**Post-hyperventilation Apnea with Spindle Activity on Electroencephalogram: A Case Report**

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**Abstract:**
Loss of consciousness occurs in post-hyperventilation apnea, but its pathophysiology remains unclear. We herein report a patient with post-hyperventilation apnea showing spindle activity on electroencephalogram (EEG). The patient was alert and breathing spontaneously before the hyperventilation test, but loss of consciousness and apnea with spindle activity on EEG occurred when the end-tidal CO₂ decreased during the hyperventilation test. She recovered consciousness and spontaneous breathing with the disappearance of the spindle activity on EEG when the end-tidal CO₂ increased after the hyperventilation test. The loss of consciousness during post-hyperventilation apnea might be due to the focal involvement of the ascending-activating mesodiencephalic reticular formation.

**Key words:** post-hyperventilation apnea, hyperventilation syndrome, spindle coma

**Introduction**
Hyperventilation syndrome (HVS) is characterized by functional hyperventilation attacks with no underlying organic abnormalities and generally carries a good prognosis (1). However, HVS has occasionally been associated with severe symptoms, including apnea. Post-hyperventilation apnea (PHA) with sustained cyanosis, hypoxemia, and loss of consciousness (LOC) has been previously reported (2), but the pathophysiology of LOC in PHA is not fully understood.

We herein report a patient with PHA showing spindle activity on EEG in the hyperventilation test (HVT) and speculate on the pathophysiology of LOC in PHA.

**Case Report**

The patient was a right-handed, 27-year-old woman. She had experienced HVS several times. Her first apnea attack occurred when she was a high school student. In 2009 and 2012, she experienced the second and third apnea attacks, respectively, after drinking alcohol. Each episode occurred subsequent to HVS, and she recovered spontaneously without treatment.

In 2016, she was rushed to the emergency department of another hospital on day 1 due to HVS after consuming alcohol and was treated with intravenous hydroxyzine. Subsequently, her respiratory rate (RR) gradually decreased, and she was intubated and artificially ventilated due to apnea, which continued for up to 1 minute. She was transferred to our medical center on day 2. On arrival, she had been intubated, but she was breathing spontaneously, and no sedative drugs were being used. Her RR was 11 breaths/min, and SpO₂ was 97% on room air. She was alert, and showed no neurological abnormalities. A blood examination revealed no abnormalities aside from an elevated white blood cell count (16,000/μL). No abnormal signals were observed on brain or cervical magnetic resonance imaging (MRI).

As the etiology of apnea remained unclear in our patient, we performed an HVT with monitoring of the SpO₂, end-tidal CO₂ (etCO₂), and EEG in order to exclude other diseases, such as epilepsy, and assess the correlation between hyperventilation and apnea (Fig. 1). The patient provided her informed consent. While she had been intubated on admission and was breathing spontaneously, we prepared a mechanical ventilator to ensure the patient’s safety in case of apnea during the HVT. Before the HVT, she was alert,
Figure 1. The time course of the patient’s consciousness, respiration, and electroencephalography on the hyperventilation test. Before the HVT, the patient was alert and breathing spontaneously (corresponding to EEG in Fig. 2A). When the etCO₂ decreased to 29 mmHg during the HVT, LOC and apnea occurred (corresponding to EEG in Fig. 2B). Later, when the etCO₂ gradually increased to 38 mmHg after the HVT, she recovered consciousness and spontaneous breathing. etCO₂: end-tidal CO₂, HVT: hyperventilation test, PDR: posterior dominant rhythm

**Discussion**

We herein report the case of a patient with PHA showing spindle activity on EEG during the HVT. In our patient, when LOC associated with PHA occurred during the HVT, EEG revealed spindle activity, which disappeared in parallel with the recovery of consciousness and spontaneous breathing. Some patients with HVS are known to develop PHA in conjunction with hypoxia, cyanosis, or LOC, requiring intubation and artificial ventilation (2). Most patients spontaneously recover from PHA, but prolonged PHA is associated with severe outcomes, including death (3).

