

## TRANSIENT GLOBAL AMNESIA

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**Abstract:** Transient global amnesia (TGA) consists of a sudden and transient loss of memory. Recent memory fades, so that the patient does not remember where he is and how he got there. The patient asks repeated and stereotyped questions because he no longer reminds the answers he has just received. The differential diagnosis is especially made with the transient ischemic attack (TIA), temporal seizure and migraine attacks. TGA is a disease whose frequency is not high and once appeared, it rarely repeats. Although the duration of the clinical signs is small and memory disorders recovery is good, the sudden appearance of TGA is sometimes dramatic and poses many problems both to patients and caregivers.

*History*

Transient global amnesia (TGA) was firstly described in literature by Guyot and Courjon in 1956. In 1964, Fischer and Adams described 17 patients with TGA, also mentioning in their work some common aspects of the disease, such as onset at middle age, sudden blackout accompanied by repetitive questions. Upon clinical examination, except for the memory disorder, there are not highlighted other signs of neurological deficit. Attacks take a few minutes or hours, then gradually memory disorders recover, but with the persistence of a memory gap.

In 1990, Hader and Worlow published an epidemiological study that analyzed 153 cases in which patients who met the criteria for clinical diagnosis, including post amnesia favourable evolution had a good prognosis. Patients with memory disorders who did not meet the full diagnostic criteria, presented instead a more severe evolution.<sup>(1)</sup>

*Epidemiology*

The incidence is approximately 5 cases per 100.000 inhabitants per year. It usually affects patients between 40-80 years old, the mean age being 61 years old. In people aged over 50 years old, the incidence increases to 23.5 cases per 100.000 inhabitants per year. No significant difference between genders has been reported. However, it seems that in men, TGA occurs most often after a physically precipitating factor, while in women it may be more frequently associated with emotional events, a history of anxiety or personality pathological disorders.

The average duration of the episode is 5.7 hours with an interval lasting between 20 minutes and 20 hours. Familial incidence is low, hereditary cases representing less than 2% of all TGAs.

*Physiopathology*

TGA pathophysiology is not well defined yet. The most popular theory is that venous congestion causes impaired blood flow to the thalamus and mesial temporal structures (amygdala and hippocampus). Venous congestion is due to retrograde venous flow as evidenced by the frequent association between TGA and some particular pathological

aspects (e.g. Valsalva manoeuvre, stress).

It looks that a fairly large number of patients had decreased jugular venous flow while performing the Valsalva manoeuvre compared to controls. This decrease of the retrograde venous flow in jugular vein brings into question a temporary impairment of cerebral venous blood flow in patients with TGA. Results of positron emission tomography (PET), MRI with diffusion (DWI), Single-photon emission computed tomography (SPECT) and magnetic resonance spectroscopy (MRS) indicated the involvement of different cortical regions, among which: the thalamus, amygdala, hippocampus, frontal cortex and cerebellum vermis. Generally, territories of vertebrobasilar arterial system appear to be most affected. This leads to the conclusion that TGA is a syndrome caused by a variety of causes that have different mechanisms of action.<sup>(1,2,3,4)</sup>

*Etiology*

The causes leading to the appearance of the nerve pathology are still unknown. There were taken into consideration various conditions, such as an atypical variant of migraine or temporal lobe seizures.

Patients who have TGA show a higher incidence of migraine crises. Numerous studies reveal the presence of migraine attacks, in history, in 14-25% of patients. However, patients with TGA rarely show throbbing headache, nausea, photophobia.

In temporal lobe epilepsy, amnesia is a common symptom. In TGA, electroencephalography (EEG) changes specific to seizures are missing. Transient epileptic amnesia is short (less than an hour) and has a tendency to recurrence.

Other authors found that patients with TGA have an age profile and risk factors similar to transient ischemic attack (TIA), but the essential difference is that TGA has a much lower incidence for stroke, heart attack or death during the follow-up period.<sup>(4,5)</sup>

TGA ischemic etiology is suggested by numerous studies. One of these was performed on 34 patients, mostly women, aged between 42 and 70 years old, who were evaluated by diffusion-weighted magnetic resonance imaging, with a resolution of 1.5 Tesla. This study supports the

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ischemic etiology of TGA, but the pathophysiological mechanism involved requires detailed studies.

In 14 of the patients included in the study, there has been highlighted the emergence of hyperintense punctuate lesions with a diameter between 1-3mm that were localized exclusively on the lateral side of the hippocampus corresponding to the CA1 region. Hippocampal arteries irrigate differently the hippocampus depending on regions; CA1 region is irrigated only by a large ventral artery, instead the other regions are irrigated by a large dorsal artery and several small arteries. Therefore, CA1 region has a small number of microvessels being thus, more vulnerable to ischemia.(6)

Another similar study also proved the ischemic etiology of TGA, aiming at the different objectification of lesions depending on the time elapsed from the occurrence of disease symptoms. Initially, the patients were performed diffusion-weighted magnetic resonance imaging (DWI) within the first 24 hours of symptoms onset, then they were imagistically re-evaluated within 72 hours.

