CASE REPORT

Long lasting recurrent familiar transient global amnesia after betablocker treatment withdrawal

Martin Vyhnalek, Martin Bojar, Jaroslav Jerabek and Jakub Hort

Memory Disorders Clinic, Department of Neurology, Charles University, 2nd Medical School and Motol University hospital, Prague, Czech Republic.

Correspondence to: Martin Vyhnalek
Memory Disorders Clinic, Dept. of Neurology, Charles University, 2nd Medical School and Motol University Hospital.
V Uvalu 84, 150 06 Prague 5, Czech Republic
TEL: +420-224436800, FAX : +420-224436820, EMAIL: vyhnalek@centrum.cz

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Abstract

The etiology of Transient Global Amnesia (TGA) is not yet clear. A small part of TGA has a familiar occurrence. We report a case of recurrent, long-lasting familiar amnesia occurring after betablocker treatment withdrawal in a migrainous patient. We suggest that familiar TGA could be caused by the mechanism of vasospasm rather than venous congestion and that the abnormal cerebral vasomotor control could be the hereditary substrate in this condition.

INTRODUCTION

Transient global amnesia (TGA) is a neurological condition characterized by an abrupt onset of severe anterograde amnesia usually lasting a few hours with no accompanying focal neurological symptoms. The incidence is reported to be 5–10/100 000/year and the age of onset is typically in the 6th and 7th decades [1].

The mean duration of a TGA attack is 4 hours and the maximum duration of amnesia, according to the Hodges criteria, is 24 hours [2]. The annual TGA recurrence rate is estimated to be 2,5% [1].

Although the first report of TGA dates back almost 40 years, the etiology of TGA still remains unclear. Neuropsychological profiles of patients during a TGA attack are consistent with transient hippocampal dysfunction and several studies bring evidence for this statement [3].

As demonstrated by recent studies, patients with TGA don't manifest patterns of acute arterial ischemia as seen in transient ischemic attack (TIA). Ischemia due to venous congestion or vasospasm has been suggested [3, 4].

Frequent amnesic episodes that last for several minutes are often of epileptic origin [1].

Several authors have reported increased incidence of migraine in TGA patients. However, actual findings don't support the hypothesis of TGA as a migrainous attack (a migraine differs from TGA in age of onset, number of recurrences and triggering events while TGA is not commonly associated with headaches) and speculate mainly about a common substrate of migraine and TGA – a paroxysmal dysregulation at the brainstem level [5].

Other known triggering factors of TGA episodes are cold water diving, Valsalva maneuvers, hyperventilation and stress [1].

Since the early eighties, seven TGA families have been reported (Table 1). Regarding the low incidence of TGA in the general population, the coincidental occurrence in one family is unlikely.

The hereditary substrate in familiar TGA is not known.

We report a case of recurrent long-lasting familiar TGA occurring after betablocker treatment withdrawal and we discuss the possible etiological background of these episodes.

CASE REPORT

The patient is a 54 year old male, who has experienced 2 episodes of amnesia.

The first occurred at the age 52 while having breakfast. One hour after the symptoms onset he was admitted to our neurological department. He was repeatedly asking the same questions about where he was and what was going on. Neuropsychological examination revealed massive isolated anteroretrograde amnesia. The neurological examination was otherwise normal and the patient didn't report any other complaints and denied having a headache. The acute brain CT and carotid and vertebral artery ultrasonography were normal. The symptoms lasted for about 48 hours and didn't leave any sequelae except for memory gap for the hours of the attack.

His second attack occurred about 2 years later in the morning without any particular provocation. He was again admitted to our department, manifesting the same symptoms as during the first episode, and the amnesia lasted again for about 48 hours.

Brain MRI performed six hours after the onset did not reveal any signs of acute ischemia on diffuse-weighted imaging sequences (DWI). The standard T2 scans were also normal except for few hyperintensities in periventricular white matter not exceeding 3mm in diameter. No signal abnormalities were detected in either of the hippocampi, thalamus and basal ganglia.

The EEG during the second episode didn't show any epileptic abnormality. Transesophageal echocardiography and transcranial doppler ultrasonography with application of contrast medium were normal with no evidence of right left intracardial or pulmonary shunt.

The basic blood analysis was normal. The blood pressure was 140/80.

The patient was treated chronically for hypertension by perindopril, indapamid, and atenolol.

He had suffered from migraines without aura in his adolescence and young adulthood.

One month before the first episode of amnesia he had withdrawn from a chronic therapy by atenolol he had been taking for 5 years for hypertension. Three weeks after this discontinuation the patient experienced three episodes of migraines without aura, and he told us that he had not had a migraine since age 20. After the first episode of amnesia the atenolol treatment was restored. The second amnesic episode was preceded by the replacement of atenolol with betaxolol 1 month before the onset of amnesia.

