have recurrent episodes. Recurrence rates over a 5-year span have been reported as 3% to 26%; however, this range includes cases and studies recorded before the diagnostic criteria were developed in 1990.[6] Although the clinical criteria for TGA can be helpful in diagnosing the disorder, there is no standardized workup because TGA has no clear etiology or known underlying mechanism. Many causal theories exist, however, and have evidence to support them.

TABLE 3

Clinical criteria for transient global amnesia, as defined by Hodges and Warlow[7]

Amnesia must be witnessed by another
Acute onset of anterograde amnesia
Patient is alert—no change in consciousness
No loss of personal identity
No focal neurologic deficits
No recent history of head trauma or seizure
Amnesia resolves in 24 hours

Possible underlying conditions. One proposed explanation is ischemia of the hippocampus. This raises questions of whether vascular risk factors place people at higher risk.[8] Recent studies have not confirmed this theory, and patients with diabetes, hypertension, or hyperlipidemia appear not to be at higher risk of TGA. Still, it is interesting that TGA is a disease affecting older adults and that evidence of small-vessel ischemia is often discovered incidentally.[6,8]

On the other hand, some experts take into account the high association of TGA with migraines documented in multiple studies, and therefore propose a spreading depression as the cause.[5] Another hypothesis is a valvular insufficiency of the jugular veins that allows reflux, resulting in venous ischemia of the hippocampal area, especially during a Valsalva maneuver.[9] Indeed, jugular valve insufficiency has been noted in up to two-thirds of TGA patients. However, if valvular insufficiency is truly the mechanism of disease, why do recurrence rates remain so low?[10]

MRI may be helpful. Given the many theories of TGA origin, several imaging mechanisms have been tried with mixed results: single photon emission computed tomography, magnetic resonance imaging (MRI) with diffusion-weighted imaging, and positron emission tomography.

The lack of reliable results makes it difficult to establish diagnostic criteria. Some generalized guidelines are as

In TGA, episodic memory—critical in making new memories—is affected.

follows:

If there are any neurologic findings or concern about a transient ischemic attack or cerebrovascular accident, obtain an MRI. This should include diffusion-weighted imaging, which may reveal a transient lesion in the hippocampus.[6] If the patient has recurrent episodes, or has episodes that last less than 1 hour, suspect the possibility of seizure and consider arranging for an electroencephalogram.[4,6] Likewise, recurrence may also be due to a patent foramen ovale (PFO) causing paradoxical emboli and transient ischemia of the hippocampus. In 1 study, the rate of PFO in the TGA arm was 55%; it was 50% in those with recurrent episodes.[11]

PRACTICE POINTERS

- Order an MRI if your patient with a suspected case of TGA has any neurologic findings or if you are concerned about transient ischemic attack or cerebrovascular accident.
- If the patient has had recurrent episodes, or has episodes that last less than 1 hour, suspect the possibility of seizure and consider an electroencephalogram.
- Reassure TGA patients that there will be no memories of the event itself, as their memory-making ability was impaired, and that there are no long-term sequelae.

Although the clinical criteria can aid in diagnosis, there is no standardized work-up for TGA.

Our patient's outcome

In the 24 hours after admission, the patient's anterograde amnesia gradually resolved. She was able to remember the medical staff caring for her and retain orientation to her situation. However, she was unable to regain memories of the events immediately surrounding the onset of amnesia. During her hospitalization, the patient underwent a thorough work-up, including carotid artery Doppler ultrasound and echocardiogram with agitated saline (bubble study), both of which yielded normal results. Her MR angiography showed patent cerebral vessels. As mentioned, an MRI of the head showed a remote lacunar infarct of her left upper pons and nonspecific subcortical white matter disease was noted, consistent with chronic small vessel disease. The patient was discharged with reassurance, and she has done well. JFP

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