Transient global amnesia: Minor inconvenience or early warning sign?

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Transient global amnesia (TGA) is a clinical diagnosis and is often a diagnosis of exclusion. However, despite the benign nature of this condition, it has been associated with underlying life-threatening medical conditions (e.g., myocardial infarction, dissecting aortic aneurysm, arrhythmias). Our case report highlights the importance of early recognition of those with cardiovascular risk factors who present with acute onset altered mental status to look for underlying medical comorbidities.

Keywords: Transient global amnesia, Myocardial infarction, Sympathetic surge

1. Introduction

Transient global amnesia (TGA) is a clinical diagnosis characterized by the sudden and reversible onset of anterograde amnesia accompanied by repetitive questioning without associated focal neurological deficits, usually occurring in the middle-aged or elderly population. Although TGA is relatively benign, underlying life-threatening medical conditions (e.g., myocardial infarction [1–3], dissecting aortic aneurysm [4,5], arrhythmias [6], tumor [7]) have been associated with TGA and should be considered to prevent catastrophic outcomes. We report a case of TGA with underlying non-ST-elevation myocardial infarction (NSTEMI).

2. Case report

A 69-year-old female with past medical history of hypertension being treated with metoprolol, presented with an acute episode of altered mental status. Emergency medical service was called once the staff at the facility noticed she was suddenly confused. She was noted as having a ''moment of memory lapse'', then appeared disoriented with repetitive queries. No other neurological symptoms or signs were reported. At baseline, she is fully conversant and entirely independent in activities of daily living. She recalled waking up in her usual state of health and going to the nearby senior center, as she frequently does for daytime activity since the passing of her husband this past year. She previously spent all her time

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caring for him because of his advanced Alzheimer's. She also reported increased stress recently due to her computer classes at a local public school. In addition, she had been having suboccipital pressure sensation and notably had migraines in the past, but denied any migraines or headaches for several years now. She also denied any dizziness, anxiety, nausea, paresthesia, chest pain, shortness of breath, abdominal pain, dysuria, or any other symptoms.

Upon arrival to the emergency department, she was found to be hypertensive to 171/79 mmHg. On examination, she continued perseveration of the same questions/statements (What happened? Where did I come from? Who brought me here?). Otherwise alert and oriented to person, place, and time with no aphasia or cognitive deficits. Physical examination revealed no focal neurological or epileptic signs or symptoms. A brain computed tomography without contrast showed diffuse cerebral atrophy, otherwise no acute findings or prior infarcts. Biological parameters and diagnostic tests ruled out metabolic disorders (i.e., hypoglycemia, hypocalcemia), infection, fluid/electrolyte derangement as underlying etiology of her acute presentation and the lack of disturbance of consciousness and altered cognition excluded delirium. However, her troponin was elevated to 0.79 ng/mL (normal $\leq$0.04 ng/mL). Aspirin (ASA) was given and the patient was admitted for elevated troponin. Repeat troponin began to trend up so she was placed on a heparin drip. Troponin peaked to 3.06 ng/mL and electrocardiogram revealed T-wave inversions in the anteroseptal leads (more prominent in V1) and mild ST-segment (<1 mm) elevations in the inferior leads, therefore cardiology was consulted.

Given the elevated troponin as a sign for stress and the preservation, neurology was consulted to evaluate for possible TGA. A neurologist evaluated the patient and she demonstrated poor short-term memory with anterograde amnesia. Immediate recall was 3/3; delayed recall 0/3 which improved to 2/3 after many prompts/guessing. According to neurology, the clinical picture was consistent with anterograde amnesia of short-term memory and given psychosocial stressors including recent loss of husband, and current occipital headache with prior history of migraines. TGA appeared most likely; however, neurology also considered the possibility of complex partial seizure(s), and could not rule out small new infarct.

On follow-up evaluation the next morning, 12 hours after presentation, the patient remained hemodynamically stable. When asked why she was brought to the hospital, she stated ''my mind wasn't working'' and was told that she was asking the same questions repeatedly. The patient remembered going to the senior center to practice a salsa dance performance for an upcoming event. She stated having a vague recollection of being there but had no idea how she got to the hospital or where her belongings were. On mini-mental status examination, she was awake, alert, and oriented to person, place, time, and could state her birthday but indicated that she was 48 years old. Her speech was fluent without dysarthria. She could name, repeat, and follow complex commands crossing the midline, able to say the months of the year in reverse, and did not repeat questions. Immediate recall was 3/3, delayed recall 1/3. The amnesic gap resolved within 18 hours from the onset of symptoms.

Close work-up unveiled non-ST-elevation myocardial infarction and the patient subsequently was admitted to the cardiac care unit where a transthoracic echocardiogram estimated global left ventricular ejection fraction at 25% with severe left ventricular systolic dysfunction and delayed diastolic relaxation. A coronary angiogram performed later demonstrated nonobstructive coronary artery disease.

