A 75-Year-Old Man With Memory Loss

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Introduction. The wife of a 75-year-old previously healthy man calls her internist to report her husband's acute episode of what she calls "confusion".

Patient history. Detailed questioning while obtaining the patient's medical history revealed the actual symptom as loss of memory for any events during approximately the last 24 hours. For example, on the morning preceding the event, the patient had placed several folders on his table that were due the next day at his accounting office. When he saw them in the evening, he repeatedly asked his wife about the folders and their due date. Still, he managed to spend the afternoon golfing without any problems and drove himself home without issues before returning home in the evening.

The patient's wife brought him to the office, but there was no complaint of pain or other neurologic symptoms. His personal medical history was unremarkable with no diabetes mellitus, cardiovascular disease, nor chronic medicines other than a statin. The patient did not have bowel or bladder incontinence nor ocular/auditory manifestations. A phone call to a golfing partner revealed he was asymptomatic and fully alert at the end of the golf round.

Physical examination. The patient's physical examination was unremarkable. He did not have an elevated temperature, and all vital signs were within normal ranges. An oral examination showed no evidence of tongue or lip biting. He was awake, alert, and in no distress. He was, however, questioning where he was and how he had gotten there.

Diagnostic examination. A thorough neurological examination was within normal ranges with no signs of paresis, deficits, or lateralizing. He was sent for an urgent head CT, which was preliminarily reported as unremarkable.

Correct Answer: D. He is experiencing an episode of transient global amnesia.

The details surrounding the patient's history, examination, and preliminary radiology are consistent with the diagnosis of transient global amnesia, an unusual, but not completely rare diagnosis. Indeed, there are recent reviews of the entity with emerging guidelines for diagnosis and evolving imaging data to help confirm such findings.[1,2] Although new data on useful imaging studies are emerging, the diagnosis is still made on clinical findings and involve the following:[2]

- An attack is witnessed by another individual
- Dysfunction is limited to repetitive queries and amnesia
- No other major neurologic signs or symptoms (e.g., consciousness, focal signs, epileptic seizure, head trauma)
- Memory loss is transient, usually lasting hours to a day.[2]

These criteria fit the presented patient well and make Answer D the most likely correct diagnosis. The absence of any neurologic symptoms or signs over the course of the event and evaluation along with a clean CT essentially excludes stroke or brain hemorrhage (Answer A). There is no antecedent history or physical findings of head trauma, so this is not a concussion related event (Answer C). Although he manifests anterograde memory loss, he is not confused in that he knows who he is, recognizes his wife, and even his longtime friend and physician. Further, he denies classical auditory/visual aura phenomena, so a seizure or atypical migraine (B and E) are unlikely here.

Discussion. Transient global anesthesia has an epidemiology of peak incidence in the seventh decade, and a slight preponderance for men. If there are any genuine "risk factors" associated, they are migraine history and perhaps the standard cardiovascular risk factors seen in patients in the 60-75-year-old population.[1] The syndrome typically occurs suddenly, with acute anterograde memory loss in an otherwise awake, alert patient and no other practical explanation. Transient acute memory loss has a differential diagnosis including variants of epilepsy, stroke/transient ischemic attack, or variants of migraine syndromes. However, none of the characteristics associated with these diagnoses–obtundation, confusion, lateralizing neurologic findings, visual/auditory aura, or head trauma–will be present. In fact, their absence is required to make a diagnosis of transient global amnesia.[3]

Although termed "global", the amnesia is quite specific. What is global is the amnesia for all events in the previous hours to, at most, a few days prior to onset. More distant memory for person, events, education, and skills are not lost. The "transient" aspect of

the syndrome name is a brief period from 2 to 24 hours. The lost memory period shrinks over that time period with essentially complete resolution and recovery in all cases.[3]

There certainly are many conditions of acute and temporary memory loss that, on the surface, are initially in the differential. But generally, these conditions–post-concussive, non-convulsive seizures, migraine syndrome–will have accompanying symptoms and recognizable associated findings/history to separate them from transient global amnesia.[3]

In the era prior to MRI brain imaging, the ubiquitous cerebral CT scanning tests for essentially all neurological situations, (e.g. stroke, brain hemorrhages), was normal/negative in transient global amnesia cases. In fact, such negativity was deemed part of making the decision on the diagnosis. But new studies and technology beget new data, and although subtle, MRI technology seems to have yielded a positive finding in transient global amnesia. That finding is a punctate lesion in the hippocampus (the area of the brain associated with memory formation) which is delayed in appearance by 12-48 hours.[4] This perhaps explains why it was not noted in earlier brain imaging studies. In a reasonably large (390 patients) study, punctate lesion in the hippocampus area was found in 70% of cases that had been clinically diagnosed as transient global amnesia.[5] The exact place for this finding, and its degree of sensitivity, remain to be seen.

What's The Take Home? Transient global amnesia is an uncommon, but not rare, neurological syndrome characterized by acute onset of anterograde amnesia of recent events, which is generally reversible within 24 hours. The sole neurological deficit is the anterograde amnesia, and the only "findings" accompanying this diagnosis would be repetitive questioning by the patient such as "Where am I? How did I get here?" Their neurological amnesia dysfunction is limited to recent events, as they are able to remember who they are and can function with their prior training and life experiences.

A convenient set of clinical diagnostic criteria includes the attack episode being witnessed, the amnesia and repetitive questioning being the only neurologic dysfunction, absence of any other neurologic etiologies (seizure, head trauma, focal findings), and reversible and self-limiting (transient) time course of about 24 hours or less. Routine CT imaging does not show signs of this finding, but refined MRI imaging has been shown to manifest small lesions in the hippocampus region, which are delayed and do not appear until 12-48 hours after the event. The major candidates for pathophysiology for the syndrome are vascular and/or migraine based but remain conjectural and unknown at this time. The prognosis is good, with essentially 100% reversion to normal memory within a day or so and no apparent long-term risk for increased later vascular or seizure events.

Patient Follow-Up. The initial onset of symptoms had been approximately 5 pm on Day 1. After returning home from the emergency room at about midnight, some memory had returned. By mid-morning, 10 am, on Day 2, anterograde memory was essentially complete. The patient remained neurologically intact and is currently symptom free at 9 months.

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