A CASE OF PROHORMONE CONVERTASE DEFICIENCY DIAGNOSED WITH TYPE 2 DIABETES MELLITUS

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Objective

Prohormone convertase is an enzyme that converts many biologically inactive prohormones into biologically active peptides. Its deficiency is characterized by deficiency of variable levels in all the hormone systems. In relation to this, postprandial hypoglycemia has been reported but, a case of prohormone convertase deficiency presenting with a diagnosis Type 2 diabetes mellitus has not been previously reported.

Case Report

A 14-year-old girl referred to the pediatric endocrine clinic due to her excess weight. It has been learned that her weight is too high for twelve years. In her history, she was admitted to the hospital with the cause of watery diarrhea 12 days old and was hospitalized with the cause of dehydration and acidosis due to diarrhea. It was learned that there were several hospitalizations due to diarrhea, 3.1 kg of body weight at 36 days and 3.5 kg at 3.5 months of age and sufficient weight gain could not be achieved and diarrhea continued until 1 year old. Our case started to gain weight rapidly from 2 years old.

There was no consanguinity between parents in the family history and there was no individual defining diarrhea. While the mother was obese only in the family, there was no individual who had diabetes. Physical examination on admission revealed that height: 148.2 (-2.013 sds), weight: 99.85 kg (+4.73 sds), body mass index (BMI): 45.46 kg/m^2 (+4.49 sds), blood pressure: 120/70 mmHg, thyroid was nonpalpable, puberty Tanner stage 5, acanthosis nigricans was both in the axilla and neck, stria was present in the arms, upper legs and around waist. The mother's height was 148 cm (-2.32 sds), the father's height was 175 cm (-0.21 sds) and the mid-parental height was 155 cm (-1.25 sds).

In the laboratory tests glucose was 258 mg/dl, insulin 75.1 µIU/ml and HbA1c 9.6 % and according to these tests the patient was hospitalized with the diagnosis of diabetes mellitus. In the blood glucose monitoring, her fasting blood glucose were 150-200 mg/dl, postprandial glucose were 200-300 mg/dl, c-peptide was 7.21 ng/ml (0.9-7.1) and islet antibody: 0.37 U/L (<1), anti GAD antibody: 0.29 IU/ml (<1), anti insulin antibody: 0.73 U/ml (<12).

Diabetic diet and2x850 mg metformin treatment initiated with the diagnosis of type 2 diabetes in this patient. Cholesterol: 227 mg/dl (95-237), LDL cholesterol: 154 mg/dl (38-140), HDL cholesterol: 37 mg/dl (>35), triglyceride: 174 mg/dl (37-131), AST: 33 U/L (<47), ALT: 26 U/L (0-27). Abdominal ultrasonography revealed stage 3 fatty liver.

Prohormone convertase deficiency was considered due to the history of treatment resistant diarrhea in the period of infancy in her history and after that start of weight gain. Proinsulin level at diagnosis was > 700 pmol/L (3.60-22). In genetic analysis, we noticed that c.685G> T (p.V229F) homozygous mutation in the PCSK1 gene. However, it should be noted that this mutation was not reported related with this disease. Other hormone insufficiencies that may be seen in the deficiency of prohormone convertase were investigated and was not determined.

It was observed that the blood glucose profile improved within 7 days following the diagnosis of type 2 diabetes and 1800 caloric diabetes diet and metformin treatment started. Fasting blood glucose was 99 mg/dl and postprandial blood glucose was 134 mg/dl.

Conclusion

We concluded that it is important to consider the diagnosis of prohormone convertase deficiency in infants with recurrent resistant diarrhea during infancy. Our case demonstrated that if obesity starts to develop after childhood associated with recurrent serious diarrhea episodes in the history, diagnosis should be considered.