Thyroglobulin deficiency: A rare cause of neonatal stridor

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INTRODUCTION

Nonimmune neonatal goitrous hypothyroidism is a rare cause of neck mass and stridor.

Retropharyngeal extension, described in 7% of cases of goitre spreading outside the thyroid bed[1] 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)

CLINICAL PROGRESS

- Treatment with levothyroxine 11.5 mcg/kg/day was started to normalise serum TSH concentrations thereby mitigating thyroidal trophic 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, Isthmectomy 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.

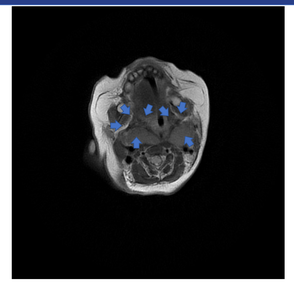

Figure 1:Enlargement of thyroid gland with retropharyngeal extension of both lobes (arrows indicate the thyroid enlargement) (axial MRI image)

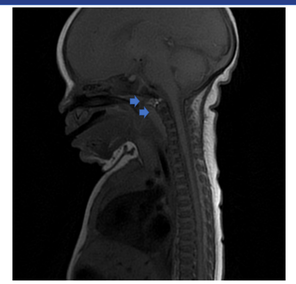

Figure 2: Thyroid goitre (area indicated by arrows) causing subglottic stenosis (sagittal MRI image)

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.

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

Table 1. Biochemical Investigations-timeline

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 hypothyroidism.[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]

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