Thyroglobulin deficiency: A rare cause of neonatal stridor

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INTRODUCTION

Nonimmune neonatal goitreous hypothyroidism is a rare cause of neonatal stridor. Retropharyngeal extension, described in 7% of cases of goitre spreading outside the thyroid bed, represents a diagnostic dilemma that requires a systematic multimodality imaging approach combined with hormonal and genetic analysis.

CASE PRESENTATION

An eight-day-old term male infant admitted to the Neonatal Intensive Care Unit (NICU) due to persistent stridor.

Assessment
- Clinical examination of his neck was normal
- Microlaryngoscopy and bronchoscopy (MLB): Subglottic stenosis
- MRI neck: Large goitre with retropharyngeal extension
- Hormonal investigations pre treatment
  - Neonatal screening: TSH 17 mU/L
  - TSH 28.7 mU/L (NR: 0.35 - 5.50 mU/L)
  - Free T4: 6 pmol/L (NR: 10.4 - 22.7 pmol/L)
  - Free T3: 9.2 pmol/L (NR: 4.6 - 10.1 pmol/L)
  - Serum thyroglobulin(TG): <0.2 ug/L (NR 7.82-79.5 ug/L)
  - Normal urine iodine levels (mother and baby)
  - Normal Maternal Thyroid function
  - Negative Thyroid stimulating immunoglobulins (TSI) and Thyroid peroxidase antibody (TPO) at birth

CLINICAL PROGRESS

- Treatment with levothyroxine 11.5 mcg/kg/day was started to normalise serum TSH concentrations, thereby mitigating thyroidal tropism, stimulation and goitre growth (subsequent thyroid function as shown in Table 1)
- Due to persistent respiratory distress, intubation and ventilation were required.
- Since two weeks of medical treatment had not ameliorated goitre size, laryngoscopy was performed at 22 -days old to facilitate extubation.
- Levothyroxine dose was optimised.
- Repeat MLB showed improvement of subglottic stenosis.
- Follow up MRI scan: Reduction of the goitre size without any focal thyroid lesions.
- The baby was extubated on day 43 of life and discharged home on thyroxine 5.7 mcg/kg/day at 2 months of age.

CONCLUSIONS

- Dyshormonogenetic retropharyngeal goitre is a rare case of persistent stridor in the neonatal period.
- TSH elevation, combined with raised FT3:FT4 ratio and disproportionately low serum thyroglobulin levels in the context of goitre and TSH elevation, should trigger molecular evaluation for thyroglobulin mutations.
- Thyroid dysfunction associated with thyroglobulin mutation can range from euthyroid goitre to severe congenital dyshormonogenesis.2
- Suppressive therapy with thyroxine is not always effective in reducing the size of goitre and surgical intervention may be required.
- Maintaining adequate maternal iodine levels is important as there have been described cases of neonatal goitre secondary to maternal iodine insufficiency.3

REFERENCES


PERMISSIONS

We would like to acknowledge Mrs Greta Lyons, research nurse, who supported us with the sample collection.

CONTACT INFORMATION

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Table 1. Biochemical investigations-timeline

<table>
<thead>
<tr>
<th>Biochemistry</th>
<th>Before treatment</th>
<th>1 week post levothyroxine</th>
<th>At discharge</th>
<th>Reference range</th>
</tr>
</thead>
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<tr>
<td>TSH</td>
<td>28.79</td>
<td>5.54</td>
<td>2.51</td>
<td>0.35 - 5.50 mU/L</td>
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<tr>
<td>FT4</td>
<td>6.0</td>
<td>16.2</td>
<td>15.9</td>
<td>10.4 - 22.7 pmol/L</td>
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<tr>
<td>FT3</td>
<td>9.2</td>
<td>7.4</td>
<td>5.0</td>
<td>4.6 - 10.1 pmol/L</td>
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<tr>
<td>TG</td>
<td>&lt;0.2</td>
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<td></td>
<td>7.82 - 79.5 ug/L</td>
</tr>
<tr>
<td>TSI</td>
<td>&lt;10</td>
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<td>&lt;0.56 iu/L</td>
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<tr>
<td>TPO</td>
<td>33</td>
<td></td>
<td></td>
<td>0 - 60 iu/ml</td>
</tr>
</tbody>
</table>

Histopathology and immunohistochemistry

Features in keeping with dyshormonogenesis due to defective thyroglobulin synthesis.

Genetic analysis:

Heterozygous for a single pathogenic TG splice site variant NM_003235.4:c.5976-2A>C; second pathogenic variant not detected.

ACKNOWLEDGEMENTS

Thyroid disease: Syndromes and Gene Reviews

Table 2. Biochemical investigations-timeline