Hypothyroidism in Context of 1q44 Microdeletion Syndrome and DOLK-CDG

Dr. Bogdan Mihai Pascu, Dr. Elisa Lincă
INSMC Alessandrescu Rusescu Hospital Bucharest, Romania

INTRODUCTION

1q44 microdeletion syndrome has a quite variable clinical phenotype, with various degrees. DOLK-CDG is a rare condition with an autosomal recessive pattern. Neurological involvement is often noticed in both of this conditions. 1q44 microdeletion syndrome and DOLK-CDG have not yet been reported on the same patient and neither was hypothyroidism for DOLK-CDG patients. Furthermore DOLK-CDG has only been described in patients having the homozygous mutation linked to a low life expectancy.

CASE PRESENTATION

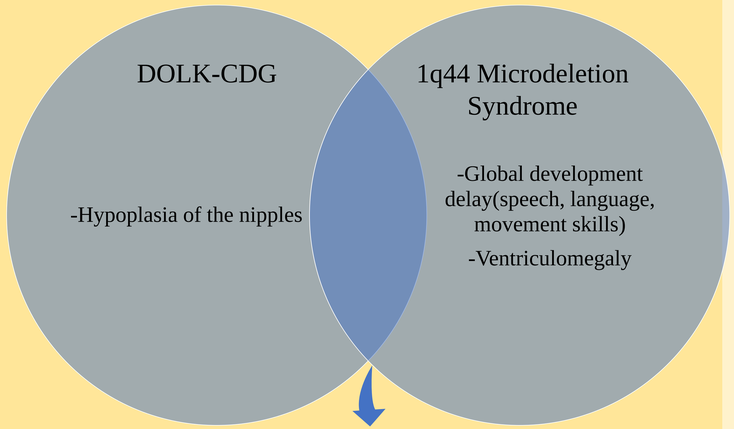
- 2 months-old girl with persistent hypotonia arising shortly after birth → Diagnosis: *Central mild hypotonia*
- Recurrent febrile convulsions → Diagnosis: *Febrile seizures*
- 1y-old: Delayed motor skills and language acquisition, failure to thrive, mild facial dysmorphism
- Personal medical history:

-Amniocentesis and fetal MRI → corpus callosum normally developed, borderline lateral ventriculomegaly

-Born at 39 week, 3540g, Apgar Score:7, perinatal asphyxia

-Newborn neurological examination: normal for the GA, TFUS: corpus callosum and ventricles in normal range

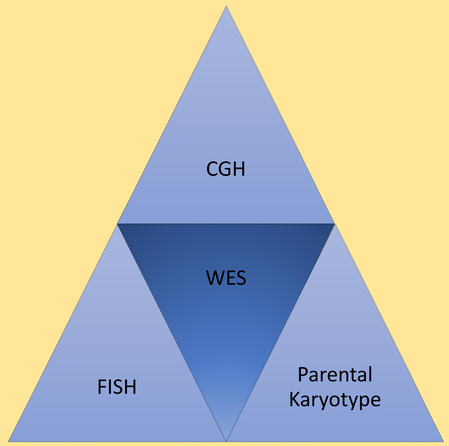
- Family history: sibling 1 with normal development and no consanguineous parents; mother: HBsAg
- Interdisciplinary collaboration was required for further investigations



LABORATORY, IMAGING AND GENETICS STUDIES

1y4m-old → Thyroid hemiagenesis

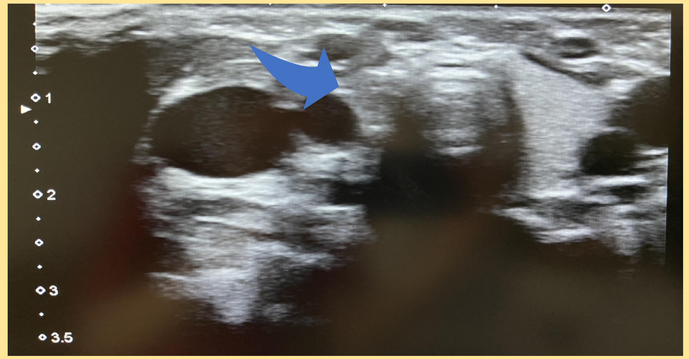
Hypothyroidism treatment with Levothyroxine 25mcg was initiated. The hormonal therapy normalized the TSH level and improved the clinically appearance of the child.



- *WES*→ A likely pathogenic 1734kb-large one copy loss within chromosomal region 1q44

→Two heterozygous variants of uncertain significance (Class 3) were identified in the DOLK gene

- *FISH* → Uncertain
- *Parental Karyotype*→ Normal
- *Brain MRI*→ Mild lateral ventriculomegaly and a reduction in the thickness of the corpus callosum
- *Array-CGH* → 1q44 microdeletion syndrome



DISCUSSION

The pattern and severity of DOLK-CDG vary among affected individuals. 1q44 microdeletion syndrome is a newly described syndrome with various degrees of development delay. Thyroid hemiagenesis is a rare form of thyroid dysgenesis, with a prevalence about 0.05-0.2% in normal population. In our case a multidisciplinary and complex approach was needed, including a pediatrician, endocrinologist, neurologist and a geneticist. Long term follow-up and treatment are essential.

REFFERENCES

1. https://rarediseases.info.nih.gov/diseases
2. https://chromodisorder.org/wp-content/uploads/2020/02/New_1q43-44.pdf
3. E. Szczepanek-Parulska, et al. Thyroid hemiagenesis: incidence, clinical significance and genetic background 2017, The Journal of Clinical Endocrinology & Metabolism
4. M.T. Lieu, et al.Severe, fatal multisystem manifestations in a patient with dolichol kinase-congenital disorder of glycosylation 2013, Molecular Genetics and Metabolism, 110(4), 484–489