

A Case Study On “Ondine's Curse: A Challenging Case of Congenital Central Hypoventilation Syndrome

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Abstract:

Congenital Central Hypoventilation Syndrome (CCHS) is also known as Ondine's Curse. A rare hereditary condition known as congenital central hypoventilation syndrome (CCHS) affects babies and is evidenced by breathing difficulties during sleep without apparent respiratory warning manifestations. It is a globally underreported illness caused by a mutation in the PHOX2B gene. Affected people are increasingly able to endure life to adulthood due to increased survival rates that were achieved by early detection and care. The clinical characteristics, diagnostic difficulties, and management strategies for CCHS are covered in the current study.

Keywords: Ondine's Curse, PHOX2B gene, Hypoventilation, Genetic disorder, Management strategies.

Introduction:

A mutation in the PHOX2B gene develops congenital central hypoventilation syndrome (CCHS), a rare inheritable condition impacting the autonomic nervous system (ANS)¹. Typically, during nonrapid eye movement sleep, neonates with CCHS exhibit symptoms such as apnoea, oxygen deprivation, along with elevated carbon dioxide levels, but they do not exhibit overt signs of respiratory distress². Mellins et al first described the syndrome in 1970, describing a case in which a child experienced inadequate breathing due to central nervous system causes despite normal respiratory triggers, such as increased carbon dioxide levels, and after ruling out primary conditions in the lungs, heart, chest, and neuromuscular system³. Despite the fact that more than 1,000 cases have been documented worldwide, the true incidence probably exceeds estimated rates of one in 200,000 live births in France and one in 148,000 in Japan^{4,5}. Some cases have been documented in older children and young adults, with severe respiratory difficulties or respiratory infections following general anaesthesia^{6,7}. Better detection of CCHS and early attention have culminated in higher rates of survival, allowing numerous impacted individuals to mature into adulthood. This discussion aims to explore the clinical characteristics, diagnostic complexities, and management hurdles encountered in CCHS patients. This investigation examines the clinical features of CCHS, along with the diagnostic challenges and medicinal techniques.

Case Presentation:

A 4 years old male patient was brought to the pediatric department with a chief complaint of recurrent episode of cyanosis, especially during the sleep. Parents reported the child appearing breathless and occasionally turning blue, leading to concerns of potential respiratory distress.

Upon clinical examination, the child exhibited signs of respiratory distress during the hospital stay.

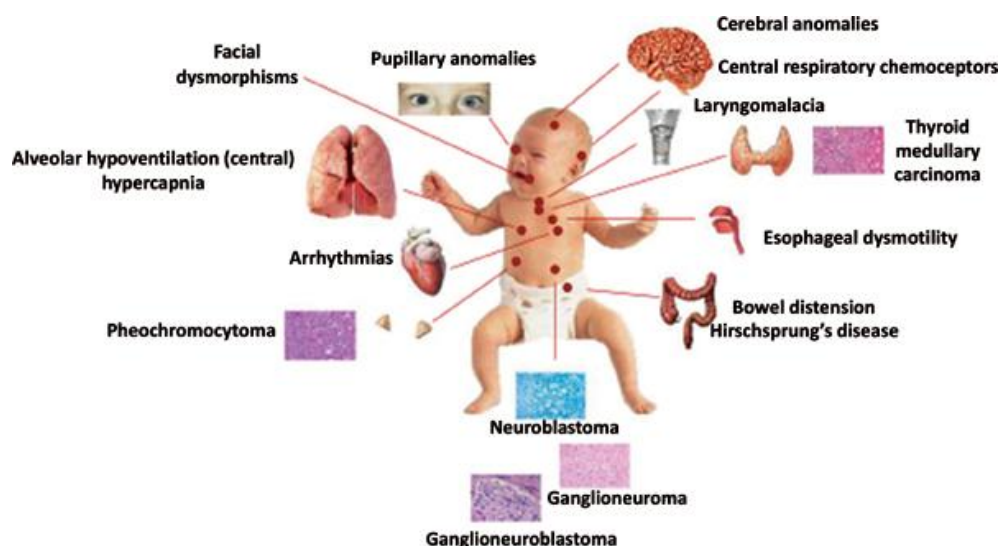


Fig: 1 Neonatal Congenital Central Hypoventilation Syndrome

Diagnostic Assessment:

