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Congenital Central Hypoventilation Syndrome in an Adult With Diaphragmatic Pacing Failure

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Abstract

Congenital central hypoventilation syndrome (CCHS) is a rare disorder of autonomic nervous system dysregulation caused by mutations in the PHOX2B gene. While volitional respiration remains intact, autonomic ventilatory responses to hypoxemia and hypercarbia are absent or attenuated, often culminating in significant alveolar hypoventilation. CCHS initially presents in the neonatal period, with patients often requiring temporary tracheostomy followed by diaphragmatic pacing. While prognoses in the past were grim, with advances in proper ventilatory support, many patients with CCHS are successfully transitioning to adult care, where they face a different set of challenges. We present the case of a 46-year-old woman with CCHS and a non-functional diaphragmatic pacemaker who presented with acute hypoxic and hypercapnic respiratory failure precipitated by an upper respiratory tract infection. The case highlights the vulnerability of adult CCHS patients and discusses the role of non-invasive positive pressure ventilation (NIPPV) in long-term management.

Categories: Pediatrics, Pulmonology, Internal Medicine
Keywords: avaps, cchs, congenital central hypoventilation syndrome, cor pulmonale, diaphragmatic pacemaker, hypercapnic respiratory failure, non-invasive ventilation, phox2b, polycythemia

Introduction

Congenital central hypoventilation syndrome (CCHS) is a rare, lifelong disorder of autonomic nervous system dysregulation caused by heterozygous mutations in the paired-like homeobox 2B (PHOX2B) gene [1,2]. The hallmark of CCHS is alveolar hypoventilation with markedly attenuated or absent central and peripheral chemoreceptor responsiveness to hypoxemia and hypercarbia, which is most pronounced during non-rapid eye movement sleep but may also affect wakefulness in more severe phenotypes [1,3]. Beyond respiratory control, CCHS is associated with diffuse autonomic nervous system dysfunction, including cardiovascular dysregulation (decreased heart rate variability, sinus pauses, and arrhythmias), gastrointestinal dysmotility (e.g., Hirschsprung disease), tumors of neural crest origin, ophthalmologic abnormalities, and altered thermoregulation [1,3].

Lifelong artificial ventilatory support is the cornerstone of CCHS management. Options include positive pressure ventilation via tracheostomy, non-invasive positive pressure ventilation (NIPPV), and diaphragmatic pacing through phrenic nerve stimulation [1,4]. Diaphragmatic pacers offer the advantage of increased mobility and improved quality of life, particularly for patients requiring daytime ventilatory support or for whom nocturnal NIPPV becomes intolerable [1]. However, phrenic-nerve pacing systems have recognized long-term limitations and modes of failure. These implanted systems connect a subcutaneous radiofrequency receiver to the phrenic nerve; an external antenna transmits an electromagnetic pulse that stimulates the nerve and produces diaphragmatic contraction. Over time, transcutaneous signal transmission may attenuate as subcutaneous tissue changes, receivers may calcify, electrodes or the phrenic nerve may be injured, and hardware may simply fail or be outgrown, any of which can result in inadequate diaphragmatic activation and progressive or abrupt hypoventilation [5]. A dysfunctional diaphragmatic pacemaker may therefore leave patients vulnerable to acute or gradual hypoventilation.

CCHS was initially reported by Dr. Robert Mellins in 1970. Improved outcomes have allowed a growing number of patients with CCHS to reach adulthood, where they must transition from pediatric programs experienced in their care to adult systems often unfamiliar with the syndrome and with diaphragmatic pacing. Pacer revisions are not readily available at most centers. We present a case of an adult CCHS patient with diaphragmatic pacer dysfunction and discuss challenges transitioning to NIPPV.

Case Presentation

A 46-year-old woman with a history of CCHS and a history of childhood diaphragmatic pacemaker implant was admitted with a one-week history of cough, nasal congestion, and sore throat. She had been lost to follow-up from her pediatric care team and had difficulty establishing care with an adult provider familiar with CCHS. She reported using a bilevel positive airway pressure (BiPAP) that was over 10 years old. She had also stopped using her diaphragmatic pacemaker during this time, as it was no longer working, and thus, she

no longer had her transmitter.

On presentation, she was alert and conversant, with normal blood pressure and heart rate, and faint bibasilar rales on auscultation. She was hypoxemic in the emergency department, requiring supplemental oxygen. Admission vital signs and laboratory data are summarized in Table *1*.

