A Case Report of TRBeta Mutation Leading to Raised T4 Levels

Dr Tomlinson ND[1], Dr I Banerjee[2] , Professor K Chatterjee[3] , Dr Smith TD[4], Dr Mukherjee A[5]

[1]Royal Oldham Hospital, Pennine Acute Hospitals NHS Trust, [2]Royal Manchester Children's Hospital,
[3]Cambridge University Hospitals, [4-5]Royal Oldham Hospital, Pennine Acute Hospitals NHS Trust

Introduction

- We present **a five year old girl** with thyroid hormone resistance, subsequently discovered to be heterozygous for **TRbeta mutation.**
- This case highlights the necessity to investigate, in detail, all children with **persistently high thyroxin** with **normal TSH levels** in order to aid future management and the necessity to follow them up.

Case Report

Birth: Normal delivery, weighing 3.34kg (50th centile)

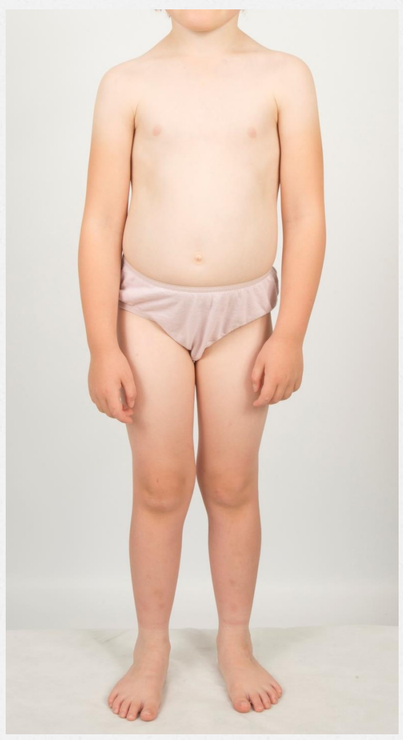
6 months old: Referred for **poor weight gain** (2nd centile)
- Blood tests = Elevated **free T4 (43.4**) with **normal TSH (3.10)**
- Systemic examination was normal and remained so over the following months
- Repeat thyroid function tests showed **persistently elevated T4 with normal TSH**

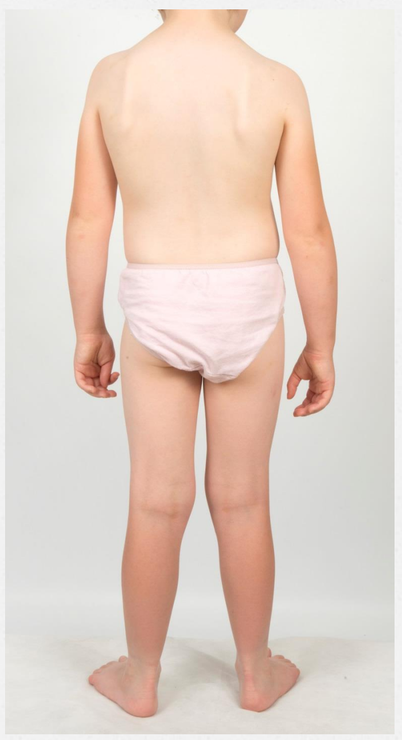
2 ½ years old: Genetic analysis revealed heterozygosity for TRbeta mutation
- Mum has no mutation detected and SDs father cannot be tested for unavoidable reason

Since then…
- ✓ Slow growth
- ✓ Idiopathic thrombocytopenic purpura
- ✓ Vitamin D deficiency
- ✓ Coeliac disease

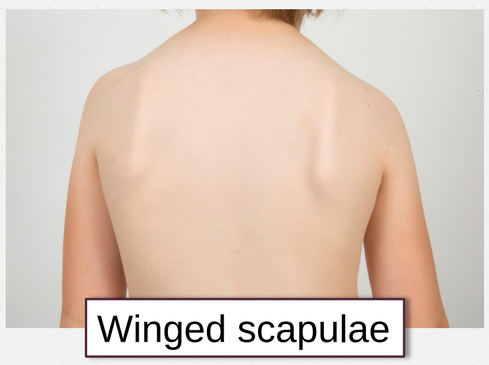
Broader antibody testing has not revealed an underlying autoimmune aetiology to date

Recently:
- ✓ Gross motor skills generally delayed
- ✓ Investigated for recurrent falls and abnormal gait:

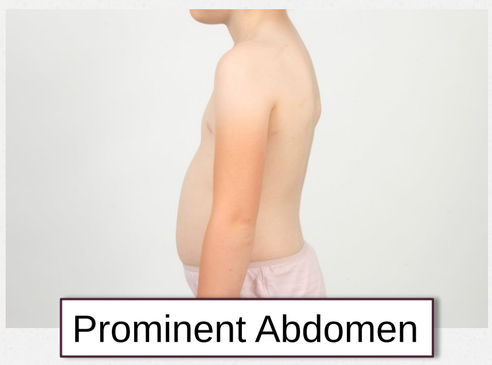




Right sided hemi hypotrophy with drooped shoulder and pelvis as well as flared ribs



Winged scapulae



Prominent Abdomen

TR-beta mutation

- **Resistance to thyroid hormone** action is due to mutations in the **beta-isoform** of the thyroid hormone receptor.
- Patients display **inappropriate central secretion** of Thyroid hormone from the hypothalamus and of TSH from the anterior pituitary. This is despite **elevated levels of thyroid hormone** (T4 and T3).
- Mutation of the beta thyroid hormone receptor is usually either **autosomal dominantly** inherited or is a **de novo mutation**, resulting in defective patterns of gene expression.
- This is a rare disorder, usually presenting with **goitre**.

Conclusion

- TRbeta mutation should be considered in children with persist**ently elevated T4 levels with a normal TSH.**
- Other immune conditions like **ITP** and changes in **body habitus** are new associations, cause of which is yet not identified.

Cambridge University Hospitals NHS Foundation Trust

Central Manchester University Hospitals NHS Foundation Trust

The Pennine Acute Hospitals NHS Trust