Progressive Paranoid Psychosis in a 20-Year-Old With Central Congenital Hypoventilation Syndrome

A 20-year-old man with a history of congenital central hypoventilation syndrome presented with recent-onset psychosis, catatonia, and a diagnosis of schizophrenia. Psychiatric symptoms were resistant to conventional treatment. A fluorodeoxyglucose positron emission tomography scan of the brain obtained during the hospitalization revealed a hypometabolism distribution more consistent with hypoperfusion than with primary central nervous system disease. Increased mechanical ventilation was successfully used to treat the psychiatric symptoms. *Pediatrics* 2014;134:e900–e902

**AUTHORS:** Alex Dranovsky, MD, PhD,a Joshua P. Needleman, MD,b Jessica Sylvester, MD,c Ronald VanHeertum, MD,d and Philip R. Muskin, MDc

*aDivision of Integrative Neuroscience, cConsultation Liaison, Department of Psychiatry, and dDepartment of Radiology, Columbia University Presbyterian Medical Center, New York, New York; and bDivision of Pediatric Pulmonology, Department of Pediatrics, Maimonides Medical Center, Brooklyn, New York*

**KEY WORDS**

schizophrenia, psychosis, congenital central hypoventilation syndrome, PET scan, catatonia

**ABBREVIATIONS**

FDG—fluorodeoxyglucose

PET—positron emission tomography

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Address correspondence to Alex Dranovsky, MD, PhD, Division of Integrative Neuroscience, Columbia University/New York State Psychiatric Institute, Box 87, 1051 Riverside Dr, New York, NY 10032. E-mail: ad722@columbia.edu

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A 20-year-old man with a history of congenital central hypoventilation syndrome presented to our emergency department with failure to thrive, catatonia, and tachycardia. The patient had a history of hypoventilation at birth and was supported with 24-hour mechanical ventilation for his first 5 years. After 5 years, he was converted to nighttime mechanical ventilation at the family's initiative. The patient thrived on this ventilatory regimen administered via a tracheostomy finishing normal secondary education and enrolling in college.

Over the year before presentation, the patient developed symptoms consistent with schizophrenia, including amotivation, avolition, increasing paranoia, and both auditory and visual hallucinations. The symptoms were accompanied by a significant decline in function, which resulted in 3 hospitalizations during the year for failure to thrive. Several independent assessments resulted in diagnoses of chronic paranoid schizophrenia, major depressive disorder, and congenital central hypoventilation syndrome. During the same period, awake PaCO2 was documented as fluctuating between 45 and 70 mm Hg without mechanical ventilation. Pulse oximetry results obtained during that year were unavailable. The patient presented to our emergency department after 2 weeks of refusing to eat and with profound psychomotor slowing. He was receiving nocturnal mechanical ventilation with tidal volume of 700 mL at 22 breaths per minute. Evaluation of pulmonary function revealed PaO2 of 50 to 70 mm Hg and oxygen saturation of 95% to 100%. The patient was also being treated with 10 mg of aripiprazole and 20 mg of citalopram daily for his psychiatric symptoms.

On admission, the patient was minimally responsive to questions, exhibited increased axial rigidity, and was assessed to be catatonic. Vital signs were significant for heart rate of 140 beats per minute. Laboratory studies (complete blood count, electrolytes, thyrotropin, rapid plasma reagin, cobalamin, folate, urine toxicology) were normal. Arterial blood gas analysis obtained during his admission revealed hypoventilation with PaCO2 measurements that ranged from 49 to 61 mm Hg. At no time was he noted to be hypoxemic while receiving mechanical ventilation. Arterial pH was 7.33 to 7.36 except for a single value of 7.32. When off mechanical ventilation, he was observed to have significant oxyhemoglobin desaturation without distress. This desaturation responded to coached deep respirations.

In addition, computed tomography and magnetic resonance scans of the brain, electroencephalogram, and 24-hour continuous cardiac monitoring showed no significant abnormalities. The family refused lumbar puncture.

The catatonia did not resolve with lorazepam treatment. The patient was then aggressively treated with first increasing dosing of aripiprazole and then risperidone. Only modest improvements were seen at that time, and 24-hour mechanical ventilation was provided. The patient then demonstrated resolution of the catatonia with gradual improvement in mental status and increasing interaction. His paranoid ideation decreased along with a progressive decrease of auditory and visual hallucinations. However, he continued to have tachycardia and psychomotor slowing with impairment in rapid alternating hand movements, notwithstanding the increased ventilation. These motor deficits resolved after addition of modafinil 100 mg. The tachycardia resolved only after the addition of metoprolol 25 mg.