According to the patient, his father and his sister had experienced one similar episode of amnesia at the age of 50 and 52, lasting for 12 and 1 hours, respectively.

His mother suffered from migraines without aura all her life, his father and his sister didn't have migraines.

DISCUSSION

The episodes of amnesia described in this study fulfilled all but one TGA criteria – the duration of both amnesia episodes in our patient was 48 hours and so exceeded twice the upper limit according to the Hodges criteria. Why do we think that our patient presented an authentic TGA?

The symptoms in our patient were typical for TGA: massive transient anteroretrograde memory impairment with no focal neurological deficit and complete recovery except lasting amnesia for the episode. Recurrence and familiar pattern is also in favor of TGA.

The longer lasting amnesias are often suspected from ischemia. The absence of signal changes on DWI 6 hours after the onset dispute possible ischemic etiology and is consistent with other recent studies which find no DWI abnormalities in acute phase of TGA, but only 24 hours after amnesia onset [10].

Our patient featured increased vascular risk factors including hypertension and manifesting signs of subtle vascular microangiopathy on a MRI scan. According to some studies, subtle cerebral angiopathy is a frequent finding in patients with TGA and could eventually explain the high prevalence of TGA in the 6th and 7th decades [1].

Recent findings of delayed DWI changes in TGA speak for transient ischemic dysfunction in memory-relevant structures induced by hemodynamic factors other than those causing TIA. The predisposition for hippocampus is explained by its distinguished vascular architecture and the glutamate excitotoxicity in this region, causing its transitory dysfunction [3]. There are two theories explaining the hippocampal ischemia occurring during TGA. On one hand, ischemia by venous congestion is hypothesized because of the high percentage of insufficient valves in the jugular veins of TGA patients and by the Valsalva maneuver being a common precipitating factor of TGA [3].

On the other hand, the presence of cerebral vasoconstriction is supported by frequent comorbidity with migraines and pathological vascular brain reactivity in TGA patients [11].

Contrary to the reports of sporadic TGA, in all but one of the published familiar TGA cases, no precipitating factor for venous congestion was found. Neither was it recognized in our patient. Recurrence of TGA seems also to be higher in familiar than in sporadic cases.

Beta blockers such as propranolol and metoprolol are the first drugs of choice for the prophylaxis of migraine. As TGA recurrence is quite rare, the prophylactic medication is not typically used and little information is available about its effect.

In one patient reported by Berlit, metoprolol was proven to be effective in the prophylaxis of recurrent postcoital amnesia. Similarly as in our patient, its withdrawal has provoked further recurrences [12].

Table 1

Summary of familial TGA cases reported in literature. Family from this article listed in the last row.

Author, family number	Sex, age of first TGA	Number of episodes	Duration (hours)	Provocation	Migraine
Munro JM 1982 (6)	Man 53y	2	8h, 3h	Unknown	No
	Father 56y	3	3h	Unknown	No
	Sister 66y	1	12h	Unknown	No
Dupuis MJ 1987 (7)	Woman 64y, 69y	2	4h	Migraine	Yes (with alexia and aphasia)
	Twin sister 68y	2	12h		Yes (with alexia and aphasia)
Stracciari A 1986 (8)	Woman 72y	1	3h	Unknown	Yes
	Brother 52y	1	6-8h	Unknown	Yes
Corston 1982 (9)	Man 63y	3	18h	Unknown, shower	No
	Brother 62, 65y	2	30min	Unknown	No
	Brother 74-81y	2	18h	Unknown	No
	Brother 75-77	2	24h	Physical exercise	No
Hodges 1990 (2)	Man 60y	1	8h	Unknown	No
	Sister &	1	Unknown	Unknown	Unknown
	Mother	1			
	Woman 66y	1	Unknown	Unknown	Unknown
	Brother	1	Unknown	Unknown	Unknown
	Man 54y	2	48h, 48h	Unknown	Yes
	Father 50y	1	12h	Unknown	No
	Sister 52y	1	1h	Unknown	No

Provocation by betablocker treatment withdrawal and replacement, absence of classical precipitating factors, occurrence only several days after migraine attack and the recurrent pattern support the hypothesis of cerebral vasoconstriction as the underlying mechanism of TGA in our patient.

The hereditary predisposition of migraines is well known although the hereditary substrate has not yet been identified in most cases and it seems that multiple genes directly or indirectly involved in cerebrovascular reactivity are implicated [13].

The long duration of amnesia in our patient compared to his relatives could be explained by the concomitancy of paternal (TGA) and maternal (migraine) susceptibility genes implicated in TGA pathophysiology.

CONCLUSION

We present a case of recurrent 48 hour-lasting familiar amnesia in relation to migraine with possible provocation by betablocker treatment withdrawal.

We suggest that hereditary TGA could be caused by the mechanism of vasospasm rather than venous congestion (presumed in the most of sporadic cases) and that the abnormal cerebral vasomotor control could represent the hereditary substrate.

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