Hypothyroidism in the presence of elevated T3 - significance of transporter proteins

Introduction

Thyroid hormones are essential for normal growth and functioning of all organs and tissues in the human body. They are particularly important for appropriate neuronal development during infancy and early childhood. Thyroid hormones mediates its' action via binding of intra-cellular T3 to the thyroid specific nuclear receptor. Inability to transport T3 into the cell can have detrimental effects in the central nervous system as seen in patients with mono carboxylate transporter 8 (MCT8) deficiency, which is the protein involved in neuronal uptake of T3. This was initially reported in 1944 as part of X-linked mental retardation syndromes and was eponymously named "Allan-Herndon-Dudley Syndrome".

Case report

A 25 month old male child was referred to Endocrinology for interpreting thyroid function abnormality detected while being evaluated for global developmental delay (GDD). The patient was extensively evaluated in view of the severe cognitive and motor developmental delay. Routine blood screens including hemogram, renal and liver function tests were normal. Work up for inborn errors of metabolism including organic aciduria were negative. A repeat electroencephalography was done which was also normal. Neuroimaging with MRI scan revealed mild
cerebral atrophy with evidence of hypomyelination. Thyroid function tests (TFT) showed slightly elevated TSH, slightly low FT4 levels and elevated FT3 levels. In view of GDD, central hypotonia, peripheral spasticity with hyperreflexia, asthenic built, and persistently elevated T3 levels with low T4 and slightly elevated TSH levels, we suspected the possibility of Allan Herndon Dudley syndrome in our patient. In order to confirm our diagnosis, we analysed the SLC16A2 gene on the X chromosome which codes for the MCT8 protein using next generation sequencing. The genetic test revealed a hemizygous missense variant [c.1468G>A; p.Gly490Arg; rs794727799] in exon 6 of the SLC16A2 gene in the patient.

Conclusion

Males presenting with congenital hypotonia, cognitive impairment with motor delay, and peripheral dystonic movements should be evaluated with TFTs which include TSH, T4 or FT4 and T3 or FT3. The signature pattern of AHDS - elevated T3/FT3, low or low normal T4/FT4, and normal to slightly elevated TSH should

prompt further confirmation with a genetic test. Early detection of AHDS enables early treatment initiation which may hold promise for better outcomes.