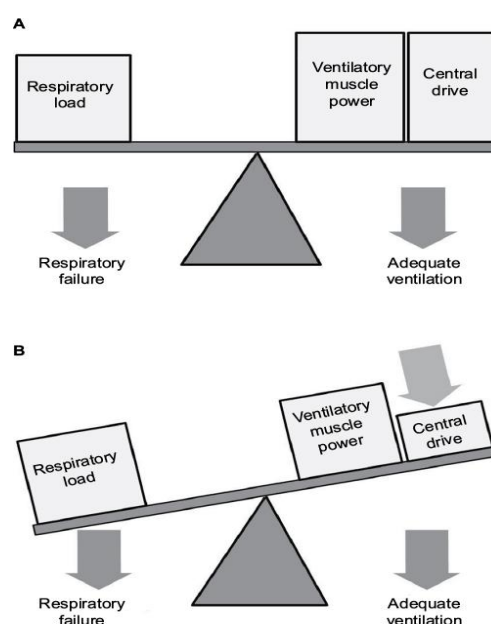


Fig: 2 The Respiratory Balance

1. Polysomnography (PSG):

Diagnostic Criterion: Abnormalities in respiratory parameters during sleep, such as hypoventilation or an elevated apnea-hypopnea index.

Values: Decreased respiratory rate, increased carbon dioxide (PaCO_2) levels during sleep, and desaturation.

2. Arterial Blood Gas (ABG) Analysis:

Diagnostic Criterion: Elevated levels of carbon dioxide (hypercapnia) during wakefulness or sleep.

Values: PaCO_2 levels typically above normal range (>45 mmHg).

3. Genetic Testing:

Diagnostic Criterion: Detection of mutations in the PHOX2B gene.

Values: Identification of mutations in the PHOX2B gene, confirming a diagnosis of CCHS.

These diagnostic tests, in combination with clinical presentation (such as episodes of hypoventilation, particularly during sleep), contribute to confirming a diagnosis of Congenital Central Hypoventilation Syndrome. The values obtained from these tests, especially increased PaCO₂ levels during sleep and genetic testing revealing PHOX2B mutations, are crucial for definitive diagnosis.

Treatment:

Medication includes Omeprazole or Lansoprazole – 0.5 to 1 mg/ kg/ day ,levetiracetam – 20mg/kg/ day divided into two doses , Oxygen Therapy, Melatonin, Methylxanthines, Benzodiazepines or Sedatives, laxatives such as polyethylene glycol or stool softeners dosage is based upon the age and the severity of constipation.

A multidisciplinary approach to management was used, which included continuous positive airway pressure (CPAP) during sleep, surgical surgery, and respiratory therapy. The patient's family was thoroughly trained in respiratory event recognition and response, and long-term ventilatory support was started.

1. **Mechanical Ventilation:** To guarantee sufficient oxygenation, the majority of people with CCHS need long-term mechanical ventilation, particularly when they sleep. Non-invasive ventilation (NIV) techniques like bilevel positive airway pressure (BiPAP) and continuous positive airway pressure (CPAP) may be used in this situation.

2. **Phrenic Nerve Stimulation:** Newer therapies stimulate the diaphragm to help with breathing through phrenic nerve stimulation systems. This technique is not commonly accessible and remains in its trial stages.

Follow-up and Outcomes:

Frequent follow-up evaluations showed decreased respiratory episodes and improved oxygen saturation values. With continued assistance and instruction, the difficulties associated with adjusting to long-term ventilatory support were overcome. Individualised therapy interventions resulted in a considerable improvement in patient's quality of life.

Discussion:

This case underscores the need for heightened clinical suspicion in cases of unexplained hypoventilation, even in the absence of overt symptoms. Additionally, the importance of genetic testing for confirming CCHS diagnosis and guiding personalized treatment strategies is highlighted. Education and support for the patient and family members are critical to understanding the condition, managing equipment, and responding to emergencies. Psychological support for the patient and family to cope with the challenges of living with a chronic respiratory condition. Genetic counselling and testing for family members to identify carriers or affected individuals, as CCHS is a genetic disorder.

Conclusion:

In conclusion, the case of this apparently healthy 4-year-old girl highlights the many different expression of Congenital Central Hypoventilation Syndrome (CCHS), emphasising its potential to manifest beyond infancy." The diagnosis of CCHS after episodes of cyanosis while rest and

recurring respiratory infections emphasises the need of investigating CCHS in such situations. Early detection through thorough examination, including genetic testing, is critical for quick intervention and specialised care, ensuring improved care as well as quality life expectancy for affected individuals even after the traditional newborn stage.

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