

Amnestic syndrome due to bilateral isolated sequential hippocampal infarctions: A case presentation

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Abstract

Transient global amnesia, acute ischemic stroke, seizures and status epilepticus, limbic encephalitis and various types of encephalopathies are included in differential diagnosis of acute-onset amnestic syndrome. Isolated hippocampal infarction is a rare cause of acute-onset amnestic syndrome. In this case presentation, we report a patient who developed permanent and severe cognitive impairment after acute-onset amnestic syndrome due to bilateral isolated hippocampal infarctions occurring nine months apart and a review of the pertaining literature is presented.

Keywords: Hippocampus, infarction, neuropsychological test, amnestic syndrome

INTRODUCTION

The hippocampus is a part of the limbic system, which is mainly involved in episodic memory. It has an important role in the consolidation of information in short- and long-term memory and spatial navigation processes (1).

Blood supply of the posterior two-thirds of the hippocampus originates from the anterior, middle, and posterior hippocampal arteries, which are branches of the posterior cerebral artery (PCA). The anterior one-third of the hippocampus receives arterial blood from the anterior choroidal artery, which has a highly variable anatomic distribution (2).

Acute neurologic disorders including transient global amnesia (TGA), acute ischemic stroke, seizures and status epilepticus, limbic encephalitis (paraneoplastic subtype, non-paraneoplastic subtype, which is mainly caused by voltage-gated potassium channel antibodies or infectious subtype) and encephalopathies due to anoxia, and various causes may affect the hippocampus (3).

We report a patient who developed permanent and severe cognitive impairment after acute-onset amnestic syndrome due to bilateral isolated hippocampal infarctions occurring in two episodes nine months apart.

