Clinical commentary

Epileptic Disord 2020; 22 (2): 225-8

Transient epileptic amnesia diagnosed using long-term electroencephalography

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Received August 14, 2019; Accepted December 15, 2019

ABSTRACT – Transient epileptic amnesia (TEA) is a distinct syndrome affecting middle-aged persons without concurrent brain disease or disposition to epileptic seizures. Seizures are characterized by amnesia, usually lasting less than one hour, and interictal memory deficits that are common. Effective antiseizure treatment is usually rapid in patients with TEA, which underlines the need for prompt diagnosis. Here, we report a 58-year-old male patient with recurrent episodes of antero- and retrograde amnesia. MRI was normal and diagnosis was made using long-term EEG (27 hours), revealing 10 right-sided temporal lobe seizures with subtle clinical symptoms lasting up to 86 seconds. Details of the video-EEG are presented. Treatment with levetiracetam resulted in complete recovery and seizure freedom that was confirmed on a second long-term EEG. Given the favourable outcome with antiseizure treatment, our case study illustrates the role of long-term EEG monitoring in patients with recurrent transient amnesia to establish a correct diagnosis [*Published with video sequence*].

Key words: transient epileptic amnesia, seizure, MRI, long-term EEG monitoring, levetiracetam

Transient epileptic amnesia (TEA) is a sub-type of temporal lobe epilepsy associated with ictal and interictal memory disturbances. Its principle manifestation is recurrent, brief episodes of isolated memory loss with other cognitive functions remaining intact (Butler, *et al*., 2007; Milton, *et al*., 2010; Zeman and Butler, 2010). Amnesia may be anterograde, retrograde or both, and memory disturbances often persist between episodes (Butler and Zeman, 2008; Zeman and Butler, 2010). Focal cognitive seizures with memory deficits only and seizures with additional temporal lobe features, such as olfactory hallucinations or oral automatisms, may occur in the same patient (Butler, *et al*., 2007; Bilo, *et al*., 2009) and a substantial proportion of patients may report other epileptic phenomena, with episodes of memory deficit/amnesia (Mosbah, *et al*., 2014). The onset of attacks in TEA is usually in middle-aged, otherwise healthy, subjects, and around 60% of the patients are men (Muhlert, *et al*., 2010; Zeman and Butler, 2010;

VIDEO ONLINE

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doi:10.1684/epd.2020.1148

Mosbah, *et al*., 2014; Nicastro, *et al*., 2014). In addition, seizures with memory deficit/amnesia, as a prominent ictal symptom, have been reported in patients with non-convulsive status epilepticus (Vuilleumier, *et al*., 1996) or after intracerebral haemorrhage (Maheu, *et al*., 2004). Once TEA has been diagnosed, attacks often respond promptly to anticonvulsants, typically lamotrigine or levetiracetam, among others (Bilo, *et al*., 2009, Gallassi, 2006, Zeman and Butler, 2010), although some patients may require polytherapy (Mosbah *et al*., 2014). The diagnosis of TEA in patients with witnessed recurrent episodes of amnesia without other cognitive deficits is based on the presence of either interictal discharges, a concurrent onset of other clinical features of epilepsy or a rapid response to antiepileptic drugs (Gallassi, 2006; Butler, *et al*., 2007; Zeman and Butler, 2010). The most important differential diagnosis is transient global amnesia (TGA), an isolated reversible, anterograde episode of amnesia, lasting between one and 24 hours (Quinette, *et al*., 2006). Despite the clinical challenge of differentiating between the common diagnosis of TGA and rare diagnosis of TEA, only few descriptions of ictal electroencephalographic (EEG) changes in patients with typical TEA have been published so far (Tassinari, *et al*., 1991; Meo, *et al*., 1995; Butler, *et al*., 2007; Bilo, *et al*., 2009; Mosbah, *et al*., 2014); most publications on TEA reported interictal findings.