Lesion detection rate in DWI obtained 24 hours after onset ranged between 6 and 80%, in contrast to that obtained within 48-72 hours of onset, which showed a significant increase in the detection rate up to 71-84%. In patients in whom there has been evidenced at least one lesion upon the early examination, at least one or more lesions were highlighted upon the examination 72 hours after onset. So, lesion detection rate in TGA using DW-MRI sequence increased along with advancing in time from onset of symptoms by more than 24 hours.(7)

Among the causes that produce TGA, the following are mentioned: intense exercise, emotional stress, pain, hot-cold exposure, intercourse and Valsalva manoeuvre. All these factors have a common physiological trait: increased venous return towards superior vena cava.

There are drugs that should be taken into account in order to set the etiologic diagnosis. In this category, there can be included sedative-hypnotic medication (especially when prescribed for transatlantic flights) or preventive administration of midazolam for certain medical procedures.(1,8)

Consumption of alcohol or drugs can produce sudden emergence of memory disorders. Patients show confusion but only as long as they are under their influence.

Unlike patients with TIA, those with TGA show more frequently emotional problems (depression, phobias) in their personal pathological antecedents.

## Clinical picture:

Diagnostic criteria were summarized as follows:

- the attack has to be proven and reported by a witness;
- presence of retrograde amnesia;
- no disorders of consciousness and loss of personal identity;
- no other cognitive disorder than amnesia;
- no history of traumatic brain injury;
- seizure duration is more than 24 hours; average of memory disorders between 2 and 8 hours. If memory impairment disorders lasts over 24 hours, an ischemic stroke or a brain hemorrhage can be suspected;
- exclusion of other causes of amnesia.

Besides these diagnostic criteria, a common feature of TGA is represented by repetitive questions asked by patient like "why am I here?", "how did I get like this?" In this period of time, the patient cannot retain new information.

One of the common features is the persevering phenomenon in which the affected people mechanically repeat

phrases or questions with identical intonation and gestures. They may experience confusion about place, time and sometimes the identity of other people.

Memory impairment can be profound and often it is accompanied by anxiety. Sometimes, patients forget things or activities that happened before the onset of amnesia.(4,9,10,11)

## Differential diagnosis

- ✓ Transient ischemic attack, specifically that localized in the posterior vertebrobasilar territory.

Studies show that TGA patients have fewer risk factors than those with coronary or cerebrovascular atherosclerotic heart disease. TGA prognosis is much better than that of TIA.

- ✓ Cardioembolic stroke.

Temporal lobe seizures. TGA is not associated with impaired consciousness or with tonic-clonic stereotyped seizures. Brain EEG does not reveal irritative brain waves.(12)

- ✓ Frontal lobe epilepsy

Migraine crises - show throbbing headaches, nausea, photophobia, phonophobia.

Lacunar infarct - shows focal neurological signs and cardiovascular risk factors for ischemic lesions

- ✓ Syncope

## Paraclinical examinations

EEG is routinely performed to rule out seizures.

Cranial CT is performed in order to eliminate the likelihood of a stroke, especially if vascular risk factors are highlighted.

Cranial MRI is the method of choice particularly in DWI sequences, which may reveal early acute ischemic changes. DWI high resolution imaging usually reveals ischemic lesions in the hippocampus.

If the patient presents to the Emergency Room (ER) and MRI cannot be performed, it is imperative to be performed at least a cranial CT.(9,13)

SPECT highlights the existence of a diffuse cerebral hypoperfusion that improves upon the following check-ups.

PET - cerebral blood flow appears to be transiently interrupted in some specific areas of the brain involving memory (thalamus and/or mesial temporal structures, particularly the amygdala and hippocampus).

A PET study revealed a decrease in cerebral blood flow and oxygen consumption throughout the entire right lateral frontal cortex, associated with a less significant decrease of the metabolism of lentiform nucleus and homolateral thalamus.

These changes, which have improved after repeating PET three months later, suggest the existence of a right prefrontal metabolic depression, probably secondary to the thalamic dysfunction.(14)

## Evolution and prognosis

We recommend patient's check-up after an interval of about 1 month. Relapses are rare and the risk of recurrence attack after five years varies between 3-20%. Episodes usually last for a shorter period of time and do not affect memory subsequently.

TGA prognosis is very good. The disease does not affect morbidity and mortality and is not a risk factor for ischemic stroke.(11)

## Treatment

The disease is currently considered benign and therefore, it is not indicated to administer a therapeutic tool. Still, it is necessary to follow-up the health of such patients for a certain period of time (1-6 months).

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