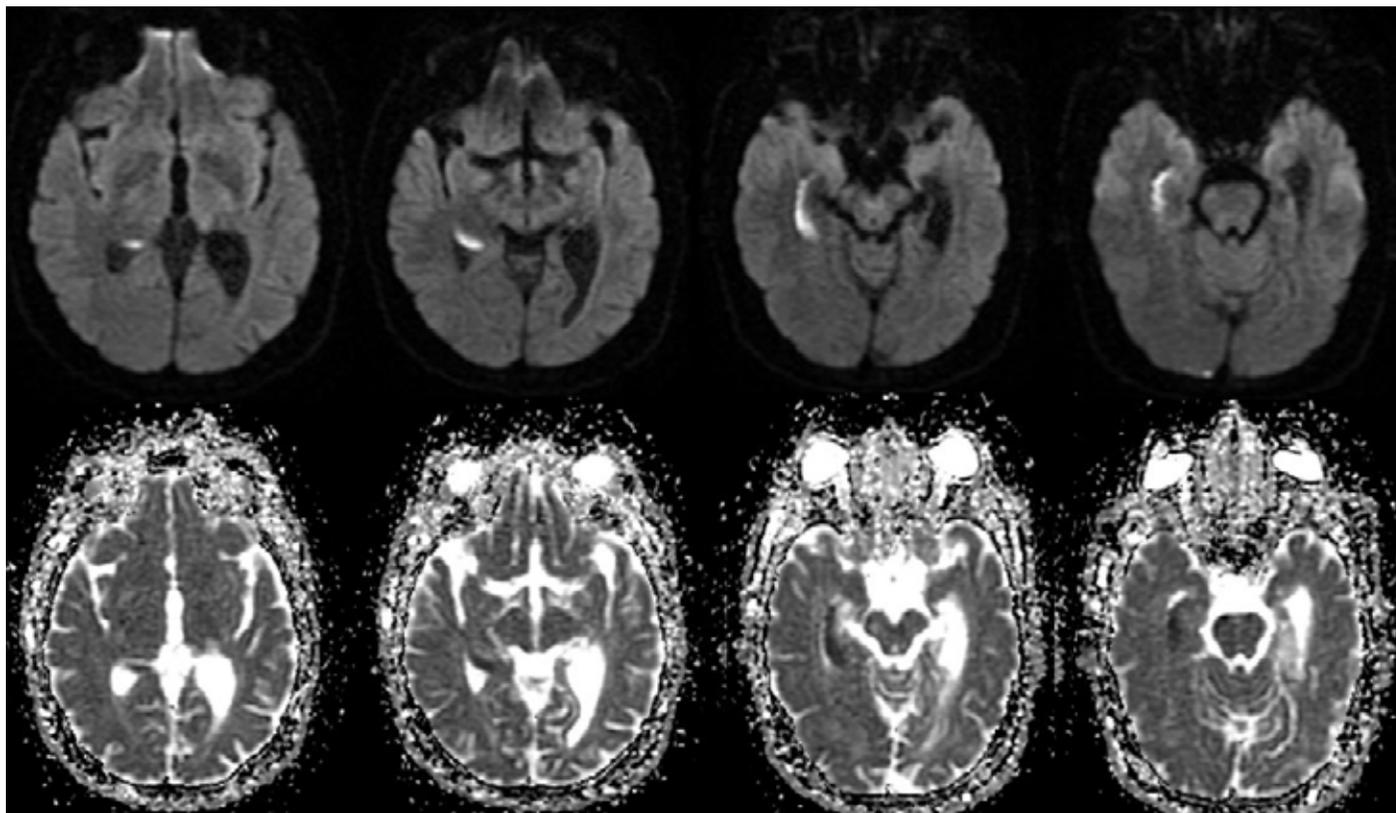
CASE PRESENTATION

A 61-year-old man was admitted to the emergency service with acute-onset episodic memory deficit. He repeatedly asked the same questions despite being answered each time. In the neurologic examination, anterograde and retrograde amnesia were evident. The patient was unable to recall recent events such as his hospitalization due to a myocardial infarction one month ago. His somatic neurologic examination was otherwise unremarkable.

The patient had hypertension and ischemic heart disease and he had been admitted with a similar amnestic syndrome and numbness of the right arm nine months ago. His forgetfulness improved in a couple of months but the numbness of the right arm persisted. He had stopped using antiplatelet treatment, which had been initiated 9 months ago.

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Figure 1. Acute infarction in the right hippocampus in diffusion (above) and ADC (below)-weighted MRI.

Diffusion-weighted magnetic resonance imaging (MRI) showed acute right hippocampal infarction (Figure 1). Intravenous thrombolytic and/or endovascular treatment could not be given because he had presented to the emergency department 8 hours after the beginning of his symptoms. Acetyl salicylic acid (300 mg) was administered. His blood glucose level was 499 mg/dL and insulin treatment was administered. He had not been previously treated for diabetes mellitus, his glycated hemoglobin (HbA1C) was 10%.

The cranial MRI that was performed 8 months ago showed encephalomalasic changes in the left hippocampus and enlargement of the adjacent lateral ventricle representing the previously isolated left hippocampal infarction. The new cranial MRI showed hyperintensity in the right hippocampus in T2 and fluid attenuation inversion recovery (FLAIR)-weighted images in addition to encephalomalasic changes in the left hippocampus (Figure 2). There was no contrast enhancement. Intracranial MR angiography showed a very thin left PCA. The proximal right PCA was very thin and the distal part could not be visualized in MR angiography (Figure 3). An electrocardiogram (ECG) showed normal sinus rhythm, non-specific ST-T changes, and premature ventricular beats. Transthoracic echocardiogram (TTE) showed mild tricuspid valve regurgitation, with an ejection fraction of 55%. Twenty-four-hour rhythm Holter monitoring revealed rare premature atrial, ventricular, ventricular couplets and ventricular bigeminy beats. However, atrial fibrillation, ventricular tachycardia, and

“pause” were not detected. His vitamin B12 was 98.8 pg/mL and replacement treatment was started. Cranial MRI was performed 1 month later and the second stroke showed disappearance of the hyperintensity in the right hippocampus in T2 and FLAIR-weighted images; the left hippocampal atrophic lesion persisted.

