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CASE REPORTS

# An unusual cause of diaphragm pacer failure in congenital central hypoventilation syndrome

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Congenital central hypoventilation syndrome is a rare genetic disorder affecting ventilatory response to hypercapnia and/or hypoxemia. We describe a case of diaphragm pacing (DP) failure in a 38-year-old woman with congenital central hypoventilation syndrome who used DP as ventilatory support only during sleep for 24 years. Diagnostic evaluation began with examination of external DP equipment, but adjustment did not elicit adequate diaphragm contractions. Clinical evaluation and transtelephonic monitoring showed absent function of the right pacer and diminished function of the left pacer. The patient had surgical exploration of her internal DP components. The operation revealed that the right pacer receiver had significant circumferential calcium accumulation. After replacement of the receivers in subcutaneous pockets closer to the skin surface, robust diaphragm contractions bilaterally occurred with stimulation. This case suggests DP failure can result from development of calcification and increased distance from the skin surface to the receivers due to weight gain.

**Keywords:** congenital central hypoventilation syndrome, diaphragm pacing, complication, malfunction

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**BRIEF SUMMARY**

**Current Knowledge/Study Rationale:** Patients with congenital central hypoventilation syndrome require assisted ventilation, and one method is diaphragm pacing. Diaphragm pacing failure can occur due to malfunction of components, and an increase in body weight can interfere with diaphragm pacing function.

**Study Impact:** Calcium deposition and accumulation around internal diaphragm pacing receivers can cause diaphragm pacing malfunction. Evaluation should include assessment of the integrity of external components of the diaphragm pacers and use of transtelephonic monitoring, and a surgical approach beginning with replacement of pacer receivers may mitigate more invasive surgery.

## INTRODUCTION

Congenital central hypoventilation syndrome (CCHS) is a rare disorder caused by a mutation in the *PHOX2B* gene, leading to improper development and function of the autonomic nervous system.[1–3] Those with CCHS have absent or reduced ventilatory response to hypercapnia and/or hypoxemia, and, therefore, they require assisted ventilation either during sleep only or full-time. Most patients initially present as neonates with apnea, cyanosis, and/or profound hypercapnia and hypoxemia requiring assisted ventilation and are unable to be weaned off ventilatory support. Some patients present as older children and adults following respiratory infection or exposure to anesthesia or sedating medications.[1–3] The diagnosis of CCHS is confirmed with genetic testing of the *PHOX2B* gene. While awaiting genetic confirmation, it is important to rule out other causes, such as pulmonary, cardiovascular, neurologic, or metabolic diseases. Once diagnosis is established, it is also essential to look for autonomic nervous system dysfunction, such as arrhythmia, Hirschsprung disease, and neural crest cell tumors.[1,2]

Treatment modalities include various mechanical ventilation methods, such as positive pressure ventilation via tracheostomy, noninvasive positive pressure ventilation via mask, and diaphragm pacing (DP). In CCHS patients who are ventilator-dependent only during sleep, DP allows for potential tracheostomy decannulation.[4] For patients who are ventilator-dependent full time, DP allows for periods of independence from home mechanical ventilators. Potential candidates for DP must have intact phrenic nerves and diaphragm function.[5] Complications of DP include obstructive apnea during sleep in those without tracheostomy, potential for infection by a foreign body, and increased postoperative risk for atelectasis, pneumonia, bradycardia, pneumothorax, and seizure due to hypercarbia.[1,5–8]

In DP, the external transmitter generates pulses that are transmitted by external antennae to bilateral internal receivers, which are connected to electrodes at the phrenic nerves. The receivers then send the electrical stimulation to the phrenic nerve electrodes, eliciting diaphragm contractions.[1] DP failure can result from malfunction of any of these components. Here, we present a patient with CCHS who experienced DP failure

secondary to alterations in the receivers' subcutaneous pockets; we review an approach to assessment of diaphragm pacing failure and describe a surgical approach to identify and repair the involved component.

