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Case report

Transient global amnesia with post-hyperventilation temporal sharp waves—A case report

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ABSTRACT

We report a 55-year-old woman, who presented with transient amnesia for 7 h following underwater swimming. There was no evidence of neurological disturbance except global amnesia. Sharp waves in both temporal regions were registered during the initial EEG recording, which was accentuated by hyperventilation. Right hippocampal high signal intensity was observed in DWI performed 56 h after symptom onset. The sharp waves were all disappeared on follow-up EEG recordings.

1. Introduction and background

Transient global amnesia (TGA) is defined by sudden onset of global amnesia, particularly anterograde memory deficit. It usually lasts for a few hours and is not accompanied by other neurological signs or symptoms. Brain imaging and electroencephalography (EEG) should be done to exclude structural lesions or epileptic condition[1]. Most convincing hypotheses for pathogenesis of TGA are cerebral hypoxic-ischemic insult, and migraine-like mechanism[2]. Many precipitating factors, such as valsalva maneuver, emotional change, and stressful event has been known preceded the symptom[3]. Venous congestion of memory relevant structure has been another eloquent mechanism for this reason[4]. The exact mechanism remains obscure, but certain paroxysmal insults causing transient hippocampal dysfunction may result in amnesia.

In many previous studies and case reports, epileptic discharges were not observed in typical TGA. Moreover, there has been no report about epileptic discharges caused by some precipitating maneuvers in TGA. Rather, patients who experienced transient amnesia repeatedly, and showed epileptic discharges can be diagnosed as complex partial seizure or transient epileptic amnesia (TEA).[1] We experienced a unique case of a patient with typical history of TGA and hippocampal lesion on DWI, and showed sharp waves from the temporal region which were accentuated by hyperventilation transiently.

2. Case

A 55-year-old previously healthy woman presented to the emergency room (ER) with ongoing amnesia for 2 h. She did not have a history of migraine or epilepsy. She had been swimming prior to her amnesia appeared. After holding her breath during a minute for subaqueous swimming, she became confused and anxious, and began asking questions, such as "*where am I*?", "*when did I come here*?" repeatedly. On neurological examination, she was alert and there were no abnormal neurological signs except recent memory disturbance. Anterograde and partial retrograde memory impairment evaluated with the Mini Mental State Examination (MMSE) was the only deficits in cognition. The initial EEG recordings showed repetitive medium voltage sharp waves in both temporal regions, which were more obvious in right side (Fig. 1) following the hyperventilation. Other interictal epileptic discharges were not observed. There was no abnormality on initial MRI, including diffusion weighted imaging (DWI) and MR angiography (MRA) taken at the ER.

Her memory deficits were fully recovered within 7 h following symptom onset. However, she did not recall the episode, including the fact that she had swam and dived prior to come to hospital. On the following day of admission, recovery of memory function was ascertained in MMSE, but there were mild dysfunction of immediate and delayed recall. The verbal memory (Seoul Verbal Learning test, SVLT) was more affected than the visual memory (Rey Complex Figure Test, RCFT) for her age in detailed neuropsychological test, Seoul Neuropsychological Screening Battery (SNSB). Language, visuospatial and frontal executive functions were all normal. EEG performed 2 days later, did not show any epileptic discharges, even after prolonged hyperventilation. DWI performed 56 h following

