CASE REPORT

FINAL HEIGHT IN A BOY WITH ACHONDROPLASIA TREATED WITH GROWTH HORMONE- CASE REPORT

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Abstract

Achondroplasia is the most common genetic form of skeletal dysplasia in humans. It is characterized by short stature and skeletal disproportion. Patients with this condition have comorbidities, such as cardiovascular problems, spinal cord problems, hearing and dental problems as well as psychological issues. We report final height of 147 cm in a 17-year-old boy treated with growth hormone, however without improvement in body proportions. Surgical therapy for limb lengthening had been proposed, which the patient refused. At this age he developed hypertension and was referred to a cardiologist, nephrologist, as well as to an orthopedic surgeon and psychologist. Recently, a new treatment with vosoritide has been introduced, promising better height outcome, but uncertain phenotype improvement. Multidisciplinary approach is recommended for these patients and close monitoring during childhood, adolescence and adulthood. Genetic counseling is also advised.

ПРИКАЗ НА СЛУЧАЈ

КОНЕЧНА ВИСИНА КАЈ МОМЧЕ СО АХОНДРОПЛАЗИЈА ТРЕТИРАНО СО ХОРМОН ЗА РАСТ – ПРИКАЗ НА СЛУЧАЈ

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Клучни зборови: ахондроплазија, терапија со хормон за раст, висина

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Извадок

Ахондроплазијата е најчеста генетска форма на скелетна дисплазија кај луѓето. Се карактеризира со низок раст и скелетна диспропорција. Пациентите со оваа состојба имаат коморбидитети, како што се кардиоваскуларни, проблеми со ,рбетниот мозок, со слухот и забите, како и психолошки проблеми. Утврдивме конечна висина од 147 cm кај 17-годишно момче третирано со хормон за раст, но без подобрување во пропорциите на телото. Предложена е хируршка терапија за издолжување на екстремитетите, која беше одбиена од страна на пациентот. На истата возраст кај пациентот се појавила хипертензија и бил упатен на кардиолог, нефролог, како и на ортопед и психолог. Неодамна, воведен е нов третман со восоритид, кој ветува подобри резултати во однос на висината, но со ограничени резултати за фенотипска презентација. За овие пациенти се препорачува мултидисциплинарен пристап и внимателно следење во периодот на детството, адолесценцијата и зрелоста. Кај нив се предлага и генетско советување.

Introduction

Severe growth retardation occurs in most skeletal chondrodysplasias. Among these bone disorders, achondroplasia is the most common genetic form in humans and it features short-limb dwarfism, macrocephaly with a prominent forehead, and a mid-face hypoplasia1. Patients with achondroplasia have comorbid conditions and complications ranging from infancy to adulthood. It has been reported that mortality may be higher related to heart disease, although most of them have normal or near normal life expectancy[2,3].

Growth hormone (GH) is an important factor for growth and differentiation of chondrocytes. Trials with GH treatment in achondroplasia have been reported for a long time in different countries[4-7]. Yet, a worldwide consensus has not been reached. The patient must satisfy selection criteria, such as young age, current body height, physical characteristics, MRI-CT examinations[8].

Following our publication in 2016[9], we decided to report the outcome and final height of this patient with achondroplasia.

Case report

As a reminder, our patient was diagnosed prenatally in the 7th month of gestation. The mother's pregnancy was uneventful and regularly controlled. The parents were of average height (mother 163 cm, father 172 cm). At birth, he had all clinical stigmata of the disorder. Genetic testing revealed a mutation of C 1138 G>A in the gene FGFR3 in a heterozygous constellation. Growth hormone treatment was initiated at the age of three years and four months, at a dose of 0.06 mg/kg, and adjusted accordingly to body weight in the following years. IgF1 was monitored regularly as well as glycaemia and thyroid hormones. His growth was on the 3rd percentile of the growth curve until the age of 13 years, when it started to decline. Growth hormone was discontinued at the age of 15 years, and bone age was 16 years. His height was 145 cm and weight 66 kg. The body disproportion did not improve during the growth hormone treatment.

The parents and patient were informed of the possibility of orthopedic treatment (Ilisarov procedure), which the patient refused.

At the age of 17 years, the final height was 147 cm and weight 66.5 kg (Picture 1 and 2). He complained on hypertension that had occurred on several occasions (150/100...140/95 mmHg). His blood tests were normal, but the ECG and ultrasonography of the heart revealed hypertrophy of the left ventricle. Treatment was initiated with beta blockers and antihypertensive medication suggested by a cardiologist. The clinical examination for eventual kidney disease showed no signs of pathological abnormalities. An orthopedic specialist performed CT examination of the spinal cord which was negative for compression due to foramen magnum stenosis. A cranial MRI, to identify possible ventricular enlargement, is also planned. The parents also complained that he had psychological issues although his peers were treating him well. A recommendation was given to consult a psychologist.

Discussion

The average adult height in achondroplasia in the Caucasian population is between 112 and 136 cm (mean 124 cm) for women and 118 and 145 (mean 132) for men[10]. A consensus for growth hormone treatment has not been reached everywhere. For instance, in Japan, GH treatment is included in their Clinical Practice Guidelines for Achondroplasia[8]. However, the first European consensus on principles of management of achondroplasia does not recommend GH treatment[10], although it allows patient and family to make a decision about limb lengthening.

Our patient grew an additional 2 cm following discontinuation of treatment. He did not experience a pubertal growth spurt which is typical for these patients. Pubertal sexual development was normal. GH treatment improved his height, but not the physical features of the skeletal dysplasia. Our patient's young age at initiation of treatment prevented height deficit from accumulating. The proposed surgical limb lengthening which could offer the possibility of a more proportionate adult stature, was not accepted byour patient. This decision is multifactorial and should include different specialists (physicians, surgeons, physiotherapists, and occupational therapist). This should be a shared decision with the family and the patient[10]. Patients with achondroplasia tend to have comorbidities, such as foramen magnum stenosis, ventricular enlargement, spinal canal stenosis, kyphosis, obstructive sleep apnea and respiratory symptoms, hearing loss, and cardiovascular issues[8].

Other patients with achondroplasia have also been treated with GH at our Department, but with unsatisfactory results probably due to older age or other factors. Mutations of the FGFR3 gene result in suppression of chondrocyte differentiation and proliferation, leading to impaired endochondral ossification and all clinical symptoms.

Recently, a new treatment has been introduced, a biological analogue of endogenous c-type natriuretic peptide which blocks the FGFR3 signal and is a potent stimulator of endotracheal ossification[11]. Clinical trials have shown improvement of growth, however there is limited data on clinical features improvement.

Conclusion

GH treatment in our patient improved the final height, however without results regardingskeletal disproportion. Surgical limb lengthening was refused by our patient. Hopefully, new medications will overcome these obstacles. At present, the focus is on adequate diagnosis prenatally and at birth, lifelong support and management, avoiding and treating complications that come with this condition, multidisciplinary approach and continuous monitoring throughout childhood, adolescence and adulthood. Future genetic counseling of the family is also advised.

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