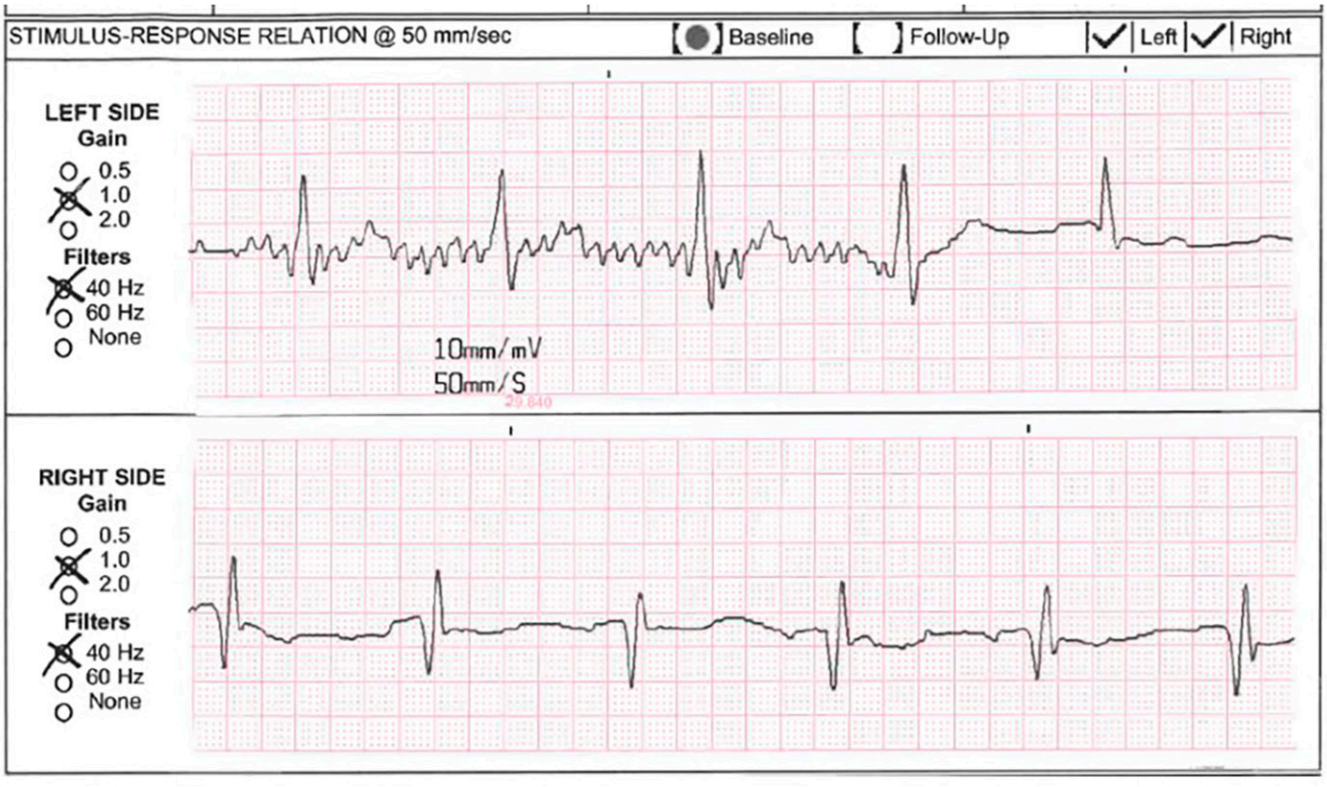
## REPORT OF CASE

A 38-year-old woman with CCHS, with the *PHOX2B* 20/33 polyalanine repeat expansion mutation, required ventilatory support only during sleep. Thoracoscopic implantation of diaphragm pacers was performed at age 14 years. At that time, bilateral monopolar electrodes were placed under the phrenic nerves thoracoscopically and sutured in place on the pericardium.[5] The electrode lead wires were separately brought out of the thoracic cavity through the diaphragm, connected to the diaphragm pacer receivers, and placed into subcutaneous pockets in the right and left upper quadrants of the abdomen. There were no complications. The DP worked well, and her tracheostomy was decannulated at age 15 years. The patient successfully used DP all night without tracheostomy into adulthood, including throughout her 2 pregnancies and progressively increasing weight gain.

At age 38 years, after almost 24 years of nightly use, the patient experienced malfunction of both diaphragm pacers over the course of 2 days. She noted that she woke up in the morning with a headache and felt groggy, reporting that she experienced these symptoms only when she was not well ventilated. She also felt as though her diaphragm was not being stimulated, especially on her right side. Familiar with the use of diaphragm pacing, the patient checked the transmitter batteries, integrity of the antenna, and alignment of the antenna over the internal receivers but still was not able to elicit diaphragm contractions. She presented to the emergency department at Children's Hospital Los Angeles (CHLA), where her oxygen saturation was 88% and her capillary blood gas showed pH 7.39, $pCO_2$ 56 torr, and $HCO_3^-$ 34 mEq/L. She was admitted to CHLA for initiation of noninvasive positive pressure ventilation via mask due to suspected diaphragm pacer failure. On follow-up visit, DP function was evaluated in the CHLA pulmonology clinic. While awake, the patient's baseline settings demonstrated no diaphragm contractions bilaterally. Even with the right tidal voltage at the maximal amplitude setting of 999 on the device (output voltage 10 V), there was no palpable right diaphragm contraction. When the left amplitude on the device was turned up to 800, higher than her baseline settings of 532, only weak left diaphragm contraction was elicited. Transtelephonic monitoring performed at a maximal setting of 999 (output voltage of 10 V) confirmed absent function of the right pacer and the significantly diminished function of the left pacer (**Figure 1**). As the patient desired to continue with diaphragm pacing, surgical exploration was planned.