Case study

We provide ictal video and EEG of a 58-year-old, right-handed man who was referred to the emergency department because of a first episode with brief memory disturbance. Earlier the same day, the patient had experienced an episode of transient amnesia that began abruptly when he was at work. During this episode, he called his son who noticed that the patient suffered from anterograde amnesia. The patient appeared confused and kept repeating questions regarding where he was and what he was up to. He also could not remember the password for his work computer. After a few hours, the symptoms disappeared. The patient's family had further noticed loss of remote autobiographical memories. For example, the patient did not remember a family voyage six months ago. Neither could he remember attending a close friend's funeral three days ago, where he helped carry the coffin. During these episodes, no cognitive dysfunctions other than amnesia was observed. There were no signs of impaired consciousness and the patient remained responsive. The patient had no recall of the attacks. The past medical history was unremarkable. When we examined the patient, he had fully recovered, and routine physical and neurological examination revealed no abnormalities. A detailed neuropsychological assessment was therefore not performed. On routine 21-electrode EEG, no focal changes or epileptiform discharges were observed; 1.5 tesla standard magnetic resonance imaging (MRI) was also without abnormalities. The patient was discharged with the diagnosis of an "atypical transient global amnesia".

One year later, the patient was referred again to the Epilepsy Clinic as he had several recurring episodes of both anterograde and retrograde amnesia in the meantime. In addition, the patient began to complain about fatigue and that he was no longer able to exercise to the same extent as before. A long-term video-EEG was performed. Within 27 hours, the patient had 10 right-sided temporal lobe seizures that lasted between 32 and 86 seconds (*figure 1*); one during wakefulness and nine during sleep-wake transition. The patient was tested (*video sequence*) during one seizure. He was very briefly non-responsive and unable to recall simple instructions given during the seizure, but otherwise without clinical manifestations.

Treatment with levetiracetam at 500 mg, twice daily, was initiated. Clinically, the patient reported complete remission of all symptoms, had no further amnestic episodes and could work as an executive manager. A follow-up long-term video-EEG (20-hour) after two months confirmed that the seizures had effectively resolved.

Discussion

The publication of several case series of patients with amnesia as the predominant ictal symptom suggests a consistent clinical picture of patients with TEA, and several authors proposed to list TEA as a distinct epilepsy syndrome (Gallassi, 2006; Butler, *et al*., 2007; Zeman and Butler, 2010). Our prototypic patient fulfils all the diagnostic criteria for TEA and this case is one of the few with ictal EEG recordings.

Our findings of mainly sleep-related seizures are perfectly in line with the results described by Tassinari *et al*. (Tassinari, *et al*., 1991) and Burkholder *et al*. (Burkholder, *et al*., 2017). In addition, we provide a video sequence confirming the very subtle ictal symptoms. In our opinion, a lack of symptoms such as automatisms or other motor symptoms is the major quintessence of the video illustrating the clinical challenges of diagnosing TEA. At initial diagnosis, the patient was diagnosed with "atypical TGA" due to retrograde amnesia, which is uncommon but does not exclude the diagnosis of TGA (Bartsch, *et al*., 2006). Unfortunately, we did not perform detailed neuropsychological testing between the episodes given that persisting memory deficits have been described in TEA

