

Increased troponin levels can detect transient global amnesia mimics

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Summary

Transient global amnesia (TGA) is a well-defined syndrome with temporarily impaired memory formation lasting several hours. Retrospective case series with diffusion-weighted magnetic resonance imaging (DWI) demonstrated that on average 5.4% of putative TGA cases are actually mimicked by strokes. To avoid a delay in stroke diagnosis – because DWI in TGA is usually deferred by a day or two – results from one large retrospective case series indicate that acutely elevated cardiac troponin levels will preselect those at highest risk of stroke as a TGA mimic and so are in need of urgent imaging and also cardiological work-up. Prospective studies will have to ascertain whether measuring troponin in suspected TGA will be helpful and improve outcome.

Introduction

Transient global amnesia (TGA) is an idiopathic entity with a complete loss of memory acquisition that resolves within a few hours. Patients demonstrate no other neurological or cognitive deficits, there is no loss of personal identity, previously acquired skills are not impaired, and characteristically they seem to realise that something is amiss and keep asking the same questions. Although the underlying pathophysiology still remains an enigma, we know from experience that physical or emotional stress are possible triggers [1]. The diagnosis of TGA is based on the clinical criteria set out by Hodges and Warlow [2]. Diffusion-weighted magnetic resonance imaging (DWI) can support a diagnosis of TGA and rule out other causes of amnesia,

for example certain types of ischaemic stroke. Uni- or bilateral punctate DWI lesions can be detected in the hippocampus 24–72 hours after the initial symptoms in up to three quarters of TGA patients [1]. A non-punctate DWI signal in the hippocampus and/or extra-hippocampal DWI lesions are characteristic of ischaemic amnesia. This minireview examines the question of how often DWI shows that the clinical diagnosis of TGA was wrong and amnesia was caused by stroke.

Results and discussion

A search of PubMed resulted in five retrospective case series with robust numbers that gave us an estimate of how frequently clinical TGA is mimicked by stroke using DWI as the diagnostic standard to detect extra-hippocampal or non-punctate hippocampal lesions [3–7]. This occurs in the range of 0 to 11.1% of cases (with an average of 5.4% based on a total of 783 episodes), see table 1 for synopsis. Because patient selection was based on clinical TGA criteria in these publications, prognosis was inherently favourable (resolution of amnesia <24 hours). Several case reports, on the other hand, describe patients who initially might easily be considered to be suffering from TGA but their amnesia persisted well beyond 24 hours, and their imaging consequently demonstrated ischaemic amnesia with non-punctate hippocampal and/or extra-hippocampal lesions [8]. Are 5.4% of missed stroke diagnoses an acceptable margin of error? How could we specifically select patients in need of urgent imaging?



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Table 1: Stroke as a TGA mimic (synopsis of case series). A non-ischaemic stroke was seen only in one of the 783 cases: left temporal haemorrhage due to cerebral amyloid angiopathy [4]. TGA = transient global amnesia.

First author and reference number	Number of stroke cases	Total number of cases	Stroke as percent of total
Szabo [3]	11	390	2.82%
Werner [4]	12	166	7.23%
Ganeshan [5]	14	126	11.11%
Santana [6]	5	45	11.11%
Simaan [7]	0	56	0%
Total:	42	783	5.36%

