ΑΣΥΝΗΘΙΣΤΗ ΕΚΔΗΛΩΣΗ ΠΑΡΟΔΙΚΗΣ ΣΦΑΙΡΙΚΗΣ ΑΜΝΗΣΙΑΣ ΜΕΤΑ ΑΠΟ ΕΝΔΟΣΚΟΠΙΚΗ ΕΞΕΤΑΣΗ ΤΟΥ ΓΑΣΤΡΕΝΤΕΡΙΚΟΥ

Μαρία Μαΐλη[1], Κλέαρχος Ψυχογιός[2], Οδυσσέας Καργιώτης[2], Αποστόλης Σαφούρης[2], Μαρία Χονδρογιάννη[1], Κωνσταντίνος Μελάνης[1], Αλέξανδρος Τριανταφύλλου[1], Γεώργιος Τσικαλάκης[1], Στέλλα Φανουράκη[1], Ελένη Μπακόλα[1], Αικατερίνη Θεοδώρου[1]

[1] *Β΄ Νευρολογική Κλινική, Πανεπιστημιακό Γενικό Νοσοκομείο «Αττικόν», Ιατρική Σχολή, Εθνικό και Καποδιστριακό Πανεπιστήμιο Αθηνών, Αθήνα*
[2] *Μονάδα Αυξημένης Φροντίδας Αγγειακών Εγκεφαλικών Επεισοδίων, Θεραπευτήριο Μετροπόλιταν, Πειραιάς*

Περίληψη

Εισαγωγή: Η παροδική σφαιρική αμνησία αποτελεί ένα κλινικό σύνδρομο, άγνωστου υποκείμενου αιτιοπαθογενετικού μηχανισμού, το οποίο χαρακτηρίζεται από αιφνίδιας εγκατάστασης διαταραχή της εμπροσθόδρομης και σε μικρότερο βαθμό της οπισθόδρομης μνήμης, χωρίς εγκατάσταση μόνιμης γνωσιακής βλάβης. Συνήθως συνοδεύεται από αλλοίωση μικρής διαμέτρου, με περιορισμό της διάχυσης στην ακολουθία μοριακής διάχυσης στην μαγνητική τομογραφία εγκεφάλου, στην περιοχή του κροταφικού λοβού και χαρακτηριστικά στην περιοχή CA1 του ιπποκάμπου. Οι κλινικές εκδηλώσεις της παροδικής σφαιρικής αμνησίας είναι συνήθως μικρής διάρκειας, έως και 24 ωρών. Παρόλα αυτά, επεισόδια μεγαλύτερης διάρκειας με άτυπα χαρακτηριστικά έχουν περιγραφεί στη βιβλιογραφία. **Μέθοδοι**: Στην παρούσα εργασία παρουσιάζουμε ένα περιστατικό με παρατεταμένο αμνησικό επεισόδιο, διάρκειας 24 ωρών, μετά από ενδοσκοπική εξέταση του γαστρεντερικού. Στην ασθενή είχε προηγηθεί χορήγηση γενικής αναισθησίας. **Παρουσίαση Περιστατικού:** Ασθενής 70 ετών προσήλθε στο Τμήμα Επειγόντων Περιστατικών, με κυρίαρχη εμπροσθόδρομη και συνυπάρχουσα ηπιότερη οπισθόδρομη αμνησία, μετά από λήψη γενικής αναισθησίας στα πλαίσια διενέργειας ενδοσκοπικής εξέτασης του γαστρεντερικού. Εκτενής διαγνωστικός έλεγχος απέκλεισε άλλα πιθανά αίτια της αμνησίας. Μαγνητική τομογραφία εγκεφάλου διενεργήθηκε 24 ώρες μετά την εκδήλωση των συμπτωμάτων, αποκαλύπτοντας στικτή βλάβη με περιορισμό της διάχυσης εντός του δεξιού ιπποκάμπου, συμβατή με οξεία ισχαιμία. Η ασθενής διαγνώστηκε με παροδική σφαιρική αμνησία, σχετιζόμενη με την προηγηθείσα ιατρική πράξη. **Συμπεράσματα:** Η κλινική εικόνα και τα απεικονιστικά ευρήματα της ασθενούς μας ήταν συμβατά με την διάγνωση της παροδικής σφαιρικής αμνησίας. Η παρουσίαση αυτού του περιστατικού υπογραμμίζει την σημασία της έγκαιρης και σωστής αναγνώρισης των επεισοδίων παροδικής σφαιρικής αμνησίας, ακόμα και όταν οι κλινικές εκδηλώσεις ή η διάρκεια των συμπτωμάτων δεν είναι τα πλέον τυπικά. Πολύ σημαντικό επίσης είναι να αποκλειστούν άλλες πιθανές διαγνώσεις που μπορεί να απαιτούν άμεση θεραπεία και αντιμετώπιση.

