A Rare Cause of Congenital Hypothyroidism: Brain -Lung -Thyroid Syndrome

A. ARASLI YILMAZ [1], Ş. SAVAŞ ERDEVE[1] , D. YÜKSEL[2], Ü. ÖZTOPRAK[2] , S .ÇETİNKAYA[1]
1. Health Sciences University, Dr Sami Ulus Obstetrics and Gynecology, Child Health and Diseases Training and Research Hospital, Pediatric Endocrinology, Ankara, Turkey
2. Health Sciences University, Dr Sami Ulus Obstetrics and Gynecology, Child Health and Diseases Training and Research Hospital,Pediatric Neurology, Ankara, Turkey

ESPE 2021
The 59th Annual Meeting Online
22-26 September 2021

INTRODUCTION

Brain-lung-thyroid syndrome (BATS) is a rare autosomal dominant inherited syndrome that develops due to mutations in the NKX2-1 gene, which is a thyroid transcription factor, and is characterized by respiratory distress in the neonatal period, congenital hypothyroidism, and choreatetosis.

Approximately half of affected patients have the complete triad, with 30% affected by the neurological phenotype (motor developmental delay, gait difficulties, choreatetosis, hypotonicity, ataxia, dysarthria, dystonia, thirst, hunger, sleep problems) and hypothyroidism, while about 13% only have the neurological phenotype.

In cases accompanying pulmonary dysfunction; neonatal respiratory distress, asthma, and frequent lung infections can be seen.

Herein, a case with a heterozygous mutation in the NKX2-1 gene is presented with interesting family characteristics.

CASE REPORT

3 months old female,

She was diagnosed with congenital hypothyroidism at the age of one month and started treatment was referred to our clinic for follow-up.

She was born at term, weighing 3300 gr, and developed meconium aspiration in newborn period. She was first child of nonconsanguineous parents.

Neurodevelopmental retardation in her mother.

Diagnosed with hypothyroidism during pregnancy in her mother and used levothroxine (LT4) treatment.

Choreiform movement disorder in her mother and grandfather.

CASE REPORT

In the physical examination of the patient at the age of 3 months;

Weight :5680gr (43 p) (-0,16 SDS)
Head circumference:40cm (50 p)(0 SDS)
Anterior fontanel: 1x1cm
Puberty:Tanner stage 1
No goiter.
Other system examinations were normal

Laboratory and imaging results at 3 months of age while receiving LT4 treatment (6,5 mcg/kg/day)

Thyroid Function Tests:TSH:2,593 µIU/ml ST4:1,32 ng/dl
Thyroid US :Right lobe 5 x 5 x 13mm ,left lobe 5 x 6 x 11 mm
The isthmus was not clearly observed.
Homogeneous parenchyma of both lobes.
Total Thyroid Volume :0,32 ml(-1,59SDS)

Follow-up
In the first year of follow up altough drug compliance was sufficient and her course was euthyroidic;
At the age of 1 year :
She could not sit without support.
At the age of 2,5 years :
Choreiform movements started.
At the age of four years 10 months:
She could only walk with support
Her speech consisted of 2 word sentences.

Table :1 Investigations for the etiology

Urine amino acids	Normal
Phenylanin:(mg/dl)	2.6
Pterin: Normal	Normal
Dihydropteridine activity: Normal	Normal
Tandem MS	Normal
Lysosomal Enzymes	Normal
VLCFA	Normal
Cranial MRI	Normal
Echocardiography	Normal
Electroencephalography	Normal
Array CGH	Normal

The patient's investigations for the etiology are summarized in Table1.
In whole exome sequencing analysis**, c.703G>T mutation was found in exon 3 in the NKX2-1 gene in our case, her mother and grandfather**. (Figure-1).
She, receives LT4 and tetrabenazine treatment and continues a special education program.

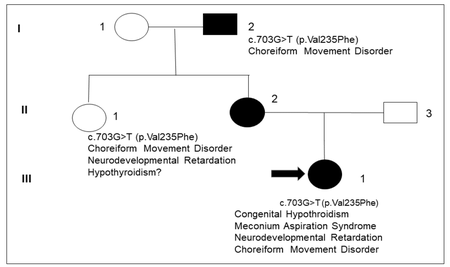

Figure 1:Pedigree of case

CONCLUSIONS

NKX2-1 mutation should be considered in cases of congenital hypothyroidism accompanied by neurological and / or pulmonary findings or family history indicating that these systems are affected.

It should be noted that the disease phenotype and severity can vary considerably even within families with the same mutation, as in our family sample.

REFERENCES

1.Patel NJ, Jankovic J. NKX2-1-Related Disorders In GeneReviews®. Editedby Pagon RA, Adam MP, Ardinger HH, Bird TD, Dolan CR, Fong CT, Smith RJH, Stephens K. Seattle (WA): University of Washington, Seattle. 2014; 1993–2015 .

2. Kharbanda M, Hermanns P, Jones J, Pohlenz J, Horrocks I, Donaldson M. A further case of brain-lung-thyroid syndrome with deletion proximal to NKX2-1. Eur J Med Genet. 2017; 60:257-260.

3.Parnes M, Bashir H, Jankovic J. Is Benign Hereditary Chorea Really Benign? Brain-Lung-Thyroid Syndrome Caused by NKX2-1 Mutations. Mov Disord Clin Pract. 2019; 6: 34–9. .

CONTACT INFORMATION

e-mail:draslihanarasli@hotmail.com

Phone: 0312 305 65 10