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 chordee. Approximately half of affected patients have the complete triad, with 30% affected by the neurological phenotype (motor developmental delay, gait difficulties, chordee, hypotonia, 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 NKX-2-1 gene is presented with interesting family characteristics.

CASE REPORT

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

- Weight: 5680g (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.

Follow-up

In the first year of follow up although 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.

The patient’s investigations for the etiology are summarized in Table 1.

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.

Table 1: Investigations for the etiology

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine amino acids</td>
<td>Normal</td>
</tr>
<tr>
<td>Phenylalanin: (mg/dl)</td>
<td>2.6</td>
</tr>
<tr>
<td>Pterin: Normal</td>
<td></td>
</tr>
<tr>
<td>Dihydroptero呤ine activity: Normal</td>
<td></td>
</tr>
<tr>
<td>Tandem MS</td>
<td>Normal</td>
</tr>
<tr>
<td>Lysosomal Enzymes</td>
<td>Normal</td>
</tr>
<tr>
<td>VGLFA</td>
<td>Normal</td>
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<tr>
<td>Cranial MRI</td>
<td>Normal</td>
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<td>Echocardiography</td>
<td>Normal</td>
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<tr>
<td>Electroencephalography</td>
<td>Normal</td>
</tr>
<tr>
<td>Array CGH</td>
<td>Normal</td>
</tr>
</tbody>
</table>

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


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