Autoimmune, paraneoplastic, infectious processes, and seizure were considered in the differential diagnosis. An electroencephalography (EEG) showed left hemispheric slowing. Cerebrospinal fluid (CSF) was acellular with 47 mg/dL of protein and 155 mg/dL glucose, concurrent blood glucose was 278 mg/dL. Oligoclonal bands were not detected. Thorax and abdominal computed tomography (CT) scans were normal. Urologic examination and urinary ultrasonography (USG) were normal. Gastro-colonoscopy showed erosive gastritis, bulbitis, and a sliding hiatal hernia, and colonoscopy showed grade 2 internal hemorrhoids. Tumor markers (CEA, AFP, B-HCG, Ca-19-9) were negative. Vasculitis markers (ANA, anti-dsDNA, anticardiolipin IgG and IgM, lupus anticoagulant, microglobulin beta 2, RF, P and C- ANCA, homocysteine, protein C, protein S and anti-thrombin III) were within normal limits.

The patient had no formal education and he was able to read but not write. He had worked as a dessert chef for 11 years until he had his first stroke. Then, he stopped working and had his second stroke 9 months later. He was left-handed. He scored 14 points

Figure 2. From left to right; MRI performed 8 months ago (FLAIR images), within the first 24 hours after the beginning of acute-onset amnesic syndrome and 1 month later, respectively. Encephalomalastic changes in the left hippocampus and enlargement of adjacent lateral ventricle are seen in all images. The right hippocampus is hyperintense in FLAIR images performed within the first 24 hours after the beginning of acute amnesic syndrome (in the middle) and the right hippocampus is normal in FLAIR images performed 1 month later (in the right).