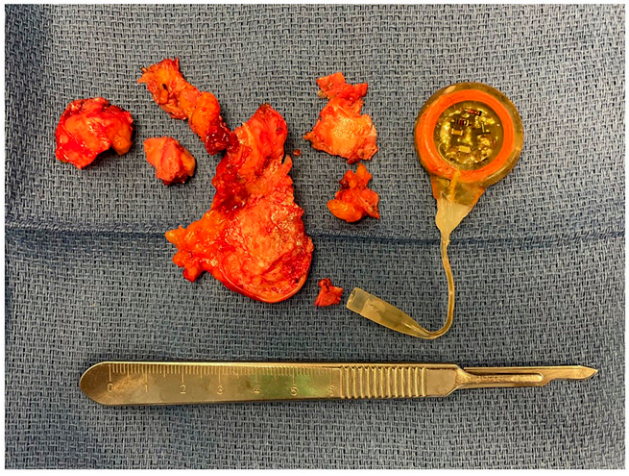
The patient had surgery 6 months after initial discovery of DP failure. The abdominal pouch on the right side was opened,

**Figure 1**—Transtelephonic monitoring.




Diaphragm pacer artifact on the left side is absent on the right side, confirming failure of right-sided diaphragm pacer.

**Figure 2**—Right diaphragm pacer receiver with calcifications.



The calcified tissue excised at surgery is shown next to the receiver.

and the receiver was noted to be encapsulated by a significant amount of calcification. The right receiver was removed by cutting through the calcified encasement (**Figure 2**). This original right receiver was then tested in a more superficial subcutaneous pocket. This demonstrated contraction of the diaphragm, suggesting that the nonfunctioning of the right receiver was likely due to the calcification and increased distance from skin surface due to marked weight gain. As the present receiver was 24 years old, it was replaced, and the new receiver was placed in a more superficial subcutaneous pocket. The wound was closed with a final check, eliciting strong right diaphragm contractions at an amplitude setting of 450 on the device.

The surgical technique for the left side was the same as for the right. There was no calcification around the left receiver. When placing the old receiver in a more superficial subcutaneous location, the DP worked well at the normal voltage setting. For the same reason as on the right, the left receiver was replaced. Before and after wound closure, the left DP produced excellent diaphragm contraction at the 450 amplitude setting. Because there were robust diaphragm contractions at normal voltage stimulation, the phrenic nerve electrodes were not replaced. The patient tolerated the operation well.

Upon follow-up in the pulmonology clinic of Children's Hospital Los Angeles a month after the surgery, the patient's new DP receivers worked well, and strong diaphragm contractions were elicited bilaterally at the 450 amplitude setting. Transtelephonic monitoring performed at this time confirmed function of both pacers bilaterally. Polysomnography is planned to assess optimal DP settings prior to initiation of DP as ventilatory support for sleep only.

## DISCUSSION

We present this unusual case of DP failure in a 38-year-old woman with CCHS who had been ventilated by diaphragm pacing during sleep for 24 years. She used the same internal DP components during this time. Failure of the mechanical components for diaphragm pacing has been described before, including previous reports on inadequate DP caused by weight gain.[4,8] Our case highlights the potential for calcium accumulation around the receivers to diminish percutaneous electrical transmission enough to render the DP nonfunctional. It also supports previously described findings on the effect of weight gain on DP function.[4]

In order to evaluate our patient's DP failure, we began with the assessment of external equipment, clinical assessment of diaphragm contraction, and finally transtelephonic monitoring. The clinical assessment involved testing baseline DP settings to check for contractions and then increasing the tidal volume voltage one side at a time.[6] Once clinical assessment was complete, transtelephonic monitoring could confirm results. If there were no contractions or only weak contractions elicited, new internal DP components or a different method of ventilation would be required.

Although we had originally planned to replace all DP components, we began the surgical approach by examining the receiver components and exchanging them for new ones as necessary. Testing of the receivers with new antennae during the operation could determine whether the phrenic nerve electrodes also needed replacement. In this case, the new receivers were enough to elicit strong diaphragm contractions. This approach minimized patient risk and potential damage to the phrenic nerves in the event that only the receivers needed replacement.

From this unusual case, we conclude that calcium can encase DP receivers and that calcium deposition can accumulate to a significant amount over time. This case also underscores how increasing distance from skin surface, such as that occurring with weight gain, can interfere with DP function. Calcification of internal DP components is an uncommon cause of DP failure but suggests that calcium deposition and accumulation should be considered when evaluating patients for DP malfunction and/or failure, especially in those who have used DP long-term. Our case emphasizes the importance of routine follow-up and periodic evaluation of DP function to confirm optimal performance.

## ABBREVIATIONS

CCHS, congenital central hypoventilation syndrome
DP, diaphragm pacing

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## SUBMISSION & CORRESPONDENCE INFORMATION

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## DISCLOSURE STATEMENT

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