CASE REPORT

Airway obstruction in congenital central hypoventilation syndrome

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SUMMARY

Congenital central hypoventilation syndrome (CCHS) is the failure of the autonomic system to control adequate ventilation while asleep with preserved ventilatory response while awake. We report a case of a patient with CCHS who presented with intrathoracic and extrathoracic airway obstruction after tracheostomy tube decannulation and phrenic nerve pacer placement. Nocturnal polysomnography (NPSG) revealed hypoxia, hypercapnia and obstructive sleep apnoea, which required bilevel positive airway pressure titration. Airway endoscopy demonstrated tracheomalacia and paretic true vocal cords in the paramedian position during diaphragmatic pacing. Laryngeal electromyography demonstrated muscular electrical impulses that correlated with diaphragmatic pacer settings. Thus, we surmise that the patient's upper and lower airway obstruction was secondary to diaphragmatic pacer activity. Thorough airway evaluation, including NPSG and endoscopy, may help identify the side effects of diaphragmatic pacing, such as airway obstruction, in patients with CCHS.

BACKGROUND

Idiopathic congenital central hypoventilation syndrome (CCHS) is characterised by generally adequate ventilation while the patient is awake and alveolar hypoventilation during sleep. Severely affected children can hypoventilate while they are awake and asleep. While asleep, children with CCHS experience progressive hypercapnia and hypoxaemia with decreased ventilator sensitivity to these factors. There is a lack of arousal responses and sensations of dyspnoea to the endogenous challenges of isolated hypercapnia, hypoxaemia and the combined stimulus of hypercarbia and hypoxaemia.[1–4] Most children with CCHS do not survive infancy unless they receive ventilator assistance during sleep and may require tracheotomy tube placement and lifetime mechanical ventilation. Diaphragm pacing systems are commercially available and help to generate breathing using the child's own diaphragm as the respiratory pump. No pharmacological respiratory stimulant has shown to be effective for children with CCHS.[5–8]

The incidence of CCHS is estimated to be 1 in 200 000 live-births and results from a polyalanine repeat expansion mutations in the paired-like homeobox (PHOX) 2B gene in more than 90% of cases. In 2006, there were only about 200 known cases worldwide, but these numbers are considered to be an underestimation.[9] CCHS is most commonly associated with central apnoea. Although less common in patients with CCHS with tracheostomy and mechanical ventilation, obstructive apnoeas should be recognised promptly by physicians.

We report the case of child with CCHS and obstructive apnoea secondary to tracheomalacia and vocal cord paresis. This case report is important because it is the first that describes upper airway abnormalities including vocal cord paresis and glottic obstruction presumably due to the use of diaphragmatic pacers.

CASE PRESENTATION

We present a 6.5-year-old Caucasian girl who was born full term. Owing to cyanosis during sleep, decreased respiratory effort, hypoxaemia and hypercapnia, she was intubated and subsequently had tracheostomy tube placement by 2.5 months of age. Weaning of ventilatory support was initiated at 18 months of age. She underwent phrenic nerve pacemaker placement at 3.5 years old, and genetic testing revealed PHOX 2B mutation, which confirmed the diagnosis of CCHS. By 4 years of age, she had tracheostomy tube decannulation after a normal nocturnal polysomnography (NPSG). She required diaphragmatic pacing while asleep with settings of rate 14 bpm and voltage of 7.5 V on the left and 5.7 V on the right. She also uses bilevel positive airway pressure (BiPAP) intermittently while asleep with settings of 14 and 7 cm H_2O.

By 6 years old, she developed loud snoring, humming and stridor during sleep, and daytime sleepiness with an Epworth Sleepiness Scale score of 15. Physical examination was unremarkable with normal range vital signs. Inspection of the oropharyngeal area demonstrated no anatomical abnormalities. Cardiopulmonary examination was unremarkable.

INVESTIGATIONS

The first night NPSG was initiated with baseline diaphragmatic pacing but not BiPAP. However, within 49 min, oxygen saturation (SpO_2) decreased to 68% and the end tidal CO_2 ($ETCO_2$) remained above 60 torr which prompted titration of BiPAP to 16/10 cm H_2O with resolution of hypoventilation and hypoxaemia. After 90 min, BiPAP was discontinued to assess for sleep apnoea. Without BiPAP, the patient had an apnoea–hypopnoea index of 11.5/h with inspiratory squeaks and loud humming noises during exhalation. Therefore, BiPAP was restarted at 14/7 cm H_2O with resolution of sleep disordered breathing.

