Giriş

• Although the majority of the cases with obesity have a multifactorial etiology, rare monogenic forms of obesity exist.
• Several genetic disorders have been described that lead to early onset monogenic obesity.
• Leptin (LEP), leptin receptor (LEPR), melanocortin 4 receptor (MC4R), proprotein converting protein subtilisin / kexin-type 1 (PCSK1) and proopiomelanocortin (POMC) are the genetic mutations that have been most frequently shown to cause monogenic forms of obesity.
• In this study, we aimed to present two cases who applied with early onset morbid obesity and hyperphagia in whom we detected homozygous missense and homozygous frameshift mutations in LEPR.

Case 1

• A 6-month-old girl presented to our outpatient clinic with morbid obesity.
• The parents were first degree cousins.
• She had hyperphagia and rapid weight gain at the age of 3 months.
• She had no red hair.
• On physical examination:
  • Weight: 13.1 kg (+4.76 SDS)
  • Height: 71 cm (+1.61 SDS)
  • Body mass index (BMI): 25.9 (+4.4 SDS)

Olgu 2

• A girl with a birth weight of 3250 g was admitted with hyperphagia and excessive weight gain at 8 months of age.
• There was a consanguinity (first cousin marriage) between his parents
• On physical examination:
  • Weight: 19.8 kg (+7.94 SDS)
  • Height: 73 cm (+1.21 SDS)
  • Body mass index (BMI): 37.1 (+6.9 SDS)

Genetic

• Molecular analysis:
  • In molecular analysis; C.1938G>T (p.W646C) variant and C.946C>A (p.P316T) homozygous missense mutation in the LEPR gene were detected.
  • In the molecular analysis of the first family, both parents and her sibling have been shown to be heterozygous for the same gene.
  • In molecular analysis; homozygous novel c.1220-1221insT frameshift mutation was detected in the LEPR gene.
  • In the molecular analysis of parents; both parents were shown to be heterozygous carriers.

Conclusion

• Leptin and LEPR play a key role in body weight and energy homeostasis.
• LEPR mutations are rare, autosomal recessive and result in hyperphagia and early onset monogenic obesity.
• Until now, the number of reported LEPR gene mutations is less than 60.
• The mutation detected in case 1 [(C.946C>A (p.P316T)] was previously reported in the literature.
• The mutation detected in case 2 [C.1220-1221insT ] was shown for the first time in our patient.
• In conclusion, we think that monogenic obesity should be kept in mind and genetic studies should be done in patients with early onset severe obesity, hyperphagia and history of consanguinity.