

Heterozygous AGPAT2 Mutation, Diabetes, and Lipodystrophy in Extremities

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A 29-year-old male patient applied to the emergency department with complaints of polydipsia, polyuria, and weight loss of 15 kg in a month although he was eating too much. Randomly measured blood glucose was 650 mg/dL, glucose in urine was found as 1000 mg/dL, and ketone was negative. Arterial blood gas analysis did not reveal any acidosis. The case was admitted to the clinic with a hyperosmolar-hyperglycemic situation.

At admission to hospital, general state was good, he was conscious and cooperative. Physical examination revealed the following: height 168 cm, weight 69 kg, and body mass index was 22.4 kg/m². His muscle mass was good although his fat mass was reduced; he had a severe insulin resistance and nonketotic, nonacidotic hyperglycemia. With all given, he was thought to have Lipodystrophy (LPD) syndrome, so his leptin levels and mutation analysis were sent to be examined. There was no retinopathy in the fundus of the patient who had microalbuminuria. In his neurological examination, there was no polyneuropathy. Laboratory

results revealed hemoglobin A1c (HbA1c) of 16.6%, while anti-glutamic acid decarboxylase was negative and lipids were in normal range. 6 months after being discharged, HbA1c value regressed to 6.9%, so intensive insulin therapy was changed with pioglitazone.

Magnetic resonance imaging (MRI) was performed in order to assess the fat distribution. MRI showed that head, neck, thorax, and abdominal fat mass was preserved, but fat both in upper and lower extremities' distal parts decreased in amount significantly. A heterozygous R159C (CGC>TGC) mutation was detected on the *AGPAT2* gene. With family's warning, we examined the 37-year-old sister who had also muscular appearance on extremities. Based on biochemical data (HbA1c value: 7.9% and fasting blood glucose: 217 mg/dL), she was diagnosed with diabetes mellitus (DM), but there was no hyperlipidemia. She also had a heterozygous R159C (CGC>TGC) mutation on the *AGPAT2* gene.

Autosomal recessively inherited *AGPAT2* mutation causes generalized fat loss clinically, but phenotypic and genetic heterogeneity is very common. Even though our case and his sister had heterozygous mutation, may we interpret the findings of partial lipodystrophy and non-ketotic DM as a new phenotype? The case and his sister cannot be assessed in any known classification of LPD. LPD syndromes must be considered by means of differential diagnosis and valid therapy in case of preliminary diagnosis of type 1 DM and maturity-onset diabetes of the young in non-obese diabetics who get diagnosed at a young age.

Key words: Heterozygote *AGPAT2* mutation, diabetes, lipodystrophy, infertility, MODY