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Rapid-Onset Obesity with Hypothalamic Dysfunction, Hypoventilation, and Autonomic Dysregulation (ROHHAD) Syndrome: A Case Report

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Abstract

Introduction: Rapid-onset obesity with hypoventilation, hypothalamic dysfunction, and autonomic dysregulation (ROHHAD) is a rare disease. To date, there have been only few reported cases of ROHHAD syndrome.
Case Presentation: We report a 5-year-old- Iranian girl who had normal growth and development until her 4th year of life. At that time, the patient developed weight gain, constipation, coldness in the extremities, and hyperhidrosis. She first presented to our children's hospital with a suspected mediastinal mass on chest radiography. After surgery and resection of the mass (a ganglioneuroblastoma), extubation was unsuccessful, with tachycardia and hypertension occurring after each attempt. After 48 days in the ICU, we were still unable to wean her from mechanical ventilation. Finally, based on the rapid weight gain, hypoventilation, hypothalamic dysfunction, and signs of autonomic dysregulation, the patient was diagnosed with ROHHAD syndrome.
Conclusions: Only a few case reports have described ROHHAD syndrome, and it is therefore difficult to manage. In children with rapid and early-onset obesity associated with hypothalamic-pituitary endocrine dysfunction, ROHHAD syndrome should be considered in the differential diagnosis.

Keywords: ROHHAD, Iran, Obesity

1. Introduction

Rapid-onset obesity with hypoventilation, hypothalamic dysfunction, and autonomic dysregulation (ROHHAD) syndrome is a very rare disease that was first reported in a 3-year-old boy in 1965 (1). Its prevalence is reported to be less than 1 in 1,000,000, and it usually occurs during early childhood. Children with ROHHAD syndrome appear healthy at first, but eventually present with rapid weight gain (> 20 pounds over 6 - 12 months) that occurs after the age of 1.5 years (2-4). Over the following months and years, other manifestations will develop, including alveolar hypoventilation, hypothalamic dysfunction, and autonomic dysregulation (3, 5). The autonomic dysregulation is usually initiated by a ganglioneuroblastoma, which involves mature gangliocytes and immature neuroblasts (5, 6). The high prevalence of cardiorespiratory arrest in ROHHAD patients, a lack of medical awareness about the disease, and delay in diagnosis and treatment can lead to poor therapeutic outcomes (6, 7). Therefore, consideration of ROHHAD syndrome in obese children with hypoventilation is necessary. In this article, we describe the first case of ROHHAD syndrome in Iran, which was diagnosed 1 year after the rapid onset of obesity.

2. Case Presentation

A 5-year-old Iranian girl was admitted to a local hospital with a history of cough and cyanosis. Her arterial blood gasses showed hypoxia, and a mediastinal mass was suspected on chest radiography. After 10 days, she was referred to our central pediatric hospital in good general condition for further investigations. She underwent thoracotomy with resection of the 5A~3A 1.5-cm mass, and the pathologic examination showed a ganglioneuroblastoma. After surgery, the patient was admitted to the intensive care unit.

The patient was a single child born to healthy, unrelated parents by cesarean delivery at term. She was a normal, healthy infant with a weight of 2,600 g. She experienced normal growth and development until the age of 4, when her weight increased by 15 kg due to hyperphagia. Her obesity was evaluated but was not considered problematic. In addition, she had a 1-year history of snoring,

constipation, coldness in the extremities, hyperhidrosis, and mood changes.

On physical examination, the patient's vital signs were as follows: heart rate of 125 beats/min, respiratory rate of 12 breaths/min, blood pressure of 120/65 mmHg, and axillary temperature of 36°C. Her weight was 40 kg (> 95th percentile) with a height of 120 cm (> 95th percentile). The patient had a round face, facial plethora, and slight buffalo neck. No other abnormalities were observed. Laboratory findings showed hyponatremia, hyperprolactinemia, and central hypothyroidism (Table 1).

Table 1. Patient's Laboratory Findings

Parameters	Value
Na+	125 mEq/L
Blood glucose	85 mg/dL
Total cholesterol	176 mg/dL
Triglyceride	104 mg/dL
TSH	0.38 μIU/mL
T4	0.8 ng/dL

On follow up, the patient was extubated, after which she had a recurrent cyanotic attack due to apnea. Therefore, we performed tracheostomy and mechanical ventilation. After weaning from mechanical ventilation, she experienced tachycardia and hypertension. Since seizures were suspected, MRI and electroencephalography were performed and which were normal. Several central and peripheral nervous system disorders, as well as lung and cardiac diseases, were ruled out. Based on the findings, the patient was diagnosed with ROHHAD syndrome. After 48 days, she was discharged in good condition.

3. Discussion

To the best of our knowledge, this is the first case of ROHHAD syndrome reported in Iran. ROHHAD is a very rare syndrome that is characterized by rapid-onset obesity with hypoventilation, hypothalamic dysfunction, and autonomic dysregulation. There have been few case reports, and treatment strategies range from surgery to autoimmune drugs, such as cyclophosphamide. Severe obesity is complicated by sleep apnea and hypoventilation in this syndrome. The underlying pathogenesis of ROHHAD is unclear, and studies that have sequenced genes, such as paired-like homeobox 2B (PHOX2B), have not been revealing (3). The early diagnosis of ROHHAD is very effective at decreasing the likelihood of cardiopulmonary arrest. In our case, rapid weight gain was the first manifestation. Obesity has a wide range of differential diagnosis (8). Because of the rarity of ROHHAD syndrome, it is not considered in the differential diagnosis for rapid weight gain in children. It seems that consideration of other ROHHAD manifestations in obese children can be beneficial for the early diagnosis of this syndrome. In our patient, the weight gain had been evaluated separately without consideration of other symptoms, such as constipation, coldness in the extremities, and hyperhidrosis. In conclusion, clinicians must be aware of the possibility of ROHHAD in children with rapid weight gain, and this syndrome should be included in the differential diagnosis.

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Footnote

Authors' Contribution: All authors contributed equally to this case report.

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