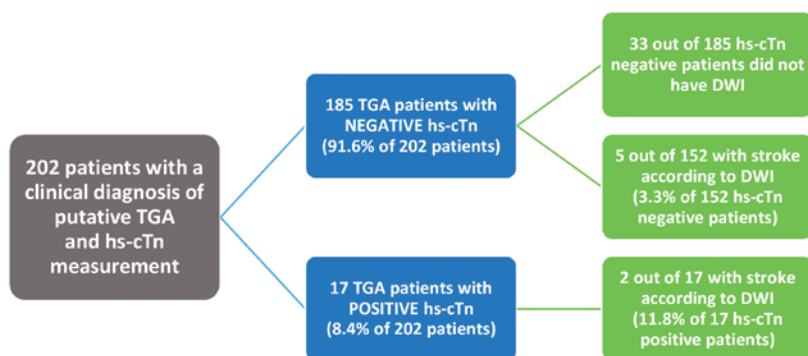


Figure 1: Cardiac troponin status as a predictor of stroke as a TGA mimic. Eisele et al. measured cardiac troponin levels with a highly sensitive test (hs-cTn) in the emergency department in 202 patients with a clinical diagnosis of putative transient global amnesia (TGA) [9]. Positive hs-cTn status was highly predictive of DWI lesions compatible with stroke as a TGA mimic. Figure compiled from the numbers in [9]. DWI = diffusion-weighted magnetic resonance imaging.

Eisele et al. reported an interesting observation that would allow us to home in on those patients whose putative “TGA” is actually due to stroke [9]. This is based on the fact that various acute brain lesions can have cardiac manifestations [10]. They measured cardiac troponin levels with a highly sensitive test (hs-cTn) in the emergency department in 202 patients with a clinical diagnosis of TGA (their patient sample overlaps with those presented by Szabo [3]). In 17 of these 202 patients they found increased levels of hs-cTn (8.4%). Further evaluation of this group demonstrated two cases of takotsubo cardiomyopathy. This non-ischaemic heart condition can be triggered by emotional or physical stress – hence the term “stress cardiomyopathy” – and is not always benign [11]. Likewise, physical and emotional triggers are also a well-known phenomenon in TGA [1]. One of the two patients with takotsubo cardiomyopathy and a clinical TGA diagnosis demonstrated an intracardiac thrombus and numerous cerebral

DWI lesions (compatible with an acute embolic stroke). Another patient with increased troponin demonstrated no cardiac symptoms or abnormalities, but also had DWI lesions compatible with an embolic stroke. In the 152 troponin-negative patients with DWI there were 5 cases of ischaemic amnesia (3.3%). If we compare the rate of ischaemic amnesia in troponin-positive patients (11.8%) with that in troponin-negative patients (who also had DWI) we find a roughly 3.5-fold “enrichment” of stroke cases, see figure 1 for synopsis. Although this result could have come about by chance (margin of error $\leq 10\%$ using a chi-square statistic), this is so far the only published strategy of how to possibly select patients in the emergency room at risk of ischaemic amnesia and a potentially adverse outcome, and so request urgent imaging and a timely cardiology consultation. For instance, takotsubo cardiomyopathy – concurrent with TGA – could result in acute heart failure, life-threatening arrhythmias or left ventricular thrombus formation [11]. But we cannot automatically infer causality from increased troponin levels and cardiac dysfunction in the setting of stroke as a TGA mimic, because not all troponin-positive patients demonstrated a stroke pattern in their DWI and also some troponin-negative patients suffered from ischaemic amnesia [9].

In conclusion, the name “TGA” should not be used as an umbrella term for every type of amnesia, but is reserved for an *idiopathic* entity with a benign prognosis. Sometimes subtle clinical clues – easily missed – indicate that amnesia might be due to cerebral ischaemia [12], a seizure or some other cause [13], and sometimes we lack such clues altogether [3–7]. The specificity of the established clinical criteria for TGA is very high, but not perfect. Prospective studies will have to determine whether the simple strategy of measuring troponin in suspected TGA will actually detect a mimic more frequently and improve outcome. Additionally, any study regarding the specificity of these diagnostic criteria will also have to consider the fact that DWI might not always be the perfect reference standard. Ischaemic amnesia tends to be particularly frequent in the posterior circulation [12], and this where DWI lacks optimal sensitivity [14].

References

You find the complete bibliography in the online version of the article at <http://doi.org/10.4414/sanp.2022.w10111>.

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Key points

- The specificity of the current clinical criteria for TGA is very high, but not perfect.
- Strokes mimic about 5% of putative TGA cases. And if it is not TGA in the idiopathic sense, then prognosis regarding outcome might be more serious.
- The likelihood of detecting a TGA mimic is increased when cardiac troponin is elevated.
- Prospective studies will have to ascertain whether this simple approach will improve outcome.