Neonatal diabetes and congenital hypothyroidism, a rare condition: report of 2 cases with different genetic causes

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Nothing to disclose

INTRODUCTION

•Neonatal diabetes (ND) is a rare monogenic form of diabetes characterized by the onset of hyperglycemia within the first six months of life. ND can be transient (TND) or permanent (PND).

•The most frequent causes are mutations in *KCNJ11, ABCC8* and i*nsulin* gene. Up to 40% of patients with ND remain without a genetic diagnosis.

•A specific molecular diagnosis has important clinical consequences for appropriate treatment, associated conditions, prognosis and genetic counseling.

METHODS

•We describe two clinical cases of neonatal diabetes and congenital hypothyroidism.

•Clinical characteristics in table 1, laboratory and imaging tests in table 2.

Table 1. Clinical characteristics

	Case 1	Case 2
Gestation, wk	35	38
Birth weight, g	1550	2300
Birth length,cm	39.5	45
Birth weight, centile	< 3rd	< 3rd
Hyperglycemia	Second day of life	20th day of life
Family history	Unremarkable	Unremarkable
Associated conditions	Congenital hypothyroidism Cholestasic jaundice Chronic diarrhea Small interauricular communication	Congenital hypothyroidism Tetralogy of Fallot

Table 2. Laboratory and imaging tests

	Case 1	Case 2
TSH (mIU/ml) *Reference* 1.7-9.1	1132	35,6
C- peptide (ng/ml) *Reference* 0.8-4.2	0.1	<0,5
Thyroyd ultrasound	Severe thyroid hypoplasia	Normal
Abdominal ultrasound	Normal	Pancreatic agenesis

RESULTS

•Molecular tests were performed at Molecular Genetics Laboratory, University of Exeter Medical School, Exeter, UK.

•Mutations in *KCNJ11, ABCC8 and INS* genes were excluded.

•Sequence analysis identified a novel ***de novo* heterozygous *STAT3* missense mutation p.Gln643 Arg (c.1928A>G)** in case 1 and a **heterozygous GATA6 mutation p.Cys447Arg** (**c.1339C>T)** in case 2**.**

•Both cases were managed with basal bolus-insulin therapy.

CONCLUSIONS

- We present two cases of neonatal diabetes associated with congenital hypothyroidism.
- *GATA6* mutation is a known cause of permanent ND due to pancreatic agenesis associated with congenital hypothyroidism.
- Mutations in *STAT3* have been recently associated with early-onset autoimmune disease including enteropathy, primary hypothyroidism, fibrotic lung disease, juvenile arthritis and ND.
- A specific molecular diagnosis has important clinical consequences as it may influence diabetes treatment and prognosis.

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55ESPE 691--P1
Endocrinology and Multisystemic Diseases
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DOI: 10.3252/pso.eu.55ESPE.2016
Poster presented at: ESPE 2016 PARIS