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SLEEP MEDICINE PEARLS

There is more to an elevated bicarbonate

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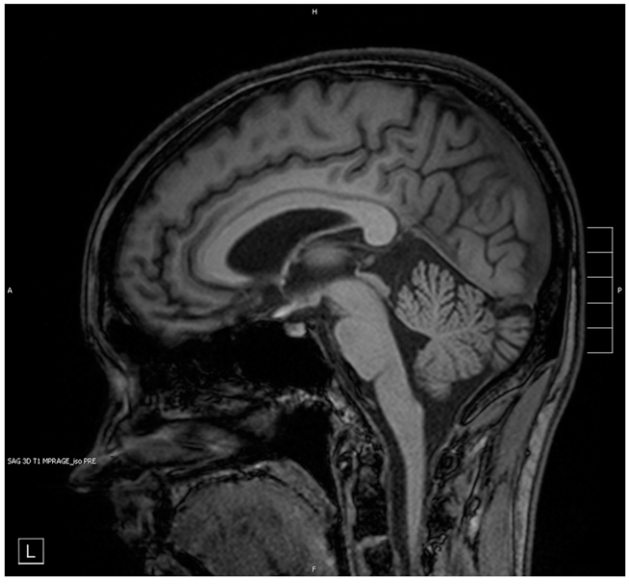
A 26-year-old woman with a history of autoimmune epilepsy presented to the hospital for further management of seizures, which were increasing in frequency. Phenytoin was being tapered because it was thought to be causing side effects such as ataxia. Her first seizures were reported in 2014 and were refractory, requiring vagal nerve stimulator placement and multiple antiepileptics. Physical examination revealed a thin woman, alert, oriented, with good muscle strength, and positive only for bilateral nystagmus horizontally. Laboratory data revealed an elevated bicarbonate level at 30 mmol/L in 2015. It ranged from 34 to 39 mmol/L during this admission. No trauma was reported. A magnetic resonance image revealed findings stable for Rasmussen encephalitis with volume loss involving the left frontal lobe, left anterior temporal lobe with cortical and subcortical thinning, and volume loss involving the basal ganglia and brainstem (**Figure 1**).

QUESTION: What may be causing her abnormal bicarbonate levels? Is additional testing needed? If so, what?

Figure 1—Magnetic resonance image, brain sagittal view, revealing cortical and brainstem atrophy.



ANSWER: She has chronic hypoventilation secondary to Rasmussen encephalitis. Additional testing is as below.

DISCUSSION

For further evaluation, arterial blood gas levels were obtained and were 7.36/62.8/108/34.8 (pH/ partial pressure of carbon dioxide [$PaCO_2$]/ partial pressure of oxygen[PaO_2]/bicarbonate). Pulmonary function tests were normal. Maximal inspiratory pressure was normal. Chest x-ray was without any acute findings. She was placed on bilevel positive airway pressure initially but required intubation for further management of her seizures. She will be prescribed a bilevel positive airway pressure on discharge for hypoventilation with follow-up in a sleep clinic. *PHOX2B* mutation testing was done, and it was negative.

Causes of hypoventilation disorders include congenital central alveolar hypoventilation syndrome, rapid-onset obesity with hypothalamic dysfunction, hypoventilation, and autonomic dysregulation, idiopathic alveolar hypoventilation, and hypoventilation secondary to medications or medical disorder.[1] Medical conditions that can cause central hypoventilation are brain tumors, structural abnormalities, infections of central nervous system (encephalitis in this case), or those secondary to trauma.[2] The mechanisms by which hypoventilation can occur include impairment in respiratory drive or defect in neuromuscular system or ventilator apparatus. The main chemoreceptors of respiratory center are central medullary chemoreceptors and peripheral chemoreceptors in the carotid body.[1] Chemoreceptors work by sensing the pH and thus measuring the level of carbon dioxide. They relay information to the medulla, which controls the respiratory muscles. Normally, if there is acidosis, ventilation will be increased to blow out carbon dioxide, and if there is alkalosis, ventilation is decreased. Ventilation is altered if this negative feedback response involving the chemoreceptors, motor neurons, and respiratory muscles fails. Chronic hypoventilation can be detrimental to the nervous system and cardiovascular system.[3] Rasmussen encephalitis is progressive chronic encephalitis with intractable seizures. Diagnostic criteria are based on clinical, electroencephalographic, magnetic resonance imaging, and histopathologic findings.[4] Involvement of the brainstem is most likely contributing to hypoventilation in this patient. Regulation of breathing is through feedback from $PaCO_2$ and PaO_2. $PaCO_2$ feedback is through the carotid body and central chemoreceptors in the brainstem.[5] Central chemoreceptors are located within the ventrolateral surface of medulla. They respond to elevated $PaCO_2$ and elevated H^+. Symptoms of hypoventilation can include dyspnea, insomnia, and frequent arousals. Lack of symptoms does not rule out hypoventilation. In patients with normal lungs like in our patient, significant hypoventilation can be present with oxygen saturation in the low normal range.[6]

SLEEP MEDICINE PEARLS

1. Sleep-related hypoventilation disorders can be acquired or congenital.
2. Central chemoreceptors respond to elevated $PaCO_2$ and H^+, and although peripheral chemoreceptors primarily respond to low PaO_2, they can respond secondarily to $PaCO_2$ and H^+.
3. Lack of symptoms does not rule out hypoventilation.
4. As the severity of hypoventilation increases, symptoms increase from only abnormalities in sleep to daytime symptoms and result in respiratory failure.

CITATION

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REFERENCES

1. Berry R, Wagner M. CSA and sleep-related hypoventilation disorders. In: *Sleep Medicine Pearls*. 3rd ed. Philadelphia, PA: Elsevier Saunders; 2014;388:392–394.
2. Cielo C, Marcus CL. Central hypoventilation syndromes. *Sleep Med Clin.* 2014; 9(1):105–118.
3. Muzumdar H, Arens R. Central alveolar hypoventilation syndromes. *Sleep Med Clin.* 2008;3(4):601–615.
4. Bien CG, Granata T, Antozzi C, et al. Pathogenesis, diagnosis and treatment of Rasmussen encephalitis: a European consensus statement. *Brain*. 2005; 128(Pt 3):454–471.
5. Nattie E. CO2, brainstem chemoreceptors and breathing. *Prog Neurobiol*. 1999; 59(4):299–331.
6. Berry R. Central sleep apnea and hypoventilation syndromes. In: *Fundamentals of Sleep Medicine*. Philadelphia, PA: Elsevier Saunders; 2012:393.

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