

Melanocortin-4 Receptor Mutation and Obesity

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Although the mortalities and morbidities that come along with being over-weighted or obese are known since Hippocrates time, in middle age, obesity was acknowledged as wealth and prosperity. However, nowadays with the definition of World Health Organization, obesity is the fat accumulation in excessive or health-disturbing amounts. Polygenic obesity is 25-40% affected by genetic factors. Children who have at least one obese parent, has 2-3 times more chance to become obese. Besides the environmental factors, genetic factors should be investigated more since the rates of childhood obesity are increasing day by day.

When family history is questioned, all the first-degree relatives are morbidly obese. O.H.'s weight was over the 90th percentile and, for this reason, Ege University Faculty of Medicine Pediatric Endocrinology Department took him into the follow-up program. He has been investigated because of his childhood obesity and he has been the

index case in his family with melanocortin receptor (MC4R) mutation at age 10. All the family members are morbidly obese. Hypertension was found in two people and type 2 diabetes mellitus was found in 3. All the cases that completed their development were in the normal height range. There was not any anomaly in the gonadotropin axle of the cases which were in the reproductive period.

His grandmother (his father's mom) had homozygous MC4R mutation, but other family members had heterozygous MC4R mutation. Grandmother who was always over-weighted told us that she even gained more weight in a fast way after she was 30. Body mass index was 54.2 kg/m² and hemoglobin A1c was 8.4%. Although she had homozygous MC4R mutation, - because it slows down the gastric peristalsis although it does not stimulate the satiety center – glucagon-like peptide-1 receptor agonist, exenatide, was added. The therapy did not succeed. The case was planned to be discussed in the obesity council in terms of bariatric surgery.

MC4R mutation shows autosomal dominant inheritance. MC4R mutation's exact prevalence is not yet known, but it is assumed that its prevalence in morbidly obese people is 4%. In MC4R mutation cases where medical nutrition therapy, exercise, behavior therapy, and medical therapy would not help, surgery must be a priority. The family that we described shows us that endocrinologists need to do the MC4R mutation screening more often in case of positive family history.

Key words: Melanocortin-4 receptor mutation, obesity, diabetes, bariatric surgery, GLP-1 receptor agonists