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Obesity hypoventilation syndrome in a 12-year-old child requiring therapeutic phlebotomy: Case report and review of the literature

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Abstract

The childhood obesity epidemic involves unusual and underrecognized complications associated with this clinical and public health problem. Obesity hypoventilation syndrome (OHS) is defined as the triad of obesity, daytime hypoventilation, and sleep-disordered breathing in the absence of an alternative neuromuscular, mechanical or metabolic explanation for hypoventilation. We herewith report a 12-year-old boy who was diagnosed with OHS. The patient improved with phlebotomy and bi-level positive airway pressure. To the best of our knowledge, this is the first reported case of secondary polycythemia due to OHS requiring therapeutic phlebotomy.

Keywords

obesity; obesity hypoventilation syndrome; positive airway pressure; secondary polycythemia; therapeutic phlebotomy

Most of the available literature on obesity hypoventilation syndrome (OHS) refers to adults and there is a paucity of data in the pediatric age group. In 2010 it was estimated that approximately one-third of children in North America are obese or overweight.¹ The present case report describes a potentially life-threatening complication of extreme obesity.

Pulmonary complications resulting from obesity include pulmonary hypertension, asthma, obstructive sleep apnea (OSA), OHS and pulmonary embolism.² A high index of suspicion is needed to identify and treat this potentially fatal pulmonary complication in children.

Case report

A 12-year-old obese boy presented to the pediatric clinic for evaluation of dyspnea on exertion. His mother reported snoring and restless sleep since 7 years of age. The mother also reported that the “gasping episodes” at night persisted despite tonsillectomy and adenoidectomy, done when he was 7 years old. Moreover, the mother reported declining school performance, which she attributed to daytime sleepiness. He denied any fatigue, chest

pain, palpitations, or cough. Further history revealed excessive weight gain starting at 3–4 years of age. He was being followed for a weight-control program and dietary counseling, with low visit and lifestyle change compliance. At 11 years of age, he was started on metformin 500 mg twice daily. He also had a history of mild intermittent asthma for which he used albuterol as needed. There was no known history of underlying heart disease. Family history was unremarkable. His development was age appropriate. His height was 154 cm, weight 115.8 kg, and body mass index (BMI) 48.24 kg/m². On initial assessment, oxygen saturation was 86% on room air, and blood pressure was 132/90 mmHg. Physical examination showed injected conjunctiva, peripheral cyanosis of hands and feet and bilateral pitting edema. There was mild acanthosis nigricans of the neck, with normal genitalia (Tanner stage 1) and no dysmorphism. He had a perineal rash, which was presumably due to irritation due to nocturnal enuresis. Neurologic examination was normal.

He was placed on nasal cannula oxygen but did not maintain oxygen saturations. He was transferred to pediatric intensive care unit step down for close monitoring of respiratory status as well as initiation of bi-level positive airway pressure (BiPAP). Initially, he required up to 65% oxygen with BiPAP but slowly it was weaned to 35% by 24 h. BiPAP settings were 20/10 mmHg.

Laboratory investigations indicated striking abnormalities. At admission, hemoglobin was 22.3 g/dL and hematocrit 69%. Initial venous blood gas showed a pH of 7.21, pCO₂ 81, HCO₃ 26.5 mmol/L. Fasting blood sugar was 89 mg/dL, triglycerides 86 mg/dL, high-density lipoprotein cholesterol 33 mg/dL, serum insulin 63.7 µIU/mL and HbA1c 5.5. Liver enzymes were normal. Serum fT3, fT4, cortisol, and leptin were within normal limits. Chest X-ray showed cardiomegaly. Electrocardiogram on admission showed sinus arrhythmia with right axis deviation, left atrial enlargement and incomplete right bundle branch block. Echocardiogram demonstrated an anatomically normal heart with mild–moderate right ventricular enlargement with flattening of ventricular septum. He was also started on aspirin 81 mg daily to prevent thrombotic complications that could result from polycythemia. He was started on furosemide. Serum erythropoietin was normal. Nuclear medicine perfusion was negative for pulmonary embolism. Pulmonary function test confirmed restrictive impairment (forced vital capacity, 48% predicted). It also showed severe obstructive impairment (forced expiratory volume in 1 s, 39% predicted) with a significant positive bronchodilator response. Polysomnography indicated very severe OSA that even at extremely high pressure settings (22/16 mmHg) continued to be moderate, at 9.2 respiratory events per hour of sleep; significant hypoxia with oxygen saturation mostly in the 80s (nadir at 71%); and hypoventilation with significantly elevated transcutaneous CO₂ up to 72 mmHg. After starting BiPAP, repeat blood gases showed improvement in pH, pCO₂ and pO₂. Acidosis and hypercarbia returned, however, after the initial improvement. Further increments in BiPAP settings were not tolerated by the patient and, due to the possibility of barotrauma at higher pressure, it was decided to perform therapeutic phlebotomy in view of the hypoxemia and refractory respiratory acidosis. Hematocrit was persistently elevated despite the patient being on i.v. fluids. On day 3, the patient underwent phlebotomy to remove 10% of blood volume in two different sittings, 5 h apart, replacing it with fresh frozen plasma. The phlebotomy volume was calculated using the formula phlebotomy volume = blood volume × (hematocrit observed – hematocrit desired)/hematocrit observed.

