A Rare Presentation of Friedreich’s Ataxia in Pediatric Case: Diabetes Mellitus

Serpil Baş1, Saygın Abali1, Zeynep Atay1, Ziya Gurbanov1, Sevda Çam1, Dilşad Türkdoğan2, Serap Turan1, Abdullah Bereket1

1Marmara University Faculty of Medicine, Department of Pediatric Endocrinology and Diabetes, İstanbul, Turkey
2Marmara University Faculty of Medicine, Department of Pediatric Neurology, İstanbul, Turkey

**Introduction:** Friedreich’s ataxia (FA) is an autosomal recessive neurodegenerative disorder resulting from a mutation of a gene locus on chromosome 9. The most common molecular abnormality is a GAA trinucleotide repeat expansion in intron 1 of the frataxin (FXN) gene; normal individuals have 5 to 30 GAA repeat expansions. FA is characterized by progressive gait and limb ataxia with associated limb muscle weakness, absent lower limb reflexes, extensor plantar responses, dysarthria, and decreased proprioception. Patients are at risk of getting glucose intolerance and 20% progress to overt diabetes. The cause of diabetes in FA is poorly understood. Diabetes can result from a shortage in insulin secretion, from a poor response to insulin (insulin resistance), or from a combination of both.

**Case:** A 15.5-year-old girl was admitted to the hospital with weakness, vomiting, weight loss, polyuria, and polydipsia in the last month. History revealed the presence of gait disturbance and pain in soles for 3 years. On physical examination, cachexia, dehydration, and ketonemic odor were noted. Thyroid gland was soft and bilaterally 4 cm on palpation. Neurological examination demonstrated ataxic gait pattern, pes cavus, intentional tremor, lower limb areflexia, and flexor plantar response. Blood glucose was 390 mg/dL with ketonuria but without acidosis. Insulin and c-peptide levels were 1.53 μIU/mL and 1.08 ng/mL, respectively, and continued up to 11 years of age. In the patient who had thyroid-stimulating hormone, prolactin, and GH deficiencies, glucagon was started at 8 years due to rapid progression of puberty and continued up to 11 years of age. In the patient who had thyroid-stimulating hormone, prolactin, and GH deficiencies, a new point mutation was detected in the FXN gene analysis revealed more than 66 GAA trinucleotide repeats in intron 1 which is a homozygous state and consistent with FA.

**Conclusion:** FA must be considered in patients who presented with diabetes and ataxia. In our case, for the first time, non-autoimmune hyperthyroidism was detected in FA.

**Key words:** Friedreich’s ataxia, diabetes mellitus, frataxin, hyperthyroidism

Central Precocious Puberty in a Patient with Multiple Pituitary Hormone Deficiency Due to POU1F1 (PIT1) Gene Mutation

Zehra Yavaş Abali1, Şükran Poyrazoğlu1, Firdevs Baş1, Oya Uyguner2, Güven Toksoy2, Rüveyde Bundak1, Nurçin Saka1, Feyza Darendeliler1

1İstanbul University Istanbul Faculty of Medicine, Department of Pediatric Endocrinology, İstanbul, Turkey
2İstanbul University İstanbul Faculty of Medicine, Department of Medical Genetics, İstanbul, Turkey

**Background:** Multiple pituitary hormone deficiency (MPHD) associated with central precocious puberty (CPP) has been widely reported in cases of arachnoid cyst, septo-optic dysplasia, brain tumors, or after cranial irradiation. However, MPHD due to deficiency of transcription factors that regulate the development of hypothalamo-pituitary system is rarely reported in combination with CPP. CPP may delay the diagnosis of growth hormone (GH) deficiency and adversely affects adult height. In this report, a patient with MPHD due to POU1F1 (PIT1) deficiency and CPP is described because of its rarity.

**Case:** A 20-month-old boy presented with short stature. He had the diagnosis of central hypothyroidism and has been receiving L-thyroxin therapy since the age of 3 months. He was born at 34 gestational weeks [birth weight 0.6 standard deviation (SD), birth length -1.2 SD], and had no perinatal asphyxia. Severe short stature (length 62 cm, -6.6 SD) was detected. There was no dysmorphic features. Testicles were scrotal and pre-pubertal. GH deficiency and prolactin deficiency were detected and there were no abnormalities in cranial and pituitary magnetic resonance imaging except for pituitary hypoplasia. While he was on GH (started at age 2 years) and L-thyroxin therapy, puberty started at 79/12 years. Gonadotropin-releasing hormone (GnRH) analogue was started at 8 years due to rapid progression of puberty and continued up to 11 years of age. In the patient who had thyroid-stimulating hormone, prolactin, and GH deficiencies, a new point mutation was detected in the POU1F1 gene (homozygous p.I244S); the parents were carriers for this mutation.

**Conclusion:** In humans, the relation between POU1F1 gene and CPP is not exactly known. In animal studies, it was shown that POU1F1 gene has effects on the GATA2 gene which has an important role on gonadotropin production and also plays a role in GnRH receptor gene functions, regulation of gonadotropin production, and in prevention of excess gonadotropin production. Further clinical and experimental studies are needed to detect the relation between POU1F1 functions and CPP.

**Key words:** MPHD, CPP, POU1F1, GATA2