Given the patient's clinical course, we considered the possibility that the psychiatric symptoms were related to progressive neural adaptations to chronic unrecognized hypercapnia and hypoxemia. We hypothesized that a prolonged exposure to a slightly lowered oxygenation produces slow and persistent changes in brain metabolism. Decreased glucose brain metabolism was previously reported in individuals suffering from obstructive sleep apnea (a more common form of chronic intermittent hypoxemia and hypercapnia), and similar adaptations could have taken place in this patient. A fluorodeoxyglucose (FDG) positron emission tomography (PET) scan was thus obtained to assess brain metabolism (Fig 1). The PET scan revealed a metabolic deficits in the bilateral thalami, temporal cortices, and cerebellum. The frontal and prefrontal cortices were less affected, and the striatum was spared.

We believe that the results of the PET scan provide strong evidence for the relationship of this patient's psychiatric and pulmonary disorders. The metabolic derangements in the temporal cortices are anatomically consistent with temporal metabolic derangements associated with hallucinations of epileptic
psychosis. The thalamic deficits are consistent with amotivation, avolition, psychomotor slowing, and catatonia. Tachycardia is consistent with metabolic defects in hypothalamic circuitry. Voluntary (behavioral) control of respiration is under cortical and thalamic governance. Therefore, impairment in respiration is consistent with thalamic dysfunction, which would itself be exacerbated by hypoventilation. PET scans of patients with paranoid schizophrenia are more likely to demonstrate temporal and thalamic activation with lateralized normalization after acute treatment. Thus, the pattern of glucose uptake seen in schizophrenia is the opposite of the pattern seen in this patient's scan. The FDG-PET imaging was repeated 2 weeks later after the symptoms improved and exhibited findings similar to the first scan.

We have described an unusual case in which symptoms commonly seen in schizophrenia developed in the context of uncommon congenital central hypoventilation. More common causes of intermittent hypoventilation such as obstructive sleep apnea have been associated with mood and anxiety disorders and, less impressively, with other psychiatric illness. However, it is difficult to know whether psychiatric consequences of sleep apnea are the result of intermittent hypoventilation or sleep disturbance, which can exacerbate many psychiatric conditions. PET imaging revealed pathology in brain regions known to underlie the presenting symptoms. Thus, even though the presenting symptoms were consistent with schizophrenia, this case represents a schizophrenia-like syndrome that may have an atypical pulmonary etiology. Our findings suggest that chronic silent hypoventilation may decrease metabolic activity in the brain, resulting in slow neural adaptations with complex behavioral sequelae. Our hypothesis is supported by the observation that the patient arrived on nighttime mechanical ventilation with psychiatric symptoms, which improved only after the ventilation was provided during the day and night and with increased tidal volume.

It is important to note that the neuroimaging findings in this case were obtained after a period of mechanical ventilation was increased and during the time of gradual psychiatric improvement. Moreover, psychiatric improvement dramatically lagged the immediate correction of blood oxygenation and \( P_{CO_2} \), supporting the notion that the metabolic changes are slow and mechanistically distinct from the changes in blood oxygenation. Similarly, changes in glucose utilization as measured by FDG-PET can lag behind behavioral changes. Persistence of PET findings after sustained increased ventilation further support our hypothesis and could be used to explore a temporal relationship between behavioral changes and FDG uptake.

The patient’s clinical course and ultimate diagnosis and treatment emphasize the difficulty in discerning hypoventilation in the absence of respiratory distress. Chronic hypoventilation, as in this case, can be silent for years, is easily masked by supplemental oxygen, and can only be definitively determined by invasive measures of \( P_{CO_2} \) tension. The challenge in a patient with a control of breathing disorder is to ascertain ventilation, by measuring \( P_{O_2} \), as well as oxygenation, without disrupting the natural breathing pattern with noxious stimuli. Furthermore, linking the pulmonary and psychiatric symptoms in patients with similar presentations may dictate different medical management than in cases of typical schizophrenia. First, because such patients may not have a primary psychiatric disorder, they would benefit from short-term treatment with antipsychotic medication, which reduces the risks of long-term antipsychotic use. Second, similar patients would make better candidates for surgical intervention, such as a phrenic nerve pacemaker, because an internal pacemaking device may be disturbing to someone with active paranoia.

**CONCLUSIONS**

A PET scan assisted in determining the appropriate diagnosis for this patient, which informed us of the underlying brain pathophysiology associated with his symptoms. Additionally, this patient’s improved outcome and treatment plan was made possible by the close interaction between different specialties involved in managing the diverse symptoms.

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