Λέξεις-κλειδιά: παροδική σφαιρική αμνησία, ενδοσκόπηση γαστρεντερικού συστήματος, μαγνητική τομογραφία εγκεφάλου, αναισθησία

AN ATYPICAL FORM OF TRANSIENT GLOBAL AMNESIA AFTER GASTROINTESTINAL ENDOSCOPY. A COMPLICATED DIAGNOSIS

Maria Maili[1], Klearchos Psychogios[2], Odysseas Kargiotis[2], Apostolis Safouris[2], Maria Chondrogianni[1], Konstantinos Melanis[1], Alexandros Triantafyllou[1], Georgios Tsikalakis[1], Stella Fanouraki[1], Eleni Bakola[1], Aikaterini Theodorou[1]

[1] *Second Department of Neurology, National and Kapodistrian University of Athens, School of Medicine, "Attikon" University Hospital, Athens, Greece*
[2] *Stroke Unit, Metropolitan Hospital, Piraeus, Greece*

ABSTRACT

Background: Transient global amnesia (TGA) is a clinical syndrome of unknown physiology characterised by a sudden onset of anterograde amnesia and a milder reduction of retrograde episodic long-term memory, without compromise of other neurologic functions. It is usually accompanied by vanishing

punctate magnetic resonance imaging (MRI) diffusion-weighted imaging (DWI) lesions in hippocampal CA1 area. Episodes of TGA are of brief duration, usually lasting up to 24h. However, episodes with atypical characteristics have been also described. **Methods**: We report a case of prolonged amnestic syndrome, lasting up to 24 hours, following gastrointestinal (GI) endoscopy and previous sedation with general anaesthetics. **Results:** A 70-year-old female was admitted to the Emergency Department, with profound anterograde amnesia and variable retrograde amnesia, after recovery from sedation due to GI endoscopy, a few hours earlier. A thorough diagnostic workup excluded alternative causes of amnesia. The Brain MRI performed 24h following symptoms onset, revealed hyperintense DWI punctate signal within the lateral part of the right hippocampus, consistent with acute hippocampal ischemia. She was ultimately diagnosed with TGA related to a medical procedure. **Conclusion:** Our patient's clinical and imaging features were consistent with the diagnosis of TGA. This case highlights that clinical neurologists should not be deterred by atypical amnestic symptoms lasting >24-hours, if the patient's clinical/radiologic presentation is consistent with TGA. However, they should carefully rule out other conditions that need immediate treatment.

Keywords: transient global amnesia, gastrointestinal endoscopy, MRI, sedation

INTRODUCTION

Transient global amnesia (TGA) occurs usually in middle-aged or elderly individuals and is characterised by the abrupt onset of anterograde amnesia, accompanied by repetitive questioning.[1,2] Apart from the amnesia, there are no focal neurological deficits. Attacks last for minutes or hours and the ability to lay down new memories is gradually recovered, leaving only a dense amnestic gap for the duration of the episode and often the hours leading up to it. Guyotat and Courjon[1] first described these amnestic episodes and in 1964 Fisher and Adams[2] reported attacks coined the term 'TGA'.

Emotional stress (ie, triggered by gastric endoscopy, birth/death announcement, and difficult/exhausting workday), physical effort (ie, gardening, house work, sawing wood, sexual intercourse, weight lifting), and water contact/temperature change (ie, hot bath/shower and cold swim) are described most frequently immediately before an attack and are considered "close events".[3] Interest was centreed on the phenomenology of the attacks and their aetiology, as this form of amnesia is sometimes difficult to differentiate from other amnestic syndromes (psychogenic, post-traumatic, epileptic, stroke, encephalopathy, and toxin/drug ingestion).[4]

In 1990, Hodges and Warlow[5] suggested that the etiological uncertainty of TGA mainly resulted from the lack of both clear diagnostic criteria and well-documented epidemiological studies. They attempted to address this problem by conducting a study of 153 cases, some of them fulfilling strict diagnostic criteria. They showed that while clinical features were not particularly relevant for separating 'pure TGA' patients from other amnestic patients, meeting the criteria was a significant predictor for a good outcome, as they designated a group of patients with a good prognosis and no higher prevalence of vascular risk factors than in other forms of transient amnesia. Amnestic patients who did not fulfil the TGA criteria had a significantly worse outcome. After that, many case reports and group studies have been published, but no comprehensive survey has been carried out to characterize the clinical features of this syndrome more accurately.

