A Case of Neonatal Diabetes with Hyperferritinemia: A Distal *PTF1A* Enhancer Mutation

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Introduction

▪Neonatal diabetes, defined as the onset of diabetes within the first six months of life, is very rare disease.

▪Several genetic factors caused to neonatal diabetes have been identified to date. *PTF1A* (pancreatic transcription factor 1a) play a key role in early pancreas development and cerebellar neurogenesis.

▪Biallelic mutations in *PTF1A* have been reported in patients with pancreatic and cerebellar agenesis, whereas mutations located in a distal pancreatic-specific enhancer region causes isolated pancreatic agenesis.

▪In here, we present a case with neonatal diabetes, high ferritin level, and cholestasis who has initially been misdiagnosed as hemochromatosis. Following further genetic analysis, distal *PTF1A* enhancer mutation have been identified.

History and Physical Examination

▪ Two and half month male was referred to our hospital from another center because of hyperglycemia and cholestasis.

▪He was born with a birth weight of 1830 gr at 36 gestational week from mother with oligohydramnios.

▪The parents were relatives (first-degree-cousin).

▪On physical examination, his weight was 1900 gr (<3p), height was 44 cm (<3p) and low ear, triangle face and micrognathia were observed. Both of testes were in scrotum (2/2 cc).

Clinical Follow-Up

▪Insulin infusion was initially started.

▪Analyses of *ABCC8/KCNJ11* were planned and glibenclamide was added.

▪Because of persistent hyperferritinemia, abdominal MRI showed increased intensity in the liver (hemochromatosis?)

▪Buccal biopsy was performed; however biopsy specimen was inadequate.

▪Pump treatment was unsuccessful because of technical problems. NPH was added and normoglycemia was achieved.

▪No mutation in *ABCC8/KCNJ11* was found; therefore glibenclamide treatment was stopped.

▪Because of inadequate weight gain and steatocrit in skool, pancreatic enzyme replacement was started.

▪During the treatment, normal serum ferritin levels were achieved.

Laboratory

Parameters	Value	Normal range
Glucose (mg/dL)	317	30-60
BUN (mg/dL)	6	4-12
Creatinine (mg/dL)	0.7	0.3-1
Sodium (mmol/L)	135	133-146
Potassium (mmol/L)	5.4	3.7-5.9
Hemoglobine (gr/dL)	8.6	13-20
ALP (IU/L)	235	25-75
AST (IU/L)	21	25-75
ALT (IU/L)	16	13-45
İnsulin (µU/mL)	0.4	2.6-24.9
C-peptide (ng/mL)	< 0.1	0.9-7.1
Ammonia (µg/dL)	53	27-115
Lactate (mmol/L)	35.7	4.5-19.8
Serum iron (gr/dL)	89.5	65-175
Iron binding capacity (µg/dL)	< 20	110-370
Transferrine saturation (%)	447	20-50
Ferritine (ng/mL)	3057.58	50-200

Molecular Genetic Analysis

▪ *PTF1A* gene distal enhancer homozygous mutation (g.23508336 G>T) was found.

▪His mother and father were heterozygous for the same mutation.

Discussion and Conclusion

• Hyperferritinemia can be accompanied in cases with neonatal diabetes as an acute phase reactant.

•If no mutation is detected in *ABCC8* and *KCNJ11* in cases of neonatal diabetes, investigation of rare genetic causes should be kept in mind.