There have been only a few reports of PHA, but breath-holding spell (BHS), which resembles PHA, is a common disease in infants causing apnea, cyanosis, and LOC following crying induced by pain, anger, and fear (4). Although PHA and BHS differ in terms of the age of onset, BHS resembles PHA in terms of the development of apnea after HVS.

Apnea is generally caused by the dysfunction of the respiratory centers in the medulla and pons (5), and several studies have speculated the mechanism of PHA to be as follows: PHA occurs when the PaCO₂ is reduced to the threshold of spontaneous breathing (6); hypocapnia resulting due to HVS causes respiratory alkalosis, and this leads to reduced hydrogen ions acting on chemoreceptors and subsequent respiratory depression (6). In addition, even if hypocapnia following hyperventilation is normalized, the breathing may not immediately restart for several possible reasons. First, the threshold level of PaCO₂ is elevated after hyperventilation (7). Second, hypocapnia in the brain persists even when arterial and alveolar PaCO₂ are normalized (8). Third, the hypoxic ventilatory drive is attenuated by hypocapnia due to HVS (9). Furthermore, our patient repeatedly experienced PHA after drinking alcohol. Since a high blood alcohol concentration and EEG showed a 9- to 11-Hz posterior-dominant rhythm (Fig. 2A). We performed the HVT using volume-controlled assist-control mechanical ventilation (tidal volume 430 ml, RR 28 breaths/min, and FiO₂ 0.21). After the HVT was started, the etCO₂ gradually decreased. Four minutes later, the etCO₂ decreased to 29 mmHg, and the patient lost consciousness. The HVT was stopped after 5 minutes, but the patient did not resume spontaneous breathing, and EEG revealed spindle activity without slow activity (Fig. 2B). Mechanical ventilation was started again due to apnea. Three minutes later, the etCO₂ gradually increased to 38 mmHg, and she recovered consciousness and spontaneous breathing, with the disappearance of the spindle activity on EEG. During the HVT, the SpO₂ was maintained at more than 95% on room air. The results of the HVT suggested a correlation between hyperventilation and apnea, so we diagnosed her with PHA.

Thereafter, she was extubated and showed no relapse of PHA. Since the previous relapses of PHA had occurred after alcohol consumption, we advised her not to consume alcohol in order to prevent PHA. The patient was discharged on day 5.
Figure 2. EEG findings. (A) EEG performed before the HVT showing a 9- to 11-Hz posterior-dominant rhythm. High-pass filter, 0.5 Hz; low-pass filter, 70 Hz. (B) EEG at the end of the HVT showing spindle activity. High-pass filter, 0.5 Hz; low-pass filter, 70 Hz. HVT: hyperventilation test

Conclusion

We herein report the case of a patient with PHA showing spindle activity on EEG during the HVT. Our clinical and EEG observations suggested that the occurrence of LOC in PHA was due to the focal involvement of the ascending-activating mesodiencephalic reticular formation, leaving the thalamocortical connections intact (13, 16). The appearance of spindle activity with LOC and the disappearance of the spindle activity with the recovery of consciousness in our patient might therefore suggest that the LOC in PHA occurs due to the transient and focal involvement of the ascending-activating mesodiencephalic reticular formation with intact thalamocortical connections.

Furthermore, the almost simultaneous occurrence of LOC and apnea in our patient might suggest that PHA is correlated with the focal involvement of the brainstem, which includes the ascending-activating mesodiencephalic reticular formation and respiratory centers in the medulla and pons. In addition, hypocapnia causes a decreased cerebral blood flow (CBF) (17), and the CBF reactivity to hypocapnia in the vertebral artery in particular is larger than that in the other cerebral arteries (18). Therefore, a decreased CBF in the brainstem might be correlated with LOC and apnea in PHA, although this is only speculative, as we did not monitor the changes in the CBF during hyperventilation.
sary to elucidate the pathophysiology of PHA.

Disclosures

Informed consent was obtained from the patient. This study was approved by the ethics committee of Kobe City Medical Center General Hospital. The authors declare no conflicts of interest.

The authors state that they have no Conflict of Interest (COI).

References


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