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Endoped Abstract

Challenges in Growth Hormone Therapy for Prader–Willi Syndrome

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Abstract: Prader-Willi syndrome (PWS) is the most common syndromic cause of life-threatening obesity, scoliosis and obstructive sleep apnea (OSA) being the major concerns for these patients. We report the case of a five year-old girl with PWS admitted for growth hormone therapy. Initially she had medium-severe OSA that required tonisllectomy and severe scoliosis. At six months follow-up after intitation of therapy, she had a good response with better height and body fat index, OSA improvement, but progression of the scoliosis severity. With this case report we underline that, while growth hormone therapy in PWS patients is efficient and not directly related to scoliosis and OSA exacerbation, careful monitoring during therapy is recommended.

Keywords: growth hormone therapy; Prader–Willi Syndrome; chromosomal region 15q11-13

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Introduction

Prader–Willi syndrome (PWS) is the most common syndromic cause of life-threatening obesity and is associated with the under-expression of the paternally-derived chromosomal region 15q11-13 [1]. PWS is characterized by the dysregulation of growth hormone (GH)-insulin like growth hormone 1 axis [2]. GH therapy (GHT) is approved and recommended for PWS with or without GH deficiency to improve growth, body composition and body mass index, motor development, cognitive function, and result in an improved quality of life [3]. Scoliosis and obstructive sleep apnea (OSA) are major concerns for these patients. Although the role of GHT in the natural history of scoliosis is not clear, and careful monitoring during treatment is recommended, the development of OSA during GH therapy is of particular concern due to several reports of sudden death in individuals with PWS undergoing GH therapy [4,5].

Case Report

A five-year-old girl diagnosed with PWS at the age of four was admitted to the Endocrinology Department of "Elias Emergency Hospital" for evaluation of associated endocrinopathies. From her history, we learned that she was born at 36 weeks with intrauterine growth restriction (2235 g), and had surgery for congenital hip dysplasia at the age of two and three. Her polysomnogram (PSG) reported medium–severe OSA. An otorhinolaryngology exam revealed tonsils hypertrophy. The cardiologic assessment, abdominal and thyroid ultrasound were normal. After tonsillectomy, she was reevaluated for GHT. At admission, she was 5.6 years old, height = 104.7 cm (−1.91 SD), weight = 24 kg, BMI = 21.9 kg/m^2 (>>p97), with characteristic phenotype (almond-shaped eyes, thin upper lip, downturned corners of mouth, narrow nasal root), dextroconvex scoliosis, lipomastia, no hyperpigmentation or discoloration, global obesity, tooth decay, normal external genitalia, Tanner 1, no polyuria-polydipsia syndrome, normal thyroid. The laboratory investigations were unremarkable. On repeated PSG, she had moderate OSA, without alveolar hypoventilation. The patient's osteodensitometry revealed a Z score of +1.8 and 55.6% body fat. Bone age was equal to chronological age. Orthopedic examination revealed severe scoliosis with a Cobb index of 54 degrees and recommended kinethotherapy and brace wearing. The patient was started on subcutaneous somatropinum 0.5 mg/m^2/day, daily regimen, 7/7 with good initial results, under clinical supervision of an endocrinologist, a pulmonologist and an orthopedist. After six months, her PSG improved, with better height (recovered + 0.37 SD), BMI (21 kg/m^2) and body fat index = 49.1%, but with a progression of scoliosis with surgical indication (the patient was noncompliant in brace wearing).

Conclusions

GHT improves linear growth and body composition and early treatment results in more favorable outcomes [6]. Obstructive sleep apnea prevalence is ~80% in PWS [7].

Screening for OSA and adenotonsillectomy, if needed, is highly recommended in PWS before GH treatment and PSG should be repeated 3–6 months after initiation of GH therapy [8]. The prevalence of scoliosis is 37–86% and increases with age; 44% of children with scoliosis have a Cobb angle above 20 degrees. Many children with scoliosis (13%) need brace treatment or surgery [5].

GHT increases the height velocity of PWS patients but does not necessarily induce scoliosis. Starting the therapy early may not be an exacerbating factor of scoliosis but careful monitoring during treatment is recommended [9].

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