

BRIEF COMMUNICATION

An Infant with Congenital Central Hypoventilation Syndrome: Transient Burst Suppression Electroencephalogram



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1. Introduction

Congenital central hypoventilation syndrome (CCHS), an autonomic disorder without anatomic abnormalities, is characterized by carbon dioxide insensitivity and the absence of a ventilatory response,¹ particularly during sleep. Seizures in CCHS are derived primarily from either autonomic nervous system dysfunction or hypoxemia. However, a burst suppression (BS) pattern has not been reported in CCHS. In this report, we present a female neonate with severe postnatal apnea and seizure-like movements. She was finally diagnosed with CCHS using the identified *PHOX2B* gene mutation.² An electroencephalogram (EEG) when she was 1 month old revealed multiple episodes of a BS pattern accompanied by spasms during quiet sleep, but these disappeared when she was 2 months old. Based on our review of the relevant literature, this is the first report that describes CCHS in an infant with a transient BS EEG.

2. Case Report

A female neonate was admitted to the neonatal intensive care unit and supported on nasal continuous positive airway pressure because of general cyanosis and delayed crying after birth. She was a preterm infant born after 36 weeks of gestation to a 44-year-old mother through a normal spontaneous vaginal delivery. Her birth body weight was 2900 g. Her Apgar scores were 6 at the 1st minute and 7 at 5 minutes. She showed no postpartum metabolic acidosis. The mother's prenatal examination was regular, and her family history was negative.

The infant was alert. Her physical examination showed no obvious abnormalities, and her neurological examination revealed no hypotonia or hypertonia; her muscle power was Grade 5, and her deep tendon reflex scores were 3+ in all extremities. No anatomic abnormalities were detected through transfontanelle ultrasonography. When she was 2 days old, the infant developed extremely frequent central apnea episodes, and then cyanosis and bradycardia when sleeping; however, when awake, she was active. Because of this, she was intubated for apnea.

Initially, neonatal seizures were suspected. She was treated with 20 mg/kg of phenobarbital as a loading dose, and then 6 mg/kg/d combined with aminophylline as a maintenance dose to control her apnea, but in vain. Moreover, her laboratory studies—arterial blood gas and plasma amino acid analyses—were normal.

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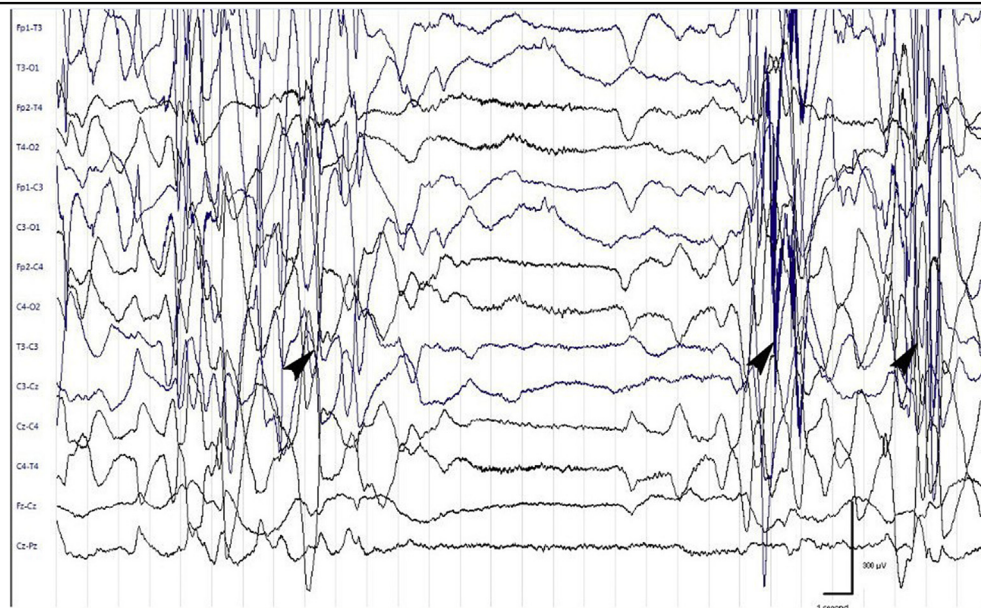


Figure 1 Continuous video electroencephalogram monitoring at 1 month revealed bouts of spasm attacks (arrowhead) associated with a generalized high-voltage ($> 300 \mu\text{V}$) sharp wave followed by an extremely low-amplitude ($< 15 \mu\text{V}$) background.

A 30-minute EEG showed multiple focal spikes and sharp waves in both hemispheres, but no clinical seizures were observed. When she was 1 month old, she had episodic bouts of spasms in addition to apnea during quiet sleep. A 24-hour real-time video EEG detected synchronous generalized high-voltage ($> 300 \mu\text{V}$) spikes, followed by an extremely low-amplitude ($< 15 \mu\text{V}$) background, accompanied by spasms (Figure S1), during sleep (Figure 1). These frequent events (every 2–3 minutes) occurred predominantly during sleep. However, the background of the awake EEG was normal for a 1-month-old baby. The infant was active and alert when she was awake. The phenobarbital regimen was continued, but her apnea was not mitigated even after adding an antiepileptic drug. A follow-up real-time 24-hour EEG when she was 2 months old showed no clinical seizures or BS patterns. A genetic analysis revealed a polyalanine stretch with a $(\text{GCN})_{35}/(\text{GCN})_{20}$ repeat expansion in the *PHOX2B* gene, thereby confirming the diagnosis of CCHS (Figure S2). The patient died from apnea when she was 6 months old—her parents requested only palliative care but not ventilation.

3. Discussion

Studies have reported a correlation between increasing alanines and the severity of defects in the respiratory drive.³ The infant in our study had 35 polyalanine repeat expansion mutations, the maximum number of polyalanine repeat expansion mutations known so far, which accounted for her severe apnea. However, apart from anoxic seizures, the association between CCHS and epilepsy remains unknown, and no study has yet explored EEG patterns in CCHS.

The BS pattern implies the presence of an epileptic coma, an asphyxic deep coma, or encephalopathy associated with serious neurodevelopmental outcomes. There are two possible explanations for the pathophysiological BS activities: thalamo-cortical hyperexcitability⁴ and cerebral hypometabolism⁵; both might simultaneously occur and present in BS.⁶ The interburst background activity was $<$

$15 \mu\text{V}$ and did not respond to stimulation, which was different from the trace alternant EEG pattern.⁷ This report demonstrated that infants with CCHS might have transient BS in EEG; however, the mechanism of transient BS is unclear and needs to be elucidated.

Conflicts of interest

The authors declared that they have no conflicts of interest relevant to this article.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.pedneo.2015.11.003>.