Parameter	Value	Reference range
Blood pressure	154/94 mmHg	90-120/60-80 mmHg
Heart rate	80 beats/min	60-100 beats/min
BMI	28 kg/m^2	
SpO_2 (room air, on arrival)	80%	≥95%
pH (arterial, 30% FiO_2)	7.36	7.35-7.45
$PaCO_2$ (arterial, 30% FiO_2)	74 mmHg	35-45 mmHg
PaO_2 (arterial, 30% FiO_2)	93 mmHg	80-100 mmHg
Hemoglobin	16.7 g/dL	12.0-15.5 g/dL (women)
HCO_3	37 mmol/L	20-31 mmol/L
Brain natriuretic peptide (BNP)	162 pg/mL	<100 pg/mL
D-dimer	2.43 µg/mL FEU	<0.50 µg/mL FEU

TABLE 1: Admission vitals and laboratory findings.

The arterial blood gas demonstrated a compensated respiratory acidosis with marked hypercapnia, consistent with chronic alveolar hypoventilation with an acute component, and the elevated hemoglobin was consistent with secondary polycythemia from chronic hypoxemia.

The elevated D-dimer prompted computed tomography angiography (CTA) of the chest, which was negative for pulmonary embolism. The CT chest was, however, notable for bilateral diaphragmatic pacers as seen in Figure *1A* and mild cardiac chamber dilation with pulmonary edema as shown in Figure *1B*. Transthoracic echocardiography demonstrated a left ventricular ejection fraction of 50% with a dilated right ventricle and right atrium and an estimated right ventricular systolic pressure of 51 mmHg, consistent with pulmonary hypertension and right heart strain. Taken together, the findings were interpreted as chronic alveolar hypoventilation (from CCHS) complicated by secondary polycythemia and pulmonary hypertension/cor pulmonale, with an acute deterioration driven by both the viral respiratory infection and volume overload/pulmonary edema.

