Angelman syndrome and hypothyroidism – coincidence or unique correlation?

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Abstract

Angelman Syndrome (AS, MIM 105830), classified among neurogenetic disorders, occurs with estimated frequency of 1:10 000 to 1:40 000. The characteristics features apart from neurodevelopmental impairment and seizures include peculiar face traits, absent speech, outburst of laughter, ataxia, stereotyped jerky (puppet-like) movements.

The authors report three children with Angelman syndrome who were also diagnosed with hypothyroidism.

CASE REPORT

After the first description of Angelman syndrome (AS) by an English paediatrician Harry Angelman in 1965 and later in 1987 – identification of a deletion of chromosomes 15q 11–13 by Magenis *et al.*, subsequent work has shown that AS can be caused by various genetic mechanisms, as well as genotype-phenotype adjustment has been attempted [1].

We report of three cases that may add something new to the phenotype of AS, as to our knowldge there have not been descriptions of thyroid dysfunction in this group of patients. Out of 15 children with AS followed up in our Department, three (with del 15q11.2) were also diagnosed with hypothyroidism. Assays of thyroid hormones were performed while differentiating causes of psychomotor retardation prior to diagnosis of AS in two patients (at the age of 2 and 4 years respectively), whereas in one case it was found out in the course of neurologic follow-up of a child with previously diagnosed AS, at the age of 13 years. All children had negative screening for congenital hypothyroidism at birth. Initial concentrations of thyroid stimulating hormone (TSH) were moderetely elevated (5–10 mIU/l) along with free thyroxine (fT4) at the lower borderline, suggesting sublinical hypothyroidism. In two cases positive antibodies against thyroid peroxidase (TPO) were found. This constellation of thyroid parameters is most often seen in patients with early Hashimoto's disease, also observed in paediatric population[2]. None of these patients presented with goiter. On ultrasound examination the thyroid gland was of normal localisation, volume and vasculisation, as well as as homogenous echo was registered. Treatment with levothyroxine at the dosage of 1 μg/kg/24h was introduced. In patients with primary hypothyroidism, the absence of TPO antibodies raises a possible

diagnosis of transient hypothyroidism following an undiagnosed episode of subacute or postviral thyroiditis. In patients with transient hypothyroidism along with negative antibodies, a trial of a reduced levothyroxine dosage after 4 months may reveal recovery of thyroid function thus avoiding permanent levothyroxine replacement. In case of our patients attempts to withdraw this therapy and verification of initial diagnosis of hypothyroidism resulted in destabilisation of thyroid parameters, however without evident clinical features of hypothyroidism, other than the whole picture of AS. Exact diagnosis may be possible after thyroid biopsy to differentiate possible lymphocytic thyroiditis, however this procedure has not been decided in our patients, having in mind their comfort and minor effect on further management.

While searching for causes of thyrotropinaemia one also has to bear in mind that some antiepileptic drugs such as carbamazepine and phenytoin may alter metabolism of thyroid hormones and levels of thyroglobulin. Because of polymorphic seizures the patients mentioned here are treated with lamotrigine, valproic acid and topiramate.

Recently Grasberger *et al*. (2005) [3] identified a locus for congenital non-goitrous hypothyroidism on chromosome 15q 25.3–26.1 [3]. There are also reports of patients with Prader-Willi syndrome with rearrangements within chromosome 15 and hypothyroidism[4].

The dilemma remains – is the hypothyroidism in patients presented by us an isolated and accidental finding? Hereby we postulate that patients with AS should be followed more carefully for their endocrine function.

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