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Daytime polysomnography was performed with diaphragmatic pacing but not BiPAP which revealed mild snoring and noisy asynchronous breathing without significant sleep apnoea. The patient's pacemaker rate was increased from 14 to 18 breaths/minute which resulted in modest improvement in SpO_2 and $ETCO_2$. The pacer voltage was decreased from 7.5 to 7 V on the left and from 6.5 to 5 V on the right. This resulted initially in hypopneas but then led to further improvement in the $ETCO_2$ and SpO_2.

A second NPSG with diaphragmatic pacing and BiPAP was performed. BiPAP was titrated from 10/5 to 16/11 cm H_2O with no apnoeas, hypopnoeas, respiratory effort-related arousals, hypoxaemia or hypoventilation during the study. However, the patient displayed a drop in SpO_2 and rise in $ETCO_2$ in lateral position. This positional effect was not significantly changed by further increases in the BiPAP pressure.

Initial airway evaluation showed 50% anteroposterior tracheal narrowing on inspiration along with a vocal cord paresis in the paramedian position. During a second airway evaluation, the glottic airway functioned normally with fully abducting vocal cords on inspiration when the pacemaker was turned off. With initiation of diaphragmatic pacing, there was significant glottic narrowing with vocal cords fixed at the paramedian position. A laryngeal electromyography (EMG) was performed with the EMG electrode placed into the left thyroarytenoid muscle. Diaphragmatic pacing resulted in concurrent muscular contractions of the vocal cords, quadriceps and deltoid muscles. CT of the head, neck and brain did not show significant abnormalities.

DISCUSSION

Although CCHS is primarily associated with hypoventilation and central apnoea, one must not be misled and should always consider other aetiologies of sleep-disordered breathing in this very unique and rare population. Moreover, obstructive events are a rare entity as most children receive a tracheotomy and remain on mechanical ventilation. Previous reports describe obstructive apnoeas in children with CCHS and need for additional ventilation with continuous positive airway pressure in approximately 50% of children with CCHS in the first year of life and during respiratory infections to overcome symptoms of airway obstruction.[10 11] A case report of resolution of obstructive sleep apnoea syndrome (OSAS) after adenoidectomy in a child with CCHS was previously reported.[12]

Central control is mandatory in maintaining upper airway patency, as demonstrated by fibre optic videoendoscopy in an infant with CCHS showing normal ventilation on a negative pressure ventilator while awake, but phasic epiglottic collapse during passive inspiration during sleep.[11] Several reflex mechanisms play a role in keeping the upper airways patent and in maintaining the balance between negative closing pressures and opening pressures. Studies on the relationship between central control of upper airway and respiratory muscle function in response to isocapnic hypoxia indicate that the genioglossus muscle behaves like a respiratory muscle and that central control of upper airway and respiratory muscles are intimately related.[13] Whether such reflex mechanisms are affected or impaired in CCHS remains questionable.

This case report is the first that describes upper and lower airway abnormalities including glottis obstruction, tracheomalacia and vocal cord paresis (VCP) presumably due to the use of diaphragmatic pacers. Tracheomalacia is usually described as primary or secondary and consists of loss of airway support leading to airway collapses during expiration and resulting in airflow limitation, air trapping and stridor.[14] We hypothesise that the aetiology of the tracheomalacia in our patient can also be, in part, secondary to previous tracheostomy. Tracheostomy or endotracheal intubation can destroy tracheal cartilage at the stoma or inflatable cuff site, respectively, which weakens the tracheal wall.[15] Incidence of tracheomalacia secondary to tracheostomy is approximately 10% in children.[16] VCP is a known complication of multiple and prolonged intubation and can also be secondary to cardiothoracic surgery by lesion of the recurrent laryngeal nerve. Bilateral VCP is more likely associated with a lesion of the central nervous system such as hydrocephalus or Arnold-Chiari abnormality. However, paresis occurring only during sleep raises the suspicion of autonomic control of breathing, reflex mechanisms in neurological control of vocal cord movement and possibly current spreading from diaphragmatic pacing as demonstrated by laryngeal EMG.

Learning points

- Although congenital central hypoventilation syndrome (CCHS) is primarily a disorder characterised by central hypoventilation and apnoea, one must not underestimate the importance of intrathoracic and extrathoracic airway abnormalities and electrophysiological interactions secondary to current spread from diaphragmatic pacers in the differential diagnosis of ventilation compromise and sleep-disordered breathing.
- Management of children with CCHS requires a meticulous follow-up and coordination of care to achieve a successful outcome for each child.
- Children should be evaluated on a 12-month basis by a centre with recognised expertise in CCHS. The evaluations should include a detailed recording during sleep and wakefulness in a respiratory physiology laboratory to monitor adequacy of ventilation.

Competing interests None.

Patient consent Obtained.

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