Review of: "Clinical Characteristics of Short-Stature Patients With Collagen Gene Mutation and the Therapeutic Response to rhGH"

Jun Mori[1]

1 Osaka City General Hospital

Potential competing interests: The author(s) declared that no potential competing interests exist.

Commentary: Clinical Characteristics of Short-Stature Patients With Collagen Gene Mutation and the Therapeutic Response to rhGH

Jun Mori

Division of Pediatrics Endocrinology and Metabolism, Children's Medical Center, Osaka City General Hospital

In a recent paper (1), Chen and colleagues investigated the frequencies of collagenopathies by using next-generation sequencing and evaluated the phenotypes, mainly focusing on the response of recombinant human growth hormone (rhGH) in short-stature children with skeletal abnormalities. Genetic analysis in children with idiopathic short stature and small for gestational age reveals genetic abnormalities, especially those related to bone formation, in about 15% of children (2, 3). Since this study is a high-risk screening for children with skeletal abnormalities, gene mutations in the extracellular matrix of cartilage were found as frequently as 65 out of 106 (61%). However, as the authors have stated, there is a possibility that large CNV have not been found. Whether rhGH treatment works for patients with collagenopathy is of great concern to pediatrics endocrinologists. Achondroplasia, FGFR3 related disorder, is the most common form of skeletal dysplasia. In Japan, rhGH treatment has been approved for achondroplasia and hypochondroplasia for more than 20 years. In this study, rhGH treatment improved FGFR3-related disease, but not significant. Long-term rhGH treatment to achondroplasia contributes about 2% of final height (4). rhGH treatment is effective to the patients with type 1 collagen mutations, achondroplasia, hypochondroplasia, Schmid type metaphyseal dysplasia, but not pseudoachondroplasia and spondyloepiphyseal dysplasia congenita (5, 6), even though the genotype phenotype correlation was unknown. It is necessary to accumulate information on genotype-phenotype correlation, including response to rhGH treatment.
This study is retrospectively assessed and the details about rhGH treatment, such as the dose and initiation age, are missing. Randomized and double-blind tests with various doses (e.g. 0.033mg/kg/day and 0.066 mg/kg/day) are needed to verify the effect of rhGH in patients with collagenopathies. There are concerns about side effects such as scoliosis in rhGH treatment for collagenopathies. Long-term data on side effects are needed, however rhGH treatment for short-stature patient with collagen gene mutation is promising.

1. Chen M, Miao H, Liang H, Ke X, Yang H, Gong F, Wang L, Duan L, Chen S, Pan H, Zhu H. Clinical Characteristics of Short-Stature Patients With Collagen Gene Mutation and the Therapeutic Response to rhGH. Front Endocrinol 2022 https://doi.org/10.3389/fendo.2022.820001
2. Flechtner I, Lambot-Juhan K, Teissier R, Colmenares A, Baujat G, Beltrand J, Ajaltouni Z, Pauwels C, Pinto G, Smara-Boustani D, Simon A, Thalassinos C, Le Merrer M, Cormier-Daire V, Polak M. Unexpected high frequency of skeletal dysplasia in idiopathic short stature and small for gestational age patients. Eur J Endocrinol (2014) 170(5):677-84. Doi: 10.1530/EJE-13-0864.
3. Freire BL, Homma TK, Funari MFA, Lerario AM, Vasques GA, Malaquias AC, Arnhold IJP, Jorge AAL. Multigene Sequencing Analysis of Children Born Small for Gestational Age With Isolated Short Stature. J Clin Endocrinol Metab 2019 104(6):2023-30. Doi: 10.1210/jc.2018-01971.
4. Harada D, Namba N, Hanioka Y, Ueyama K, Sakamoto N, Nakano Y, Izui M, Nagamatsu Y, Kashiwagi H, Yamamuro M, Ishiura Y, Ogitani A, Seino Y. Final adult height in long-term growth hormone-treated achondroplasia patients. Eur J Pediatr (2017) 176(7):873-879. Doi: 10.1007/s00431-017-2923-y.
5. Antoniazzi F, Monti E, Venturi G, Franceschi R, Doro F, Gatti D, Zamboni G, Tatò L. GH in Combination With Bisphosphonate Treatment in Osteogenesis Imperfecta. Eur J Endocrinol (2010) 163(3):479-87. Doi: 10.1530/eje-10-0208
6. Kanazawa H, Tanaka H, Inoue M, Yamanaka Y, Namba N, Seino Y. Efficacy of growth hormone therapy for patients with skeletal dysplasia. J Bone Miner Metab (2003) 21(5):307-10. Doi: 10.1007/s00774-003-0425-7.