He appeared more alert and comfortable. There was a reduction in daytime sleepiness. Blood gases also showed improvement in pH, pCO₂ (Fig. 1). Hematocrit dropped from 69% at admission to 56.6% after the phlebotomy. After 2 weeks the patient was discharged home on sleep-time BiPAP (20/10 mmHg) with oxygen (FiO₂, 35%). At 1 month follow up, pH was normal and hematocrit was 48.9%. Six months after discharge, the patient continued to require BiPAP but was off oxygen.

Discussion

Obesity hypoventilation syndrome is defined as obesity (BMI > 30 kg/m²), chronic alveolar hypoventilation leading to daytime hypercapnia and hypoxia (PaCO₂ > 45 mmHg and PaO₂ < 70 mmHg) and sleep-disordered breathing.³ Other causes of hypoventilation are, for example, kyphoscoliosis, neuromuscular disorders, severe hypothyroidism, severe underlying pulmonary disease, and other central hypoventilation disorders. Approximately 10–20% of patients with OSA have OHS.⁴ The classic symptoms include loud snoring, nocturnal choking episodes, apnea, excessive daytime somnolence, and morning headaches. Physical exam includes plethoric obese patient with enlarged neck girth, crowded oropharynx, prominent P2 and pedal edema.³

The pathophysiology of obesity hypoventilation is not well understood. The postulated mechanisms include abnormal respiratory mechanics resulting from obesity, impaired central response to hypercapnia and hypoxia, leptin resistance and sleep-disordered breathing.³

Positive pressure therapy is the mainstay of management for OHS. Both continuous positive airway pressure (CPAP) and BiPAP are effective in reversing daytime hypercapnia in OHS.³ An initial trial of CPAP may be considered in stable patients, especially in ambulatory care settings, but some patients may not respond to CPAP and may require non-invasive mechanical ventilation via BiPAP or volume ventilation. BiPAP should be considered in patients with CPAP failure, patients with acute-on-chronic respiratory failure, and patients who have OHS without OSA. Titration of expiratory positive airway pressure and inspiratory positive airway pressure is done to achieve eucapnia, normoxia and improved work of breathing.³

Oxygen therapy may be necessary in up to half of the patients with OHS.³ The need for supplemental oxygen drops in patients compliant with PAP therapy.³ Tracheostomy, by bypassing the upper airway, helps normalize hypercapnia and is reserved for severe OHS not responding to other therapies. Weight loss improves pulmonary mechanics and helps reverse hypercapnia.

Dayton *et al.* noted that in patients with severe chronic lung disease and secondary polycythemia, phlebotomy produced subjective benefit in those patients with evidence of CHF and initial hematocrit >65%.⁵ Phlebotomy has been shown to improve cerebral blood flow, subjective wellbeing and exercise tolerance.^{6–8} It also improves myocardial contractility and left ventricular function.⁹

The definitive test for alveolar hypoventilation is arterial blood gas performed on room air during wakefulness. Given that this is a relatively invasive procedure, several screening tools have been proposed. Screening questionnaires such as the validated STOP-Bang questionnaire can identify patients at high risk of OSA. The STOP-Bang questionnaire, used in preoperative patients, is a scoring model combining the STOP (snoring, tiredness, observed apneas, and increased blood pressure) questionnaire and Bang (BMI ≥ 35 kg/m², age >50 years, neck circumference >40 cm, and male gender). A positive screen (3 questions answered yes) is highly sensitive for moderate–severe OSA and is useful to exclude patients with the disease.¹⁰ Mokhlesi *et al.* suggested three clinical predictors of OHS: serum HCO₃[−], apnea hypopnea index, and lowest oxygen saturation during sleep.⁴ Increased serum HCO₃[−] caused by metabolic compensation of chronic respiratory acidosis is common in patients with OHS. In a cohort of obese patients with OSA referred to the sleep laboratory for suspicion of OSA, a serum HCO₃[−] threshold of 27 mEq/L had a 92% sensitivity in predicting hypercapnia on arterial blood gas.⁴

Conclusion

This is the first reported case of successful use of therapeutic phlebotomy for secondary polycythemia resulting from obesity.

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Fig. 1.
Trend of (---) pH, (—) pCO₂ (mmHg) and (···) hematocrit (%) over time. BiPAP, bi-level positive airway pressure