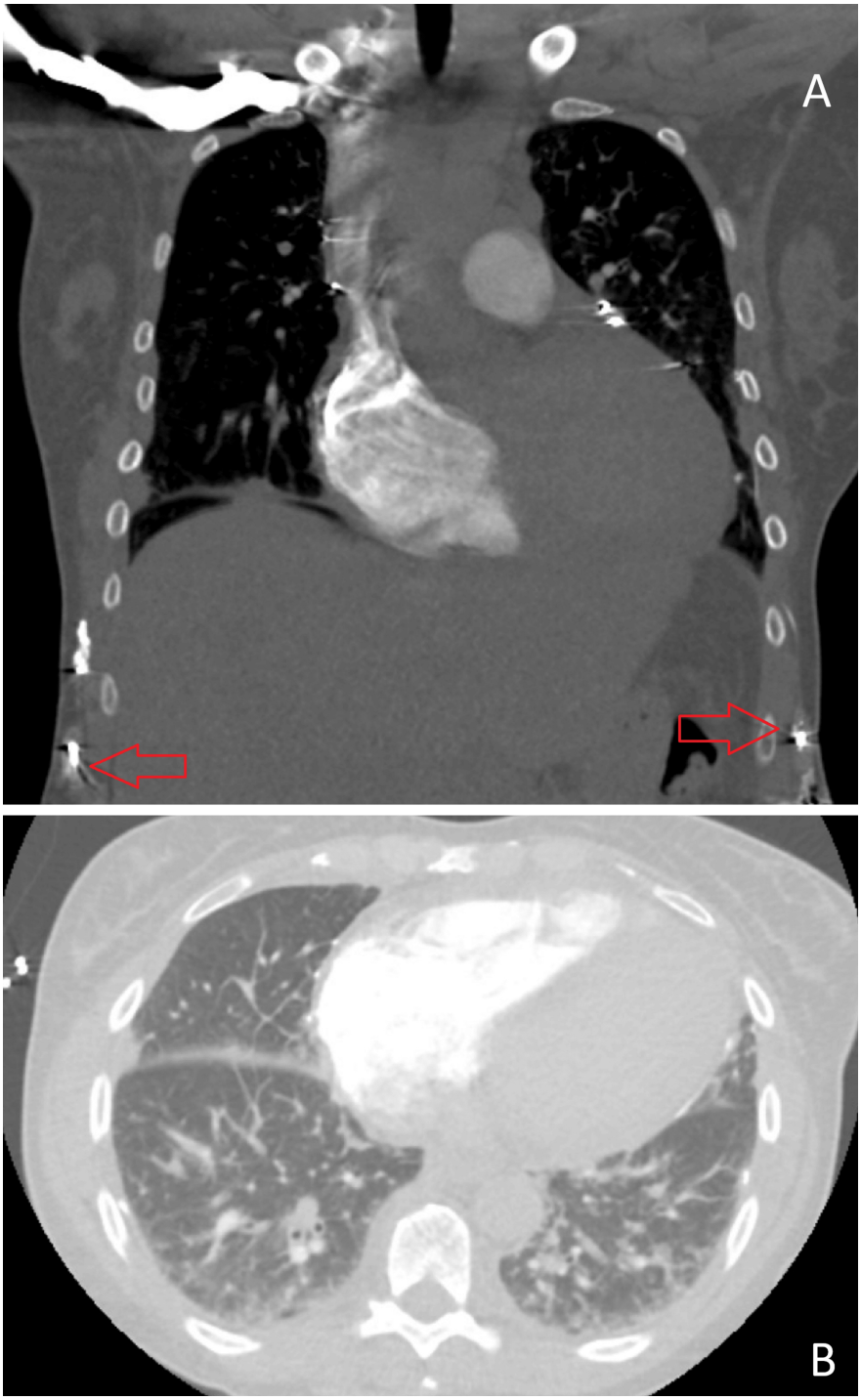


FIGURE 1: Computed tomography angiography (CTA) of the chest.

CTA chest was negative for pulmonary embolism. (A) Coronal view showing bilateral diaphragmatic pacer receivers external to the rib cage (red arrows). (B) Axial view at the level of the heart showing bilateral pulmonary edema, fluid in the minor fissure, mild right ventricular enlargement, and poor contrast filling of the left ventricle.

CTA: Computed tomography angiography.

Diuresis was initiated, with improvement in oxygenation. Given her hypercapnic respiratory failure, loss of the transmitter, and outdated BiPAP device, we started the patient on average volume-assured pressure support via our hospital's Philips Respironics V60. For preliminary settings, we specified a target tidal volume of 490 mL, corresponding to ~8 cc/kg, and a respiratory rate of 16 breaths/min, which was her daytime resting respiratory rate. Expiratory positive airway pressure (EPAP) was set to 5 cmH_2O, with an IPAP range of 7-20 cmH_2O. These settings were titrated at the bedside to the patient's comfort while she was

awake. Due to high flow rates and air leaks, end-tidal CO_2 monitoring for NIPPV is often inaccurate, and transcutaneous CO_2 monitoring was not available. Therefore, while the patient remained hospitalized, venous blood gases were obtained each morning to ensure the efficacy of the settings. End-tidal CO_2 monitoring was used during the day to ensure CO_2 normalization.

Over the course of her admission, the patient demonstrated clinical improvement, with resolution of hypoxia and improvement in hypercapnia. The diagnosis of hypercapnia secondary to CCHS, along with a blood gas demonstrating a persistent compensated $PaCO_2$ of 66 mmHg, supported qualification for a home non-invasive ventilator prior to discharge. A ResMed Astral 150 with intelligent volume-assured pressure support (iVAPS) and auto-EPAP was set to target alveolar ventilation (Va) of 6.2 L/min based on the abovementioned target tidal volume and respiratory rate. EPAP was set to a range of 5-10 cmH_2O and pressure support was set to 1-15 cmH_2O. iVAPS was selected for its ability to automatically adjust inspiratory pressure to maintain a target tidal volume, thereby providing consistent ventilatory support across varying respiratory mechanics [1,6].

As an outpatient, a PAP titration polysomnogram with transcutaneous CO_2 monitoring was performed to assess and optimize settings and patient comfort. Ultimately, iVAPS settings of Va 6.6 L/min, EPAP 10 cmH_2O, PS 4-10 cmH_2O, and a respiratory rate of 16 breaths/min effectively improved stabilized $TcCO_2$ at 41 mmHg. Efforts to reassess her diaphragmatic pacer are ongoing.

Discussion

CCHS patients face extraordinary challenges as children. Pediatric care for CCHS has evolved substantially, and adult medicine must now follow suit. This case illustrates several important clinical considerations in the management of adult patients with CCHS.

