Neonatal pituitary-thyroid axis dysregulation with combined thyroid hormone and thyrotopin resistance in infant with Trisomy 21 and maternal subclinical hypothyroidism

Asthा Soni1, Mohammed Diḍ2, Shivaram Avula3, Sze May Ng1
1 Department of Paediatrics, Southport and Ormskirk Hospital NHS Trust
2 Department of Endocrinology, Alder Hey Children’s Hospital NHS Foundation Trust
3 Department of Radiology, Alder Hey Children’s Hospital NHS Foundation Trust

Authors declare no conflict of interest

Background

Trisomy 21 may be associated with a dysregulated pituitary thyroid axis with higher plasma TSH and lower Free thyroxine (FT4) than controls. This may be due to genomic imbalance from trisomy of chromosome 21. Some workers have considered this to be a form of congenital hypothyroidism (CH) and a randomised control trial1 has demonstrated significant benefit from treatment with thyroxine. Transient (CH) in newborns is recognised in association with maternal thyroperoxidase (TPO) antibody positivity. ‘Thyroid hormone resistance’ (RTH) in infancy has also been described in CH.

Case Report

A term infant born to a primigravid mother was confirmed to have Trisomy 21. The mother had plasma TSH of 7mU/L, FT4 of 11 pmol/L and TPO positivity during the third trimester. Her thyroid function tests (TFT) and antibody status normalised following delivery. The infant was identified as a possible baby with CH on the neonatal screening program. He was observed on Day 10 despite his TFTs (table 1) as he appeared well. TPO antibodies were absent. 99mTc-Pertechnetate scan showed uptake within a bilobed structure in the lower neck. (Figure 1) Scan time was 5 min and 17 seconds, at the upper limit of normal. Ultrasound scan showed normal appearance of the thyroid gland in the neck (Figure 2).

His plasma TSH was elevated on Day 16 as compared with the largest published study1 involving neonates with trisomy 21. He had prolonged jaundice and a widely open posterior fontanelle, consistent with CH. Thyroxine replacement was started at 37.5 micrograms daily as the neonatal screening program in the UK demands treatment of all infants with CH by Day 21. Treatment had to be reduced progressively (table 1) due to mild features of overtreatment despite raised plasma TSH reminiscent of what has been well described in RTH. The elevated plasma thyroid hormones failed to normalise plasma TSH. He remains well on 12.5 mcg of thyroxine with normal FT4, but mildly elevated TSH at 6 months of age.

Discussion

RTH has been described in Trisomy 21 in the literature in the absence of any mutations2–3 known to affect TH or thyroid hormone receptors. Maternal TPO positivity might have additionally contributed to the picture. Treatment with a small dose of thyroxine was needed to lower the TSH which still remained above the reference range. The unusual thyroid function and its subsequent behaviour in this infant with Trisomy 21 and CH are not completely explained by combined thyroid hormone and TSH resistance that has been previously described.

Conclusion

There may be genes other than the TSH receptor or thyroid hormone receptor implicated in patients with trisomy 21 who display unusual features of the pituitary thyroid axis as in this patient.

References