



NEONATAL DIABETES, GALL BLADDER AGENESIS AND CHOLESTATIC GIANT CELL HEPATITIS: A NOVEL HOMOZYGOTE MUTATION IN PDX-1 GENE

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Background:

Neonatal Diabetes Mellitus (DM) is a DM form which is encountered in the first six months of life, inherited monogenically and is accompanied by additional anomalies. It is known that Pancreatic Duodenal Homeobox-1 (PDX-1) gene mutation is related to neonatal diabetes, pancreas agenesis and intrauterine growth retardation. Here the aim was to present a newly defined mutation in PDX-1 gene in a case born with IUGR, diagnosed with neonatal DM and in which exocrine pancreas deficiency and gallbladder agenesis were detected.

Case Presentation:

Blood glucose was measured as 185 mg/dl in the first hour after birth and insulin infusion was given at intervals to the case whose blood sugar was >250 mg/dl during observation and the case was referred to our clinic.

In the physical examination of the male baby born with a weight of 1520 gr in the 37th week as G1P1 from a 19 year old mother with a story of 1° cousin marriage in her parents, the birth weight was 1400 gr(<3p), height was 42,5 cm (<3p) and the head circumference was 31 cm (<3p) and they were smaller when pregnancy week was considered. Referral blood sugar was found 216 mg/dl and it reached up to 500 mg/dl in the follow-ups.

Cholestatic giant celled hepatitis was detected in the liver needle biopsy of the patient whose c-peptide level-amylase-lipase was low, faecal elastase level was >200 ng/ml and had direct hyperbilirubinemia and mild height in liver function tests. Insulin infusion between 0.01-0.02 unit/kg/hour was given. Conventional insulin treatment was started by making consultation with pediatric endocrinology department. Blood sugar regulation was provided with insulin pump to the case whose satisfactory nutrition couldn't be provided due to exocrine pancreas function disorder and who was experiencing hypoglycemia and hyperglycemia even though 0.2 U/kg/day SC insulin dose was given. Gallbladder imaging was impossible in ultrasonography and magnetic resonance cholangiography. A new homozygote mutation was detected in PDX-1 gene Exon 2 with Whole Exom sequencing method [c.593G>C;p.Arg198Pro(p.R198P)]. It was observed that the parents had heterozygote mutation. Pancreas enzyme replacement, ursodeoxycholic acid, fat-soluble vitamin support was given for exocrine pancreas deficiency and cholestasis. Cholestasis presentation regressed when total parenteral nutrition was cut. The patient was discharged with insulin pump and supporting treatments in the postnatal fourth month.

Conclusion:

Although PDX-1 was known as a transcription factor defined for insulin transcription regulating mechanisms, it was detected to play a very significant role including pancreas and islet functions and we think that the new mutation we defined would contribute to the literature.