CCHS patients begin life within a medical community keenly aware of their vulnerabilities. As they transition to adult care, they face the challenge of assimilating into health care systems that are much less familiar with their condition [7]. A deceptively benign physical examination often belies profound, well-tolerated hypercapnia because these patients do not sense or respond to hypoxemia and hypercapnia. Adult providers must therefore be especially vigilant for nocturnal hypoventilation, the exaggerated risks of anesthesia and opioids, and the sequelae of chronic hypoventilation, including pulmonary hypertension, cor pulmonale, secondary polycythemia, and arrhythmias [1,7]. Pulmonary hypertension and cor pulmonale have been reported in up to 78% of CCHS patients in early cohorts, and echocardiographic surveillance for right ventricular hypertrophy and cor pulmonale is recommended at least annually [8,9]. Anesthetic exposure poses particular risk; a systematic review by Basu et al. [10] found that novel presentations of CCHS after sedation or anesthesia for minor procedures often led to diagnosis, and that undiagnosed CCHS led to complications including hypoxia, apneas, seizures, and unplanned intensive care admissions. Although our patient was awake and alert on admission and able to advocate for herself, CCHS patients may present obtunded due to hypercapnia. On subsequent outpatient visits, our patient obtained a medical alert bracelet to identify her condition in case of emergency.

After initial tracheostomy, CCHS patients generally transition to NIPPV or diaphragmatic pacing in early childhood [3,7,8]. For those who primarily use diaphragmatic pacing, several challenges emerge over time. Diaphragmatic pacemakers for CCHS are placed within the chest and connect a subcutaneous receiver to the phrenic nerve. An external antenna placed over the receiver transmits an electromagnetic pulse that stimulates the phrenic nerve, causing contraction of the diaphragm. These systems are inherently not MRI-compatible. The amplitude of the transmitted signal drives the force of diaphragmatic contraction and can be titrated to achieve a desired tidal volume. With age, transcutaneous signals may attenuate as subcutaneous fat increases, requiring recalibration of transmitter amplitudes to overcome the additional resistance [9]. Receivers may also develop calcifications, ultimately culminating in pacer failure. Kwon et al. described a case of diaphragm pacing failure in a 38-year-old woman with CCHS who had used diaphragmatic pacing for 24 years; surgical exploration revealed significant circumferential calcium accumulation on the right pacer receiver, and replacement of the receivers in subcutaneous pockets closer to the skin surface restored robust diaphragm contractions bilaterally [5]. The exact etiology of our patient's pacer failure was unclear and never fully elucidated. There were no calcifications surrounding the pacer on imaging. She also, unfortunately, no longer had her transmitter. Had a transmitter been available, tidal volume voltages could have been increased one side at a time while monitoring for diaphragmatic contractions. If still ineffective, Kwon et al. described assessing pacer components intraoperatively during replacement to identify malfunctioning components [5]. Few surgeons have experience with pacer replacement in adults. Thus, our patient ultimately remains reliant on NIPPV, which has some advantages. While diaphragmatic pacing effectively treats central apnea, it does not treat obstructive sleep apnea (OSA). The negative inspiratory pressure generated by diaphragmatic pacing does not splint the upper airway open in the same manner as positive pressure ventilation [8].

Many modes of NIPPV exist, and while an ideal mode for adult CCHS patients has not been defined, several considerations are essential. Spontaneous ventilator modes (e.g., continuous positive airway pressure (CPAP)

and BiPAP in spontaneous mode) are insufficient for CCHS patients due to their lack of respiratory drive and inability to trigger breaths reliably [8,9,11]. Ventilators with a backup battery are preferred in the event of power loss. The ability to set high-leakage alarms or low-minute ventilation alarms, and the ability to store and review these alarms, may be helpful early in the setup phase while settings are being optimized or when awaiting a polysomnographic titration [9]. The option to have auto-EPAP is also beneficial for patients with concomitant OSA. For these reasons, we opted to use the ResMed Astral 150 with iVAPS for our patient. In a study of eight children with CCHS, Khayat et al. [11] suggested that iVAPS was associated with a reduction in peak transcutaneous CO_2 during NREM sleep compared to traditional spontaneous/timed (S/T) mode (median 43.0 vs. 46.5 mmHg, $p = 0.05$), suggesting that iVAPS may offer advantages in controlling the variable hypoventilation that occurs across sleep stages. The American College of Chest Physicians, in collaboration with the American Association for Respiratory Care, the American Academy of Sleep Medicine, and the American Thoracic Society, has recognized that volume-assured pressure support modes should be considered in patients with persistent hypercapnia despite standard BiPAP support and in those with significant dyssynchrony or oxygenation requirements that cannot be met by standard BiPAP devices [4].

