Clinical and neuropsychological changes after the disappearance of seizures in a case of transient epileptic amnesia

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A B S T R A C T

We encountered a female patient with late-onset temporal lobe epilepsy who presented with transient amnesia as the sole ictal manifestation, an accelerated rate of forgetting daily life events, and a retrograde memory deficit. We describe the memory function of the patient both before and after the administration of antiseizure medication. After the patient’s seizures were controlled with antiseizure drugs, her neuropsychological memory performance scores showed improvement. We presumed that the disappearance of seizures was associated with a decrease in the accelerated rate of forgetting medication. However, her lost memories were not recovered after the seizures were controlled by antiseizure medication.

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1. Introduction

Memory disturbance is common among people with temporal lobe epilepsy (TLE). Transient epileptic amnesia (TEA) [1] is a subtype of TLE and is characterized by brief, recurrent episodes of transient amnesia during which other cognitive functions are preserved [2,3]. The condition typically arises in middle and old ages. Most patients with TEA experience interictal memory difficulties such as an accelerated forgetting rate and isolated autobiographical memory deficit [2,3]. The former is characterized by the normal acquisition and retention of memories over short periods of up to 30 min but abnormally fast forgetting over periods of days or weeks after the event. The phenomenon has been termed long-term amnesia or accelerated long-term forgetting [3,4]. The latter is characterized by a patchy loss of memories of salient personal events, such as family events or holidays or weddings, from the remote past extending back over many years [3]. The performance of patients with these three types of memory deficit on standard neuropsychological memory tests that assess the retention of new memory after delays of 30–40 min is usually normal [2].

We encountered a woman with late-onset TLE who presented with transient amnesia as the sole ictal manifestation, an accelerated rate of forgetting of daily life events, and a retrograde memory deficit that specifically affected her autobiographical memory. We herein investigated her memory function both before and after the administration of antiseizure medication and discussed the findings about the relationships between her seizures during the study period and her memory function.

2. Case presentation

Ms. A was a 67-year-old right-handed woman who was referred to us due to transient amnesia and memory disturbance. She was the product of a normal pregnancy and delivery, and her development was normal. Her family history was unremarkable. She had no history of head injury, neurological illness, or drug abuse. After graduating high school, she was employed as an office worker; after getting married, she became a homemaker. She was living with her husband, daughter and two granddaughters. Six months prior to her first attendance at our clinic, her family observed several episodes of transient amnesia of approximately 15 min in duration. These episodes were characterized by a sudden onset of disorientation regarding her location or her purpose for being at the location. Although impaired consciousness was absent and responsiveness was maintained, she had no recall for events during these attacks. She was unaware of her seizures. One morning, soon after getting up in her house, she asked her daughter where the switch for the heater was. She looked at her husband and could not recognize him. On another occasion, when she and her family went on a day trip by car, she suddenly repeated, “Why am I here?” She could respond when spoken to, although her responses were slightly superficial. At the same time as these episodes occurred, she also began to experience a baseline memory disturbance. She described accelerated forgetting as follows. She started to worry about her inability to remember what she had done approximately one month previously. When she consulted our clinic for a third time two months later, she did not remember that she had undergone a psychological examination at our clinic one month previously. She also described a patchy loss of remote autobiographical memories. Patchy memory loss of family travel and ceremonial occasions had occurred over the past 3 years. Even if she saw commemorative
Neuropsychological results.

Table 1

| Test          | Before medication | 1 year after disappearance of seizures |
|---------------|-------------------|---------------------------------------|
|                |                   |                                       |
| WAIS-III      |                   |                                       |
| Verbal IQ     | 97                | 97                                    |
| Performance IQ| 75                | 80                                    |
| Full scale IQ | 86                | 89                                    |
| WMS-R         |                   |                                       |
| Verbal memory | 77                | 84                                    |
| Visual memory | 58                | 95                                    |
| General memory| 67                | 86                                    |
| Attention/concentration | 98 | 98                                    |
| Delayed recall| 69                | 83                                    |

Butler et al. described patients with “pure” attacks of TEA, in which amnesia was the only ictal symptom [3]. They excluded cases where witness accounts were unavailable, unreliable, or indicated more extensive cognitive impairment during all attacks.

