An Obese Case with Homozygous Leptin Receptor Mutation

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Here, we aim to present the characteristics of a 27-month-old male morbid obese case with a leptin receptor (*LEPR*) mutation and to emphasize the current approaches.

Patient's DNA sample was studied in France. *PCSK1, LEPR, LEP, MCR4, POMC* genes' reference sequences were compared with SeqScape@ (Applied Biosystem).

When he was 9 months old (height: 75 cm, weight: 19 kg, head circumference: 48 cm), he was referred to our clinic in order to clarify his obesity; there was no dysmorphism on his physical examination. His birth weight was 3870 grams and he was fed with breast milk only. The weight gain was noticed after the second month of life. There were not any obese and/or diabetic cases in the family and the patient did not have any medication history. Laboratory results were as follows: fasting glucose 88 mg/dL, fasting insulin 4.6 mU/mL, alanine aminotransferase 19 U/L, total cholesterol 172 mg/dL (upper limit), triglyceride 209 mg/dL (high), adrenocorticotropic hormone 16.5 pg/mL, cortisol 12 µg/dL, hemoglobin A1c 5.3%. Ophthalmologic and cardiologic evaluations were normal. Cranial imaging was normal, but abdominal imaging revealed that the kidneys merge from the lower poles at the middle line (horseshoe kidney). Genetic mutation analysis was negative for Prader-Willi syndrome. At the last control (when 27 months old), height was 93.5 cm (1.18 SDD), weight was 27 kg (5.9 SDD), and body mass index was 32.1 kg/m^2 (4.86 SDD). For the last 3 months, he had been presenting urinary tract infection and renal stone which was followed by nephrology -family history was positive for kidney stones. We could not measure serum leptin levels. Molecular analysis for monogenic obesity found a new mutation, homozygous c.2929G>T (p.Glu977), on the *LEPR* gene that causes stop codon. The parents were heterozygous for this mutation.

There is an early and dramatic weight gain in infantile cases with *LEPR* mutation. Hypogonadotropic hypogonadism and thyrotropin deficiency is a common endocrine problem in these patients and for this reason, follow-up is important. There is no specific therapy other than diet. MCR4 agonist usage is in experimental phase. Bariatric surgery is an option although it is risky and not so efficient in older children.

Key words: Obesity, infant, leptin, leptin receptor, mutation