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THYROID FUNCTION TESTS

"No Detectable TSH" doesn't always mean a patient has hyperthyroidism or central hypothyroidism

BACKGROUND

The most frequently ordered test to screen patients for thyroid disease is the TSH. This hormone is released by the pituitary gland in response to the blood levels of active thyroid hormones (free T_4 and free T_3). TSH levels are opposite the thyroid hormone levels. Therefore, if the blood thyroid hormone levels are low, the TSH will be elevated and vice versa.

Occasionally, when screening a person who does not appear to have obvious thyroid disease, a TSH will be found to be very low or not detectable. In those cases, if the free T_4 is low, one might consider the diagnosis of central hypothyroidism (a problem with the pituitary gland) or the effect of another illness on TSH levels. If the free T_4 is normal or high, then a diagnosis of hyperthyroidism might be considered. However, this study illustrates a different diagnostic possibility, showing that the physician must keep an open mind when evaluating thyroid tests, especially when the patient does not have any symptoms.

In a prior study, a group of 20 patients who had a TSH that was not detectable by the commonly used assays, was found to have a mutation involving one of the chains that make up the TSH molecule. The TSH with this mutation was found to have normal function, but almost half of the patients were inappropriately treated because their TSH levels were not detectable.

The current article describes all studies done on a new family carrying the same mutation, and reports results that indicate that the mutation described changes only a very small portion of the molecule that is needed for the attachment of the TSH to the antibodies used in the assays, therefore TSH is not detected although is present in normal quantities and has normal function.

THE FULL ARTICLE TITLE

Pappa T et al TSHβ variant with impaired immunoreactivity but intact biological activity and its clinical implications. Thyroid 2015;25:869-75. Epub June 15, 2015.

SUMMARY OF THE STUDY

The first member of the family that was studied was a 4 year old boy. He had a TSH that was not detectable, a free T_4, free T_3 and total T_4 that were normal. His 10 year old brother had identical thyroid tests. Their mother, older brother and sister had a normal TSH. The father declined testing. None of them had evidence of thyroid disease.

Their blood samples were analyzed by 5 different available commercial assays (that use different technologies and reagents).In addition, studies were done to make sure that there was no evidence of another substance that was interfering with the tests. Computer modeling was done that showed that the variant TSH behaved normally once it attached to the active site at its receptor.

WHAT ARE THE IMPLICATIONS OF THIS STUDY?

As mentioned before, the samples from this family were analyzed using 5 different commercially available assays. The two boys, who were homozygous for the mutation described, did not have a detectable TSH in two of the assays, but normal in other three. Therefore, after all results were evaluated, it was concluded that the mutation does not affect function, but it does not allow the TSH to interact with the antibodies used for detection in some commercial assays.

This study is important for patients because it shows that patients who have these types of mutations may be told that they have thyroid disease because their TSH is low and that they need treatment, when actually their thyroid function is normal. This particular mutation may be present in 0.2% to 0.3% of the general population, and may be up to 5 times more common in individuals from Bangladesh, India, Sri Lanka and Pakistan.

In cases like this, when an individual does not appear to have a thyroid problem yet the TSH is very low or not detectable, and the rest of the thyroid function panel is normal, it may be worth repeating the TSH at a facility that uses a different assay.

— Jessie Block-Galarza, MD

ATA THYROID BROCHURE LINKS

Thyroid Function Tests: http://www.thyroid.org/thyroid-function-tests/

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THYROID FUNCTION TESTS, continued

ABBREVIATIONS & DEFINITIONS

Central hypothyroidism: a rare cause of hypothyroidism where the thyroid gland is normal and the problem is inadequate TSH secretion from the pituitary gland.

Genes: a molecular unit of heredity of a living organism. Living beings depend on genes, as they code for all proteins and RNA chains that have functions in a cell. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring.

Homozygous: Having identical pairs of genes for a particular hereditary characteristic.

Mutation: A permanent change in one of the genes.

Thyroxine (T_4): the major hormone produced by the thyroid gland. T_4 gets converted to the active hormone T_3 in various tissues in the body.

Triiodothyronine (T_3): the active thyroid hormone, usually produced from thyroxine.

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.