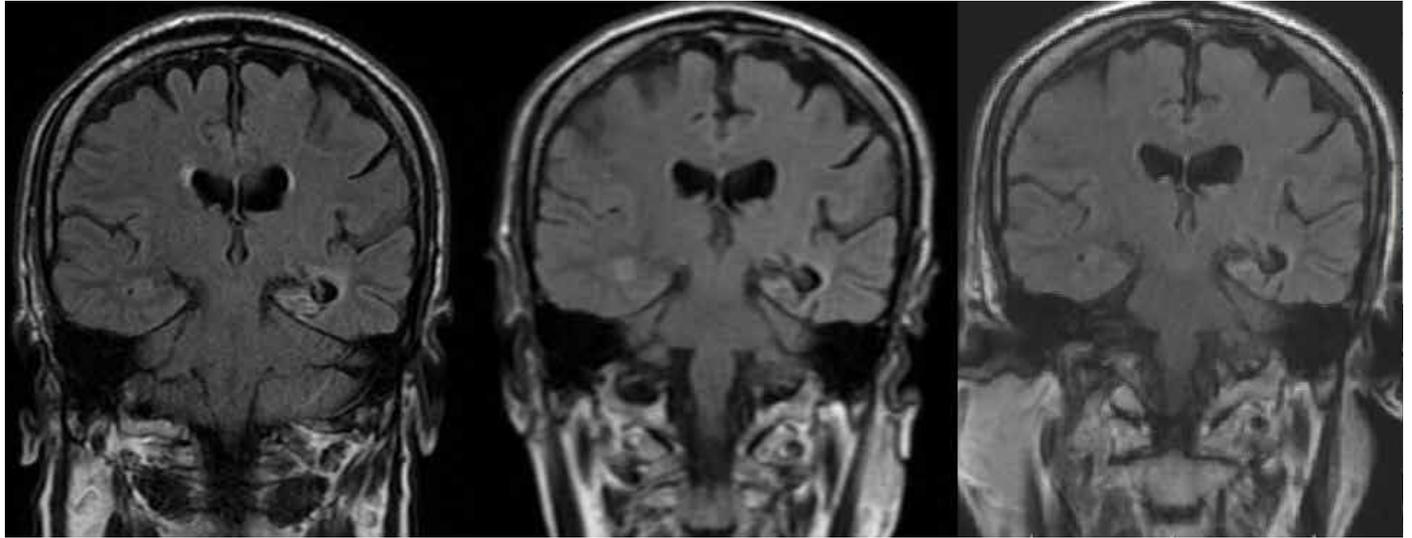
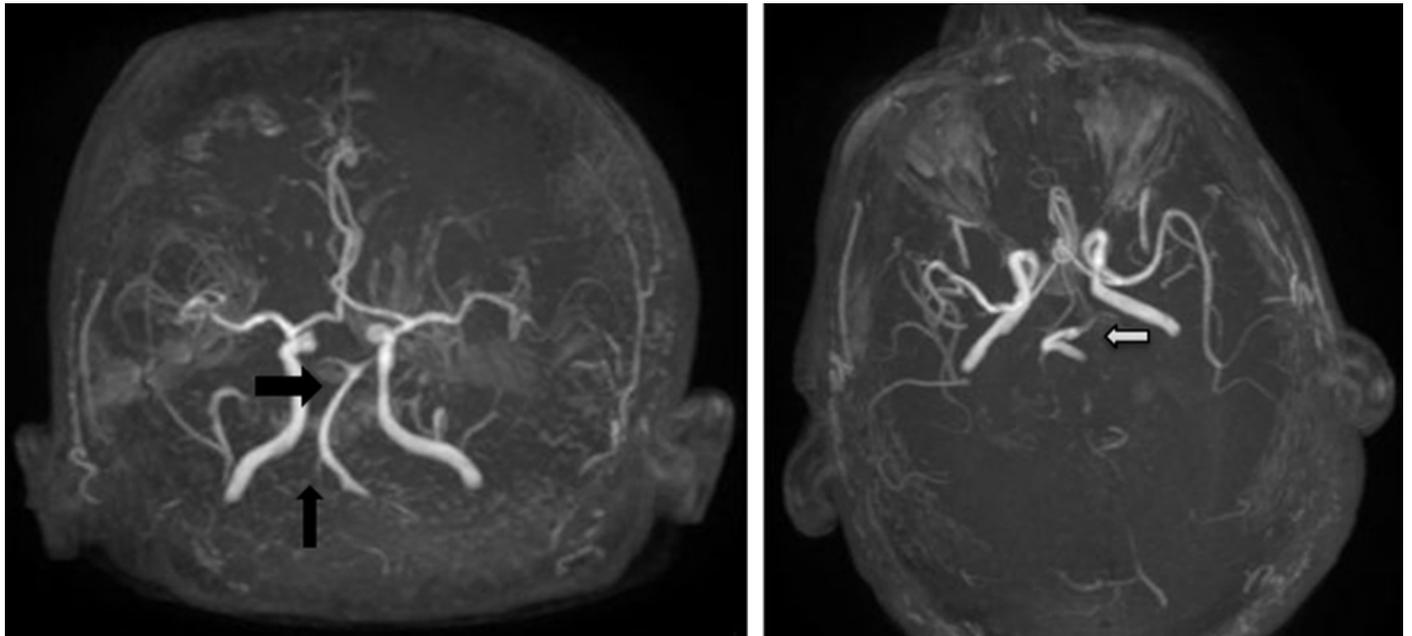


Figure 3. Intracranial MR angiography shows a very thin left posterior cerebral artery (PCA) (white arrow with black frame). Proximal of the right PCA is very thin and distal part cannot be visualized in MR angiography (thick black arrow). The right vertebral artery is hypoplastic (thin black arrow).