As mentioned earlier, medical procedures represent a precipitating factor. Gastrointestinal (GI) endoscopies are frequently used as diagnostic tool to identify abnormalities within the GI tract. Endoscopic procedures are invasive and may cause pain and discomfort. Therefore, combination of sedatives and analgesic agents is given to increase a patient's tolerance and cooperation.[6] Commonly used drug combinations in GI endoscopic procedures are drugs with a hypnotic effect such as midazolam, propofol in combination with an opioid such as fentanyl. With the use of various neurocognitive test, researchers have shown an association between the drugs used in and in sort term reversible decline in cognitive function.[7] In addition, case reports of TGA have been reported in the literature, following GI endoscopy.

A rare, acute-onset anterograde amnestic syndrome occurring in the setting of opioid use, closely linked to fentanyl, is of special interest.[8] This opioid-associated amnestic syndrome (OAS) is characterized by diffuse lesions of the hippocampus bilaterally on diffusion-weighted Magnetic Resonance Imaging (MRI), because of excitotoxic effect in this anatomic area.[9] Reports indicate that OAS lasts for weeks to months and in some instances, a year or longer. Opioid-associated amnestic syndrome can be easily distinguished from TGA when there is an impaired level of consciousness or sufficient follow-up observation. However, OAS cases may present with similar features to those of TGA, including frequent repetition, and absence of altered levels of consciousness. Moreover, the possibility of "transient" OAS cases of

shorter duration (and potentially attributed to TGA) could be considered.

Herein, we describe an atypical case, prompting questions about our current diagnostic criteria and the underlying pathophysiological mechanisms that contribute to TGA.

CASE DESCRIPTION

A 70-year-old female with history of weight loss in the last months, presented to the emergency department (ED) accompanied by anaesthesiologist, with sudden onset confusion and memory loss following gastrointestinal endoscopy a few hours earlier. According to the gastroenterologist's referral note, the patient had received standard doses of midazolam, fentanyl, and propofol, but was unreasonably slow to recover despite the administration of naloxone and flumazenil, and after regaining consciousness she was disoriented in space and time. The patient did not have any past medical history, did not report similar episodes of memory loss, and she did not receive regularly any medication.

In the ED, the patient had normal vital signs and she was alert, with profound anterograde amnesia and mild retrograde amnesia. The clinical examination revealed no focal neurological signs. A thorough diagnostic workup (Brain Computed Tomography, CT-Angiography, Doppler ultrasound of the cervical/cerebral arteries, laboratory testing) excluded alternative causes of amnesia. The electroencephalogram (EEG) was performed within 24 h from symptom onset, showing no epileptic evidence.

Initial brain MRI was performed 24h after the symptom onset, revealing increased signal within the lateral part of the right hippocampus on the diffusion-weighted imaging (Figure 1A), associated with a corresponding reduction in the apparent diffusion coefficient (Figure 1B), consistent with acute hippocampal ischemia.

Within 24 hours of her hospitalisation, the patient remained confused and worried. She had complete amnesia of the event that occurred around the introspection and could not engrave any new information. She kept repeating "how did I get here", "what happened to me", and forgetting any new information within seconds. Secondary stroke prevention with antiplatelet agents was administered. Within 24-48 hours of hospitalisation, the patient fully recovered without any acute reperfusion treatment. After that, she was able to engrave new information while she had complete amnesia of the event.

The clinical picture and diagnostic workup are compatible with an episode of atypical transient global amnesia (TGA). Although rare, this has been described in the literature as an episode of TGA following GI endoscopy. The patient was discharged in stable condition, without any residual neurological dysfunction, with instructions for re-evaluation in the Outpatient Stroke Clinic. Follow-up brain MRI, performed 1 month later, did not reveal any abnormal findings (Figure 1C) and provided evidence for the reversibility of diffusion restriction in the right hippocampus.

DISCUSSION

We consider, after excluding other pathological conditions, that the clinical picture of our patient, with the prolonged duration of amnesia and the lesion with diffusion restriction within the lateral part of the right hippocampus, refers to an atypical form of iatrogenic induced TGA, although it does not absolutely comply with the established clinical criteria.[10] Possible explanations might include the emotional stress of instrumentation, associated pain, autonomic activation from passing the scope and medication use (although TGA is also recorded fol-

