A Hypogonadotropic Hypogonadism Case as a Consequence of GNRHR Mutation

Esra Döğer[1], Özge Yüce[1], Nurullah Çelik[1], Hamdi Cihan Emeksiz[1], Ali Kemal Topaloğlu[2], Aysun Bideci[1]

[1]Gazi University Faculty of Medicine, Department of Pediatric Endocrinology, Ankara, Turkey

[2]Çukurova University Faculty of Medicine, Department of Pediatric Endocrinology, Adana, Turkey

Hypogonadotropic hypogonadism may occur as a result of hypothalamic pituitary axle-associated pathologies and also may accompany variable syndromes. So far, hypogonadotropic hypogonadism was reported as being associated with numerous gene mutations. These cases mostly apply to clinics with puberty delay. Here, we present a case of hypogonadotropic hypogonadism which presented with adolescence delay.

A 15-year-6-month-old female patient applied with complaints of puberty delay and lack of breast development. She had applied to a different hospital 5 months ago with lack of breast development and hair growth and estradiol (E2) and medroxyprogesterone acetate therapies had been initiated. Her history had nothing specific, but we learned that her parents were first-degree cousins and her 24-year-old brother has been receiving testosterone therapy due to pubertal delay.

Her physical examination revealed the following: weight 57.8 kg (50-75 p), height 158.1 cm (25-50 p), breast - Tanner stage 2, pubis - Tanner stage 1, and normal smelling capabilities. Laboratory results were as follows: follicle-stimulating hormone 0.19 mIU/mL, luteinizing hormone 0.03 mIU/mL, E2 20.2 pg/mL, prolactin 5.9 µg/L, karyotype 46 XX, bone age 12 y 6m. On her pelvic ultrasonography, uterus was 24x14x20 mm, right ovary was 15x8 mm, left ovary was 15x9 mm; pituitary gland was 7x6.5x15.8 mm (smaller than usual). We have started hormone replacement therapies to the patient with the diagnosis of hypogonadotropic hypogonadism. A c.743-1 G>A splice mutation was detected on gonadotropin-releasing hormone receptor (GNRHR) exon 4 in our patient's and her brother's gene analysis.

A lot of gene mutations play a role in hypogonadotropic hypogonadism etiology. GNRHR mutations were described as the most common reason of normoosmic isolated hypogonadotropic hypogonadism. Given that consanguineous marriage is common in our country, the *GNRHR* gene must be the first to look for especially in autosomal recessive familial cases.

Key words: Hypogonadotropic hypogonadism, GNRHR mutation, hypogonadism etiology, hypogonadotropic hypogonadism genetics