Bell's palsy following Growth hormone therapy in a patient with Prader-Willi syndrome: the first report

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ABSTRACT. Prader–Willi syndrome (PWS) is a complex genetic disorder with different manifestations in infancy and childhood including obesity, type 2 diabetes mellitus, mild to moderate intellectual impairment and learning disabilities. In this syndrome, growth hormone therapy improves outcomes. For the first time, here we report a 11-year-old boy with PWS who presented with three episodes of unilateral facial palsy after starting growth hormone therapy.

KEY WORDS: Prader-Willi syndrome, Bell's palsy, Growth Hormone

INTRODUCTION

Prader–Willi syndrome (PWS) clinical manifestation may present in infancy and child hood with hypotonia, feeding problem, poor growth and development. Affected individuals in childhood develop as more appetite, hyperphagia, obesity, type 2 diabetes mellitus, mild to moderate intellectual impairment, learning disabilities, and some other manifestations.

Genetically, PWS occurred due to genomic imprinting resulting in dysfunctional genes in a specific region of chromosome 15. Briefly, some genes are actively expressed if only a copy is inherited from father, and a paternal chromosome 15 segment is deleted in 70% cases of PWS. Maternal uniparental disomy mainly occurred in the rest of cases (25%), besides some other rare causes for PWS including chromosomal rearrangement (translocation). Although growth hormone therapy has been recommended for PWS to improve the disease outcomes, it has some complications too (1,2).

Bell's palsy is a lower motor neuron unilateral facial paralysis or the evidence of an aural, a neurological, or a local cause. Bell's palsy has been reported upon IGF therapy in growth hormone insensitivity syndrome (GHIS), GH gene deletion, and diabetes mellitus (3,4). Also, an association and coincidence has been very recently reported between Bell's palsy and obesity (5), which the latter is a symptom of Prader-Willi syndrome too. Here, we report a 11-year-old boy with Prader-Willi syndrome. It is more likely an unfavorable effect of growth hormone therapy in children.

CASE REPORT

A 11-year-old boy presented with unilateral facial palsy. The patient was first examined at the age of 4 years because of obesity, weakness, and poor development. At that time, and mainly due to a generalized and prolonged hypotonia, paternal genes on chromosome 15 were evaluated using an MLPA kit (MLPA-ME028-B1; MRC Holland, Amsterdam, The Netherlands) to detect copy number changes and aberrant methylation patterns in the 15q11 locus using an ABI Prism 310 genetic analyser. The evaluation was also carried out in all available family members and an aberrant methylation pattern was found in the region 15q11-q15 in the patient. Therefore, he was diagnosed with Prader Willi syndrome (PWS) either via uniparental disomy or imprinting defects, so a further molecular analysis was recommended to differentiate them using STR analysis and imprinting center sequencing.

Early diagnosis and treatment may improve quality of life in these patients, so we begin human growth hormone (HGH) administration based on Federal Drug Administration (FDA) approval at 9 years old. Linear growth, muscle tone and decreases body fat were improved by HGH replacement but a facial asymmetry was noted with a unilateral peripheral facial nerve deficit without history of trauma or seizure by 6 months after HGH replacement therapy. All other cranial nerves and his blood pressure were normal, and there was no remarkable finding in physical exam.

The laboratory tests including fasting blood glucose and insulin, lipid profiles, complete blood count, serum electrolytes, liver function tests, coagulation tests and the cerebrospinal fluid were in normal ranges. Any intracranial abnormality or evidence of mastoiditis was not obtained in cerebral axial computed tomographic (CT) scan and axial T1- and T2-weighted magnetic resonance imaging (MRI). Growth hormone was discontinued, and the patient was treated with oral hydrocortisone. However, Bell's palsy was recurred three times more despite GH discontinuation. The results of biochemical and CBC tests are summarized in the table 1. Genetic testing was approved by the local ethics committees (**Rasht** University of Medical sciences). With informed consent from the parents and in accordance with the Declaration of Helsinki, genomic DNA was extracted from peripheral blood lymphocytes, and a further genetic assay was performed in the Molecular Genetics Laboratory.

Table 1. Patient's Test Results

Test	Result	NL Range
Fasting Blood Sugar (FBS)	90	80-126 mg/dL
Fasting insulin level	12	1.8–24.6 mU/L
Lipid profiles		
HDL	50	36–84 mg/dL
LDL	110	64–136 mg/dL
Total Cholesterol	200	125–244 mg/dL
Complete blood count (CBC)		
RBC	4.5	4.0–4.9
WBC	8	4.5–10.5
Hemoglobin	12	11.0–13.3
Serum electrolytes		
Sodium	137	135–148 mmol/L
Chloride	110	102–112 mmol/L
Potassium	4	3.5–5.8 mmol/L
Phosphorus	4.5	3.2-6.3 mg/dL
Liver function tests		
Alkaline Phosphatase	200	115–336
SGOT	35	5-40 U/L
SGPT	36	7 to 56 U/L
Coagulation tests		
Prothrombin Time (PT)	13	11–15 sec
Partial Thromboplastin Time (PTT)	48	42–54 sec

DISCUSSION

The benefits of HGH treatment in patient with Prader-Willi syndrome are well established including increased linear growth, improved body composition, decreased body fat, increase motor function and psychomotor development (1). Side effects of GH was reported in children and adolescents not including Bell's palsy.
It is the first report of Bell's palsy in PWS which was improved by the hormone discontinuous. Despite the safety profile of growth hormone treatment, Bell's palsy association with or secondary to GH therapy has been previously reported in a case as a GH unfavorable side effect or a coincident (3). It may be a co-incidence of Bell's palsy and PWS, but also it may be a consequence of GH therapy as a side effect too. A predisposition or susceptibility to Bell's palsy could also be considered in some genetic diseases such as PWS. To confirm this possible tendency, and to better understanding of Bell's palsy in Prader-Willi syndrome, further studies are recommended.

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CONFLICT OF INTEREST

Authors have no conflict of interest

ESTABLISHED FACTS AND NOVEL INSIGHTS

- It is the first, here we report a 11-year-old boy with PWS and facial (Bell's) palsy after starting growth hormone therapy.
- A predisposition or susceptibility to Bell's palsy could also be considered in some genetic diseases such as PWS

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