



Case Report

Graves' Disease: Uncommon Condition in Males in Paediatric Age Group – A Case Report

Neha Chowdary*, Asha Benakappa and Dakshayani

Department of Paediatrics, Bangalore Medical College and Research Institute, India

ARTICLE INFO

Received 07 June 2015
Received in revised form 02 July 2015
Accepted 07 July 2015

Keywords:

Graves disease,
Proptosis,
Thyroid uptake scan.

Corresponding author: Department of Paediatrics, Bangalore Medical College and Research Institute, India.
E-mail address: excelneha@gmail.com

ABSTRACT

Graves' disease is an autoimmune disorder that is the most common cause of hyperthyroidism in paediatric patients. There is production of thyroid-stimulating immunoglobulin (TSI) by stimulated B lymphocytes which results in diffuse toxic goiter. It occurs in approximately 0.02% of children. It may occur at any time during childhood, but its frequency increases with age, peaking during adolescence. Most children with this disorder have a positive family history of some form of autoimmune thyroid disease. Genetic and environmental factors also play a role. Enlargement of the thymus, splenomegaly, lymphadenopathy, infiltration of the thyroid gland and retro-orbital tissues with lymphocytes and plasma cells, and peripheral lymphocytosis are well established findings. This case report aims to highlight that a 9 year old male child who had a significant family history of hypothyroidism was diagnosed to have Graves' disease. Usually it has a female predominance, 5:1 female to male ratio and a peak incidence in 11 to 15 year olds.



Introduction

Graves' disease is rare in children but is responsible for the vast majority of hyperthyroidism cases in children and adolescents.¹ Girls are affected four to five times more frequently than boys, although no gender difference is noted in patients younger than 4 years of age.¹

It is the most common cause of thyrotoxicosis, accounting for about 95% of juvenile thyrotoxicosis.²

Serum TSAb (TSH receptor stimulating autoantibodies) level is a sensitive, specific, and reproducible biomarker for this disease and correlates well with disease severity and extra thyroidal manifestations.³

In whites, Graves' disease is associated with HLA-B8 and HLA-DR3; the latter carries a 7-fold relative risk.⁴

The ophthalmopathy that occurs appears to be caused by antibodies against antigens shared by the thyroid and eye muscle.⁴

The signs of diffuse toxic goiter are exophthalmos, lid retraction, lid lag, impaired convergence, ophthalmoplegia.⁵

Prepubertal children are the most difficult to treat with remission attained in less than 15%.⁶ When antithyroid drugs (ATDs) are prescribed, only Methimazole should be administered, as Propylthiouracil is associated with an unacceptable risk of severe liver injury.⁸ ATDs act by inhibiting oxidation and organic binding of thyroid iodide to impair thyroid hormone production.⁹ Remission is defined as being biochemically euthyroid or hypothyroid for one year or more after discontinuation.⁹ In the pediatric age group, remission rates range from 20-30% following use of drugs for two years or more.⁹

Alternative treatments, mostly Radioactive Iodine, rather than thyroidectomy are considered in cases of relapse.¹⁰

Case Description

A nine year old male child, admitted to Vani Vilas hospital of Bangalore Medical College and Research Institute, and second born to a non-consanguineous parentage belonging to lower middle socioeconomic status according to modified Kuppuswamy scale, with uneventful antenatal, natal and neonatal period and normal development, immunized upto date as per the National Immunization schedule of India, presented with protrusion of eyeballs as noticed by the mother since six months which progressed gradually, change in behaviour since six months in the form of increased irritability, stubbornness and anger, and loss of weight as noticed by the mother due to loosening of clothes.

There was significant family history of hypothyroidism in the father and paternal grandmother.

On examination, child had tachycardia. Thinness was present (Body Mass Index 12.6). Child had a triangular face with parietal bossing. There was a staring look with bilateral proptosis, upper limbus and lower sclera visible, conjunctival chemosis also present. A soft smooth diffuse swelling 3 x 4.5cm in the neck, non tender and moved with deglutition. Hands were warm and moist with no tremors. Systemic examination was normal.

Investigations included a complete haemogram that was normal. Thyroid profile showed an increase in free thyroxin and a decrease in thyroid stimulating hormone. FNAC of thyroid suggested a hyperplastic goiter. Thyroid peroxidase antibody and TSH (Thyroid stimulating hormone) receptor antibody titres were high.

Additional investigations included ^{99m}TcO4 Thyroid uptake scan which showed features suggestive of borderline increased trapping function of thyroid gland which clinched the diagnosis of Graves' disease.

ECG showed sinus tachycardia

Differential Diagnosis considered was Autoimmune Thyroiditis. Thyroid peroxidase antibody and TSH receptor antibody titres can be positive in both but the only differentiating feature was that the thyroid uptake scan showed increased uptake, which occurs in Graves' disease whereas in autoimmune thyroiditis there is decreased uptake.