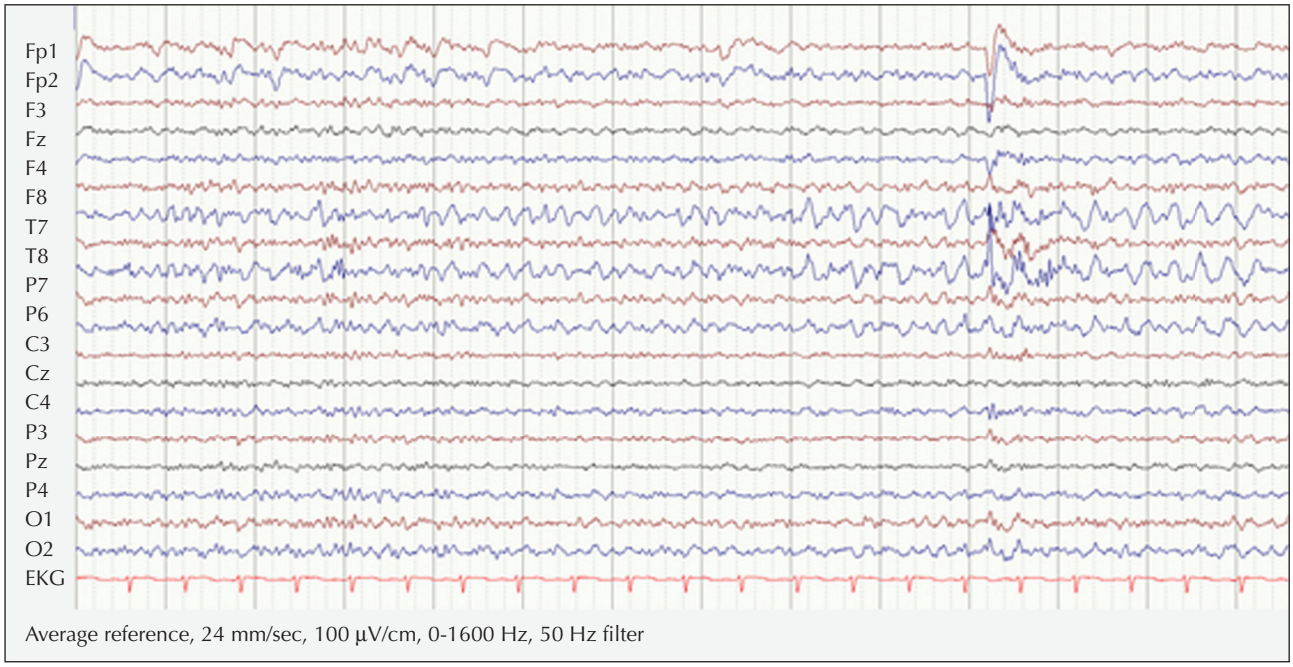

Figure 1. Ictal EEG illustrating a focal seizure from the right temporal lobe with typical ictal evolution of rhythmic theta/delta activity.

but not in TGA patients (Bartsch, *et al*., 2006; Butler and Zeman, 2008).

We observed the same discrepancy between subtle, essentially electrical, seizures and diffuse clinical symptoms, and memory deficits with no direct association with seizures previously described by *e.g.* Tassinari *et al*. (Tassinari, *et al*., 1991). Given the prompt and impressive effect of low-dose antiepileptic treatment, resulting in complete remission of all ictal activity, we are in no doubt that ictal activity seen on the EEG was related to interictal memory deficits in TEA. It is tempting to speculate that the seizures detected using surface electrodes may be only "the tip of the iceberg" and that patients are suffering from far more seizures originating from deeply localized temporal structures. This would be in line with observations by Butler and co-workers describing seizures with amnesia as predominant symptoms with and without other symptoms such as automatisms. Bilateral vs. unilateral seizures could provide an alternative explanation for the variable clinical manifestation, given that most patients described had seizures originating from both temporal lobes (Palmini, *et al*., 1992; Butler and Zeman, 2008). However, the EEG for our patient was recorded during right temporal lobe seizures, and we cannot exclude that the left side was involved based on scalp EEG.

In summary, our patient's ictal EEG and video sequence illustrates the diagnostic difficulties and pitfalls in diagnosing TEA and underlines the importance of long-term EEG monitoring to establish a correct diagnosis. □

Legend for video sequence

Patient tested during an electrographic seizure (*figure 1*) during wakefulness, demonstrating the subtle clinical manifestation of very brief non-responsiveness.

Key words for video research on www.epilepticdisorders.com

Phenomenology: ictal discharge (infraclinical), consciousness (alteration)
Localisation: temporal lobe bilateral
Syndrome: focal non-idiopathic temporal
Aetiology: not applicable

Disclosures.
The study was funded by a grant from the Regions of Southern Denmark to CPB (17/18517). None of the authors have any conflict of interest to declare.

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TEST YOURSELF

(1) What are the major clinical differences between transient global amnesia (TGA) and transient epileptic amnesia (TEA)?

(2) How would you establish a diagnosis of TEA in a patient with a witnessed episode of isolated transient amnesia (*i.e.* without other cognitive deficits associated with the episode)?

(3) Does a normal EEG in a symptomatic patient exclude the diagnosis of TEA?

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".