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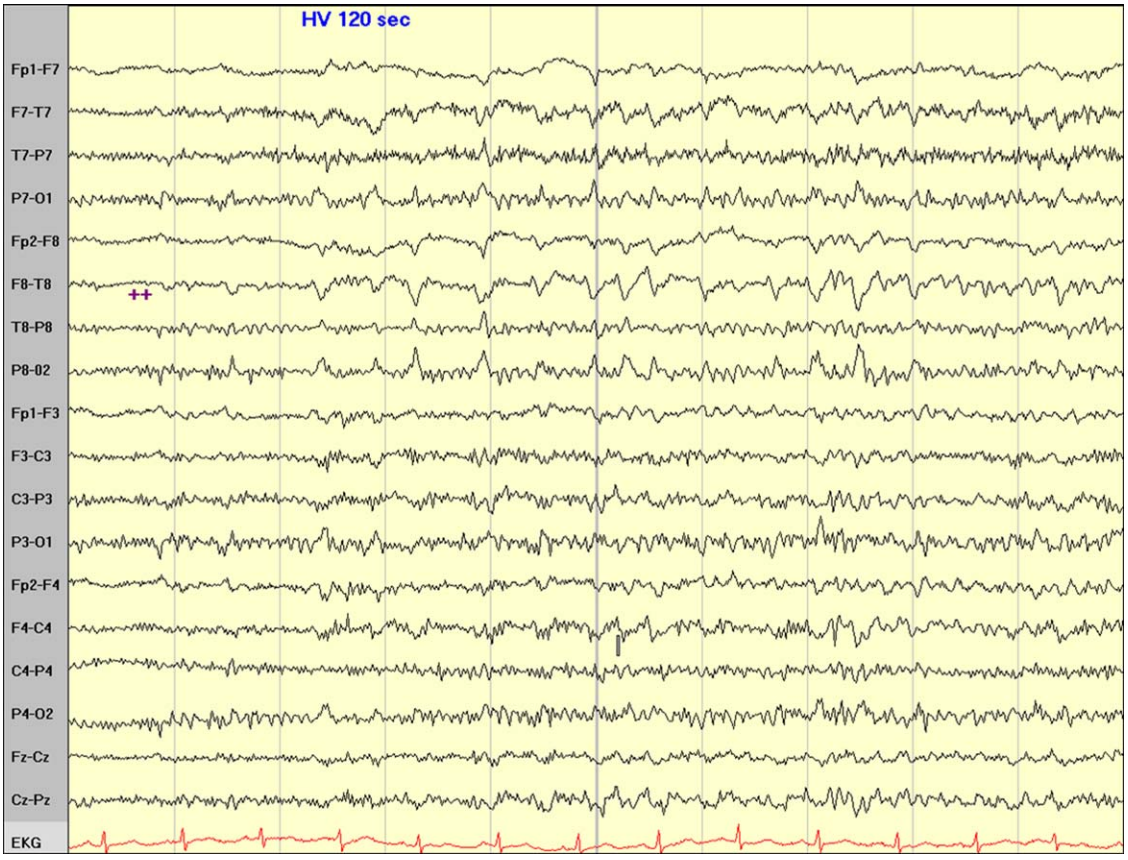

Fig. 1. EEG during an amnestic episode. Medium amplitude sharp waves occur in both temporal regions, simultaneously or independently. They were appeared during hyperventilation.

symptom onset demonstrated small, punctuated high signal intensity in the right hippocampus, the CA1 portion (Fig. 2a). Single photon emission computed tomography (SPECT) demonstrated reduced perfusion in both temporal lobes (Fig. 2b) and focal defect in the right hippocampus, which again points to the consequences of short hypoxic incident. Additional laboratory tests did not show any risk factors for stroke. She was discharged without symptom recurrence. Follow-up EEG which was taken 2 weeks later from the symptom onset, epileptic discharge was not found any more.

3. Discussion

This case fulfilled the diagnostic criteria for TGA proposed by Hodges and Warlow[4]: (1) attacks must be witnessed and information available from a capable observer who was present for most of the attack; (2) there must be clear-cut anterograde amnesia during the attack; (3) clouding of consciousness and loss of personal identity must be absent, and cognitive impairment is limited to amnesia (i.e. no aphasia, apraxia); (4) there should be no