(orientation 5/10, recording memory 3/3, attention and calculation 2/5, recalling 0/3, language 4/9) in the Mini-Mental State Examination test, which was performed 1 week after the second stroke. A neuropsychological evaluation performed one month after the second stroke showed deficits in language attention, working memory, short- and long-term memory and visuospatial abilities. He had “limbic-type” of both verbal and visual short-term memory deficits. Confrontation, naming, and “what” path abilities related with the ventral path were severely impaired. The geriatric depression scale score was 12 points, suggesting mild depression.

Written informed consent was obtained from the patient who participated in this study.

DISCUSSION

In acute neurologic disorders including TGA, acute ischemic stroke, seizures and status epilepticus, limbic encephalitis and anoxic and other encephalopathies, specific diffusion restriction patterns of the hippocampus in MRI are reported. These disorders can be differentiated according to clinical presentation, diffusion-weighted MRI, and other radiologic and laboratory findings (3).

A diagnosis of TGA was considered in our patient who presented with acute-onset anterograde amnesia, question repeats, and retrograde amnesia with an inability to remember an important recent life event.

TGA is characterized by the sudden inability to acquire and recall new information, lasting less than 24 hours (especially 4-6 hours) (4, 5). In a meta-analysis of 374 patients with TGA, it was shown that executive functions and anterograde and retrograde long-term memories were impaired in the first 24 hours, which could last 5 days; these dysfunctions subsequently improved and patients fully recovered (6). Diffusion-weighted MRI lesions, which occur after 24-48 h, are characteristic in TGA. These punctate hyperintense lesions can be single or multiple, uni- or bilateral, and are found in the lateral aspect of the hippocampus (7, 8).

Our patient's memory impairment was still present at the 1-month neuropsychological evaluation. Furthermore, DWI-weighted MRI performed in the first 24 hours showed non-punctate right hippocampal infarction with a left hippocampal encephalomalasic area, which excluded TGA as a diagnosis.

Seizures and status epilepticus may cause diffusion restriction (DR) in the hippocampus. DR was found in 5 children with new-onset psychomotor seizures in the entire hippocampus and was shown to transform into hippocampal atrophy during follow-up (9). DR is not usually limited to the hippocampus, it also involves the pulvinar nucleus and other cortical areas with resolution of lesions in the subacute/chronic stage. It is suggested that such MRI changes may occur when increased energy metabolism due to prolonged ictal activity cannot be compensated (10, 11). Hippocampal DR is closely related with ipsilateral EEG abnormalities or the side of clinical seizure onset (10, 11). Another pathology that may cause hippocampal DR is limbic encephalitis, which is characterized by subacute onset of seizures, memory deficits, confusional state, altered vigilance, and psychiatric symptoms. In paraneoplastic and non-paraneoplastic types of limbic encephalitis, hippocampal DR with hippocampal swelling and atrophy are defined but these imaging findings are seen weeks-months and even years after the clinical episodes, and most of these DRs are probably caused by T2-shine through effect (12). DR is widely seen in frontal, insular, temporal and parietooccipital regions in addition to the hippocampus and amygdala in typical herpes simplex virus encephalitis or it can be limited to the hippocampus and amygdala in human herpes virus-6 encephalitis encountered in patients who are immunocompromised (13). Other infectious diseases such as cerebellar variant of Creutzfeldt-Jakob disease may also cause DR in the hippocampus, usually in addition to other brain regions (14). Additionally, encephalopathies including anoxic encephalopathy and hyperglycemic coma may cause widespread DR involving the hippocampus (15, 16).

Our patient did not have seizures. An EEG showed left hemispheric slowing without epileptic activity. CSF was normal, tumor and vasculitis markers were negative and evidence for an occult cancer was not found; thus paraneoplastic, non-paraneoplastic and infectious limbic encephalitis, and seizures and status epilepticus were excluded.