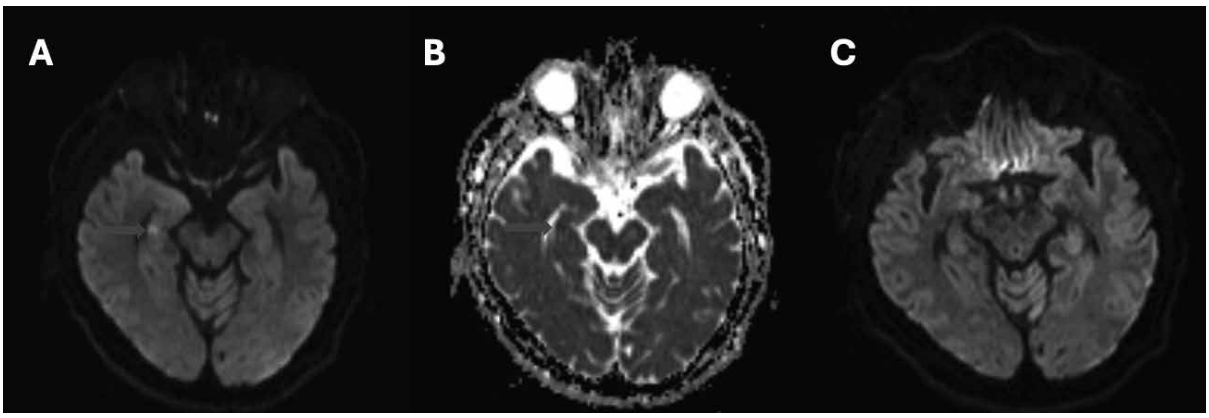

Figure: Neuroimaging findings
Figure Legend: Diffusion-weighted imaging showing a punctate area of diffusion restriction in the medial right temporal lobe 24 hours after the episode (Panel A; red arrow), with a corresponding reduction in the apparent diffusion coefficient (Panel B; red arrow) consistent with acute hippocampal ischemia. Follow-up brain Magnetic Resonance Imaging 1 month after the episode, revealing no abnormal lesions (Panel C).

lowing endoscopy without medication).

The diagnosis of TGA is based on patient's history, as well as on neurological and bedside neuropsychological examination and the exclusion of possible differential diagnoses. The diagnosis usually can be established primarily clinically in the acute stage based on the criteria of Caplan and Hodges and Warlow[5]:

- Acute onset and pronounced new memory impairment.
- Duration of at least 1 h, regression within 24 h.
- No focal neurological symptoms/deficits and no additional cognitive deficits.
- Absence of impaired consciousness or disorientation to person.
- No previous trauma or epilepsy.

Clinical symptoms beyond isolated memory impairment with antero- and retrograde amnesia, including somnolence, severe headache, vomiting, confusion, fever etc., or incomplete recovery after more than 24 h argue against TGA and require rapid differential workup to rule out other potential underlying aetiologies.

Characteristic DWI lesions are most likely to appear 24–72 h following symptom onset, especially in the CA1 region (about 30% of lesions) of the hippocampus, most of which are accompanied by T2-weighted hyperintensity and are still detectable 10–14 days after episode.[6,7] Detection of these DWI lesions support the TGA diagnosis and could be found in up to 75% of all patients. However, absence of DWI lesions does not exclude TGA.[11,12]

Nevertheless, the role of sedative medication and its potential effect on event's duration could be discussed. Various studies focus on the effect of drugs, as monotherapy or in combination, and on the duration of their effects on cognitive functions. Surveillance data from ED visits in Massachusetts between January 2019 and June 2023 do not suggest that opioid use is a risk factor for TGA. Proposed mechanistic differences between OAS and TGA might begin to offer insight into this observation. Although OAS is thought to result primarily from an excitotoxic effect of opioids on the hippocampus, the leading underlying mechanisms of TGA are vascular or migrainous in nature, including ischemia and cortical spreading depression, respectively. Additionally, patients with OAS commonly present with altered consciousness due to respiratory depression, whereas those with TGA do not.[13,14]

Two clinical cases with prolonged TGA, reported in the literature, describe a 12-year-old boy who developed prolonged retrograde amnesia following sedation with propofol[15] and a 66-year-old female with prolonged TGA, persisted for 72 h, with no clear emotional or psychological stressor.[10]

In conclusion, this case highlights a patient diagnosed eventually with an atypical presentation of TGA, because of the prolonged duration and the administered medications, that made the diagnosis controversial. Although TGA represents a rare complication of medical procedures, clinical neurologists and gastroenterologists should be aware of its possible occurrence and the potential atypical manifestations. It is difficult to distinguish whether a prolonged course of amnesia points towards a different pathophysiological mechanism of TGA or other clinical entity. Thus, it is very important to rule out other entities, mimicking transient amnestic episodes and probably requiring immediate intervention so that no valuable time will be lost.

To the best of our knowledge, this case is one of the few reported cases with prolonged, iatrogenic induced TGA, associated with MRI evidence of transient unilateral hippocampal ischemia, most probably due to a transient reduction in regional hippocampal blood flow.

CONFLICT OF INTEREST

All the authors declare that they have no conflict of interest.

FUNDING INFORMATION

No funding was received for the present study.

ETHICAL APPROVAL

The approval for the study protocol was not necessary because our institutional review board does not require approval for case reports.

INFORMED CONSENT

Informed consent was obtained from the patient in the study.

DATA AVAILABILITY

All data needed to evaluate the conclusions in the paper are present in the paper. Additional data related to this paper may be requested from the corresponding author, upon reasonable request.

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