As the population of adults living with CCHS continues to grow, with recent European CCHS Consortium data showing a 25-year survival probability of 89% for isolated CCHS, the need for adult-focused CCHS management frameworks is increasingly urgent [12]. Slattery et al. [7] have highlighted that unique considerations for adult CCHS patients include independent living, family planning, exposure to anesthesia, and substance use, all of which can interact with the underlying ventilatory deficit.

Conclusions

This case highlights the challenges faced by a growing population of adult CCHS patients with exceptional ventilatory support needs and demonstrates the feasibility of non-invasive ventilation with a volume-assured mode as both an acute intervention and a durable home therapy. The acute deterioration in this patient reflected the convergence of several processes that likely overwhelmed an already fragile ventilatory insufficiency. During such acute exacerbations, awareness and understanding of CCHS physiology and ventilatory support devices (e.g., diaphragmatic pacemakers and NIPPV) are important for adult providers. As the population of adults living with CCHS continues to grow, further research into optimal long-term ventilatory strategies and cardiopulmonary monitoring in this population is warranted.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Caleb Hsieh, Cole Liberator, Thien P. Nguyen

Acquisition, analysis, or interpretation of data: Caleb Hsieh, Cole Liberator

Drafting of the manuscript: Caleb Hsieh, Cole Liberator, Thien P. Nguyen

Critical review of the manuscript for important intellectual content: Caleb Hsieh, Cole Liberator, Thien P. Nguyen

Disclosures

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References

1. Weese-Mayer DE, Rand CM, Khaytin I, et al.: Congenital Central Hypoventilation Syndrome. University of Washington, Seattle; 2021. https://www.ncbi.nlm.nih.gov/books/NBK1427/.
2. Massie J, Gillam L: Ethical considerations with the management of congenital central hypoventilation syndrome. Pediatr Pulmonol. 2015, 50:503-10. 10.1002/ppul.23097
3. Kam K, Bjornson C, Mitchell I: Congenital central hypoventilation syndrome; safety of early transition to non-invasive ventilation. Pediatr Pulmonol. 2014, 49:410-3. 10.1002/ppul.22848
4. Gregory B, Ezenwanne C, Al Mahrizi AD, et al.: AVAPS versus BiPAP in acute hypercapnic respiratory failure: a systematic review and meta-analysis. COPD. 2026, 23:2671706. 10.1080/15412555.2026.2671706
5. Kwon A, Lodge M, McComb JG, Durham S, Shin CE, Keens TG, Perez IA: An unusual cause of diaphragm

pacer failure in congenital central hypoventilation syndrome. J Clin Sleep Med. 2022, 18:949-52. 10.5664/jcsm.9778

6. Mokhlesi B, Won CH, Make BJ, Selim BJ, Sunwoo BY: Optimal NIV medicare access promotion: patients with hypoventilation syndromes: a technical expert panel report from the American College of Chest Physicians, the American Association for Respiratory Care, the American Academy of Sleep Medicine, and the American Thoracic Society. Chest. 2021, 160:e377-87. 10.1016/j.chest.2021.06.083
7. Slattery SM, Perez IA, Ceccherini I, et al.: Transitional care and clinical management of adolescents, young adults, and suspected new adult patients with congenital central hypoventilation syndrome. Clin Auton Res. 2023, 33:231-49. 10.1007/s10286-022-00908-8
8. Maloney MA, Kun SS, Keens TG, Perez IA: Congenital central hypoventilation syndrome: diagnosis and management. Expert Rev Respir Med. 2018, 12:283-92. 10.1080/17476348.2018.1445970
9. Trang H, Samuels M, Ceccherini I, et al.: Guidelines for diagnosis and management of congenital central hypoventilation syndrome. Orphanet J Rare Dis. 2020, 15:252. 10.1186/s13023-020-01460-2
10. Basu SM, Chung FF, AbdelHakim SF, Wong J: Anesthetic considerations for patients with congenital central hypoventilation syndrome: a systematic review of the literature. Anesth Analg. 2017, 124:169-78. 10.1213/ANE.0000000000001470
11. Khayat A, Medin D, Syed F, et al.: Intelligent volume-assured pressured support (iVAPS) for the treatment of congenital central hypoventilation syndrome. Sleep Breath. 2017, 21:513-9. 10.1007/s11325-017-1478-5
12. Bokov P, Chaitidou-Kolb P, Dudoignon B, et al.: Survival in congenital central hypoventilation syndrome (CCHS): data from the European CCHS Consortium. Thorax. 2026, 10.1136/thorax-2025-224512