Hyperhomocysteinemia is a putative risk factor for ischemic stroke (IS) but the relationship between homocysteine, B vitamins, and IS is complex. A large double-blind, placebo-controlled trial randomized patients with prior ischemic stroke or transient ischemic attack (TIA) regardless of their blood homocysteine levels to vitamins B and placebo with a median follow-up of 3.4 years and failed to show any difference for recurrent stroke (17). According to recent guidelines, treatment with B vitamins might be considered for the prevention of IS in patients with hyperhomocysteinemia, but its effectiveness is not well established (Class IIb; Level of Evidence B) (18). In patients with a recent IS or TIA, routine screening for hyperhomocysteinemia is not indicated (Class III; Level of Evidence C) and supplementation with B vitamins has not been shown to prevent stroke when the patient has mild-to-moderate hyperhomocysteinemia (Class III; Level of Evidence B) (19). Our patient had a low vitamin B12 level with normal homocysteine level therefore an association with low vitamin B12 levels and IS was not considered causative. Diabetes mellitus and ischemic heart disease are among the well-documented and modifiable risk factors of stroke (18, 19). Our patient had poorly treated diabetes that could lead to intracranial atherosclerosis. Although he had ischemic heart disease, paroxysmal atrial fibrillation or evidence for a left ventricular source of cardioembolism was not found. Therefore, poorly controlled diabetes mellitus, low-flow/undetectable PCAs in MR angiography and the failure to show a source of cardioembolism suggested intracranial atherosclerosis as the underlying etiology of hippocampal infarction in our patient.

Four hippocampal infarction patterns compatible with the vascular anatomy of the hippocampus were reported in a review that researched the clinical, neurophysiologic, and MRI features of hippocampal infarction; the complete hippocampus, the lateral or dorsal parts of the hippocampal body and tail, and small circumscribed lesions in the lateral hippocampus. Interestingly, other ischemic lesions were found in the area of PCA in all patients and most presented with symptoms related with extrahippocampal involvement; only one-sixth of patients presented with acute-onset amnesic syndrome. All patients who had neuropsychological tests showed cognitive impairment. Patients with left hippocampal infarction showed impairment in verbal functions and patients with right hippocampal infarction showed impairment in non-verbal episodic long-term memory functions (20). In this study, atherosclerotic occlusion of PCA was reported similar to the presented case (20).

In a study from Turkey, five patterns of hippocampal infarction with specific clinical, neuropsychologic features and etiologic factors were reported in 19 patients with isolated hippocampal infarction. Cardioembolism and embolism from artery to artery were reported as the etiology in more than two-thirds of the patients. An embolus sparing the adjacent PCA territory and solely reaching the hippocampus may be a valid mechanistic explanation (21).

In another study by the same group, a specific subtype of vascular "major neurocognitive disorder" presenting with acute confusion was defined in 4 of 22 patients with isolated hippocampal infarction, three of whom had bilateral hippocampal infarction (22). Our patient, with isolated hippocampal infarctions resulting in impairments in frontal, verbal and visual memory functions in neuropsychologic tests, may be considered as having vascular "major neurocognitive disorder."

The diffusion MRI changes in TGA mentioned above are thought not to be typical vascular ischemic changes because it was shown that MR angiography and perfusion MRI of patients with TGA were normal (23). Furthermore, there was no difference in terms of having vascular risk factors between healthy subjects and patients with TGA with and without hippocampal lesions (24). Also, ischemic stroke involving the hippocampus often involves other parts of the PCA territory and such patients rarely present with TGA-like amnesic syndrome. These data are in line with the suggestion that hippocampal lesions in TGA are not typical vascular ischemic changes (3).

Uni- or bilateral isolated hippocampal infarction is very rare in the literature. The presented case is the first in the literature in terms of having isolated hippocampal infarctions at different times. Hippocampal infarction should be considered in the differential diagnosis of acute-onset amnesic syndrome.

Ethics Committee Approval: N/A.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

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