A Case of Achondrogenesis Type 2/ Hypochondrogenesis Due to a *De Novo* Mutation in the *COL2A1* Gene

Gönül Çatlı[1], Ayhan Abacı[1], Ahmet Anık[1], Ranad Shaneen[2], Hale Ünver Tuhan[1], Derya Erçal[3], Ece Böber[1], Niema A. Ibrahim[2], Mais O. Hashem[2], Fowzan Sami Alkuraya[2]

[1]Dokuz Eylül University Faculty of Medicine, Department of Pediatric Endocrinology, İzmir, Turkey

[2]King Faisal Specialist Hospital and Research Center, Clinic of Genetics, Riyadh, Saudi Arabia

[3]Dokuz Eylül University Faculty of Medicine, Department of Pediatric Genetics, İzmir, Turkey

Achondrogenesis type 2/hypochondrogenesis is a rare cause of micromelic dwarfism in the neonatal period. Severe short stature, narrow chest, increased lordosis, protuberant abdomen, and characteristic facies are the typical clinical findings. A 13-month-old boy was referred to our clinic for severe short stature and dysmorphic features. He was born at term with a normal birth weight and length. His past medical history was unremarkable. Parents were not related. He had a 7-year-old healthy sister and there was no individual with similar medical condition in the three-generation pedigree. On physical examination, his weight was 7.1 kg [-1.32 standard deviation score (SDS)], length was 63 cm (-5.6 SDS), and head circumference was 49.2 cm (1.84 SDS). He had relative macrocephaly and rhizomelic short stature with atypical facies (frontal bossing, flat nasal bridge, and high-arched palate), narrow chest, increased lumbar lordosis, prominent heels, and overriding toes. His testicles were 1 mL in scrotum and pubic hair was Tanner stage 1. Blood biochemistry revealed normal findings. Radiological investigations showed inadequate ossification and disorganisation in vertebra, sacrum, and pubic bones suggesting achondrogenesis type 2. Due to his severe disproportionate short stature and abnormal radiological findings, a molecular analysis of *COL2A1* gene was performed and a *de novo* mutation causing achondrogenesis type 2/hypochondrogenesis was identified (King Faisal Specialist Hospital and Research Center-Developmental Genetics Unit).

Key words: Achondrogenesis, hypochondrogenesis, *COL2A1* gene

Seven Cases of Williams-Beuren Syndrome: Endocrine Evaluation and Long-Term Follow-Up

Ayla Güven

Medeniyet University, Faculty of Medicine Göztepe Education and Research Hospital, Clinic of Pediatric Endocrinology, İstanbul, Turkey

Objectives: Hypercalcemia, hypothyroidism, and early puberty are the most common endocrine disorders defined in Williams-Beuren syndrome (WBS). Here, the endocrine evaluation and long-term follow-up of seven patients with WBS are given.

Methods: Data were obtained from patients' medical records. WBS was diagnosed by demonstration of the deletion on chromosome 7 by using FISH method (7q11.23). Anthropometric measurements and growth velocities (GV) of patients during L-thyroxine (L-T4) treatment were evaluated. Thyroid ultrasonography was performed and thyroid volume was calculated. L-T4 was started in patients with hypothyroidism and WBS.

Results: Six patients were male. Age at the diagnosis of WBS was 1.04 (3.47) decimal-year. Five of them were born small for gestational age. They all had mild hypercalcemia (9.9-11.1 mg/dL). Three of the patients had overt hypothyroidism, while subclinical hypothyroidism was detected in three patients [(0.66 (5.77) decimal-year]. At the diagnosis, serum thyroid-stimulating hormone was 10.5±6.3 μIU/mL and free T4 was 0.9±0.1 ng/dL. L-T4 was started at 5±3.9 μg/kg. Four patients had thyroid hypoplasia and one had thyroid agenesis. Growth hormone (GH) deficiency was determined in one patient. Height SDS was -3.26 at the age of 34/12 decimal-years when human GH was initiated and increased to -1.45 at the age of 6.08 decimal-years. The puberty onset age in two patients was normal. Follow-up duration was 5.3±2.2 years. Mean GV was 12.9±7.2 cm and 7.6±2 cm at the end of the first and second years of the therapy, respectively. At the last visit, L-T4 dose was 2.9±1 μg/kg. All patients had neurodevelopmental retardation and were receiving special education.

Conclusion: Hypothyroidism was the most common endocrine problem in our patients (85.7%). Untreated hypothyroidism also causes mental and motor retardation particularly in infancy period in WBS. Therefore, physicians must be alert for the possible diagnosis of WBS and to investigate the thyroid morphology and function.

Key words: Williams Beuren syndrome, hypothyroidism, growth hormone deficiency