Child was started on antithyroid medications; tablet Methimazole 0.25-1 mg/kg/day given once or twice daily in divided doses. Methimazole has a longer serum half-life and is 10 times more potent than Propylthiouracil.

On follow up after 6 weeks, there were no fresh complaints.

Discussion

The incidence of hyperthyroidism is 8 cases per 1,000,000 individuals aged 0-15 years per year as reported in the Danish population, and the lowest incidence of 1 per 1,000,000 was found in children younger than 4 years.¹

Graves' disease is frequently associated with clinical manifestations of thyroid eye disease, also called Graves' ophthalmopathy (GO).² The paediatric age group of 0-15 years comprises only 5-6% of the total number of thyrotoxic patients.² It occurs mostly in patients with a family history of autoimmune thyroid disease or in the context of associated autoimmune disorders like type 1 diabetes mellitus and Addison's disease.²

The clinical relevance of TSH receptor (TSHR) autoantibodies in pediatric disease and their predictive value at the time of diagnosis has been demonstrated. In addition to being a useful biomarker for disease activity, TSAb (TSH receptor stimulating autoantibodies) also correlated with the presence of GO independent of thyroid function, suggesting a possible

causal role of TSAb in the immunopathogenesis and in the development of the clinical phenotype of thyroid eye disease with proptosis.³

Adverse reactions occur with antithyroid drugs; most are mild, but some are life threatening.⁴ Transient granulocytopenia ($<2000/\text{mm}^3$) and urticarial rashes are common.⁴ The most severe reactions include agranulocytosis, hepatitis, lupus like polyarthritis syndrome, glomerulonephritis, vasculitis involving the skin and other organs.⁴ The most common liver disease associated with Methimazole is cholestatic jaundice, reversible when the drug is discontinued.⁴

Clinical response becomes apparent in 3-6 weeks, and adequate control is evident in 3-4 months.⁴

Antithyroid drugs are the preferred modality for treatment since its non invasive, less initial cost and low risk of permanent hypothyroidism.⁴ Other modalities of treatment include Radioactive Iodine I-131 which cures hyperthyroidism but permanent hypothyroidism is almost inevitable.⁴ Surgery in the form of thyroidectomy is the most invasive and costly therapy.⁴ Potential complications included recurrent laryngeal nerve damage, hypocalcaemia and hypoparathyroidism.⁴

Ophthalmopathy remits gradually and usually independently of the hyperthyroidism but if severe can require treatment with high dose prednisolone, orbital radiotherapy or orbital decompression surgery.⁴

Regardless of the modality that is ultimately used for treatment, patients will require long term regular medical follow up.⁷

Recent studies in adults show that despite successful treatment and a return to the euthyroid state, some patients will continue to exhibit symptoms of physical, emotional and neuropsychological illness.⁷

Anxiety, depression, lack of energy, sleep disturbance, emotional liability, impaired memory and forgetfulness are difficulties experienced by patients who had remained euthyroid for more than a year.⁷

References

1. Yo Han Ho, Eun Cho Chung, and Sin-Ae Park; A 3-Year-Old Girl with Graves Disease with Literature Review; *Annals of Pediatric Endocrinology & Metabolism*. 19.3 (2014): 154-158.
2. G E Krassas, M Segni and W M Wiersinga; Childhood Graves' ophthalmopathy: results of a European questionnaire study; *European Journal of Endocrinology*. (2005) 153; 515-520.
3. T. Diana, R. S. Brown, A. Bossowski, M. Segni, M. Niedziela et al; Clinical Relevance of Thyroid-Stimulating Autoantibodies in Pediatric Graves' Disease; *The Journal of Clinical Endocrinology and Metabolism*, May 2014, 99(5):1648–1655.
4. Nelson textbook of Paediatrics – Kliegman, Stanton, St. Geme, Schor, Behrman; 19th edition, Page 1909-1913.
5. Jwal Doctor, Aesha Trivedi, Bharat Kumar, Snehal Patel; Clinical Expression of Graves Disease in Children; *World Journal of Pharmacy and Pharmaceutical Sciences*. 2015, Vol4; 966-969.
6. Sophy Korula, Shubha Srinivasan, Geoffrey Ambler, Martin Silink, Neville Howard et al; Graves' disease in children less than 8 years of age; *International Journal of Pediatric Endocrinology*. 2015.
7. Pediatric Endocrinology – 5th edition, Fima Lifshitz, Volume 2, 416-420.
8. Graves' Disease in Childhood - Scott A. Rivkees 2015; 147-166.
9. Scott A Rivkees; Pediatric Graves' disease: management in the post-propylthiouracil Era; *International Journal of Pediatric Endocrinology*. 2014.
10. Leger; Graves' Disease in Children; *Paediatric Thyroidology*. 2014; Vol 26; 171-182.



Picture of child with Graves' Disease



Child with proptosis-upper limbus and lower sclera visible