

**Original Case Report**

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**A RARE CASE OF THYROTOXICOSIS IN PEDIATRIC PRACTICE****Renata Markosyan<sup>1,2</sup>, Natalya Volevodz<sup>3,4</sup>, Lusine Navasardyan<sup>1,2</sup> and Karmella Pogosyan<sup>2</sup>**

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**ABSTRACT:** Thyrotoxicosis observed during the first two decades of life is rare compared to that in adults, with an incidence of 0.8 per 100000 children per year (Brent G.A. 2008). Transient thyrotoxicosis may be caused by acute or subacute thyroiditis, chronic lymphocytic thyroiditis, acute or chronic administration of thyroid hormones and/or iodides. Some other rare causes of thyrotoxicosis like TSH-secreting pituitary tumours and thyroid hormone resistance (Lafranchi S.H.2013). may be represented by the following conditions, such as: McCune-Albright syndrome, germline and somatic gain-of-function mutations of the TSH receptor gene, which could be possibly associated with diffuse hyperplasia and toxic nodules. The excess of free thyroid hormones may result in thyrotoxicosis syndrome (Lafranchi S.H.2013) which may affect any of the organism system (Rivkees S.A. & Szarfman A.2010). Such factors as increased adrenergic stimulation (palpitations, tremors) and behavioral changes (restlessness, poor sleep, declining academic performance) (Rivkees S.A. & Szarfman A. 2010) may result in formation of usual symptoms in children, and are more expressed in younger patients. Other, less commonly observed symptoms are as follows: anxiety, proptosis, excess appetite, weight loss, and heat intolerance. Goiter is observed in 95% of cases and eye problems – in about 50% of children with GT. The presence of these manifestations depend on hormone elevation degree, the period of elevation, their increase rate and the patients' individual peculiarities.

**KEYWORDS:** Thyrotoxicosis, Ophthalmopathy, Graves' disease, Childhood.

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## 1. INTRODUCTION

Thyrotoxicosis during the first two decades of life is rare compared to that in adults, with an incidence of 0.8 per 100000 children per year. About 95% of thyrotoxic children have Graves' disease, in contrast to findings in adults where a significant number of toxic adenomas and multinodular toxic goitres are seen, especially in areas with a relatively low iodine intake (Srinivasan S., Misra M. 2015). It is suggested that Graves' disease in childhood is a self-limiting disorder with a remission rate of 25% every 2 years. Acute or subacute thyroiditis, chronic lymphocytic thyroiditis, acute or chronic administration of thyroid hormones and/or iodides may also result in transient thyrotoxicosis (Brent G.A. 2008). McCune-Albright syndrome as well as germline and somatic gain-of-function mutations of the TSH receptor gene, which may be associated with the presence of diffuse hyperplasia and toxic nodules, are also rare causes of thyrotoxicosis, as are TSH-secreting pituitary tumours and thyroid hormone resistance (Bahn R.S., Burch H.B. et al 2011). Thyrotoxicosis is the syndrome caused by an excess of free thyroid hormones. Any or all systems of the body can be affected (Kraem Z, R. 2001). The usual symptoms in children are due to increased adrenergic stimulation (palpitations, tremors) and behavioral changes (restlessness, poor sleep, declining academic performance) (Topliss D.J., Eastman C.J. 2004). Symptoms are more pronounced in younger patients. The other symptoms less commonly seen are anxiety, proptosis, excess appetite, weight loss, and heat intolerance (Lafranchi S.H. 2013). Goiter is present in up to 95% of cases. Eye signs present in about 50% of children with GD (Lafranchi S.H. 2013). The presence of these manifestations depend on hormone elevation degree, the period of elevation, their increase rate and the patients' individual peculiarities. The formation of the nervous system and growth of young organisms greatly depend on the thyroid hormone level. If hyperthyroidism isn't diagnosed and treated during this period of life, it can seriously affect growth and development. It can also cause brain irreversible injuries due to craniosynostosis, failure to thrive, behavior disturbances, and speech impairment, particularly in young children during the first 2 years of life (Baskin H.J., Cobin R.H. et al 2002). Thus, early diagnostics and corresponding treatment to prevent such complications are of utmost importance and Graves' disease is most probably supposed.

### Case report

The case of a 3-year-old boy with Graves' disease, goiter and exophthalmos is presented in this paper. The patient referred to "Muratsan" university hospital at the age of 3, mentioning that goiter progressively enlarged during the previous six months. His parents told that he had excessive sweating, heat intolerance and hyperactivity during past 6 months. No family history of thyroid or other autoimmune disease was reported and his mother's thyroid function test was normal. The patient's examination revealed normal mental and motor function development, height SDS was +2.4 and weight SDS was +1.2. Bilateral exophthalmos was observed, while the thyroid gland was diffusely enlarged up to grade 2B according to the World Health Organization. It was of soft texture on