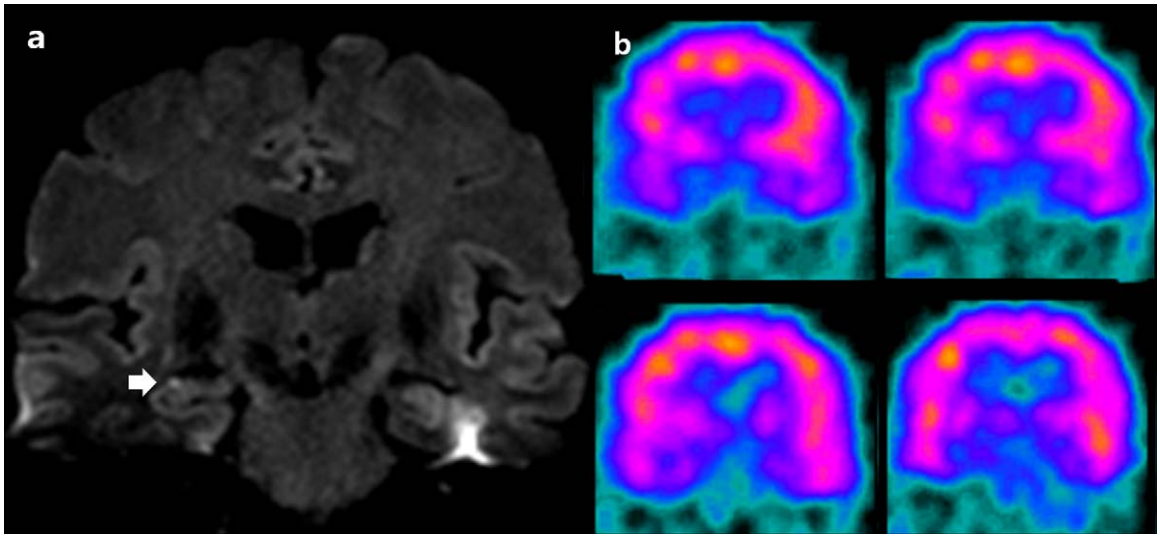

Fig. 2. Brain MRI and SPECT of the patient. (a) Diffusion weighted image after 56 h from symptom onset reveals small dot-like high signal intensity in right hippocampus (arrow). (b) SPECT after symptom recovered decreased perfusion on both temporal lobes. And perfusion defect is observed in the right medial temporal lobe.

associated focal neurological symptoms during the attack, and no significant neurological signs afterwards; (5) epileptic features must be absent; (6) attack must resolve within 24 h; (7) patients with recent head injury or active epilepsy (i.e. remaining on medication or one seizure in the past 2 years) are excluded.

Our patients attack was witnessed, and clear-cut anterograde amnesia lasted 7 h, in addition to an absence of epilepsy history. Moreover, considerable contributory factors for TGA were present. Her first imaging was normal but subsequent DWI performed 56 h after symptom onset showed punctuated high signal intensity in the right hippocampus. On EEG, which performed when the symptom persisted, medium voltage repetitive sharp waves were observed in bilateral temporal regions during the hyperventilation. However, we could not consider this patient as TEA. In contrast to the previously reported cases of TEA,[5–8] our patient showed difference in many aspects: presence of precipitating factors, no confusion other than amnesia, longer symptom period, and no history of epilepsy. Moreover, on DWI, high signal intensity on hippocampus was observed in right hippocampus, CA1 sector, which is strongly suggestible with TGA.

The selective vulnerability to metabolic and oxidative stress of the CA1 sector of the hippocampus was described as a result of hypoxemia, β-amyloid-induced neurotoxicity, and ischemia.[9,10] The exact underlying mechanisms of this region-specific vulnerability and glutamate toxicity are not well understood, but known as genomic-determined differences in the tolerability to glutamate and distribution of glutamate receptors, and an increase in excitatory synaptic transmission.[11,12] In our patient, CA1 sector of hippocampus maybe injured by ischemic insult after a prolonged breath holding and valsalva maneuver for submergence, and we could ascertain the lesion in DWI.

On the other hands, how can we explain the sharp waves after hyperventilation during the EEG recording? Hyperventilation causes hypocapnia that result in cerebral vasoconstriction. This is a well-known precipitating maneuver of EEG abnormality with cerebro-vascular lesion; such as Moyamoya disease.[13] In spite of our patient did not have a vascular abnormality on the MRA, vasoconstriction induced by hyperventilation during the EEG recording exaggerate hippocampal ischemia, and it might increase burden of the metabolic stress causing EEG abnormality.

Underlying mechanisms of ischemia-induced epileptogenesis are not well understood, glutamate has been found to be associated with both epileptogenesis and ischemia-induced injury in several research models. The ischemic penumbra has been suggested as the substrate for epileptogenesis in stroke-induced epilepsy,[14] and recent studies have demonstrated enhanced excitability in penumbral tissue. And ischemia-injured tissue also has a lower seizure threshold[15]. Decreased GABA-mediated inhibition may contribute to the ischemia-induced hyperexcitability of penumbral tissue also.[15–17] GABA-mediated inhibitory postsynaptic potentials are significantly decreased in ischemia-injured tissue.[15–17] Like ischemia-induced seizure model, in TGA, increased glutaminergic activity and calcium influx caused by ischemic insult lead neuronal cell hyperexcitability, which in turn might cause epileptic discharges. In other words, the sharp waves are not the cause of transient amnesia *per se*, but the result of focal ischemia in our patient.

This case is unique in that post-hyperventilation epileptic discharges were associated with symptoms of TGA in a patient, which has not been reported previously. Usually epileptic discharges on EEG exclude TGA. However, if the patients have a significant precipitating factor and typical symptoms of TGA, clinicians may be good to diagnose as TGA, not TEA. We conclude that in TGA, epileptic discharge especially following hyperventilation can occur. And the importance of hyperventilation during EEG recording must be recognized in patients with transient amnesia.

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