Clinical characteristics and molecular analysis of patients with neonatal diabetes

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Background

Neonatal diabetes mellitus (NDM) is a form monogenic diabetes diagnosed before 6 months of age.

Objective

To describe the clinical and molecular characteristics of NDM patients in aTurkish cohort.

Methods

Fifteen patients (13 M, 2 F) with diabetes onset before 6 months of age were included in the study.

Clinical and molecular data were evaluated retrospectively.

Result

Mean age at diagnosis was 2.4±1.5 months (median 2, range 0.5-6 m).

Gestational ages were between 35-40 weeks.

Birth weight (BW) was between 1400-3680g and BW-SDS -1.7±1.7 (median -1.1; range -5.0 – 0.6).

Small for gestational age (SGA, BW <-2 SD) ratio was 40%.

Consanguinity ratio was 66.7%.

Mean serum glucose level at diagnosis was 29.4±8.9mmol/l.

Mutations are given in Table 1.

Table1. Genotype analyses of the patients

	Patients (n)	Mutations detected
ABCC8	3	p.E382K and p.R826W
PTF1A	2	g.23508437A>G distal enhancer
Thiamine responsive megaloblastic anemia	1	p.S214fs in *SLC19A2*
Wolcott Rallison syndrome	1	p.S718TfsX723 in *EIF2AK3*
INS	1	c.-331C>G
Not known	7	-
Total	15	

- ✓ In two siblings with *ABCC8* mutations (p.E382K mutation), insulin therapy was switched to glibenclamide at the age of 15 and 11 years. They have been on sulphonylurea (SU) monotherapy for 9 years, recent HbA1c values were 6.5%.
- ✓ The third patient with ABCC8 mutation (p.R826W) was planned to transfer SU.
- ✓ The two patients with *PTF1A* mutation had exocrine pancreatic deficiency due to pancreatic hypoplasia.
- ✓ One patient with unknown genetic etiology was SGA and had also exocrine pancreatic deficiency.
- ✓ Patient with *SLC19A2* mutation has sensorineural deafness, megaloblastic anemia, AV block, still on thiamine and subcutaneous insulin therapy (0.8 U/kg/day) at the age of 7 years.
- ✓ Patients with mutations in *INS, PTF1A* and two patients with unknown genetic etiology were SGA.
- ✓ One patient had no mutation in *ABCC8* and *KCNJ11* gene. Genetic cause was not resulted in six patients.

Conclusion

- ✓ With high consanguinity ratio in this cohort, Wolcott Rallison syndrome was not the most common cause of NDM, contrary to previous reports.
- ✓ Male dominancy of our cohort was also noteworthy.
- ✓ In NDM patients with SGA and exocrine pancreatic deficiency *PTF1A* should be analysed first.

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