CASE REPORT

A rare case of idiopathic central hypoventilation syndrome

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Abstract

Central hypoventilation syndrome has been reported in children as a rare congenital disorder with associated Hirschsprung disease and several neural crest tumors. In adults, hypoventilation syndromes are usually associated with obesity, chest wall and neuromuscular disorders, and lower airways obstruction. We report a rare case of idiopathic central hypoventilation syndrome in an adult, nonobese man without any comorbidity who presented to us with chronic type 2 respiratory failure.

Keywords : central hypoventilation syndrome, polysomnography, transcutaneous CO_2.

Introduction

When arterial pCO_2 ($PaCO_2$) surpasses the upperlimit of normal level, then it is conservatively decided to be hypoventilation. Since 1942, literature has recorded data for the normal range of this parameter, with majority determining a mean value of about 38 mm Hg and the upper 95% confidence limit to be about 45 mm Hg. Consequently, a value of $PaCO_2$ greater than 45mm Hg (presumably only applicable at or near sea level) is commonly used to define the presence of hypoventilation[1]. The ventilatory control system is tightly regulated. This system is regulated by threes parameters:sensors, such as peripheral and central chemoreceptors and mechanoreceptors; central controllers that receive input and integrate the response from the above sensors; and effectors, involving the muscles of respiration, which respond to the commands of the central controllers[2]. The neurologic disorders that affect the sensors, the central controller, or the integration of the signals lead to conditions known as central alveolar hypoventilation disorders. Such disorders can lead to insufficient ventilation and an increase in $PaCO_2$(hypercarbia) and a decrease in PaO_2 (hypoxemia). The condition may be congenital or acquired, and affected children may be at risk from the neonatal period. It can be present only during sleep or during sleep and wakefulnessin more severe cases. Early detection of central hypoventilation is necessary to protect from the harmful effects of hypercapnia, acidosis, and hypoxemia on cardiovascular and neurocognitive functions[2]. We report a rare case of an adult, nonobese man with no comorbidity who presented to us with excessive daytime sleepiness and in type 2 respiratory failure.

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Case Report

Our patient was a 52-year-old man, never smoker, no history of alcohol intake, nondiabetic, nonhypertensive, with a body mass index (BMI) of 26.5 kg/m^2. He presented to our sleep clinic with history of early morning headache, excessive daytime sleepiness, and unrefreshing sleep for last 3-4 years. Patient also complained of exertional breathlessness for last 1 year, which was grade 1m MRC (modified Medical Research Council). He and his sleep partner did not report any night time snoring or witnessed apneas during sleep. There was no history of chronic cough, sputum production, wheezing, or chest pain. Patient gave no history of any abdominal complaints, syncopal attacks, palpitations, sweating, and nocturia. The patient did not give any history of drug intake, and there was no significant family history of any chronic disease. On examination, patient showed a pulse rate of 96/min, respiratory rate of 18/min, blood pressure of 128/76 mm Hg, and SpO_2 of 86% on room air. All his routine laboratory investigations were within normal limits. Thyroid function tests, serum cortisol levels, and serum leptin levels were also within normal range. His arterial blood gas analysis revealed a pH of 7.396; $paCO_2$60; paO_2 56; and HCO_3 32, suggestive of chronic respiratory acidosis with type 2 respiratory failure. His chest roentgenogram, spirometry, and maximum inspiratory / expiratory pressures were within normal limits. His ECG showed sinus rhythm with P pulmonale, and 2D-ECHO showed dilated right atrium and right ventricle with mild pulmonary hypertension (estimated mean pulmonary artery pressure of 33mm Hg) and normal left ventricular ejection fraction of 60%. His CT chest and CT pulmonary angiography revealed no abnormality. Electromyography and nerve conduction velocity studies were also normal. His MRI brain and spine was done to rule out any structural abnormality and showed normal findings. Patient underwent level 1 polysomnography (PSG) with transcutaneous CO_2 ($tcpCO_2$) monitoring(Figure 1). There were no obstructive apneas or hypopneas, no snoring, and no thoracoabdominal paradox. However, there was central hypopnea with sustained hypoventilation (Figure 2)in stage II sleep as evidenced by fall in nasal pressure flow signal by more than 30% of the baseline and an increase in the $tcpCO_2$ by more than 10 mm to a value >55 mm Hg for >10 min ($tcCO_2$ increased from 55 to 68 mm Hg). There were frequent arousals (arousal index = 34.8/h) following prolonged desaturation with no rapid eye movement (REM) sleep. Patient was diagnosed to show idiopathic central hypoventilation syndrome (CHS). Positive airway pressure therapy titration was done. EPAP was set at 5 cm H_2O as there were no obstructive events. IPAP was titrated to 16 cm H_2O using $tcpCO_2$ monitoring till there was no sleep-related hypoventilation with return of $tcpCO_2$ to baseline awake value (55 mm Hg). There were treatment emergent central sleep apneas (CSAs) even at $tcpCO_2$ of 57 mm Hg (Figure 3), and a backup rate of 12/min was added, which effectively eliminated CSA (Figure 4) and was close to patient's awake respiratory rate of 16/min.There was REM sleep on PAP therapy with an arousal index of 5/h. Patient was advised home nocturnal noninvasive ventilation (NIV) with oronasal mask on ST mode with IPAP of 16cm H_2O, EPAP of 5cmH_2O, and a backup rate of 12/min. On follow-up visit after 2 weeks, patient reported refreshing sleep with no early morning headache. Patient felt alert and active during the day with no significant breathlessness. His compliance with PAP therapy was satisfactory and his ABG revealed pHof 7.412; $paCO_2$ 40 mm Hg; paO_2 76mm Hg; and HCO_3 25. Patient's next follow-up was due after 3 months.