palpation but no detectable nodules were revealed, as well as hepatomegaly, splenomegaly, or abnormalities of the chest or abdomen weren't found out. Laboratory studies revealed normal hemoglobin concentration of 16.6 g/dL, hematocrit of 52.6%, a normal leukocyte count of 6,000/mm<sup>3</sup>, platelet of 385,000/mm<sup>3</sup> and a normal aspartate aminotransferase level of 32 IU/L, alanine aminotransferase of 24 IU/L. Radiologic examination revealed that his bone age corresponded to 4.3 years according to the Greulich-Pyle method. The laboratory studies made during his first referral revealed that thyroid-stimulating hormone level (TSH) was 0.003  $\mu$ IU/mL (normal range, 0.5-4.8  $\mu$ IU/mL), triiodothyronine (T3) was 15.8 ng/mL (1.19-2.18 ng/mL), and free thyroxine (free T4) was 21.15 ng/dL (0.8-2.2 ng/dL). Serum samples were markedly positive for thyroid-stimulating antibody (TSAb). Antithyroglobulin antibodies >300 IU/ml (Positive >100 IU/mL). Antithyroid peroxidase antibodies 266 IU/mL (Positive >60). A thyroid ultrasound investigation revealed diffuse enlargement of thyroid glands. Graves' disease was later diagnosed and thyamazole therapy in the initial dose of 5mg three times a day 15 mg/day was administered and other medicines such as  $\beta$ -blockers were not added. Euthyroid status occurred after 1 month of the therapy was started and his thyroid functions tests lab values were as follows: TSH 1.2  $\mu$ IU/mL (normal range, 0.5-4.8  $\mu$ IU/mL), triiodothyronine (T3) was 1.8 ng/mL (1.19-2.18 ng/mL), and free thyroxine (free T4) was 2.5 ng/dL (0.8-2.2 ng/dL). During 6 months the patient underwent follow-up observation in the out-patient department and continued thyamasole therapy in the dose of 2.5 mg daily, the exophthalmos and goiter are obviously improved.

## 2. DISCUSSION

It is widely known that Robert Graves was the first who identified the clinical syndrome of goiter, palpitations, and exophthalmos in 1835. Graves' disease is rarely observed in children but is responsible for the vast majority of hyperthyroidism cases in children and adolescents. Several reports on Grave's disease observed in children under 4 were available in the literature, whereas no such data haven't been reported in Armenia so far. We present this case because of its rarity and significant ophthalmopathy. The optimal treatment for Graves' disease in children is still disputable<sup>9</sup>. Antithyroid drugs (ATD), sub- or near-total thyroidectomy, and radioactive iodine are intended to be used in current treatment options. There is no specific cure for the disease and each therapeutic option has associated complications. ATD therapy is usually recommended as the initial treatment for hyperthyroidism in children and adolescents. The most commonly used ATD are thyamazole and propylthiouracil (Hamburger J.I.1985). It has recently been recommended to avoid the use of PTU because of high risk of PTU-induced hepatitis. The frequency of side effects may be dose-related and severe side effects are very low in patients administered thyamazole in a dose of lower than 10-15 mg/day. The initial starting dose of thyamazole is 0.5-1 mg/kg/day, with a maximum dose of 30 mg per day. After 2-4 weeks, when thyroid hormone secretion is effectively blocked and thyroid hormone levels become normal, the initial dose is gradually reduced by 30%-50%( Rivkees S.A,

Dinauer C.2007).The maintenance of high doses of ATD cause no additional benefit. The administration of additional  $\beta$ -blocker therapy (except in patients with asthma or cardiac failure) during the first 2 weeks of management may be favourable for the patient's symptoms reduction(Rivkees, S.A. & Szarfman, A. 2010). This treatment can be administered orally, in the dose of 2 mg/kg/ twice a day, and stopped when the patient becomes euthyroid. However, agranulocytosis, neutropenia, and drug-induced hepatitis are considered to be potentially serious complications due to medicamentous therapy, and young children usually display a relapse when the treatment was discontinued. ATD toxicity, relapse after an appropriate course of drug treatment, and the lack of compliance on behalf of the patient or the parents are considered to be indications for radical treatment in children. The presented case reports about the patient with initial ATD, who was successfully treated. According to the literature data a remission of Graves' disease on ATD therapy is connected with the restoration of euthyroidism rather than the immunosuppressive effects of the drugs (Iazar L.K. 2000). As it is shown, hyperthyroidism itself worsens the autoimmune aberration, and autoimmunity leads to the formation of more TSH receptor antibodies (TRAb) and hyperthyroidism exacerbation. Once this cycle is broken by ATD treatment administered to a euthyroid patient or in the result of surgery, the patient may experience gradual remission of the disease (Abraham P., Avenell A 2005). More prolonged use of ATD (at least 2-4 years) in children than in adults may be required to gain remission (Allahabadia A, Daykin J.2000). Compliance is therefore an important issue in the management of these children and should be improved by educational strategies(Okawa E.R, Grant F.D. 2015). These findings are compatible with the well-known confirmation that Grave's disease is less liable to treatment in patients at the age under 4, as it was in the presented case. So, taking into account unfavourable reactions, generally low remission rate and long remission periods, a certain treatment options for young children should be discussed with the family.

### 3. CONCLUSION

Thus, concluding all the above noted we would like to mention that pediatricians should be aware of the possibility of cerebral injury due to craniosynostosis, failure to thrive, and neuropsychological deficits in young children with hyperthyroidism, and special attention should be paid to the pediatric patients' age if Graves' disease is clinically suspected. The younger the patients are, the closer monitoring is necessary to be provided (Baskin H.J., Cobin R.H.2002) Against this background, we reported here a case of a 3-year-old male patient with Graves' disease along with a related literature review.

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