Although the presence of ictal EEG discharges during a typical event confirms the diagnosis of ictal amnesia [8], we could not capture a typical event because of the infrequent occurrence of seizures in the present case. Our patient showed interictal low voltage spikes on her awake EEG. These spikes were different from benign epileptiform transients of sleep because of clear phase reversal in right temporal region and appearance on awake. Witness accounts of her family were available and reliable and she did not indicate more extensive cognitive impairment during all her attacks. She did not show the concurrent onset of other clinical features of epilepsy. From these facts, we concluded that her symptoms were broadly consistent with the diagnostic criteria for pure attacks of TEA.

Interictal epileptiform abnormalities on EEG in TEA were seen in about 40% and were localized over the temporal or fronto-temporal region [9]. Interictal EEG in our patient was similar to those reports. TEA is responsive to relatively low doses of antiseizure medication [3]. After commencing extremely low dose of sodium valproate monotherapy (daily dose = 100 mg), episodes ceased in patients with TEA [10]. Like these reports, treatment with low dose of antiseizure drug abolished the attacks in our patient.

When treating patients with epilepsy-associated memory problems, we need to consider the influence of antiseizure medication, because there is a possibility that the medication itself may be a confounding factor that affects the patient’s memory function [11,12]. In the present study, the influence of antiseizure medication could be excluded because she was treatment-naïve.

Our patient not only had brief recurrent episodes of amnesia but also reported interictal accelerated forgetting and autobiographical amnesia. Her accelerated forgetting and the patchy impairment of episodic autobiographical memory were similar to the memory impairment that often occurs in TEA.

No previous reports have directly compared the pretreatment and posttreatment memory performance of patients in whom TEA was the sole manifestation of seizures. The findings regarding the relationship between seizure frequencies during the study period and memory function are controversial. Hendriks et al. noted that a high seizure frequency is particularly disruptive to the first encoding stage of the memory process [13]. Mamenskiene et al. reported that frequent seizures during the study period were related to poor long-term recall and that uncontrolled seizures can be a significant factor in the accelerated decay of memory [14]. In addition, O’Connor et al. found that forgetting increased in conjunction with more frequent seizures and that this trend was reversed by antiseizure medication [15]. In contrast, isolated seizures do not generally cause patients to forget material that they have recently learned, because there was no correlation between memory performance and seizure frequency [16,17]. We presumed that the disappearance of epileptic seizures and the temporal lobe epileptiform abnormalities in our patient was associated with subjective memory improvement and the improvement in her WMS-R scores.

In our patient, even after seizures were controlled with antiseizure medication, the memories that lost in TEA, long-term anterograde and retrograde amnesia were not recovered. It is suggested that an irreversible change in the brain occurred due to repeated clinical and subclinical activity. Structures in both the hippocampal complex and neocortex play an important role in the establishment and maintenance of long-term episodic memory representation [18,19]. It remains unclear whether epileptic activity interferes with the memory consolidation, storage and retrieval processes. The possibility that recurrent seizures are responsible for the impairment of long-term memory consolidation has been raised by several authors. Kapur suggested that repeated burst of clinical and subclinical epileptiform activity over months and years may disrupt neocortically-based neural networks that act as storage or
retrieval sites for long-term memory [20]. Manes et al. also suggested that extensive retrograde memory deficit is the cumulative effect of re-current TLE with epileptic activity demonstrated on EEG [21]. Recently a possible role for sleep in memory consolidation has been drawing attention. Slow wave sleep and rapid eye movement sleep have complementary function to optimize memory consolidation [22]. Subclinical epileptiform activity during sleep may disrupt the hippocampal complex or neocortex, which act as the storage or retrieval sites for memory. Examples of EEG recordings are shown in Figures 1 and 2.

**Fig. 1.** Interictal monopolar EEG recording shows low voltage spikes predominantly in the right temporal region.

**Fig. 2.** Interictal bipolar EEG recording shows low voltage spikes with phase reversal in the right temporal region.
remote memory, and eliminate remote episodic memory. Further study is required to understand the functional mechanism underlying the accelerated forgetting and remote episodic memory impairment.

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