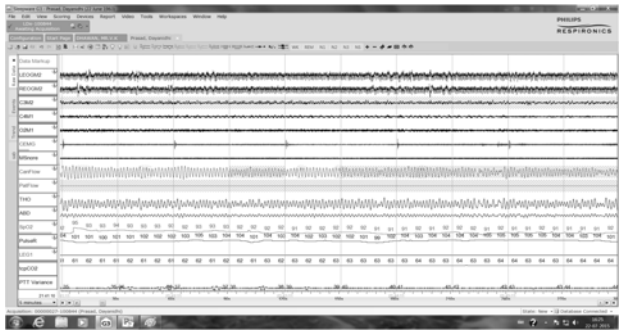

Figure 1: Polysomnography with transcutaneous CO_2 monitoring

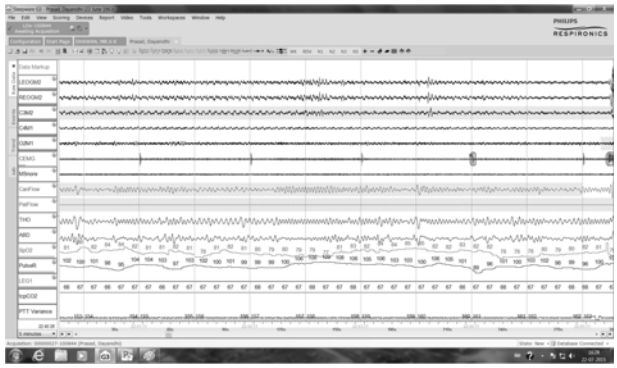

Figure 2: Sleep-linked hypoventilation with increasing $tcpCO_2$ (68) and persistent desaturation