Nearly 24 hours after the initial presentation; the patient appeared to be making new memories and returning to baseline. There was no indication for further neurologic workup. Troponin I down trended to 2.92 ng/mL and repeated electrocardiograms were unchanged from admission. She was safely discharged from the hospital on the 2nd day with routine post myocardial infarction treatment and follow-up.

3. Discussion

This case of TGA appeared to be secondary to an acute myocardial infarction. To date, three previous cases of TGA presenting along with or as a manifestation of acute myocardial infarction have been reported in the literature [1–3].

We report a case on a 69-year-old female with sudden onset altered mental status with anterograde amnesia and repetitive queries. Other than suboccipital headache, there were no focal neurological or epileptic deficits. There were no cardiac symptoms on admission or at any time during her hospital stay. She recovered from her amnestic state within 24 hours of presentation of symptoms and the findings were consistent with the diagnostic criteria for TGA as established by Caplan and

Hodges [8]. Therefore, NSTEMI and psychosocial stressors leading to TGA was postulated.

The pathogenesis of transient global amnesia remains ambiguous and the leading hypotheses centers on ischemia, seizure/epileptic discharge, TIA, and a migrainous phenomenon as possible etiologies [9]. It was previously surmised that arterial thromboembolism in patients with vascular risk factors could have attributed to the ischemic events leading to TGA [10]. These cardiovascular risk factors potentiate events such as atrial fibrillation and myocardial infarction, which are associated with intracardiac thrombus formation, and are potential sources of emboli [11,12]. Although it is plausible that the left ventricular dysfunction noted in our patient may have led to blood stasis and eventual thrombus formation, however, no such findings was noted on the echocardiogram making arterial embolism a less likely cause of TGA.

The previous suggestion of arterial thromboembolism contributing to the events of TGA were seen in certain patients with low blood pressure leading to hypoperfusion of the hippocampal tissues. However, other patients were shown to have hyperperfusion of the medial temporal region upon single-photon emission computed tomography (SPECT) performed during or immediately after an episode of TGA [10,13]. The discrepancies were attributed to the timing of the imaging studies with respect to the chronology of each individual TGA event, nonetheless, the transient hyperperfusion revelation strengthened the belief that either a migrainous phenomenon or an epileptic development may be involved in the pathogenesis as increased cerebral blood flow have been observed in those settings [14]. No SPECT scans were performed on our patient but of note, she does have a history of migraines.

Triggering circumstances such as highly emotional events/stress, physical exertion (e.g., Valsalva maneuver, painful experience), driving a motor vehicle, and sexual intercourse have been reported as possible etiology of TGA [15]. These circumstances have one thing in common; it causes a sympathetic surge leading to increased epinephrine and norepinephrine, which are potent vasoconstrictors of vascular adrenergic receptors. Arteriole vasoconstriction of the carotid arteries can transiently impede blood flow to the hippocampus and medial temporal lobe, considered the elementary sites of involvement in TGA, leading to its manifestation. Additionally, increased sympathetic activity has been associated with upregulation of clotting factors and helper T-cell cytokines inducing a hypercoagulable and thrombogenic state [16]. The inflammation associated with cytokine activation is believed to disrupt atherosclerotic plaque stability and may progress to the carotid arteries resulting in possible cerebral ischemia [17]. Inflammation in the form of leukocyte degranulation following myocardial ischemia has also been linked to cerebral ischemia due to leukocyte plugging [18]. As alluded to by Agosti et al. [3], acute myocardial infarction can trigger elevated sympathetic activity, which may be the pathophysiology.

The four chambers of the heart are abundantly distributed with sympathetic nerves that relay information between the brain and the contracting myocardium. Hyperactivity of the sympathetic nervous system has been implicated in heart failure due to abnormalities in the cardiovascular reflexes [19]. Our patient demonstrated impaired left ventricular function (EF 25%) with nonobstructing coronary arteries and this can be attributed to amplified cardiac sympathetic afferent output postacute myocardial infarction causing functional changes in the cardiac myocytes precipitating left ventricular systolic dysfunction [20]. Furthermore, the systemic vasoconstriction and increased venous tone from sympathetic stimulation can explain the elevated blood pressure seen in our patient on arrival to the emergency department. The tension on the myocardial wall from pressure overload possibly exacerbated the subendocardial ischemia and the insult led to eventual troponin leak [21].

A sympathetic efflux can occur as early as 3 hours after an acute myocardial infarction and we are speculating that this postinfarction surge contributed to the manifestations of TGA [22]. This case report as well as the others mentioned in the literature have important clinical implication as early recognition of TGA or anyone presenting with acute alerted mental status or confusion, especially ones with cardiovascular risk factors, should be evaluated carefully for potential underlying medical comorbidities.

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