Growth Hormone Treatment in an Adolescent with Pycnodysostosis

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Introduction: Pycnodysostosis is a rare skeletal dysplasia caused by autosomal recessive mutations in the cathepsin K (*CTSK*) gene and is characterized by short stature, osteosclerosis, and large fontanels. Adult height varies between 130 and 150 cm. Here, we report the short-term effect of growth hormone (GH) treatment in an adolescent with pycnodysostosis.

Case: A 7-year-old boy presented with a compliant of short stature. He was born at 37th gestational week, weighing 2400 g. His parents denied consanguinity, but they were from the same village. His height was 106.3 cm (SD score -2.85). He had typical clinical (open anterior fontanel, frontal bossing, prominent nose, brachydactyly, and teeth abnormalities) and radiological features (widened lambdoid sutures and anterior fontanel, hypoplasia of the mandible, diffuse osteosclerosis and acroosteolysis in the distal phalanges). Genetic analysis showed homozygous M1I (ATG>ATA) mutation in the *CTSK* gene, confirming a diagnosis of pcynodysostosis. During a 7-year follow-up without treatment, the patient's height reached to 133.8 cm (SD score -4.35) with an average annual growth rate of 3.9 cm. Despite the onset of puberty, growth rate was 2 cm/year over the last 6 months. Target height and predicted adult height were calculated as 168.7 cm and 142 cm, respectively. Peak GH responses in two clonidine tests were 3.9 and 9.3 ng/mL, and GH treatment was started at a dose of 2 mg/day (42 µg/kg/day). In the first six months of treatment, growth rate was determined as 9.4 cm/year, which is more than twofold increase.

Conclusion: Few publications demonstrate that GH therapy in patients with pycnodysostosis increases growth rate and provides near-normal adult height in long-term use. Short-term outcome of GH therapy in our case is consistent with the data of previous publications and suggests that early initiation of therapy would be more useful for the patients with pycnodysostosis.

Key words: Growth hormone, short stature, cathepsin K, pycnodysostosis, therapy

A Preliminary Study of the Possible Role of Cannabinoid Receptor-1 (CNR1) Gene Polymorphisms in the Development of Morbid Obesity in Obese Children

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Aim: In this study, we aimed to investigate the possible role of the Cannabinoid Receptor-1 (*CNR1*) gene polymorphisms in the development of morbid obesity in obese children.

Method: The study was carried out with 48 morbidly obese (27 female/21 male) and 52 obese (28 female/24 male) children. The relative weight ratio >140 was considered as morbid obesity. The 1359G/A polymorphism of the *CNR1* gene was determined using polymerase chain reaction restriction method. The SPSS version 13.0 and Graphpad Instat version 3 were used for the statistical analysis. The Hardy-Weinberg equilibrium was calculated using the De-Finetti program. Statistical significance was considered at $p<0.05$.

Results: The distributions of G/G, G/A, and A/A genotypes for the 1359G/A polymorphism of the *CNR1* gene were 64.6%, 31.3%, and 4.2% in morbidly obese patients, compared with 59.6%, 36.5%, and 3.8% in obese patients ($p>0.05$). The allele frequencies of G and A were 80.2% and 19.8% in morbidly obese children and 77.9% and 22.1% in obese children ($p>0.05$). In morbidly obese children, family history of obesity was determined in 25.0% (12) of mothers and in 16.7% (8) of fathers. In patients with obese mothers, A/A genotype was more common (with obese mother: 2/12, 16.7%; without obese mother: 0/36, 0.0%; $p=0.020$). In patients with A/A genotype, triglyceride ≥150 mg/dL was more frequent (A/A: 2/2, 100.0%; G/A: 2/13, 15.4%; G/G: 11/31, 35.5%; $p=0.050$).

Conclusion: In this study, no association was found between the *CNR1* gene 1359G/A polymorphism and development of morbid obesity in obese children. However, our study suggests that A/A genotype of human *CNR1* gene may play a possible role as a risk factor in the familial inheritance of obesity. Since this is a preliminary study, further investigations are needed to confirm the exact role(s) of this gene in morbid obesity in childhood.

Key words: Children, obesity, morbid obesity, gene, polymorphism