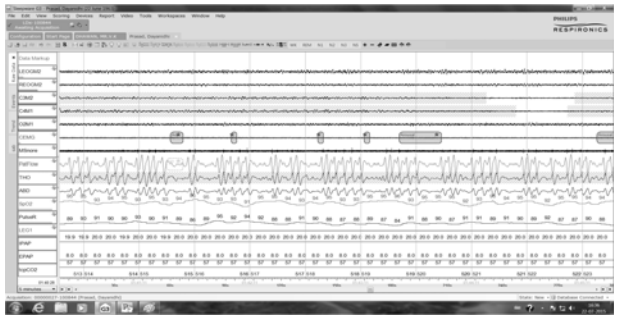

Figure 3: Treatment emergent CSA with tcpCO_2 of 57mm Hg

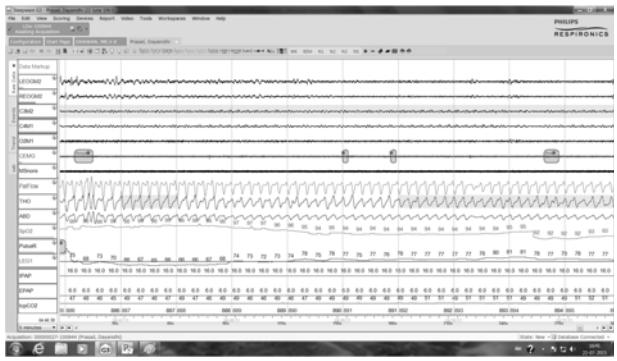

Figure 4: Backup rate of 12 added (ST mode) to abolish CSA with hypercapnia

Discussion

Congenital central hypoventilation syndrome (CCHS) is a rare disorder with usual manifestation in the newborn period or early infancy, famously referred to as Ondine's curse. A form of late-onset central hypoventilation syndrome (LO-CHS) has also been described in children of older age group (2-10 years)[3,4]. CCHS and LO-CHS are diagnosed in the absence of neuromuscular, pulmonary or cardiac disease, or an identifiable brain stem lesion. They are characterized in general by adequate ventilation while the patient is awake but hypoventilation with shallow breathing and normal respiratory rates during sleep[5]. With time, nocturnal sleep-induced hypoventilation becomes diurnal hypoventilation, with daytime awake hypercapnia owing to bicarbonate retention by kidneys and microsleeps throughout the day. While asleep,children with CCHS show progressive hypercapnia and hypoxemia[6]. Their ventilation is better in REM sleep than in non-REM sleep[6]. Absent or negligible ventilatory sensitivity is observed in them to hypercarbia while absent or variable ventilatory sensitivity to hypoxemia during sleep[7]. They show an absence of arousal response to the endogenous challenges of isolated hypercarbia and hypoxemia and to the joint stimulus of hypercarbia and hypoxemia. CCHS is associated with conditions such as Hirschsprung disease, ganglioneuroma,[8] neuroblastoma,[9] ganglioneuroblastoma, absence of heart rate variability, and eye defects,[7] including reduced pupillary light response. Feeding struggle with esophageal dysmotility in infancy, breath-holding spells, bad regulation of temperature with the basal body temperature usually <98°F, and intermittent abundant sweating episodes with cool extremities have been demonstrated anecdotally. Hypothalamic dysfunction inclusive of hyperphagia, hypersomnolence, thermal dysregulation, emotional liability, and endocrinopathies are observed only in LO-CHS.[10]

CCHS is a lifelong identification, with many patients reaching early adulthood, and these patients reveal enduring abnormalities in breath control and require lifelong ventilatory support[5]. Many ventilatory support possibilities are obtainable for the infant and the child with CCHS/LO-CHS. Infant with CCHS typically require tracheostomy and home mechanical ventilator support. The older child with entirely normal airway may be able to rely on diaphragmatic pacing by phrenic nerve stimulation while awake[11] and BiPAP mask ventilation while asleep. Those children who consistently require ventilatory support during sleep only and who are able to cooperate can be considered as candidates for noninvasive support with bilevel positive pressure mask ventilation. Published data record extended survival[12] of children with CCHS/LO-CHS and good quality of life.

Our patient is a case of idiopathic CHS with onset of symptoms in the fourth decade. He did not satisfy the definition of obesity hypoventilation syndrome as his BMI was less than 30kg/m^2. In absence of any other identifiable cause of hypercapnic respiratory failure such as neuromuscular disorder, chest wall disorder, chronic obstructive pulmonary disorder, chronic drug abuse, or brainstem lesion, our patient is an extremely rare case of adult onset idiopathic CHS. Our patient did not show any obstructive sleep apnea on PSG and demonstrated sustained hypoventilation in non-REM sleep with prolonged desaturations and frequent arousals. He did not show any REM sleep in the diagnostic PSG suggesting disturbed sleep architecture. The plausible mechanisms of this "would not breathe" type of CHS remain poorly understood and could be same as those described in the congenital variety with reduced chemosensitivity and ventilatory responses to hypercapnia and hypoxemia. Our

patient also showed hypercapnic CSA after initiation of NIV, which is attributable to defective plant gain in such patients. Plant gain is the change in the arterial $CO_2$for a given change in ventilation. When ventilation increases with NIV, $PaCO_2$ decreases considerably even though it still remains above the normal levels (this is referred to as increased plant gain). The increased plant gain increases the probability of developing central apnea if the apneic threshold $PaCO_2$ is also increased, as occurs in patients with chronic hypercapnea[13]. We were successfully able to titrate the NIV settings for our patient using $tcpCO_2$ as the guide and corrected sleep-induced hypoventilation. We did not target normocapnia in the single night titration but only corrected sleep-related increase in CO_2 from the awake value. With the treatment of sleep-induced hypoventilation using nocturnal NIV for 7 h daily, we were able to achieve daytime normocapnia after 2 weeks of regular use. This highlights the ability of nocturnal NIV to treat diurnal respiratory failure.

Conclusion

Our patient is a rare case of idiopathic CHS who presented to us in fifth decade of his life with unexplained chronic type 2 respiratory failure. After ruling out all other causes, his PSG revealed sleep-induced hypoventilation, and he was successfully treated with home nocturnal NIV. This case also highlights the importance of using $tcpCO_2$ monitoring during PSG for NIV titration in such patients.

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