# EARLY ONSET MONOGENIC OBESITY: TWO CASES WITH HOMOZYGOUS MUTATION IN LEPR GENE

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## 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 :** 13,1kg (+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

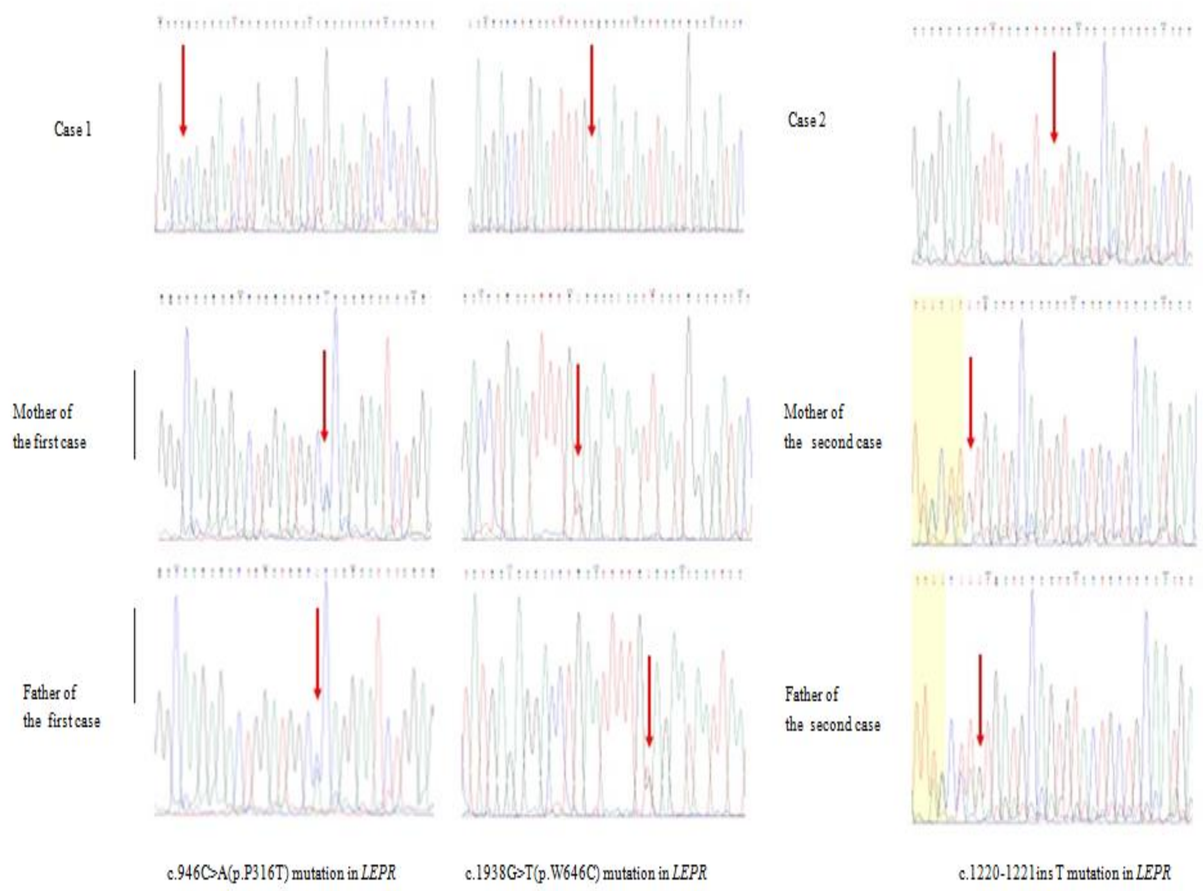
▪**Molecular analysis :**

▪ 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.