



HYPERTHYROIDISM

Hereditary Activating Mutations of the TSH Receptor Lead to Hyperthyroidism

BACKGROUND

TSH (thyroid stimulating hormone) regulates thyroid function by binding to a specific TSH receptor that turns on thyroid cells, increasing the production and secretion of thyroid hormones. The most common type of hyperthyroidism is Graves' disease, an autoimmune disorder where the patient develops antibodies that attack the TSH receptor, turning in the thyroid in the absence of TSH. Rarely, hyperthyroidism may be caused by genetic mutations in the TSH receptor that cause it to be permanently in the "on" position (activating mutations). Two forms of this genetic hyperthyroidism have been reported, one that runs in families (familial form) and one that occurs by itself (sporadic form). Despite an increase in reported cases in the recent years, the genetic forms of hyperthyroidism remain rare and are incompletely characterized. The aim of this study was to evaluate the clinical and biological aspects of the familial and sporadic forms of genetic hyperthyroidism caused by activating TSH receptor mutations.

THE FULL ARTICLE TITLE:

Hébrant A et al Genetic hyperthyroidism: hyperthyroidism due to activating TSHR mutations. *Eur J Endocrinol* 2011;164:1-9.

SUMMARY OF THE STUDY:

This study analyzes the medical history of 152 patients with the familial form of genetic hyperthyroidism coming from 27 families and 15 sporadic cases. Several TSH receptor mutations have been identified, some of them being reported in both the familial and sporadic forms. Men and women are equally affected in both the familial or sporadic forms.

Familial hyperthyroidism developed most frequently between adolescence and 30 years of age and it was

rarely present at birth or during infancy. In contrast, all sporadic cases developed at birth or during the first year of life and they were more severe than the familial forms. Sporadic forms were associated with other complications at birth, such as prematurity and mental retardation. Members of the same family bearing the same mutation had different degrees of disease severity. Non-autoimmune hyperthyroidism tended to relapse after conventional treatment.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

Similar activating TSH receptor mutations involving all thyroid cells have been described in both the familial and sporadic forms of genetic hyperthyroidism. The sporadic forms seem to be associated with stronger mutations resulting in a higher degree of thyroid activation, since hyperthyroidism appears early in life and is clinically more severe compared to familial forms. It is important to differentiate the genetic hyperthyroidism from Graves' disease because the genetic hyperthyroidism tends to relapse after antithyroid drug treatments. More patients with the sporadic forms are now able to survive with adequate treatment and will transmit the disease to their offspring. Genetic counseling is recommended for all patients with genetic hyperthyroidism.

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ATA THYROID BROCHURE LINKS

Hyperthyroidism: http://thyroid.org/patients/patient_brochures/hyperthyroidism.html

Graves disease: http://thyroid.org/patients/patient_brochures/graves.html

Thyroid Function Tests: http://thyroid.org/patients/patient_brochures/function_tests.html

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HYPERTHYROIDISM, continued

ABBREVIATIONS & DEFINITIONS

TSH: thyroid stimulating hormone — produced by the pituitary gland that regulates thyroid function; also the best screening test to determine if the thyroid is functioning normally.

TSH receptor — a molecule (protein) located on the thyroid cell surface that binds TSH and stimulates the production of the thyroid hormones within the thyroid cell.

Hyperthyroidism — a condition where the thyroid gland is overactive and produces too much thyroid hormone. Hyperthyroidism may be treated with antithyroid meds (Methimazole, Propylthiouracil), radioactive iodine or surgery.

Graves' disease — the most common cause of hyperthyroidism in the United States. It is caused by antibodies that attack the thyroid and turn it on.

Genetic hyperthyroidism — a rare form of hyperthyroidism caused by genetic mutations in the TSH receptor that cause it to be permanently in the “on” position (activating mutations).

Congenital — a condition that exists at birth.

Mutation — a permanent change in one of the genes.

Antibodies — proteins that are produced by the body's immune cells that attack and destroy bacteria and viruses that cause infections. Occasionally the antibodies get confused and attack the body's own tissues, causing autoimmune disease.